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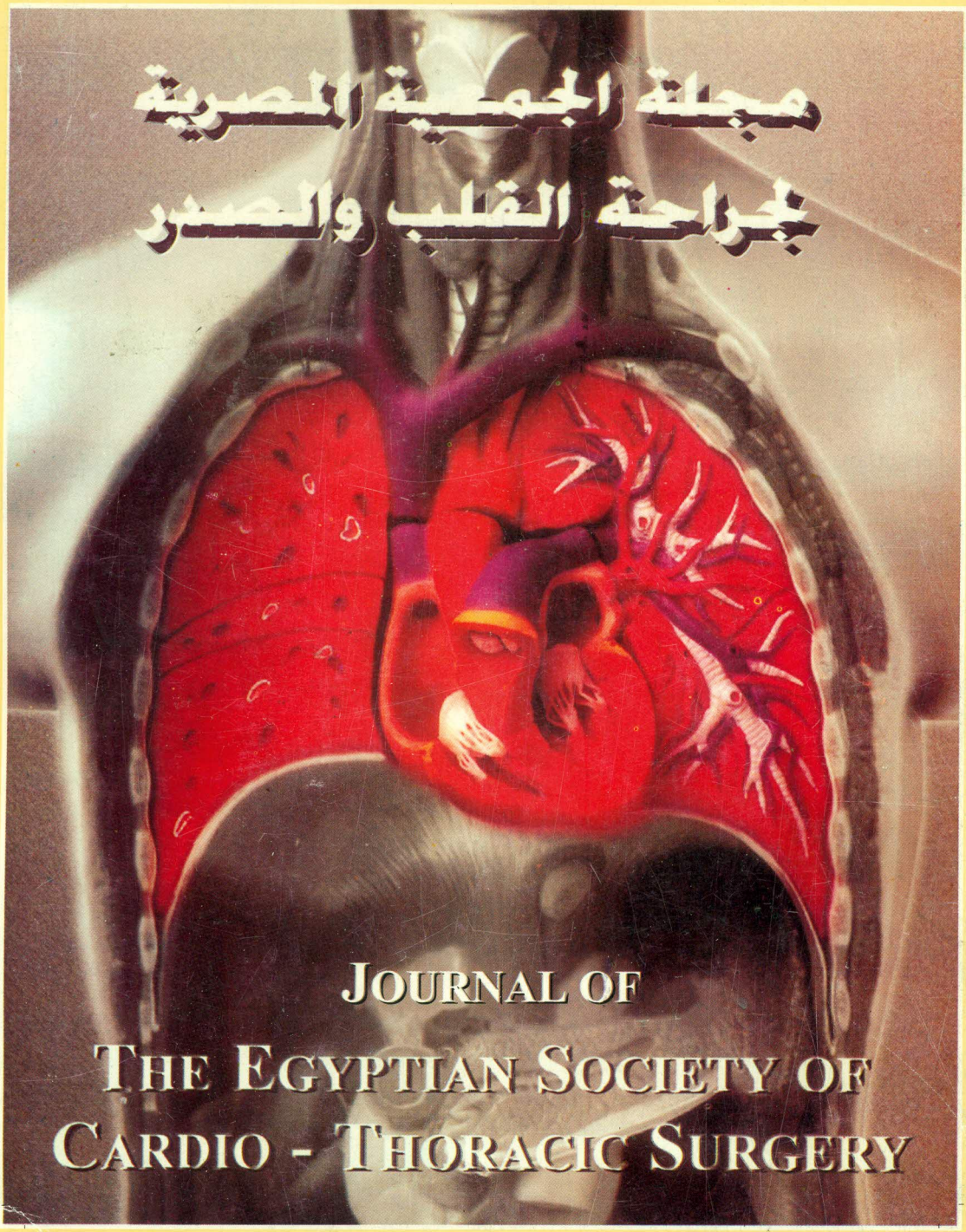

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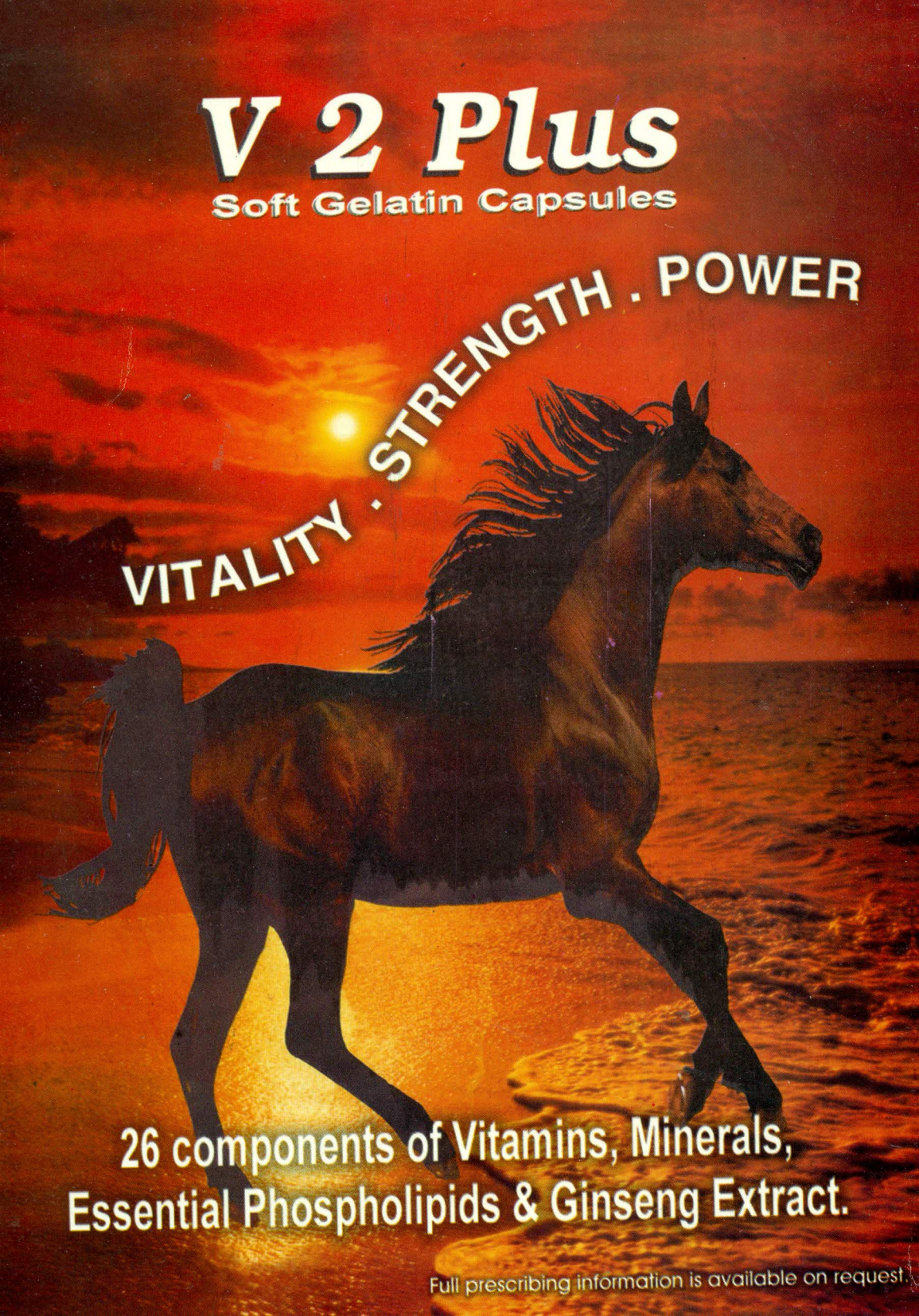
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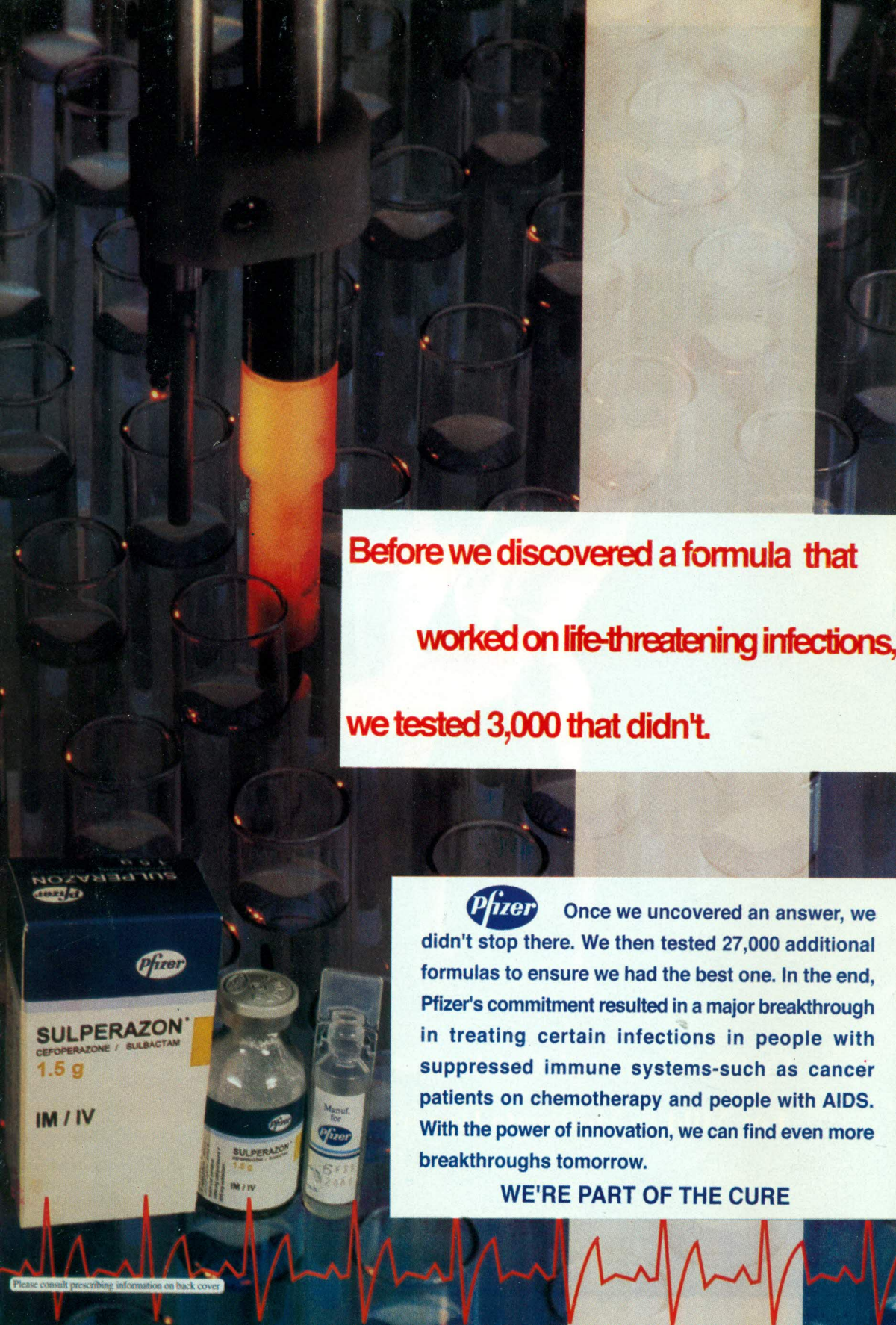
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The First "Deep-Spectrum" Antibiotic

Sulperazon IM/IV

cefoperazone/sulbactam

DESCRIPTION

Sulbactam sodium is a derivative of the basic penicillin nucleus. Chemically it is sodium penicillinate sulfone and is an off-white crystalline powder highly soluble in water. The molecular weight is 255.22.

Cefoperazone sodium is a semisynthetic broad-spectrum cephalosporin antibiotic for parenteral use only. It is the sodium salt of 7-D (-) - (4 - ethyl - 2,3 - dioxo - 1 - piperazinecarboxamido) - (4 - hydroxyphenyl) acetamido - 3 - (1 - methyl - 1H - tetrazol - 5 - yl) thiomethyl - 3 - cephem - 4 - carboxylic acid. It contains 34 mg sodium (1.5 mEq) per gram. Cefoperazone is a white crystalline powder which is freely soluble in water. The molecular weight is 667.65.

SULPERAZON brand of sulbactam sodium/ cefoperazone sodium combination is available as a dry powder for reconstitution in a 1: 2 ratio in terms of free sulbactam and cefoperazone. Vial contains 500 mg + 1000 mg of sulbactam and cefoperazone, respectively.

ACTIONS

Human Pharmacokinetics

Approximately 84% of the sulbactam dose and 25% of the cefoperazone dose administered with SULPERAZON is excreted by the kidney. Most of the remaining dose of cefoperazone is excreted in the bile. After SULPERAZON administration the mean half-life for sulbactam is about one hour while that for cefoperazone is 1.7 hours. Serum concentrations have been shown to be proportional to the dose administered. These values are consistent with previously published values for the agents when given alone. Mean peak sulbactam and cefoperazone concentrations after the administration of 3 grams of SULPERAZON (1g sulbactam: 2 g of cefoperazone) intravenously over 5 - 15 minutes have ranged between 76.8 and 128.7 mcg/ml for sulbactam and 245.7 and 254.4 mcg/ml for cefoperazone. This reflects the larger volume of distribution for sulbactam (Vd = 18.0 - 27.6L) compared to cefoperazone (Vd = 10.2-11.3L). After intramuscular administration of 1.5 g SULPERAZON (0.5 g sulbactam: 1 g cefoperazone) peak serum concentrations of sulbactam and cefoperazone are seen from 15 minutes to two hours after administration. Mean peak serum concentrations were 19.0 and 64.2 mcg/ml for sulbactam and cefoperazone, respectively.

After multiple dosing no significant changes in the pharmacokinetics of either component of SULPERAZON have been reported and no accumulation has been observed when administered every eight to 12 hours.

The pharmacokinetics of SULPERAZON have been studied in elderly individuals with renal insufficiency and compromised hepatic function. Both sulbactam and cefoperazone exhibited longer half-life, lower clearance, and larger volumes of distribution when compared to data from normal volunteers. The pharmacokinetics of sulbactam correlated well with the degree of renal dysfunction while for cefoperazone there was a good correlation with the degree of hepatic dysfunction.

In patients with different degrees of renal function administered SULPERAZON, the total body clearance of sulbactam was highly correlated with estimated creatinine clearance. Patients who are functionally anephric show a significantly longer half-life of sulbactam (mean 6.9 and 9.7 hours in separate studies). Hemodialysis significantly altered the total body clearance, and volume of distribution of sulbactam. No significant differences have been observed in the pharmacokinetics of cefoperazone in renal failure patients. Studies conducted in pediatrics have shown no significant changes in the pharmacokinetics of the components of SULPERAZON compared to adult values. The mean half-life in children has ranged from 0.91 to 1.42 hours for sulbactam and from 1.44 to 1.88 hours for cefoperazone.

Both sulbactam and cefoperazone distribute well into a variety of tissues and fluids including bile, gallbladder, skin, appendix, fallopian tubes, ovary, uterus, and others.

There is no evidence of any pharmacokinetic drug interaction between sulbactam and cefoperazone when administered together in the form of SULPERAZON.

Microbiology (In vitro Susceptibility Data)

The anti-bacterial component of SULPERAZON is cefoperazone, a third generation cephalosporin, which acts against sensitive organisms during the stage of active multiplication by inhibiting biosynthesis of cell wall mucopeptide. Sulbactam does not possess any useful antibacterial activity, except against **Neisseriaceae and Acinetobacter.** However, biochemical studies with cell-free bacterial systems have shown it to be an irreversible inhibitor of most important beta-lactamases produced by beta-lactam antibiotic-resistant organisms.

The potential for sulbactam's preventing the destruction of penicillins and cephalosporins by resistant organisms is confirmed in whole organism studies using resistant strains in which sulbactam exhibits marked synergistic effects when given together with penicillins and cephalosporins. As sulbactam also binds with some penicillin binding proteins, sensitive strains are also often rendered more susceptible to SULPERAZON than to cefoperazone alone.

The combination of sulbactam and cefoperazone is active against all organisms sensitive to cefoperazone but in addition demonstrates synergistic activity (up to fourfold reduction in minimum inhibitory concentration values with the combination versus those for each component) in a variety of organisms, most markedly the following:

- Haemophilus influenzae
- Acinetobacter calcoaceticus
- Proteus mirabilis
- Citrobacter freundii
- Bacteroides species
- Enterobacter aerogenes
- Klebsiella pneumoniae
- Enterobacter cloacae
- Staphylococcus species
- Escherichia coli
- Morganella morganii
- Citrobacter diversus

SULPERAZON is active in vitro against a wide variety of clinically significant organisms.

Gram-Positive Organisms:

Staphylococcus aureus, penicillinase and non-penicillinase producing strains.
Staphylococcus epidermidis
Streptococcus pneumoniae (formerly **Diplococcus pneumoniae**).
Streptococcus pyogenes (Group A beta-hemolytic streptococci)
Streptococcus agalactiae (Group B beta-hemolytic streptococci)
Most other strains of beta-hemolytic streptococci.
Many strains of **Streptococcus faecalis** (enterococcus)

Gram-Negative Organisms:

- **Escherichia coli**
- **Klebsiella** species
- **Enterobacter species**
- **Citrobacter species**
- **Haemophilus influenzae**
- **Proteus mirabilis**
- **Proteus vulgaris**
- **Morganella morganii (formerly Proteus morganii)**
- **Providencia rettgeri (formerly Proteus rettgeri)**
- **Providencia species.**
- **Serratia species (including S. marcescens).**
- **Salmonella and shigella species**
- **Pseudomonas aeruginosa** and some other **pseudomonas species**.
- **Acinetobacter calcoaceticus**
- **Neisseria gonorrhoeae**
- **Neisseria meningitidis**
- **Bordetella pertussis**
- **Yersinia enterocolitica**

Anaerobic Organisms:

Gram - negative bacilli (including Bacteroides fragilis, other Bacteroides species, and Fusobacterium species).

Gram-positive and gram-negative cocci (including Peptococcus, Peptostreptococcus and Veillonella species).

Gram -positive bacilli (including Clostridium, Eubacterium and Lactobacillus species).

The following susceptibility ranges (according to guidelines of the U.S. National committee for Clinical Laboratory Standards) have been established for SULPERAZON.

	Minimal inhibitory concentration (MIC), mcg / ml (expressed as cefoperazone concentration)
Susceptible	16
Resistant	64

	Susceptibility Disc Zone Size, mm (Kirby - Bauer)
Susceptible	21
Intermediate	16 - 20
Resistant	15

For MIC determinations, serial dilutions of SULPERAZON may be used with a broth or agar dilution method. Use of a susceptibility test disc containing 30 mcg of sulbactam and 75 mcg of cefoperazone is recommended. A report from the laboratory of "susceptible" indicates that the infecting organism is likely to respond to SULPERAZON therapy, and a report of "Resistant" indicates that the organism is not likely to respond. A report of "Intermediate" suggests that the organism would be susceptible to SULPERAZON if a higher dosage is used or if the infection is confined to tissues or fluids where high antibiotic levels are attained.

The following quality control limits are recommended for 30 mcg/75 mcg Sulbactam/ cefoperazone susceptibility discs:

CONTROL STRAIN	ZONE SIZE MM
Acinetobacter Spp. ATCC 43498	26 - 32
Pseudomonas aeruginosa ATCC 27853	22 - 28
Escherichia Coli, ATCC 25922	27 - 33
Staphylococcus aureus, ATCC 25923	23 - 30

INDICATIONS

SULPERAZON is indicated for the treatment of the following infections when caused by susceptible organisms.

Respiratory Tract Infections (Upper and Lower)
- **Urinary Tract Infections (Upper and Lower)**
- **Peritonitis, Cholecystitis, Cholangitis, and Other Intra-Abdominal Infections**
- **Septicemia**
- **Meningitis**
- **Skin and Soft Tissue Infections**
- **Bone and Joint Infections**
- **Pelvic Inflammatory Disease, Endometritis, Gonorrhea, and Other Infections of the Genital Tract.**

Combination Therapy

Because of the broad spectrum of activity of SULPERAZON, most infections can be treated adequately with this antibiotic alone. However, SULPERAZON may be used concomitantly with other antibiotics if such combinations are indicated. If an aminoglycoside is used, renal function should be monitored during the course of therapy. (See DOSAGE AND ADMINISTRATION SECTION)

CONTRAINDICATIONS

SULPERAZON is contraindicated in patients with known allergy to penicillins or any of the cephalosporins.

WARNINGS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-Lactam therapy. These reactions are more apt to occur in individuals with a history of hypersensitivity reactions to multiple allergens. If an allergic reaction occurs, the drug should be discontinued and the appropriate therapy instituted.

Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

PRECAUTIONS

General

Those precautions that pertain to sulbactam and cefoperazone will also pertain to the combination as discussed below.

Cefoperazone is extensively excreted in bile. The serum half-life of cefoperazone is usually prolonged and urinary excretion of the drug increased in patients with hepatic diseases and/or biliary obstruction. Even with severe hepatic dysfunction, therapeutic concentrations of cefoperazone are obtained in bile and only a 2 to 4 fold increase in half-life is seen.

Dose modification may be necessary in cases of severe biliary obstruction, severe hepatic disease or in cases of renal dysfunction coexistent with either of those conditions.

In patients with hepatic dysfunction and concomitant renal impairment, cefoperazone serum concentrations should be monitored and dosage adjusted as necessary. In these cases dosage should not exceed 2g/day of cefoperazone without close monitoring of serum concentrations.

The serum half-life of cefoperazone is reduced slightly during hemodialysis. Thus, dosing should be scheduled to follow a dialysis period.

As with other antibiotics, Vitamin K deficiency has occurred in a few patients treated with cefoperazone. The mechanism is most probably related to the suppression of gut flora which normally synthesize this vitamin. Those at risk include patients with poor diet, malabsorption states (e.g. cystic fibrosis) and patients on prolonged intravenous alimentation regimens. Prothrombin time should be monitored in these patients and exogenous vitamin K administered as indicated.

A reaction characterized by flushing, sweating, headache, and tachycardia has been reported when alcohol was ingested during and as late as the fifth day after cefoperazone administration. A similar reaction has been reported with certain other cephalosporins and patients should be cautioned concerning ingestion of alcoholic beverages in conjunction with administration of SULPERAZON. For patients requiring artificial feeding orally or parenterally, solutions containing ethanol should be avoided.

As with other antibiotics, overgrowth of nonsusceptible organisms may occur during prolonged use of SULPERAZON. Patients should be observed carefully during treatment. As with any potent systemic agent, it is advisable to check periodically for organ system dysfunction during extended therapy; this includes renal, hepatic, and hematopoietic systems. This is particularly important in neonates, especially when premature, and other infants.

Drug Laboratory Test Interactions

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution.

Usage During Pregnancy

Reproduction studies have been performed in rats at doses up to 10 times the human dose and have revealed no evidence of impaired fertility and no teratological findings. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Usage in Nursing Mothers

Only small quantities of sulbactam and cefoperazone are excreted in human milk. Although both drugs pass poorly into breast milk of nursing mothers, caution should be exercised when SULPERAZON is administered to a nursing mother.

Usage In Infancy

SULPERAZON has been effectively used in infants. It has not been extensively studied in premature infants and neonates. Therefore, in treating premature infants and neonates potential benefits and possible risks involved should be considered before instituting therapy.

Cefoperazone does not displace bilirubin from plasma protein binding sites.

Adverse reactions

SULPERAZON is generally well tolerated. The majority of adverse events are of mild or moderate severity and are tolerated with continued treatment.

Gastrointestinal - As with other antibiotics, the most frequent side effects observed with SULPERAZON have been gastrointestinal.

Diarrhea/loose stools have been reported most frequently followed by nausea and vomiting. The frequency of these reported reactions has ranged from 3.6 to 10.8%.

Dermatologic Reactions - As with all penicillins and cephalosporins, hypersensitivity manifested by Maculopapular rash, urticaria, eosinophilia and drug fever has been reported. These reactions which have been reported in 0.8 to 1.3% of the cases, are more likely to occur in patients with a history of allergies, particularly to penicillin.

Hematology: Slight decreases in neutrophils have been reported. As with other beta-lactam antibiotics, reversible neutropenia may occur with prolonged administration. Some individuals have developed a positive direct Coombs test during treatment with cephalosporin antibiotics. Decreased hemoglobin or hematocrit have been reported, which is consistent with published literature on cephalosporins. Transient eosinophilia and thrombocytopenia have occurred, and hypo-prothrombinemia has been reported.

Miscellaneous adverse events (headache, fever, injection pain, chills) occurred in less than 1% of patients.

Laboratory Abnormalities: Transient elevations of SGOT, SGPT, alkaline phosphatase and bilirubin levels have been noted in 6.3 to 10.0% of the reported cases.

Local Reactions: SULPERAZON is well tolerated following intramuscular administration. Occasionally, transient pain may follow administration by this route. As with other cephalosporins and penicillins, when SULPERAZON is administered by an intravenous catheter some patients may develop phlebitis at the infusion site.

DOSAGE AND ADMINISTRATION

SULPERAZON is available in 1.5 g strength vial.

Total Dosage (g)	Equivalent Dosage of sulb. + cefoperazone (g)	Total Volume of Reconstituted Solution (ml)	Maximum Final Conc. (mg/ml)
1.5	0.5 + 1.0	4.0	125 + 250

The usual adult dose of SULPERAZON is 1.5 to 3 g per day (i.e., 1 to 2 g cefoperazone activity) given intravenously or intramuscularly in equally divided doses every 12 hours.

In severe or refractory infections the daily dosage may be increased up to 12 g of SULPERAZON (8 g cefoperazone activity) given intravenously in equally divided doses every 12 hours. The recommended maximum daily dosage of sulbactam is 4 g (8 g SULPERAZON).

Dosage regimens of SULPERAZON should be adjusted in patients with marked decrease in renal function (creatinine clearance of less than 30 ml/min) to compensate for the reduced clearance of sulbactam. Patients with creatinine clearances between 15 and 30 ml/min should receive a maximum of 1 g of sulbactam (maximum daily dosage of 2 g sulbactam), while patients with creatinine clearances of less than 14 ml/min should receive a maximum of 500 mg of sulbactam every 12 hours (maximum daily dosage of 1 g sulbactam). In severe infections it may be necessary to administer additional cefoperazone.

The usual dosage of SULPERAZON in children is 30 to 60 mg/kg/day (i.e., 20 - 40 mg/kg/day cefoperazone activity) in 2 to 4 equally divided doses. In serious or refractory infections, these dosages may be increased up to 240 mg/kg/day SULPERAZON (i.e., 160 mg/kg/day cefoperazone activity) in 2 to 4 equally divided doses. For neonates in the first week of life, the drug should be given every 12 hours. The maximum daily dosage of sulbactam in pediatrics should not exceed 80 mg/kg/day.

Intravenous Administration

For intermittent infusion, each vial of SULPERAZON should be reconstituted with the appropriate amount (shown in table) of 5% dextrose in water, 0.9% Sodium Chloride Injection or Sterile for water Injection and then diluted to 20 ml with the same solution followed by administration over 15 to 60 minutes.

For intravenous injection, each vial should be reconstituted as above and administered over a minimum of three minutes.

Intramuscular Administration

Sterile water for Injection should be used for reconstitution. For a concentration of cefoperazone of 250 mg/ml or larger, a two step dilution is required using Sterile water followed by 2% lidocaine to approximate a 0.5% lidocaine solution (see below).

Incompatibilities

SULPERAZON has been shown to be compatible with water for injection, 5% dextrose, normal saline, 5% dextrose in 0.225% saline, and 5% dextrose in normal saline at concentrations of 10 mg cefoperazone and 5 mg sulbactam per ml and up to 250 mg cefoperazone and 125 mg sulbactam per ml. Initial reconstitution with Lactated Ringer's Solution or with 2% lidocaine HCl solution should be avoided since these mixtures have been shown to be incompatible. However, a two step dilution process involving initial reconstitution in water for injection will result in a compatible mixture when further diluted with Lactated Ringer's Solution at a sulbactam concentration of 5 mg/ml. Similarly, after appropriate initial reconstitution with water for injection SULPERAZON could be further diluted with 2% lidocaine hydrochloride to yield solutions containing up to 250 mg cefoperazone and 125 mg sulbactam per ml in 0.5% lidocaine HCl solution. Solutions of SULPERAZON and aminoglycosides should not be directly mixed since there is a physical incompatibility between them. If combination therapy with SULPERAZON and an aminoglycoside is contemplated (SEE INDICATIONS section) this can be accomplished by sequential intermittent intravenous infusion provided that separate secondary intravenous tubing is used, and that the primary intravenous tubing is adequately irrigated with an approved diluent between doses. It is also suggested that doses of SULPERAZON be administered throughout the day at times as far removed from administration of the aminoglycoside as possible.

How Supplied

One vial containing 1.5 gm Sulperazon (500 mg sulbactam + 1000 mg cefoperazone) + distilled water ampoule for injection.

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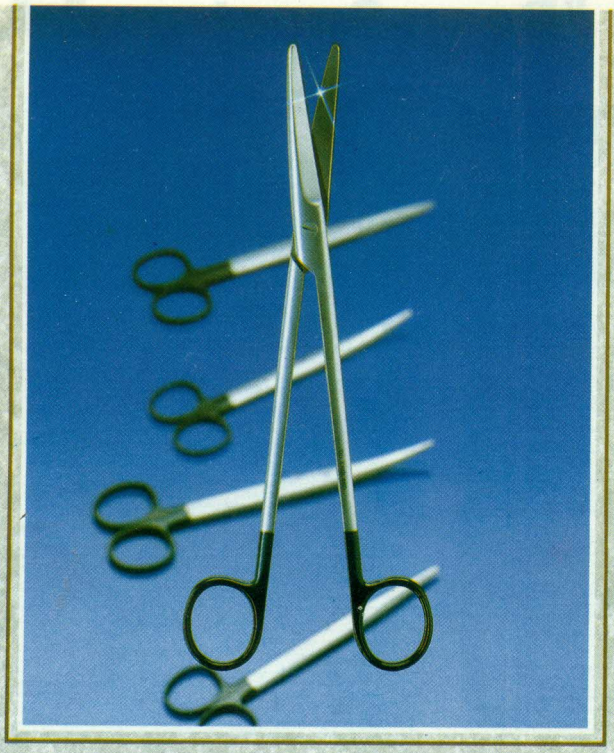

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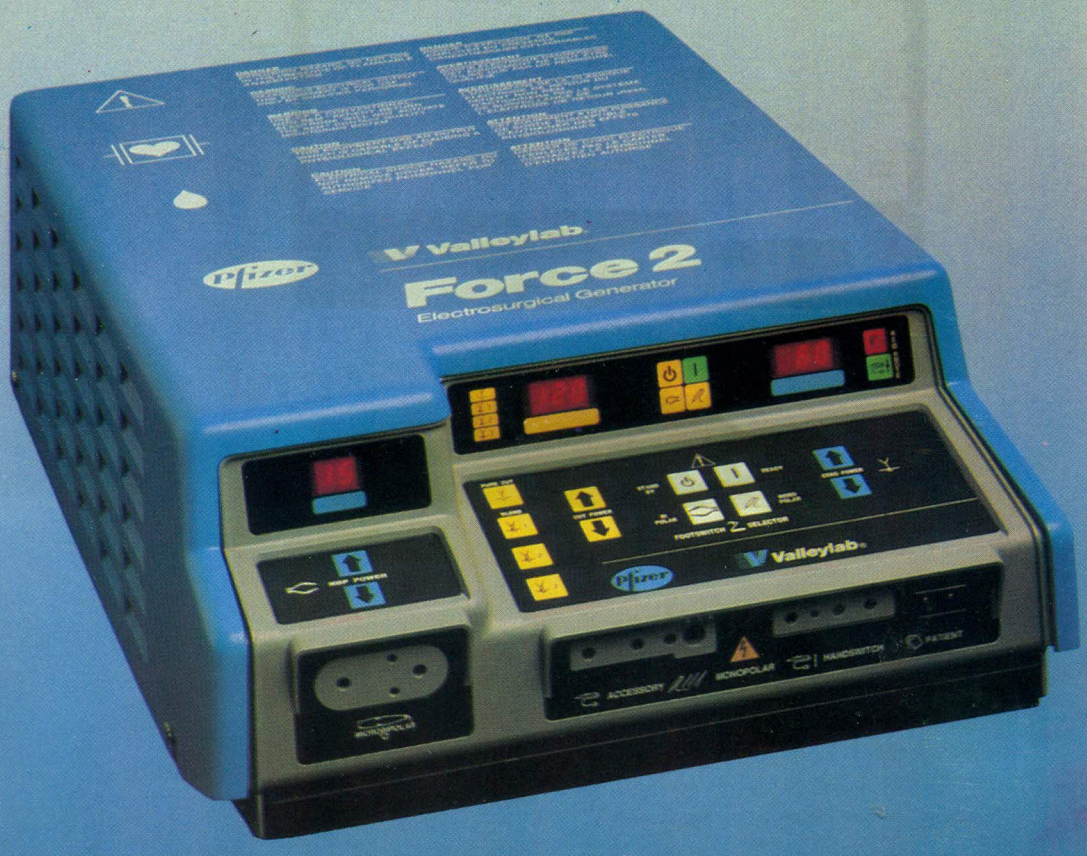

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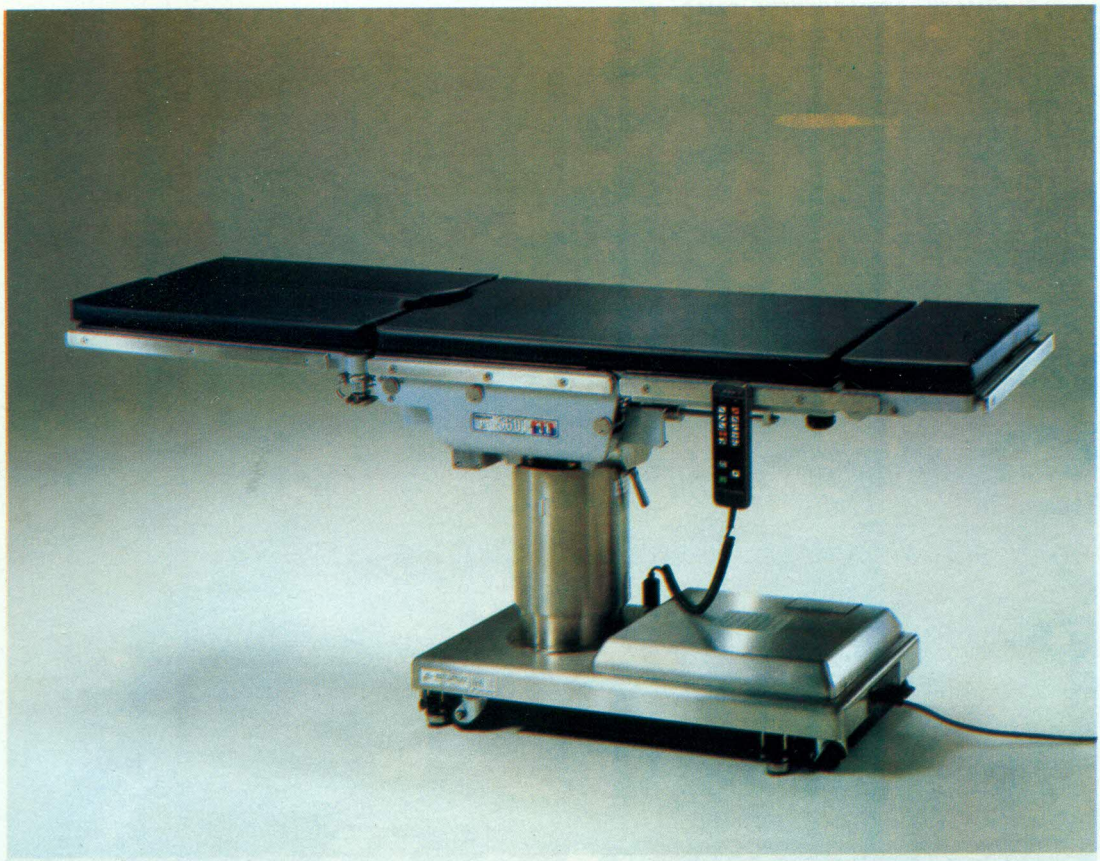

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Correspondence to be sent to:
Prof. Dr. Mohamed El Fiky, 79, Ramsis Str., Cairo, Egypt, Post Code 11111

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EDITOR

MOHAMED EL FIKY.

79, Ramsis Str.
Cairo - Egypt.
Post Code 11111.
Fax (202) 772535

Information for authors

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2- Introduction, Material, Methods, Results, Discussion and references.

3- Tables and figures should be provided separately; the position of the tables and figures in the text should be marked on the manuscript. Drawings should be with china ink.

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Aortic Valve Replacement in Patients with Small Aortic Annulus Using the Manouguian's Approach

ABSTRACT

To avoid the problem of valve prosthesis patient mismatch in the late postoperative period from January 1995 to January 1998 at Ain Shams University Hospitals, 18 patients underwent patch enlargement of the small aortic annulus by the Manouguian's approach either with aortic single valve replacement (11 patients, 3 of them were reoperations) or with aortic mitral double valve replacement (7 patients).

Their age ranged from 15 to 45 years. The aortic annulus before enlargement ranged between 14 to 20 mm with an average of 16 mm and after enlargement the diameter of the annulus ranged from 19 to 24 mm with an average of 21 mm. To enlarge the annulus fresh autologous pericardium was used in 3 patients. Haemashield dacron patch was used in 4 patients and in 11 patients pericardium fixed in gluteraldahyde was used.

There was one early death due to low cardiac output (operative mortality 5.5%). The rest of the patients are doing well with excellent haemodynamic results in the post operative follow up echocardiography.

Follow up period ranged from 4 to 35 months (average 25 months).

Patch enlargement of the small aortic annulus (Manouguian's technique is a simple safe and effective adjunct permitting the insertion of a valve one or two sizes larger than that which could be accommodated by the native annulus.

Key words: Aortic valve replacement - patch enlargement - small aortic annulus.

Ahmed El Kerdany

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INTRODUCTION

Management of the small aortic annulus presents a dilemma and a technical challenge to the surgeon during aortic valve replacement. In patients who underwent aortic valve replacement and had valve prosthesis patient mismatch, complications such as persisting or increasing left ventricular dysfunction or hypertrophy, haemolysis and sudden death are produced(1). Here we report our experience with patch enlargement of the small aortic annulus using the Manouguian's procedure(2,3,4,5) .

Department of cardiothoracic surgery, Ain Shams University - Cairo - Egypt.

Patients and Methods

Between January 1995 and January 1998 at Ain Shams University Hospitals 18 patients underwent patch enlargement of the aortic annulus using the Manouguian technique either with aortic single valve replacement (11 patients, 3 of them were reoperations) or with aortic mitral double

valve replacement (7 patients) .

Twelve were females and six were males, their age ranged from 15 to 45 years, mean (28.7±7.4).

Primary valvular diseases included rheumatic heart disease (11 patients). Congenital aortic disease (5 patients, one of them had previous resection of subaortic membrane), and 2 patients had valve prosthesis patients mismatch, both had aortic valve replacement with standard Carbomedic valve size 19, both were symptomatic and had high postoperative transvalvular gradient during rest (64 and 70 mmHg) respectively.

The predominant aortic valve lesion was stenosis in 12 patients, insufficiency in 2 patients, and mixed in 4 patients.

Operative technique

Standard cardiopulmonary bypass and moderate systemic hypothermia (28°C) were used for all patients, myocardial protection was performed with antegrade cold blood enriched crystalloid cardioplegia (80% crystalloid, 20% blood with K level, 30 m mol/L) injected every 30 minutes.

The anterior aortic wall was incised in an oblique fashion, the aortic cusps were excised and the aortic annulus was measured and if the aortic annulus was judged to be too small to accomodate size 19 HP St Jude prosthesis, the aortotomy was extended as long as 10 mm from the top of the non coronary cusp-left coronary cusp commissure to just the confluence of the interventricular fibrous trigone, left atrial wall and the mitral annulus.

In 6 patients the atrial attachment at the base of the aorta was divided and the left atrium was incised about 1.5 cm posteriorly for better enlargement of the annulus.

A diamond shaped haemashield dacron patch (4 patients) or fresh autologous pericardial patch (3 patients) or autologous pericardial patch fixed in 0.4% gluteraldahyde (11 patients) was sutured to the V shaped defect in the anterior mitral leaflet and in the aortic root with 4/0 running polypropyline.

A mechanical prosthesis (ST Jude HP) one or two sizes larger than the original annulus was sewn into place using interrupted horizontal mattress teflon pledgeted sutures. The prosthesis was placed parallel to the original native valve position. (Figs. 1, 2, 3) .

The defect between the left atrial wall and the patch material was closed from the outside with mattres sutures through teflon felt strip.

10 patients underwent other concomitant procedures in addition to aortic valve replacement (Table 1).

Patients follow up was achieved by direct contact with the patients. All the patients had post-operative echocardlography during their 1 st postoperative visit (one month after discharge).

Results

We encountered no haemorrhage in our series. The aortic annulus before enlargement ranged from 14 to 20 mm with an average of 16 mm and after enlargement the diameter of the annulus ranged from 19 to 24 mm with an average of 21 mm. This

Table (1): Concomitant procedures performed

Procedure	No of patients
Mitral valve replacement alone with tricuspid annuloplasty	 6 1
Excision of subvalvular membrane and septal myectomy	3

Table (2) Systolic pressure gradient across aortic outlet prior and after the Manouguian's procedure

Case No.	Age	Type of valve used	LV peak systolic gradient	
			Before repair	After repair
1	37	St Jude HP 19	85	25
2	26	St Jude HP 19	65	18
3	25	St Jude HP 21	70 (Carbo 19)	15
4	22	St Jude HP 19	190	35
5	15	St Jude HP 19	90	12
6	16	St Jude HP 21	110	20
7	43	St Jude HP 21	64 (Carbo 19)	18
8	17	St Jude HP 19	10	Died
9	27	St Jude HP 19	60	22
10	35	St Jude HP 21	75	15
11	42	St Jude HP 19	70	20
12	18	St Jude HP 19	110	25
13	33	St Jude HP 19	80	14
14	45	St Jude HP 21	20	10
15	18	St Jude HP 19	75	28
16	17	St Jude HP 17	125	32
17	28	St Jude HP 19	60	18
18	21	St Jude HP 17	90	36

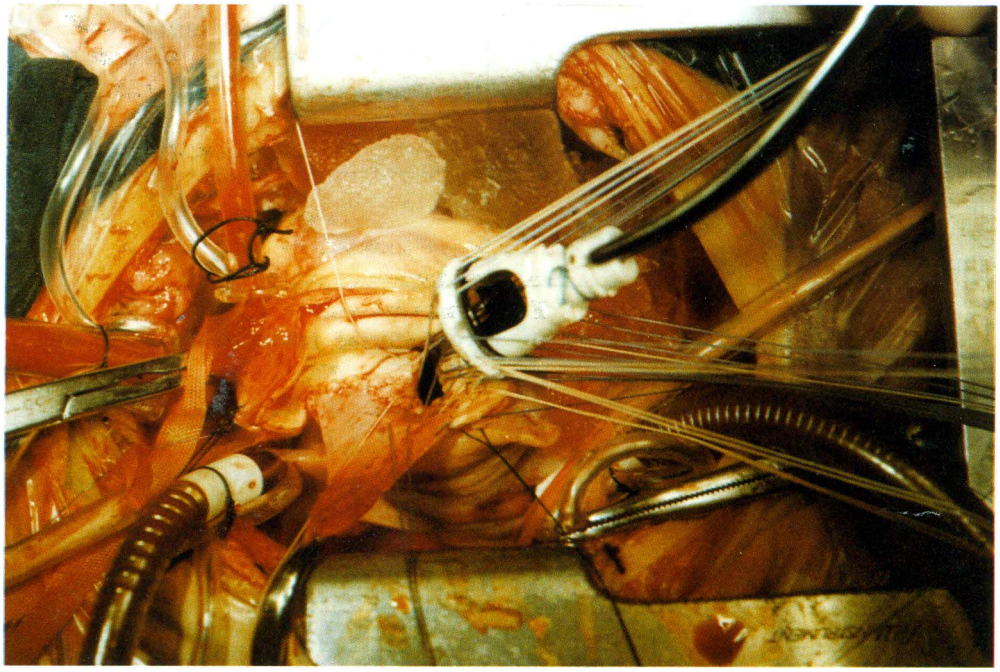

Fig. (1) The pericardial patch used to enlarge the aortic annulus

enabled us to insert a valve one or two sizes larger than that which could be accommodated by the native annulus. (Table 2).

We have one operative mortality (5.5%). In this patient the annular enlargement was not planned from the start but was done after failure to insert a size 19 HP St Jude valve. This patient died from low cardiac output in the early post-operative period.

All survivors are doing well with normal exercise tolerance in NYHA class 1. Follow up echocardlography showed excellent haemodynamic results (Table 2).

Discussion

In patients with a small aortic annulus, it is still controversial whether to use a small prosthetic valve (equal to or less than 19 mm in diameter) or to enlarge the aortic annulus (6,8). The free hand aortic allograft is considered to be the best replacement device for the small aortic valve because it results in only minimal pressure gradients, though unfortunately, allografts are not always available (10) .

However when the aortic annulus is extremely small and valve replacement can not be accomplished even with a 19 mm prosthetic valve employing the standard

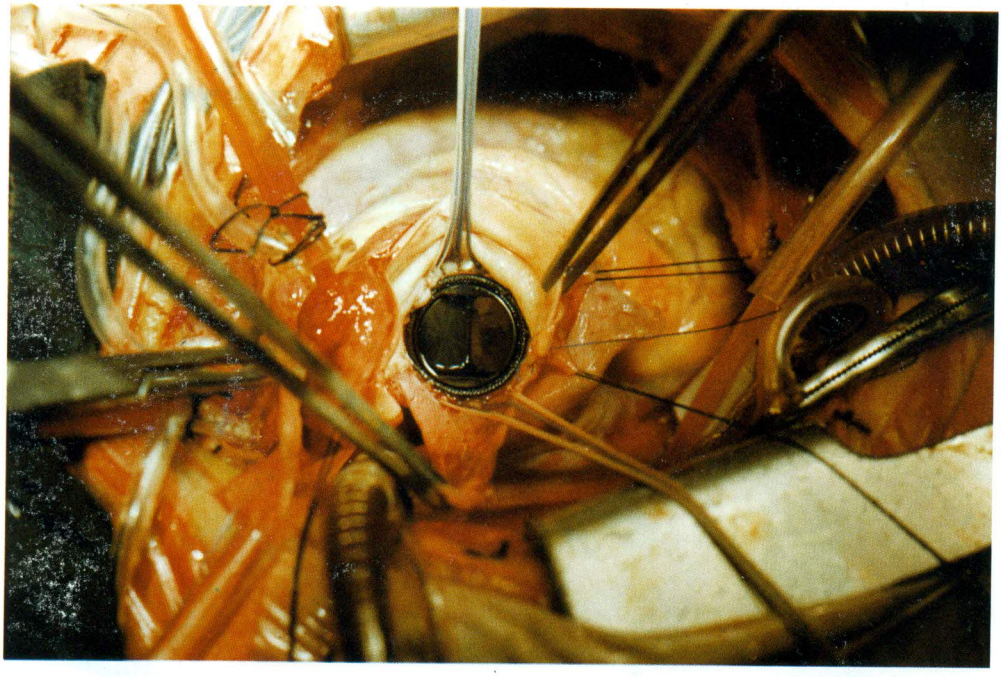

Fig. (2): The aortic prosthesis in place.

technique an annulus enlarging procedure should be considered (2,11,12) .

Placement of the aortic prosthesis in a supra annular position is a simple method of accomplishing that, this done by suturing the prosthesis to the aortic annulus along the left and right sinuses and in a supra annular position along the non coronary sinus, however this technique allows for insertion of a prosthesis only one size larger than the aortic annulus (7) .

From a clinical perspective several annulus-enlarging procedures have been reported for aortic valve raplacenent in patients with a small aortic annulus.

Niks and Colleagues (11) proposed enlargement of the aortic annulus by extending the aortotomy incision to the middle of the non coronary sinus throughout the aortic annulus, but the enlargement of the aortic annulus is limited compared to the other methods (3,5) .

Kono and associates (12) reported enlargement of the left ventricular outflow tract and the aortic annulus by extensive ventriculotomy. This procedure requires opening and enlargement of the right ventricular outflow tract and repair of the subsequent ventricular septal defect but provides a much wider enlargement of aortic annulus. Possible injuries of the major septal coronary arteries and conduction systems with the Kono

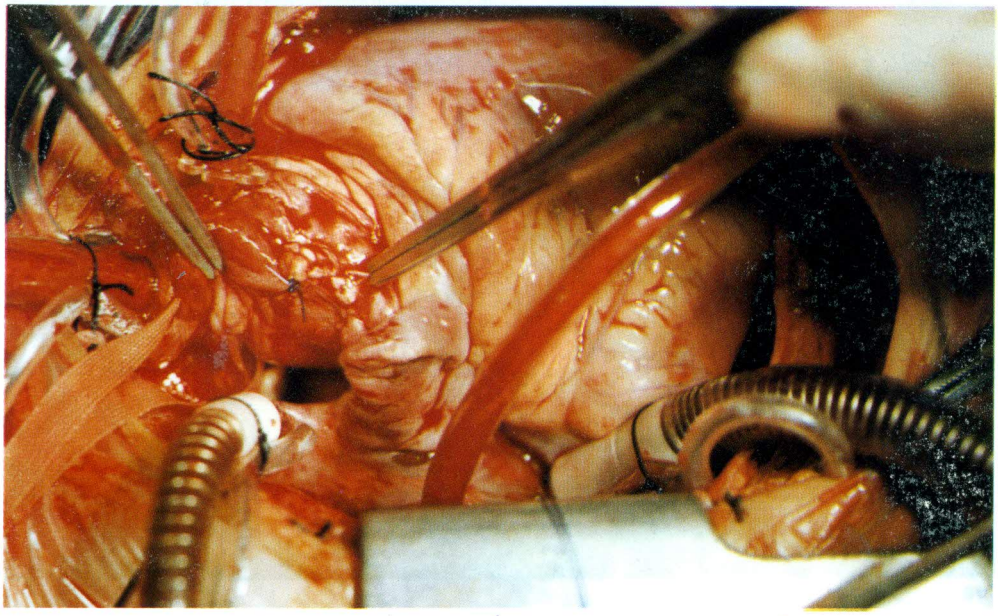

Fig. (3): The pericardial patch used to close the aortotomy.

procedure are major disadvantages (13) .

The Manouguian's procedure (3,4,5) is considered the simplest method to enlarge the aortic annulus by extending the aortotomy incision through the commissure between the non coronary cusp and the left coronary cusp into the central fibrous body and provides enlargement of the aortic annulus more than the Nick's procedure, yet less than the Kono procedure (13) .

This technique is simple and safe and we did not encounter any haemorrhage in our series.

All the patients showed marked improvement in their NYHA functional class even in the two patients in whom we did use St Jude HP size 17.

Kitamura and associates (13) reported that long term survival and freedom of morbidity after aortic annular enlargement is superior to those after standard aortic valve replacement with a small valve prostheses

Mitral prolapse and mitral regurgitation are known late complication of the Manouguian's procedure (9,14) . We have not seen yet any mitral regurgitation in our patients as we try to limit in the incision in the anterior mitral leaflet to the minimal and to use native pericardium that proved to

cause less mitral regurgitation compared to the use of prosthetic patches (14) .

Conclusion

Patch enlargement of the small aortic annulus using the Manouguian's procedure is a simple safe and effective adjunct permiting the insertion of a valve one or two sizes larger than what could have been accommodated by the native annulus and the use of St Jude HP prosthesis showed excellent haemodynamic results even in the small sizes.

References

1. Rahimtoola SH. The problem of valve prosthesis-patient mismatch. Circulation 1978, 58:20-24.
2. Manouguian S, Seybold-Epting W. Patch enlargement of the aortic valve ring by extending the aortic incision into the anterior mitral leaflet. New operative technique. J Thorac Cardiovasc Surg 1979, 78.402-12.
3. Kawachi Y, Tominaga R, Tokunaga K. Eleven year follow up study of aortic or aortic-mitral annulus enlarging procedure by Manouguian's technique. J Thorac Cardiovasc Surg 1992. 104:1259-63.
4. Mayumi H, Toshima Y, Kawachi Y, Tokunaga K and Yasui H. Simplified Manouguian's aortic annular enlargement for aortic valve replacement. Ann Thorac Surg 1995, 60:701-4.
5. Nakono S, Matsuda H, Shemazaki Y. An appraisal of patch enlargement of the small aortic annulus in 33 patients undergoing aortic valve replacement. Eur J Cardio Thorac Surg 1992, 6: 347-9.
6. Kenz I, Machler H, Rehak P, Oberwalder P, Monti M, Dacar D and Rigler B. Concomitant procedures in the small versus standard aortic root. J Heart valve Dis 1996, Vol 5: Suppl III:294-301.
7. David T, Uden D. Aortic valve replacement in adult patients with small aortic annuli. Ann Thorac Surg 1983, 36-.577-83.
8. Winter TQ, Major MD, Tri TB, Bowen TE. Haemodynamic evaluation of the St. Jude medical valve prosthesis in the small aortic annulus. J Thorac Cardiovasc Surg 1981, 81:615-20.
9. Inanaka K, Takamoto S, and Faruse A: Mitral regurgitation late after Manouguian's annulus enlargement and aortic valve replacement. J Thorac Cardiovasc Surg 1998, 115:727-31.
10. Jaffe WM, Coverdale HA, Roche AHG, Whitlockr ML, Neutze JM, Barrat - Boys BG. Rest and exercise haemodynamics of 20-23 mm allograft. Medtronic intact (porcin) and St. Jude medical valves in the aortic position. J Thorac Cardiovasc Surg 1990,100:167-74.
11. Nicks R, Cartmill T, Bernstein L. Hypoplasia of the aortic root. Thorax 1970., 25:339-46.
12. Konno S, Imai Y, Lida Y, Nakajima M, Tatsuno K. A new method for prosthetic valve replacement in congenital aortic stenosis associated with hypoplasia of the aortic valve ring. J Thorac Cardiovasc Surg 1991, 102: 202-6.

13. Kitamura M, Satoh M, Hashimoto A, Koyanagi H. Aortic valve replacement in small aortic annulus with or without annulur enlargement. J Heart Valve Dis 1996; Nov 5 Supp 3:289-93.

14. Imanaka K, Takamoto S and Furuse A. Mitral regurgitation late after manouguian's annulus enalegement and aortic valve replacement. J Thorac Cardiovasc Surg 1998; 115: 727-29.

Size 19mm Mechanical Bileaflet Aortic Valve in Small Aortic Root

ABSTRACT

Background and aim of work: Aortic valve replacement with small aortic ring escalates the challenge which any surgeon can in face to choose the right size and design of the prostheses. The aim of this study was to assess the outcome of implantation of size 19mm mechanical bileaflet prosthetic aortic valve, in different adult patients circumstances, when enlargement of the aortic ring was hazardous to be performed. Material and Methods: During 3 years period (Feb. 1992 and Feb. 1995), 41 patients underwent aortic valve replacement with small aortic root in Glenfield General Hospital. There were 12 male (29.3%) and 29 female (70.7%). The age ranged from 19 to 83, mean 64.6 years. The etiology of the diseased valves was variable. NYHA classification ranged from 2-4 with mean of 3.19. The mean peak systolic pressure gradient was 84.3 mmHg of range 30-120 mmHg. The body surface area (BSA) ranged from 1.31 to 2.1m2 of 1.57m2 mean. All patients received size 19 mm Sorin mechanical bileaflet aortic valve when it was not feasible to enlarge their aortic ring and all were followed up for 4 weeks and 6 months after the operation. Some had more than two visits. Results: There were 2 patients (4.9%) died on table and no late mortality. At a mean follow up of 7.36 months, there were a significant change in mean NYHA classification from 3.19 preoperative to 1.23 postoperative. There were also marked drop of the mean peak systolic pressure gradient through the aortic valve (pre-op. 84.31 mmHg-post-op. 18.76 mmHg). Four patients (10.6%) reported improvement in EF from poor to moderate. There was no late bleeding related to anticoagulation, thromboses, para-valvular leak or endocarditis. Conclusion: Our study demonstrated that size 19 mm mechanical bileaflet aortic valve, can be used in adult, if anticoagulation is not contraindicated and annular enlargement is not feasible. The surgical outcome is related to the age of the patient at the time of surgery, concomitant cardiac lesions, the body surface area and the gradient through the valve before and after surgery.

M Abdallah; MD and J Leverment; FRCS.

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INTRODUCTION

Up till now, there is no available ideal prosthetic valve which can meet the huge variability of patients demands. Aortic valve replacement with small aortic ring escalates the challenge which any surgeon can in face to choose the right size and design of the prostheses.

Several techniques have been developed to overcome these difficulties including enlarging the annulus. However, this technique sometimes is difficult to achieve in calcified or fragile tissues, that increases the risk in critically ill patients (1,2).

Department of Cardiothoracic Surgery, Glenfield Hospital, Leicester, UK LE3 9QP.

Therefore, replacement of the diseased valve by a prosthesis that fits into the existing root is the reasonably solution to the problem. Many controversies have been raised regarding using stentless bioprostheses (3) or mechanical prostheses inserted inside or on top of the aortic ring (4,5,6). This debate has led to find out the principles of judgement for each prosthetic valve size and design.

The aim of this study was to assess the outcome of implantation of size 19 mm mechanical bileaflet prosthetic aortic valve, in different adult patients circumstances, when enlargement of the aortic ring was hazardous to be performed. This was based on clinical assessment, suplemented by pre and post-operative echocardiography, measuring the peak systolic pressure gradient across the aortic valve and left ventricular ejection fraction (EF).

Material and Methods

During 3 years period (Feb. 1992 and Feb. 1995), 41 patients underwent aortic valve replacement with small aortic root in Glenfield General Hospital. Thirty seven patients (90.2%) were elective and 4 (9.8) were for emergency procedures.

The information were obtained from the patients clinical records including preoperative assessment, operative reports, and follow up data.

Cardiac catheterization and angiographic evaluation were done for those patients in whom these investigations had been required. Pre and postoperative echocardiography was a routine investigation for all patients.

There were 12 male (29.3%) and 29 female (70.7%). The age ranged from 19 to 83, mean 64.6 years. The etiology of the diseased valves was variable, 24 were due to calcific aortic stenosis, 10 due to rheumatic heart diseases, 3 due to congenital bicuspid aortic valve, 2 due to endocarditis and one had myxometous degeneration, with over all calcification in 36 patients. Fourteen patients had aortic stenosis (AS), 3 had aortic incompetence (A1), 16 had combined lesions (ASI), 6 had ASI with mitral stenosis (MS) and incompetence (M1), 1 had ASI, MIS and tricuspid stenosis (TS), 1 had ASI, MIS and tricuspid incompetence (T1). Three patients had previous heart operations.

NewYork Heart Association (NYHA) classification ranged from 2-4 with mean of 3.19. Fourteen patients had good EF, 20 had moderate EF and 7 had poor EF. The mean peak systolic pressure gradient was 84.3 mmhg of range 30-120 mmHg. The body surface area (BSA) ranged from 1.31 to 2.1M2 of 1.57m2 mean. Seven patients were in sinus rhythm, 13 were in atrial fibrillation (AF) and one had permanent pacemaker implantation for third degree heart block.

All these patients had their operation performed by the same surgical technique and received size 19 mm Sorin mechanical bileaflet aortic valve when it was not feasible to enlarge their aortic ring. Seven patients (17%) had concomitant mitral valve replacement, one (2.4%) had mild MI did not require surgical interference, 4 (9.8%) had concomitant coronary artery bypass surgery, one patients had atrial septal defect repair using pericardial patch and one (2.4%) had tricuspid valve repair. All patients started oral anticoagulation

Table 1: Data of early mortality.

No	Age	Sex	NYHA	Gradient	EF	BSA
1	62	F	4	100	P	1.7
2	66	F	3	60	M	1.86

Table 2: Data of patients with gradient more than 20 mmHg after surgery.

No	Age	NYHA	Gradient	EF	BSA
		Pe-po	Pe-po	Pe-po	
1	51	3-1	100-47	G-G	1.95
2	68	3-2	120-20	M-M	1.8
3	66	2-2	90-20	M-M	1.89
4	74	3-2	80-25	M-M	1.8
5	76	4-1/2	90-33	P-M	1.8
6	66	3-1	80-33	G-G	2.1
7	71	4-1	80-28	M-M	1.8
8	82	4-2	120-20	M-M	1.84

Pe: Preperative Po: post-operative.

shortly after the operation.

Local patients were followed up for 4 weeks and 6 months after the operation. Some had more than two visits. Others who were not local,' their data had been given by the referral cardiologist.

Results

Two patients (4.9%) died on table. Both were female of 62 and 66 years old, and both died from cardiogenic shock; one and two hours after insertion of intra-aortic balloon pump (IABP) respectively (table: 1). Up to 8 months from the last follow up, there were no reported mortalities.

One patient (2.7%) required IABP for 36 hours; one patient (2.7%) had post operative bleeding, wound infection followed by renal failure: One (2.7%) had atelectasis that needed suction bronchoscopy, his chest x ray improved 48 hours later: Three patients (7.7%) required permanent pacemaker implantation. Two of these patients had been in sinus rhythm and

one had been in AF before surgery. One sinus rhythm patient developed left bundle branch block (LBBB), recovered after 5 days and one AF patient converted to sinus rhythm.

At a mean follow up of 7.36 months. there were a significant change in mean NYHA classification from 3.19 preoperative to 1.23 postoperative. There were also marked drop of the mean peak systolic pressure gradient through the aortic valve (pre-op. 84.31 mmHg-post-op. 18.76 mmhg). There were eight patients (20.5%) with post operative peak systolic pressure gradient between 20 and 47 mmHg (table:2). Seven patients (17.9%) reported increase in the peak systolic pressure gradient during the second visit. This increase ranged from 5 to 7 mmhg above the initial reported peak systolic pressure gradient during the first visit. Their age ranged from 19 to 51 years old. Four of them, their BSA ranged from 1.6 to 1.69 M2 and two had BSA of 1.95 and 1.96 M2. All were in NYHA class I during the second visit.

Four patients (10.6%) reported improvement in EF from poor to moderate. There was no late bleeding related to anticoagulation, thromboses, paravalvular leak or endocarditis.

Discussion

This study has shown that, In recent years the number of referral calcified aortic diseases to our unit has increased. Female referral (70.7%) was relatively higher than male (29.3%) referral. Concomitant heart (34.1%) and other systemic diseases (68.3%) were common. This to some extent with calcification and friability of tissues made surgery demanding (7). We have tried in this study to use the same technique in managing all patients to avoid interference with the outcome.

Arrhythmia was the dominating problems in early postoperative period (53.8%) This early arrhythmia affected the blood pressure and required conversion in most of them. Ten patients (25.6%) reverted to sinus rhythm and 11 (28.2%) persisted with AF. Nineteen patients (48.7%) needed cardiac support for more than 24 hours. All of them had concomitant aortic incompetent lesion. This confirmed our experience with patients who have aortic valve incompetence. They usually require relatively longer recovery period after surgery than patients who have aortic stenosis.

All the studied patients recorded improvement in life style with significant improvement in the degree of dyspnoea. This improvement had simultaneous drop of the peak systolic pressure gradient through the valve. Eight patients (20.5%) had postoperative peak systolic pressure gradient more than 20 mmHg. These patients had BSA more than 1.8M2. Preoperative peak systolic pressure gradient above 80 mmhg and age above 51 years. Inspite of occasional presence of one of these parameters in the other studied patients, they were not in combination in one patient at the same time except in these 8 patients. It has been found that the BSA (8,9) and replaced valve index affect the cardiac output and subsequently the peak systolic gradient (7, 10, 11). It has also been found that residual obstruction after valve replacement may affect the clinical outcome (12) and even long term survival

(13,14). The other 7 patients (17.9%) who reported increase in peak. systolic pressure gradient during the second visit . This could possibly be related to the increase in physical activity, as all of them went back to work with normal life demands. They had no reported complaint for 14 months after the last visit of total follow up of 22 months. We do believe that these patients might have more benefit from annular enlargement which was not feasible during their procedure (15).

There was no bleeding related to oral anticoagulation with international neutralization ratio of 2.5 to 3. There was also no embolic manifestation or endocarditis in the studied patients.

Conclusion

Our study demonstrated that size 19 mm mechanical bileaflet aortic valve, can be used in adult. if anticoagulation is not contraindicated and annular enlargement is not feasible. The surgical outcome is related to the age of the patient at the time of surgery, concomitant cardiac lesions, the body surface area and the gradient through the valve before and after surgery.

References

1. Colleen F. Sintek, Alden D. Fletcher. Siavosh Khonsari. Small Aortic Root in the Elderly: Use of Stentless Bioprosthesis. The Journal of Heart Valve Disease 1996; 5 (Suppl. III): S 308-S 313
2. Achtelik M, Pethig K, Schafers H-J, Borst H-G. Stentless Aortic Valve replacement with the Biocor Prosthesis: Indication and Outcome. The Journal of Heart Valve Disease 1996; 5 (Suppl. III): S 314-S 316
3. Gonzalez-Juanatey JR, Garcia-Bengoechea JB, Garcia-Acuna JM Fernandez MV, Cendon AA, Roman AV, de La Pena MG. The Influence of the Design on the Medium to Long Term Hemodynamic Behavior of 19 mm Pericardial Aortic valve Prostheses. The Journal of Heart Valve Disease 1996; 5 (Suppl. III): S 317-S 323.
4. Wortham DC, Tri TB, Bowen TE. Hemodynamic evaluation of the St. Jude Medical valve prosthesis in the small aortic annulus. J Thorac Cardiovasc Surg 1981;81:615-620
5. Tatieneni S, Barner HB, Pearson AC, Halbe D, Woodraft R, Labovitz AJ. Rest and exercise evaluation of St. Jude Medical Medtronic Hall prostheses: influence of primary lesion, valvular type, valvular size,, and left ventricular function. Circulation 1989; 80 (suppl): 116-123.
6. De Brux J-L, Subayi J-B, Binuani P, Laporte J. Doppler-Echocardiographic Assessment of the Carbomedics Supra-Annular Top-Hat Prosthetic Heart valve in the Aortic Position. The Journal of Heart Valve Disease 1996; 5 (Suppl. III): S 336-S 338
7. Franzen SF, Huljebrant IE, Konstantinov IE, Nylander E, Olin CL. Aortic valve replacement for aortic stenosis in patients with small aortic root. The Journal of Heart Valve Disease 1996; 5 (Suppl. III): S 284-S288.
8. Rahimtoola SH. The problem of valve prosthesis-patient mismatch. Circ 1978; 58: 20-24.
9. Chamber J. Echocardiography and the

Small Aortic Root. The Journal of Heart Valve Disease 1996; 5 (Suppl. III): S 264-S 268.

10. Izzat NW, Birdi I, Wilde P, Bryan AJ, Angelini GD. Evaluation of the hemodynamic performance of small CarboMedics aortic prostheses using Dobutamine-stress Doppler echocardiography. Ann Thorac Surg 1995; 60: 1048-1052.

11. DePaulis R, Sommariva L, Russo F, et al. Doppler echocardiography evaluation of the CarboMedics valve in patients with small aortic annulus and valve prosthesis-body surface area mismatch. J Thorac Cadiovasc Surg 1994; 108: 57-62.

12. Sim EKW, Orszulak TA, Schaff HV, Shub C. Infuence of prosthese size on change in left ventricular mass following aortic valve replacement. Euro J Cariothoracic Surg 1994; 8: 293-297.

13. Kratz JM, Sade RM, Crawford FA, Crumbley AJ, Stroud MR. The risk of small St. Jude aortic valve prostheses. Ann Thorac Surg 1994;57:1114-1119.

14. Morris JJ, Schaff HV, Mullany CJ, et al. Determinants of survival and recovery of left ventricular function after aortic valve replacement. Ann Thorac Surg 1993; 56:22-30 .

15. Kitamura M, Satoh M, Hachida M, Endo M, Hashimoto A,-Koyanagi H. Aortic Valve Replacement in Small Aortic Annulus with or without Annular Enlargement. The Journal of Heart Valve Disease 1996; 5 (Suppl. III): S 289-S 293.

Role of Thrombolysis in Management of Acute Mechan Valve Obstruction, initial Experience

ABSTRACT

Twenty eight patients with acute mechanical valve obstruction were diagnosed clinically and echocardiographically at the Cairo University hospital from 1986 to 1998. The obstructed valves were in the Aortic position in four patients and in the Mitral position in 24 patients, one of which had a double valve replacement. All patients had tilting disc prosthesis. We compared 3 groups of patients; those who received heparin only in preparation for surgery (Gp1), those who received thrombolytic therapy (Gp2), and those who were sent directly to cardiac surgery (Gp3) as concerns their clinical status and their clinical outcome. From Gp I one patient was cured, 3 could be stabilized well enough to undergo surgery and seven patients died. In Gp2, two patients were cured, five improved but needed surgery later on, one of which developed transient upper limb ischaemia. Three patients died of cerebral embolism. In Gp3, one patient died, and the five had a successful outcome. The difference in early survival between Group 1 and Group2 was of weak statistical significance (p=0.1). The difference in early survival between Group I and Group3 was statistically significant (p< 0.025). Although the difference in early survival between Group2 and Group3 was of no statistical significance (p=0.2) only 2 of 7 survivors did not need surgical intervention.

Conclusion: Although the risk of embolism is high and maybe fatal, thrombolytic therapy is indicated in prosthetic valve patients with acute valvular obstruction, who need to be stabilized medically as a preparatory step for valve re-replacement. It cannot be considered as an alternative to surgery in Egyptian patients,.

Zeinab A. Ashour, MD and Hesham A.F. Shawky, MD

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INTRODUCTION

Background

Valvular heart disease is common in Egypt, due to the high incidence of rheumatic fever. Mechanical prosthetic valves have been used in this country since the late 1970s. The commonest and potentially lethal complication occurring in patients with mechanical valve prosthesis is thromboembolism. (1) International studies estimate this complication to occur with a frequency of about 0.5- 6/100 patient years (1,2). The most dramatic version of prosthetic valve thrombosis is acute valvular malfunction which is mainly observed in tilting disc valves. Emergency cardiac surgery is not available in all centers, and even when available the patient may not be fit for or willing to undergo another major operation. Thrombolysis was tried in various countries, with varying degrees of success and varying degrees of thromboembolism

Department of Cardiology and Department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt

(3-22) We tried to determine whether thrombolytic therapy is an alternative way of treatment for Egyptian patients with mechanical valve obstruction.

Patient population

348 female and 211 male patients with mechanical valve prosthesis were followed up from 1986 to 1998. Of these, 28 presented with acute mechanical valve obstruction. The obstruction was diagnosed clinically in all cases and was confirmed by imaging a reduced valvular excursion by flouroscopy,transthoracic echocardiography and transesophageal echocardiography whenever possible. However, a full echocardiography examination could not be performed in six patients due to extremely poor physical condition.

From 1986 to 1989, thrombolytic therapy was not available and the patients presenting during this period of time could only receive heparin. Emergency cardiac surgery was also not well established, and it was considered a great achievement, when a patient was admitted to surgery one week after the diagnosis. Later redo valve replacements on an emergency basis became more feasible, and thrombolytic agents also became available. We compared 3 groups of patients whose valvular malfunction was diagnosed clinically and echocardiographically; those who received heparin only in preparation for surgery (Gp 1), those who received thrombolytic therapy (Gp2), and those who were sent directly to cardiac surgery (Gp3) as concerns their clinical status and their clinical outcome.

Patients who received heparin only (GpI).

Gp I patients received heparin infusions so as to adjust the PTT 2-2.5 times their normal control. These were the patients who presented with acute mechanical valve obstruction prior to the availability of thrombolytic therapy, patients who refused to give a written consent for receiving thrombolytic therapy, and patients whose initial presentation was peripheral embolism. Four of these patients were pregnant at the time they experienced the acute valvular obstruction (see table 1)

Patients on thrombolytic therapy (Gp2)

These were patients whose poor medical condition did not allow immediate surgery, as well as patients who refused a redo surgery. Four patients were pregnant at the time of presentation, and a fifth had just had a premature delivery and had experienced postpartum hemorrhage. The risk of peripheral embolism as well as fetal damage in case of pregnancy was explained to the patients as well as their families and a written consent was obtained.

Each received a bolus injection of 250000 I.U. Streptokinase followed by an infusion of 100 RJ per hour for 24 up to 72 hours. (see table 2)

In case of survival transthoracic and transesophageal echoes were done repeatedly to follow up the transvalvular gradient, valve mobility as well as size and friability of the thrombus.

Patients referred directly to surgery (Gp3).

This group comprised six female patients with Mitral valve prosthesis. Although all of them had shortness of breath classified as NYHA class 3 or 4,

Table 1: Gp 1 Patients who received heparin

PATIENT	AGE	OPERATION DATE	MALFUNCTION DATE	VALVE POSITION	TYPE	GRADIENT	NYHA CLASS	OTHER PRESENTATIONS	OUTCOME
FEMALE	31y	1991	1992	Mitral	St Vincent	28	4	pregnancy related	died in DIC
FEMALE	18y	1989	1992	Mitral	Sorin	24	2		cured
FEMALE	28y	1987	1991	Mitral	Sorin	33	4	pregnancy related	died
FEMALE	25y	1987	1988	Mitral	St Vincent	-	3	pregnancy related	died
FEMALE	29y	1988	1992	Mitral	Omniscience	-	4		died
FEMALE	30y	1989	1990	Mitral	Omniscience	34	4		died
FEMALE	24y	1988	1990	Mitral	Sorin	-	4		died
FEMALE	45y	1985	1987	Mitral	Sorin	32	4		died
FEMALE	24y	1979	1993	Aortic	Sorin	86	3	pregnancy related	Successful surgery
FEMALE	39y	1985	1997	Aortic	Sorin	64 mmHg	2		cured/ needs surgery
FEMALE	48	1985	1989	Aortic	Omniscience	85	4	Embolization	died
MALE	45y	1995	1997	Aortic	Carbomedics	80	2	Embolization	cured/ needs surgery

their general condition was such that they did not need prolonged medical stabilization prior to surgery, except for one patient was pregnant at the time. Another patient presented with multiple peripheral emboli in addition to her dyspnea. A third patient had had both Mitral and Aortic valves replaced at the age of 12. The Mitral valve had a thrombus seen by TEE, whereas the Aortic valve was now too small for her as an adult (patient prosthesis mismatch)

Results

In the period from 1986 to 1998, of 348 female and 211 male patients with mechanical valve prosthesis, 28 presented with acute mechanical valve obstruction, accounting for an incidence of 4/100 patient years.

On heparin alone, one patient was cured, 3 could be stabilized well enough to undergo surgery and seven patients died. Two patients presented with peripheral retinal artery occlusion, and thus were not candidates for thrombolytic therapy.

On thrombolytic therapy, two patients were cured, five improved but needed surgery later on, one of which developped transient upper limb ischaemia. Three patients died of cerebral embolism.

Six patients were referred to surgery directly, one of which presented intially with multiple emboli to the lower limbs. One died, and the five had a successful outcome. The difference in early survival between Group 1 and Group2 was of weak statistical significance ($p=0.1$). The difference in early survival between Group 1 and Group3 was statistically significant ($p< 0.025$). Although the difference in early

Table 2: Gp 2 Patients who received thrombolytic therapy

NAME	AGE	OPERATION DATE	MALFUNCTION DATE	VALVE POSITION	TYPE	GRADIENT	NYHA CLASS	OTHER PRESEN-TATIONS	OUTCOME
FEMALE	32y	1990	1992	Mitral	Sorin	22	1		cured
FEMALE	34y	1994	1995	Mitral	Sorin	27	2		cured/needed surgery 1 year later
FEMALE	21	1990	1992	Mitral	Sorin	28	2		Needed surgery/successful
FEMALE	23	1988	1992	Mitral	Sorin	36	4	pregnancy related	Needed surgery/successful
FEMALE		1991	1994	Mitral	Sorin	-	4	pregnancy related	embolization / died
FEMALE	31y	1994	1995	Mitral/Aortic	Sorin	-	3	?Pregnancy related	embolization / died
FEMALE	30y	1989	1994	Mitral	Carbomedics	-	4	pregnancy related	embolization / died
FEMALE		1991	1995	Mitral	Sorin	34	3		needed surgery/refused
FEMALE	24y	1990	1994	Mitral	Sorin	28	2	pregnancy related	Needed surgery/successful
MALE	29y	1985	1992	Mitral	Sorin	24	2		cured

Table 3: Gp 3 Patients who had immediate surgery

PATIENT	AGE	OPERA-TION DATE	MAL-FUNCTION DATE	VALVE POSITION	TYPE	GRA-DIENT	NYHA CLASS	OTHER PRESEN-TATIONS	OUTCOME
FEMALE	19	1987	1994	Mitral Aortic	Sorin Carbomedics	24 70	3		successful
FEMALE	40	1993	1995	Mitral	Sorin	31	4		successful
FEMALE	31	1995	1997	Mitral	sorin	23	3	embolisation	successful
FEMALE	43	1987	1991	Mitral	disc	27	4		died PO
FEMALE	30	1989	1990	Mitral	disc	27	4		successful
FEMALE	20	1993	1993	Mitral	disc	32	4	pregnancy related	successful

survival between Group2 and Group3 was of no statistical significance (p=0.2) only 2 of 7 survivors did not need surgical intervention.

It is also noteworthy that the results were very dependent on the functional class of the patient. Thus all patients but one in functional class 4 NYHA on heparin or thrombolytic therapy died, and of the four patients presenting in FC 3, two died and two needed surgery later on. Those patients presenting with a lost click only or FC 1-2 all refused the idea of surgery, as they did not feel markedly unwell. Three received heparin and five were subjected to thrombolysis. All survived, however, of these eight patients only two did not need any further procedure, the rest needed surgery eventually. The difference in survival was statistically significant (23%

for FC 3-4 versus 100% for FC 1-2, p< 0.001).

When comparing the FC 3-4 patients who received antithrombotic therapy to their counterparts who were transferred to surgery directly, another striking difference in survival is noted (23% for antithrombotic therapy versus 83% for direct surgery).

Discussion

The most common and most serious complication in patients with a valve prosthesis is thrombo-embolism. Its incidence in the literature varies between 1. 5% and 11% and is generally estimated to be 0.5 -6 per 100 patient years. (1) In the Cairo University follow up series, 28 patients presented with acute valvular obstruction from January 1986 to December 1998, making the incidence of acute valvular obstruction 4/100 patient years. The high incidence of complications in our series can be attributed to the lack of proper follow up clinics in remote rural areas. The problem is made worse by the absence of emergency cardiac surgery facilities in these regions. In the past decade, thrombolysis has been advocated as an alternative to cardiac surgery in such patients, some reports claiming that it alone may suffice. (12,13,16,18) In the guidelines for prosthetic valve management recently published, thrombolysis was advocated mainly for high risk surgical candidates having Mitral or Aortic valve replacement (23).

As can be seen from the results of the Cairo University series, neither heparin nor thrombolysis could obviate the need for surgery in most cases, and so neither can be considered as an alternative to surgery, contrary to the many enthusiastic reports by other investigators (12,13,16,18). The reason is that occasionally the thrombus was seen on transesophageal examination to have become dangerously friable. Another cause in other cases was incomplete dissolution of the thrombus despite a 72 hour regimen and clinical return of an audible click. In these cases the transvalvular gradient did not diminish to the desired levels. Peripheral embolism remains a major problem, 7.2% of our series presented initially by peripheral embolism (multiple emboli to the lower limbs in one patient and retinal artery occlusion in two others). Thrombolytic therapy cased peripheral embolism in 40% of patients receiving this treatment, 30% being fatal cerebral emboli. Although our numbers are small, this is a much higher incidence than that reported in the literature, where this complication is estimated to occur in 15%-18% (12,16,20). It may be, that Egyptians respond differently to Streptokinase than other populations.

The patients whose general physical condition was good enough to be operated upon were sent directly to surgery and the outcome was far superior to either medical therapy. However, when the patient's general condition is too poor to allow immediate surgery, thrombolysis is more effective in stabilizing the patient than heparin. In our series, due to the small number of patients, the difference was of weak statistical significance (p = 0.1). This is in accordance with the guidelines recently published (23).

Conclusion

Although the risk of embolism is high and may be fatal, thrombolytic therapy is indicated in prosthetic valve patients with

acute valvular obstruction, who need to be stabilized medically as a preparatory step for valve re-replacement. It cannot be considered as an alternative to surgery in Egyptian patients.

References

1. Roudaut R, Labbe T, Lorient-Roudaut NW, Gosse P, Baudet E, Fontan F, Besse P, Dallochio M Mechanical cardiac valve thrombosis, Is fibrinolysis justified Circulation 1992; 86 (suppl II) 11 - 8 - II - 15.

2. Copeland JG, An international experience with the cabomedics prosthetic heart valve J Heart valve dis 1995 Jan; 4 (I): 56 - 62.

3. Birdi I; Angelini GD; Bryan AJ Thrombolytic therapy for left sided prosthetic heart valve thrombosis. J Heart Valve Dis 1995 Mar;4(2):154-9

4. Puleo JA; Fontanet BL; Schocken DD The role of prolonged throtnbolytic infusions and transesophageal echocardiography in thrombosed prosthetic heart valves: case report and review of the literature. Clin Cardiol 1995 Nov; 18 (11):679-84

5. Koller PT; Arom KV Thrombolytic therapy of left-sided prosthetic valve thrombosis. Chest 1995 Dec; 108 (6): 1683-9.

6. Reddy NK; Padmanabhan TN; Singh S; Kumar DN; Raju PR Satyanarayana PV; Rao DP; Rajagopal P; Raju BS Thrombolysis in left-sided prosthetic valve occlusion: immediate and follow-up results Comment in: Ann Thorac Surg 1995 Apr; 59 (4):1045 Ann Thorac Surg 1994 Aug; 58 (2): 462-70; discussion 470-1.

7. Agrawal D; Dubey S; Saket B; Bhargava M; Mehta N Lohchab SS; Satsangi DK; Nigam M; Gupta BK; Khanna SK Thrombolytic therapy for prosthetic valve thrombosis in Third World countries. Indian Heart J 1997 Jul-Aug; 49 (4): 383-6.

8. Rajasekhar D; Balakrishnan KG; Venkitachalam CG Tharakan JA; Titus T; Pillai VR; Kumar VK, Bhat A Thrombolytic therapy for prosthetic cardiac valve thrombosis. Indian Heart J 1994 Mar-Apr; 46 (2): 101-5.

9. Vasan RS; Kaul U; Sanghvi S; Kamlakar T; Negi PC Shrivastava S; Rajani M; Venugopal P; Wasir HS Thrombolytic therapy for prosthetic valve thrombosis: a study based on serial Doppler echocardiographic evaluation. Am Heart J 1992 Jun; 123 (6):1575-80.

10. Renzulli A; Vitale N; Caruso A; Dialetto G de Luca L; Schinosa T; Cotrufo M Thrombolysis for prosthetic valve thrombosis: indications and results. J Heart Valve Dis 1997 Mar; 6 (2): 212-8.

11. Sivasubramanian S; Vijayshankar CS; Krishnamurthy SM Santhosham R; Dwaraknath V; Rajaram S Surgical management of prosthetic valve obstruction with the Sorin tilting disc prosthesis, J Heart Valve Dis 1996 Sep; 5 (5): 548-52.

12. Graver LM; Gelber PM; Tyras DH The risks and benefits of thrombolytic therapy in acute aortic and mitral

prosthetic valve dysfunction: report of a case and review of the literature. Ann Thorac Surg 1988 Jul; 46 (l):85-8.

13. Silber H; Khan SS; Matloff JM; Chaux A; DeRobertis M Gray R The St. Jude valve. Thrombolysis as the first line of therapy for Cardiac valve thrombosis Comment in: Circulation 1993 Jan; 87 (l): 294-6, in: Circulation 1993 Aug; 88 (2): 808-9 Circulation 1993 Jan; 87 (l): 30-7.

14. Page A; Gateau P; Roudaut R; Lorient W; Baudet E Besse P Traitement thronibolytique dans les thromboses de prothese valvulaires. Nouv Presse Med 1980 Nov 8;9 (42): 3186-7.

15. Witchitz S Les thrombolytiques dans le traitement des thromboses de protheses valvulaires: experience de 15 cas. Haemostasis 1986; 16 Suppl 4: 106-9.

16. Torrado Gonzalez E; Ferriz Martin JA Prieto Palomino MA; Rodriguez Garcia JJ; Alyarez Bueno JM; Vera Almazan A Garrido Alcalde MR; Gonzalez de Vega N Thrombolysis of thrombosed heart valve prostheses: presentation of 2 cases and review of the literature] Rev Esp Cardiol 1990 May; 43 (5): 345-51.

17. Guerrero Lopez F; Vazquez Mata G; Reina Toral A Rodriguez Bailon I; Fernandez Mondejar E; Aranegui Lasuen P Thrombolytic treatment for massive thrombosis of prosthetic cardiac valves. Intensive Care Med 1993; 19 (3): 145-50.

18. Vitale N; Renzulli A; Cerasuolo F; Caruso A; Festa M de Luca L; Cotrufo M Prosthetic valve obstruction: thrombolysis versus operation. Ann Thorac Surg 1994 Feb; 57 (2): 365-70.

19. Ledain L; Lorient-Roudaut NW; Roudaut R; Gateau P Roques X; Colle JP; Besse P Traitement fibrinolytique des thromboses valvulaires. A propos de 16 cas. Arch Mal Coeur Vaiss 1983 Feb; 76 (2): 133-43.

20. Kurzrok S; Singh AK; Most AS; Williams DO Thrombolytic therapy for prosthetic cardiac valve thrombosis. J Am Coll Cardiol 1987 Mar; 9 (3): 592-8

21. Binder T; Baumgartner H; Maurer G Diagnosis and management of prosthetic valve dysfunction. Curr Opin Cardiol 1996 Mar; 11(2):131-8.

22. Campagnucci VP; Suzuki HY; Franken RA; Rivetti LA Thrombolytic therapy in thrombosis of prosthesis Arq Bras Cardiol 1994 Jul; 63 (l): 35.

23. Lengyel M; Fuster V; Keltai M; Roudaut R; Schulte HD Seward JB; Chesebro JH; Turpie AG Guidelines for management of left-sided prosthetic valve thrombosis: a role for thrombolytic therapy. Consensus Conference on Prosthetic Valve Thrombosis. JAm Coll Cardiol 1997 Nov 15; 30 (6): 1521-6.

Retrograde Cardioplegia in CABG for Extensive Coronay Artery Disease

ABSTRACT

Homogenous distribution of antegrade cardioplegia is not possible in patients with extensive coronary disease, redo coronary surgery and in presence of aortic incompetence. This study reviews our results with retrograde delivery of cardioplegia in 34 consecutive patients operated upon from December 1996 to November 1997. 30 were males (mean age 53.5 y, range 3,9-71y) and 11 were diabetic. All were symptomatic with angina pectoris, 8 of whom had unstable angina. Four cases had congestive pulmonary symptoms. 15 patients had an old MI. LV systolic dysfunction was mild in 13 and moderate in 5 pts.

Angiography revealed left main disease of 50% or more in 7 patients.

Three patients had emergency surgery and 12 urgent surgery.

Induction with cold crystalloid antegrade/ retrograde cardiopleqia at a 2/1 ratio was followed by retrograde cardioplegia every 15-20 min. A total of 113 grafts were constructed, 26 of which were ITA (range 1-5, mean 3.3 graft/pt.)

All patients returned back to NSR with normal A-V conduction, 28 of whom did so spontaneously. The mean cross clamp time was 59.6 min (range 15 - 112 min) and mean pump time was 72.4 min (range 25 min-144 min). Weaning off bypass was uneventfull in all case except 4, one of whom required IABP. Mean ICU stay was 2.7 days (range: 1-14 days.) and mean postop. hospital stay was 8.2 days (range:5-23 days).

Morbidity included re-exploration in 3 cases (Dry tamponade in one and bleeding in 2), AF in 4, saphenous vein harvesting site infection in two and mediastinitis and peptic ulcer bleed each in a single case. One patient died on the 14 th post op. day of low cardiac output complicated by pulmonary sepsis.

In a relatively young population with diffuse coronary pathology, retrograde cardioplegia offers optimum myocardial protection. It is safe and reproducible.

Magued A. Zikri

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INTRODUCTION

Route of cardioplegia delivery may be crucial in patients undergoing coronary artery bypass surgery. The use of the venous circulation to deliver cardioplegia is not novel. (Lillehei (1) 1956; Fabiani (2) 1984; Diehl (3) 1988; Fiore, (4) 1989).

Cairo University

Preoperative angina denotes the inadequacy of collateral circulation to provide sufficient coronary blood flow distal to occluded or stenosed coronary arteries. Homogenous cardioplegia distribution is expected to be hampered when delivered only through the diseased coronary artery tree, the so called antegrade cardioplegia route. Presence of mild aortic valve regurgitation may not allow building of enough aortic root pressure to perfuse stenotic native arteries. Moreover, patients with redo coronary surgery frequently depend on flow through diseased vein grafts or pedicled mamary artery conduits that are not suitable for antegrade delivery.

The so called retrograde cardioplegia delivery has been used with excellent and consistent results, whether alone or in combination with antegrade delivery.

With the increasing complexity of revascularisation procedures and the escalating risks factors of patients refered to surgery, we opted to explore this new avenue and present here the results of this initial study.

Patients and Methods

All patients operated upon for coronary artery bypass surgery in the period between December 1996 and November 1997 had a trial of transatrial cannulation of the coronary sinus. Out of 36 patients, cannulation of the coronary sinus was succesfull except in two instances. This report pertains to the remaining thirty four cases. All patients were operated upon by the same surgeon. Preoperative data, laboratory, electrocardiogram study, cardiac echocardiography and coronary angio informations were retrospectively analysed. Number and type of conduits, duration of cross clamp and cardiopulmonary bypass time were studied. Myocardial protection was through systemic cooling to 30 degrees, topical ice sluch in myocardial well and crystalloid modified St. Thomas's cardioplegia. Protocol for cardioplegia delivery consisted of use of antegrade/ retrograde crystalloid at a 2/1 volumetric ratio for induction for a total of 15cc/kg. This was followed by additional 200 cc via the retrograde route every 15- 20 min. Either a DLP OR Research medical coronary sinus cannulae gauge # 12-14 were used. Proximal anastomosis were done after cross clamp removal except when LIMA LAD was not used, in patients with EF less than 35%, whenever the ascending aorta had palpable plaques and in redo cases.

Spontaneous return to sinus rhythm, need for IABP or inotropic support to wean off the cardioplumonary bypass were noted. Post operative need for ventillation , inotropic support, duration of ICU stay and total hospital stay were all recorded.

Follow up was conducted by clinical examination, ECG and echocardiography at hospital discharge, at six weeks and at three months. Coronary angio was performed in cases with reccurence of angina.

Results

1-Demographic data:

Thirty four patients were operated upon, four of whom were females. Their age ranged between 39-71y (mean 53.5y). Only 12 patients were 55 or older Other relevant clinical data are depicted in Table 1.

2-Clinical presentation:

All patients were symptomatic. Twenty six patients had chronic stable angina and 8 patients had unstable angina despite

Table (1): Clinical and investigational data.

Risk factors for coronary artery disease:

- *Smoking = 24 pts.*
- *Diabetus 11 pts (Niddm = 5 , IDDM = 6)*
- *Hyperlipedemia = 10 pts.*
- *+ Family hystory = 8 pts.*
- *Overweight = 7 pts.*

ECG:

Previous MI:
Acute MI = None.
Old MI = 15 pts.
Inf wall = 10 pts.
Antrolateral wall = 1 pt
Antroseptal MI = 4 pts.

Echocardiography:

LV function:
Normal EF > 55 % = 16 pts.
Mild dysfunction EF 40-55 % = 13 pts.
Moderatedysfunction EF 30-39 % = 5 pts.
Ischaemic Mitral regurge: 3 pts.

maximum intravenous vasodilator therapy and anticoagulation. One patient had four repeated episodes of acute ischaemic mitral regurge and flush pulmonary edema with hypoxic cardiac arrest. One case had unstable angina 12 years after a primary CABG. Congestive pulmonary symptoms were present in 4 cases.

3-Preoperative evaluation:

None of these patients presented with acute MI. Fifteen had electrocardiographic evidence of an old MI. This was located in the inferior wall in 10 patients, antroseptal wall in four and antrolateral wall in one.

All patients had echocardiography to evaluate LV function, mitral incompetence and analyse semental wall motion abnormalities. (Table 1).

In three cases with EF less than 35% dobutamine stress test documented the viability of hybernating myocardium by a byphasic response to increasing doses of IV infusion of dobutamine.

Coronary angiography showed triple vessels disease in 26 pts.; double vessels disease in 6 pts. (LAD/Cx = 4 pts., LAD/RCA = 2 pts.) and in two patients, disease confined to the LAD. (Graph)

Table (2):

Coronary angio:

Left main : *total # : 7 pts.*
(including Left main disease, + RCA critical lesion: 5 pts.)

LAD : *total : 34 pts.*
100% = 8 pts.
90-99% = 21 pts.
< 90 % = 5 pts.

Cx/Ramus distribution : *total : 30 pts.*
100% = 4 pts.
90-99% = 14 pts.
< 90 % = 12 pts.

RCA: *total : 26 pts.*
100% = 11 pts.
90-99% = 13 pts.
< 90 % = 2 pts.

Table 2 .
- Number of grafted vessels : *113 grafts.*

1 graft = 1
2 grafts = 2
3 grafts = 17
4 grafts = 13
5 grafts = 1

- Conduit type:

- Arterial graft: *24 pts.*
** in situ LIMA to LAD* *22 pts.*
** in situ LIMA to OM 1* *2 pts.*
** in situ RIMA to LAD* *2 pts.*
** Free RIMA to OM 2* *1 pt.*

- Venous Grafts:
** Reversed SVG* *83 grafts* *32 pts.*

** Cephalic vein to RCA* *one graft* *1 pt.*

- Proximal Anastomosis :
to Ascending Aorta *64 anastomosis.*
Veno-venous proximal *18 anastomosis.*
Sequential graft to Om vessels *2 grafts.*

4-Urgency of operation:

Fifteen patients had non-elective surgery. Three of these were operated upon emergently (one following four episodes of flash pulmonary aedema and cardiac arrest and two for unstable angina and left main disease). Urgent surgery was performed for unstable angina in 6 and left main disease in the remaining six patients.

5-Operative findings:

The number and type of conduits are detailed in Table 3.

After the aorta was unclamped , 28 pts returned to NSP spontaneously.

Of the remaining 6 pts, only one needed multiple D/C shocks. None of the patients had, any form of conduction abnormalities. Cross clamp time ranged between 15 and 112 min with a mean of 59.6 min. Pump time ranged between 25 and 144 min with a mean of 72.4 min. Weaning off bypass was without support in 30 cases. Four cases needed additional support including recirculation for 20 min in 2 pts, pharmacologic support with epinephrine and/or norepinephrine in 2 pts and IABP in a single patient. IABP insertion was necessary in another patient on the third post op day.

Half the patients did not require any homologous blood transfusion and 15 of these benefited from reinfusion of one unit of autologous blood drawn after the induction of anesthesia. Patients that had blood transfusion were given homologous freshly donated packed RBCs. (less than two hours) except in emergency surgery (2 pts) and when blood need for postop bleeding exeeded available freshly donated blood (5 pts).

6-Post operative course:

The mean duration of ventillation was 11.6 with a range of 6 to 30 h. The mean ICU stay was 2.7 days with a range of 1- 14 days. Duration of postop hospital stay ranged between 5 and 23 days with a mean of 8.2 days.

7-Morbidity and mortality:

Eleven pts had 14 events. Three pts were reexplored, 2 for bleeding and one for low cardiac output that proved to be secondary to dry tamponade from hyperinflated lungs. Four patients developed atrial fibrillation on days 3, 4 and 7. Their ventricular rate was pharmacologically controlled by digoxin/Ca channel blockers and then were reverted to NSR using IV amiodarone.

Lower respiratory tract infection developed in 3 cases. Two IDDM patients had saphenous vein harvest site infection . Another IDDM patient had staphilococcus aureus mediastinitis managed by early drainage, povidone iodine irrigation and rewiring with satisfactory outcome. One patient had GI bleed from an occult peptic ulcer and another patient had a small pulmonary embolism that was treated conservatively

One mortality was caused by low cardiac output that developed on the third post op day in the setting of antrolateral ishaemia. This patient had a very diffusely diseased

LAD and Diag system . He expired two weeks post op in pulmonary sepsis complicating prolonged ventillatory and IABP support.

8-Follow up:

Follow-up was 100% complete (6-18

months, mean 9.6). 32 pts (94%) were in NYFC 1-2. Repeated angio for recurrent angina showed patent grafts in two cases.

Discussion

Adequate myocardial protection will remain the main stay of conventional cardiac surgery (Krukenkap, 1996) (5). The composition, temperature and, route of cardioplegia delivery do Provide a number of combinations that were tested in numerous clinical trials (Buckberk, 1988) (6) (Noyez, 1993) (5). In an attempt to introduce retrograde cardioplegia in our practice, we opted to make the route of cardioplegia delivery the only new variable in our protocol. Crystalloid cardioplegia has proved efficient in a large spectrum of cases and hypothermia has stood the test of time over the last thirty years. Retrograde delivery of cardioplegia may be done either through the coronary sinus that can be cannulated under direct vision through a right atriotomy or transatrially, or by occluding both cavae with snares around the venous drainage cannulae and including the pulmonary artery in the aortic cross clamp. (Fabiani, 1984) (Gundry, 1990) (Geha, 1993),

Proponents of Fabiani method postulate lesser liability to injure the coronary sinus, better perfiusion of the most proximal tributaries draining the right ventricle and better endocardial cooling of the right sided chamber (Eichhorn 1989) (10). The incidence of injury of the coronary sinus has been minimal with direct cannulation. We opted for the simplest method which is transatrial cannulation.

Because we are aware of the limitations of retrograde cardioplegia to initiate rapid myocardial standstill we combined for induction an antegrade dose followed by a retrograde dose. (Bhayana, 1989) (11), Chocron, 1996) (12).

Antegrade cardioplegia delivery past critically stenosed or totally occluded coronary arteries depend to a great extent on the collateral circulation to the ischaemic bed. Presence of severe or unstable angina is the sine qua none of inadequacy of such collaterals. Seven of our patients had a combination of left main lesions with additional stenosis in the left anterior descending and circumflex systems together with critical or total obstruction in the right coronary system. The efficiency of retrograde cardioplegia in patients with such, severe coronary pathology has been previously demonstrated. (Menasche, 1991) (13). Our single candidate for redo revascularisation had a subtotal left main obstruction and total right coronary obstruction with a single functioning diseased SVG to the LAD.

Comparing such a high risk group with the rest of the series would have substantiated the value of retrograde cardioplegia in such subset. The limited number of cases in this pilot study has prevented us from fractionating it into subgroups for statistical relevance purpose.

An additional benefit of retrograde cardioplegia delivery was experienced twice in this series when an unforseen mild Aortic regurge precluded use of antegrade cardioplegia. (Bura Moisa, 1995) (14).

Adequacy of myocardial protection was accessed by a combination of clinical and laboratory critiria.

Spontaneous return to NSR with normal A-V conduction, ease of wean from cardiopulmonary bypass, need and duration of administration of inotropes, length of ventillation and ICU stay and level of Creatine phosphokinase - myocardial fraction were all taken in account.

Only one patient required multiple D/C shock after declamping of the aorta. None of the patients had Atrioventricular conduction defects, either initially or post operatively. The need of electrical defibrillation after aortic unclamping was related to a higher release of Cardiac troponin I (Pichon et al 1997) (15).

Weaning from the heart lung machine was uneventfull in the majority of patients and required inotropic support in only 4 cases. One case required additional support with an IABP.

AF was present in only three cases and this low rate may be caused by the use of topical atrial cooling, conferring additional protection to the atria.

In conclusion, retrograde cardioplegia in coronary revascularisation offers optimum myocardial protection in all cases. It has to be combined with an antegrade initial dose to induce a rapid myocardial standstill. Retrograde cardioplegia has a definite advantage in patients with extensive native coronary circulation, in redo coronary surgery with diseased vein grafts or depending on pedicled mammary grafts and in patients with mild degree of aortic valve incompetence. It proved to be a safe, reproducible and affordable tool.

References

1- Lillehei C., Dewall R., Gott V., Varco R. The direct vision correction of calcific aortic stenosis by means of a pump oxygenator and retrograde coronary sinus perfusion. Dis Chest 1956; 30: 123-132.

2- Fabiani J., Rolland J., Carpentier A. Myocardial protection via the coronary sinus in cardiac surgery: comparative evaluation of two techniques, in Mohl N., Wolner E., Golger D (eds): The coronary sinus. New York, Springler-Verlag, 1984. pp 305-311.

3- Diehl J., Eichhorn E., Konstam M. et al. Efficacy of retrograde coronary sinus revascularisation in patients undergoing myocardial revascularisation: A prospective randomised trial. Ann Thorac Surg. 1988; 45: 595-602.

4- Fiore A., Naunheim K., Kaiser G. et al. Coronary sinus versus aortic root perfusion with blood cardioplegia in elective myocardial revascularisation. Ann Thorac Surg. 1989; 47:684-688.

5- Krukenkamp I. and Levitsky S. Physiological and cellular mechanisms of myocardial protection. Am J Surg. 1996; 172: 79-84.

6- Buckberg G. Antegrade cardioplegia, retrograde cardioplegia, or both? Ann Thorac Surg. 1988; 45: 589-590.

7- Noyez L., van Son J., van der Werf T. et al. Retrograde versus antegrade delivery of cardioplegic solution in myocardial revascularisation. J Thorac Cardiovasc Surg. 1993; 105:854-863.

8- Gundry S., Sequiera A., Razzouk A., McLaughlin J., Bailey L. Facile retrograde cardioplegia: transatrial cannulation of the coronary sinus. Ann Thorac Surg. 1990; 50:882-887.

9- Geha A, Lee J. Retrograde cardioplegia cannulation during cardiopulmonary bypass. Ann Thbrac Surg. 1993; 55:175-6.

10-Eichhorn E., Diehl J., Konstam M., Payne D., Salem D., Cleveland R. Protective effects of retrograde compared with antegrade cardioplegia on right ventricular systolic and diastolic function during coronary bypass surgery. Circ. 1989; 79: 1271-1281.

11-Bhayana J., Kalmbach T., Booth McL., Mentzer R., Schimert G. Combined antegrade/retrograde cardioplegia for myocardial protection: a clinical trial. J Thorac Cardiovasc Surg. 1989; 98: 956-960.

12-Chocron S., Alwan K., Toubin G. et at. Crystalloid cardioplegia route of delivery and cardiac troponin I release. Ann Thorac Surg. 1996; 62:481-485.

13-Menasche Ph., Subayi J.-B.,Veyssie L., Le Derf O., Chevret S., Piwnica A. Efficacy of coronary sinus cardioplegia in patients with complete coronary artery occlusions. Ann Thorac Surg. 1991; 51: 418-23.

14-Bura Moisa R., Zeldis S., Alper S., Scott W. Aortic regurgitation in coronary artery bypass grafting: Implications for cardioplegia administration. Ann Thorac Surg. 1995; 60: 665-668.

15-Pichon H., Chocron S., Alwan K. et al. Crystalloid versus blood cardioplegia and cardiac troponin 1 release. Circ. 1997; 96: 316-320.

Crystalloid Versus Blood-Enriched Cardioplegia Clinical and Biochemical Markers of Myocardial Injury

ABSTRACT

Two methods of myocardial preservation were compared. Sixty patients were enrolled in this study and categorized into two groups. Group I: 28 patients who received cold crystalloid cardioplegia and Group II: 32 patients who received cold blood-enriched cardioplegia. The 2 groups of patients, all underwent mitral valve replacement, were comparable as regards age, sex, New York Heart Association class (NYHA), ejection fraction, pulmonary artery pressure, left atrial size, ischemic and cardiopulmonary bypass times. Myocardial protection has been assessed from the evolution of hemodynamic parameters, reperfusion arrhythmias and the postoperative need for inotropic support. The extent of myocardial injury was also estimated by monitoring the postoperative leakage of the MB isoenzyme of creatinine kinase (CK-MB) and the more recently used cardiac troponin T (cTnT). Patients in group I had a significantly lower incidence of spontaneous defibrillation compared to group II (50% vs. 81%, $p<0.05$). They also needed more inotropic support (39% vs. 6%, $p<0.001$) as well as longer ventilation time in the postoperative period (10.4 ± 3.08 vs. 7.8 ± 2.24, $p < 0.001$). The use of crystalloid cardioplegia was associated with highly significant more release of cTnT both in the immediate postoperative period (3.19 vs. 0.72, $p<0.001$) and 24 hours after surgery (1.59 vs. 0.58, $p<0.001$) when compared with blood-enriched cardioplegia. The same finding was found in the immediate postoperative reading of CK-MB (252.14 vs. 155.22, $p < 0.001$). The areas under the curve (AUC) representing the total release of both cardiac troponin T and CK-MB were also bigger for group I indicating more degrees of myocardial tissue injury with more leakage of cardiac enzymes. Blood-enriched cardioplegia was found to be a better myocardial protective technique when compared to crystalloid cardioplegia.

Hossam El Okda, MD[1] and Mona Mostafa Osman, MD[2]

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INTRODUCTION

Myocardial protection during ischemia-reperfusion is a constant concern in heart surgery. Based on the concept of hypothermia introduced by Bigelow and associates in 1950 as one of the most important components of myocardial protection, cold crystalloid cardioplegia became a standard technique to preserve the heart during aortic cross clamping period. Buckberg in 1989 demonstrated the many advantages offered by using blood cardioplegia. We decided to conduct a prospective clinical trial to compare crystalloid cardioplegia with a simple method to deliver blood-enriched cardioplegia without the use of heat exchangers in patients undergoing mitral valve replacement. The purpose of this

1-Cardiac Surgery Department, Ain-Shams University, Cairo, Egypt.

2-Clinical Pathology Department, Ain-Shams University, Cairo, Egypt.

study was therefore to evaluate, on a clinical and biochemical basis, whether blood enriched cardioplegia maintains better myocardial protection than cold crystalloid cardioplegia.

Material and Methods

Patient population

Sixty patients admitted for elective mitral valve replacement were prospectively enrolled in the study protocol from Jaunary 1997 to May 1997. The exclusion criteria were EF less than 40 %, emergency surgery, previous cardiac operations, surgical reexploration within 24 hours of operation and significant associated diseases such as aortic valve diseases or coronary artery disease. Patients were divided into two groups:

Group 1: 28 patients aged 28.6 years ± 5.9 received crystalloid cardioplegia.

Group 2: 32 patients aged 29.4 years ± 6.6 received blood-enriched cardioplegia.

Both groups, thus comparable, underwent mitral valve replacement in the Cardiothoracic surgical department, Ain Shams University. In addition, 10 healthy subjects, 5 males and 5 females, aged 35 ± 7.2 were taken as control subjects for CKMB and Troponin T measurements.

Anesthesia

Premedication consisted of oral diazepam (5 mg) and intramuscular morphine (10 mg), given 1 hour preoperatively. Fentanyl was given at induction of anesthesia and then given as increments during the procedures. Pancuronium (0.1 mg/kg) was used for muscle relaxation, and the patients were ventilated with 50% oxygen/nitrous oxide. Heparin (4mg/kg) was given before aortic cannulation for CPB. The activated clotting time was always kept at more than 450 seconds during perfusion. Heparinization was reversed with protamine sulfate after decannulation.

Perfusion

A membrane oxygenator was used in all patients. The hematocrit was maintained between 25 - 30% during CPB, pump flow was maintained at 2.4 L.min.m2.

Surgical Technique and Cadioplegia

Cardiopulmonary bypass with moderate hypothermia (28-30°C) was used in all cases with caval and ascending aortic cannulation. Myocardial cooling was augmented with the administration of topical iced slush. All valves were replaced using interrupted Ethibond sutures 2-0 with Teflon pledgets. Only bileaflet prosthetic valves (St. Jude or Carbomedies) were used in the whole patient population.

Group I. Seven hundred to one thousand mls of crystalloid cardioplegia were infused in the aortic root at a temperature of 4°C in the onset of the aortic crossclamping. Three to four hundred mls of the same solution were administered every 25-30 minutes during the cross-clamp time. Removal of the cross-clamp was achieved without warm reperfusion cardioplegia. The crystalloid cardioplegia was composed of dextrose - saline physiological solution to which 25 mEq/L KCL, 60 mEq/L NaHCO3, 40 ml/L dextrose 25% and 100 mg/L xylocaine were added.

Group II. Three hundred mls of the cold crystalloid cardioplegic solution

having the same composition as before were discarded and then replaced with the same volume of patient's blood through the aortic root thus adding oxygenated blood to the cardioplegic solution. 10 mEq/L KCL was then added to increase the potassium content of the cardioplegia. The resulting "blood-enriched cardioplegia" was then infused in the aortic root after the application of the aortic cross-clamp.

After completion of the surgical procedure, standard deairing maneuvers were performed. Rewarming was done and weaning from CPB was instituted with the aid of inotropic support as dictated by the hemodynamic state of the patient. The chest was closed in layers once hemostasis was achieved.

Data collection and Hemodynamic study

Intraoperative data were collected for each patient. These data included duration of aortic cross-clamp time (ACT) and cardiopulmonary bypass time (CPB). Cardiopulmonary bypass weaning-off conditions were also recorded, in particular spontaneous or electrical defibrillations as well as inotropic agent doses needed if any. In the postoperative period, evidences of the need for inotropic support were carefully monitored and epinephrine was used only when seemed necessary. Also, the ventilation time required by each patient was registered.

Biochemical data

Sampling: 180 nonheparinized blood samples were drawn, 3 from each patient. The first sample was drawn before the induction of anesthesia (R1). The second one immediately after patient's arrival to the ICU (R2) and the third one 24 hours after operation (R3). All samples were immediately centrifuged at 2,000g for 15 minutes, stored at -70°C, thawed once and then analyzed in patches.

Methods: Two biochemical tests were performed to each of the 180 samples:

1) CK-MB was measured using the RANDOX CK-MB kit (Randox laboratories ltd., United Kingdom) employing the method recommended by Wurburg in 1976. This method is based on immunoinhibition principle, where the antibody in the reagent inhibits the activity of the M-subunit of CK-MB. The following reactions then occur:

$$\text{ATP} + \text{glucose} \xrightarrow{\text{(hexokinase)}} \text{ADP} + \text{G-6-P}$$

$$\text{G-6-P} + \text{NADP} \xrightarrow{\text{(G6PD)}} \text{6-gluconate} + \text{NADPH}$$

The released NADPH increasing is measured kinetically at 340 nm on a spectrophotometer. The activity is multiplied by 2 to get the activity of CK-MB in serum. The reference range for CK-MB at 30°C using this kit was 3 - 16 U/L.2) Cardiac troponin T (cTnT) was measured using Troponin T stat kit (Boehringer Mannheim GmbH, Germany) employing the method recommended by Baum in 1997 for the second generation of cTnT. However the kit used was modified by the company as calibrators and controls were containing recombient human cTnT (third generation). The assay was performed on Elecsys 1010 system. This method is based on electro-chemiluminescence principle. In the first incubation, 15 µL of sample, a biotinglated monoclonal TnT specific antibody and a monoclonal TnT specific antibody labeled with a ruthenium complex react to form a sandwich complex. While the second incubation is performed after addition of streptavidin - coated

Table (1): Demographic Information and Preoperative Characteristics of the Patients.

Variable	Group I	Group II	P value
Patients (n)	28	32	
Age (y)	28.6 ± 5.9	29.4 ± 6.6	$p = 0.32$, NS
Sex (male/female)	15/15	15/17	$p = 0.42$, NS
Rhythm (SR/AF)	7/28	10/32	$p = 0.14$, NS
NYHA Class (I/II/III/IV)	0/2/26/0	0/3/29/0	$p = 0.41$, NS
EF	50.1 ± 8.4	50 ± 7.4	$p = 0.49$, NS
PAP	58.2 ± 13.2	57.5 ± 12.7	$p = 0.42$, NS
Left atrial size	5.7 ± 0.88	5.9 ± 0.83	$p = 0.26$, NS

microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with Procell. Application of a voltage to the electrode then induces chemluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is generated by the instrument using two calibrators. Reference range for this kit is 0.01 - 0.04 ng/ml.

Statistical analysis

Data were analysed with the Statview software. Data were expressed as mean values standard deviation. F-test for normality was first done to all variables. Variables which were normally distributed in both groups I and II were compared using the unpaired t-test. On the other hand, variables proved not to be normally distributed were compared using the Wilcoxon rank-sum test. Chi-square test was done to compare the incidence of spontaneous defibrillation as well as the need for inotropic support between the two groups. Linear regression as well as forward stepwise multiple regression analysis were used to identify explanatory variables that influenced the release of cTnT and CK-MB, as expressed by the area under the curve (AUC) for both biochemical markers. Difference were considered statistically significant at a probability level of $p < 0.05$.

Results

Patients

Between January 1997 and May 1997, 60 patients were included in the study with a mean age of 29 ± 6.2 and 5.5 to 4.5 female to male sex ratio. The crystalloid and blood-enriched groups had similar preoperative characteristics, without any significant differences with respect to age (28.6 ± 5.9 vs. 29.4 ± 6.6, p = 0.32, NS) sex, NYHA class, EF (50.1 ± 8.4 vs. 50 ± 7.4%, p = 0.49, NS), left atrial size (5.7 ± 0.88 vs. 5.9 ± 0.83, p = 0.26, NS) and pulmonary artery pressure (58.2 ± 13.2 vs. 57.5 ± 12.7, p ± 0.42, NS) (table 1) .

Table (2): Intraoperative Variables.

Variable	Group I	Group II	P value
Duration of CPB	61.3 ± 15.7	59.9 ± 13.7	p = 0.37, NS
Duration of ACT	38.6 ± 12.7	39.4 ± 10	p = 0.48, NS
CPB temperature	28.3 ± 2.3	28.7 ± 1.9	p = 0.47, NS
Tricuspid repair	28.5 %	25 %	p = 0.35, NS

Table (3): Postoperative Outcome Variables.

Variable	Group I	Group II	P value
Spontaneous Defibrillation	14/28, 50 %	26/32, 81 %	$p < 0.05$, S
Need for inotropic support	11/28, 39 %	2/32, 6 %	$p < 0.001$, HS
Ventilation time	10.4 ± 3.08	7.8 ± 2.24	$p < 0.001$, HS
Mortality rate	2/ 28, 7.1%	1/ 32, 3.1%	$p = 0.09$, NS

Table (4): The Mean, Standard Deviation, Minimum and Maximum of cTnT and CK-MB for Group I.

Test, Time	Number	Mean	SD	Min.	Max.
cTnT, R1	28	0.05	0.15	0.01	0.61
cTnT, R2	28	3.19	2.79	0.59	10.67
cTnT, R3	28	1.59	1.55	0.01	5.43
CK-MB, R1	28	12.10	2.09	8.00	16.00
CK-MB, R2	28	252.14	198.48	90.00	810.00
CK-MB, R3	28	175.21	161.46	16.00	650.00

Table (5): The Mean, Standard Deviation, Minimum and Maximum of cTnT and CK-MB for Group II

Test, Time	Number	Mean	SD	Min.	Max.
cTnT, R1	32	0.03	0.06	0.01	0.29
cTnT, R2	32	0.72	0.47	0.12	2.00
cTnT, R3	32	0.58	0.40	0.11	1.67
CK-MB, R1	32	11.84	2.73	6.00	16.00
CK-MB, R2	32	155.22	219.30	8.00	960.00
CK-MB, R3	32	201.06	136.43	16.00	510.00

Table (6): Correlation Coefficients Between AUC of cTnT and CK-MB and The Different Explanatory Variables for Group I Patients.

Variable	AUC - T	(*p*)	AUC - CK-MB	(*p*)
Age	- 0.03	(NS)	- 0.04	(NS)
PAP	+ 0.42	(S)	+ 0.39	(S)
EF	- 0.65	(S)	- 0.38	(S)
LA Size	+ 0.14	(NS)	+ 0.25	(NS)
ACT	+ 0.96	(HS)	+ 0.25	(NS)
CPB	+ 0.98	(HS)	+ 0.21	(NS)

Table (7): Correlation Coefficients Between AUC of cTnT and CK-MB and The Different Explanatory Variables for Group II Patients.

Variable	AUC - T	(p)	AUC - CK-MB	(p)
Age	- 0.12	(NS)	- 0.28	(NS)
PAP	+ 0.27	(NS)	+ 0.05	(NS)
EF	- 0.47	(S)	- 0.23	(NS)
LA Size	+ 0.28	(NS)	+ 0.10	(NS)
ACT	+ 0.88	(HS)	+ 0.33	(S)
CPB	+ 0.90	(HS)	+ 0.31	(S)

Perioperative course

There were no significant differences between the two groups in the perioperative course of the procedures. The cross-clamp time was 38.6 ± 12.7 and 39.4 ± 10 (p = 0.48, NS), the CPB time 61.3 ± 15.7 and 59.9 ± 13.7 (p = 0.37, NS) and CPB temperature 28.3 ± 2.3 and 28.7 ± 1.9 (p = 0.47, NS) in the two groups respectively. (Figure 2). Tricuspid valve repair was done using Devega repair in 28.5% of group I patients and in 25% of group II (p NS).

Spontaneous defibrillation occurred in only 14 patients of the crystalloid cardioplegia group (50%) compared to 26 patients of the blood-enriched cardioplegia group (81%) ($p < 0.05$, significant). All patients received bileaflet valves (St. Jude medical or Carbomedics) with sizes ranging between 27 and 31 nun.(table 2)

Hemodynamic recovery and postoperative course.

Heart rate increased postoperatively and remained higher than preoperatively in both groups, whereas mean arterial blood pressure decreased, but only transiently. Central venous pressure tended to decrease in both groups. 11 out of 28 patients in group I needed inotropic support in the form of adrenaline (39%). This is in contrast to only 2 patients in group II (6%) ($z = 3.099$, $p < 0.001$, highly significant).

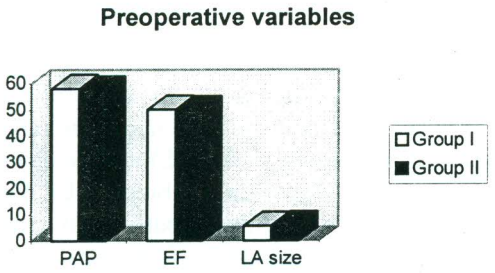


Figure (1): Different Preoperative Variables in The Two Groups

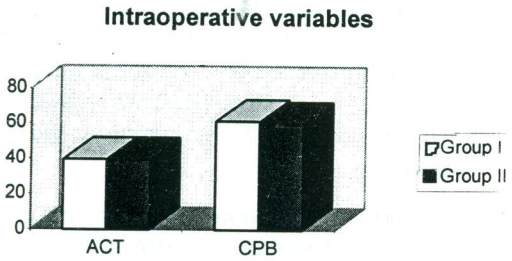
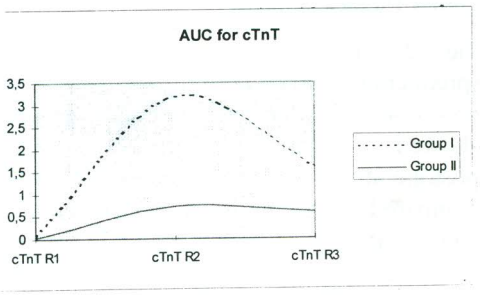
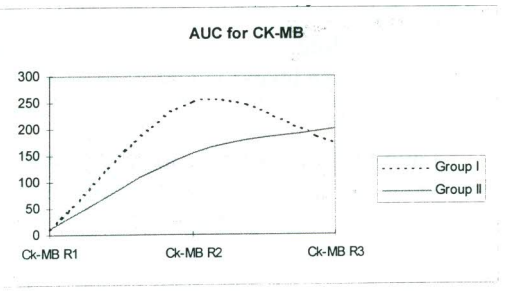


Figure (2): Ischemic and Cardiopulmonary Bypass Times in The Two Groups.



Figitre (3): The Area Under The Curve (AUC) for Cardiac Troponin T



Figitre (4): The Area Under The Curve (AUC) for The MB Isoenzyme of CK

Those patients in both groups who needed inotropic support had significantly lower preoperative EF ($T = 2.48$, $p < 0.05$, significant), longer ischemic ($T = 5.05$, $p < 0.001$) and bypass times ($T=4.82$, $p<0.001$). Ventilation time was significantly higher in group I when compared to group II (10.4 ± 3.08 vs. 7.8 ± 2.24 hours, $p < 0.001$, HS) (table 3). There were three mortalities in our series (5%), two of them in group I (6.7%) and one in group II (3.3 %). The cause of death was low cardiac output in the 2 patients of group I, whereas the only mortality in group II was due to mediastinitis.

Biochemical results

The mean values of the three readings of the cTnT and CK-MB as well as the standard deviation, minimum and maximum are shown in tables 4 and 5 for groups I and II respectively. There were no statistically significant differences between the mean values of the first readings for both enzymes and those for the 10 control healthy subjects. Using the Wilcoxon rank-sum test to compare the 2 groups, the following was found:

* Cardiac troponin T, There was no statistically significant difference between

the 2 groups as regards reading 1 (preoperative reading) with $z = -0.089$ and $p = 0.46$, NS. On the other hand, group 1 showed highly significant higher postoperative reading (reading 2) when compared to group II ($z = -5.749$, $p < 0.001$, HS). The same applied to the next day's reading (reading 3) where z was -3.438 with $p < 0.001$, HS.

* CK-MB, There were no statistically significant differences between reading 1 and 3 in both groups ($z = -0.274$, 0.83 $p =$ 0.39, 0.20 respectively, both NS). As regards reading 2, group I had significantly higher enzyme level than group II (z 4.112, $p < 0.001$, HS).

Patients who needed inotropic support in both groups had significantly higher second and third readings of cTnT when compared to those patients who were not in need for inotropic support ($z = -3.67 - 4.16$ respectively, both with $p < 0.001$, HS). The similar readings of CK-MB were also higher in patients who needed inotropic support but with no statistically significant differences indicating more sensitive cardiac troponins to myocardial tissue injury when compared to CK-MB. The 2 patients who died in group I from low cardiac output had very high levels of cTnT (10.67, 8.87 for the second reading and 5.43, 4.95 for the third reading). They also had higher levels of CK-MB (810, 540 for the second reading and 540, 260 for the third reading). On the other hand, the only patient who died in group II from mediastinitis had low levels of cTnT (0.42, 0.28) as well as CK-MB (92, 48).

Figures 3 and 4 demonstrate the area under the curve (AUC) for both cTnT and CKMB respectively, representing the total release of the two biochemical markers. The AUC for cTnT (AUC-T) was 0.1511 ± 0.1335 vs. 0.0413 ± 0.0245 in groups I and II respectively ($p < 0.05$, S). On the other hand, group 1 showed also bigger AUC for CK-MB (AUC-MB), but with no statistically significant difference (0.153 ± 0.11 vs. 0.128 ± 0.11, NS)

Pre-and intraoperative variables influencing release of the biochemical markers Correlation coefficients between the AUC-T and AUC-MB as dependent biochemical markers of myocardial injury and the different pre- and intraoperative factors that may affect them are expressed in tables 6 and 7 for group I and II respectively.

Multiple regression analysis between AUC - T (dependent variable) and pre- as well as intraoperative variables in a stepwise fashion showed the following:

*Group I (Crystalloid cardioplegia): Ischemic time as well as CPB time were the most two influencing factors to cause cTnT elevation with a multiple r of 0.98 ($r^2 = 0.96$). The next important factor to be entered in step no. 2 (i.e. to influence the cTnT level) was the left atrial size which improved the linear correlation to a multiple r of 0.98 ($r^2 = 0.97$). The last variables to cause improvement in the linear correlation between the AUC-T and any other combination of them were the EF and PAP which yielded a multiple r^2 of 0.99 with r^2 of 0.975.

*Group II (Blood-enriched cardioplegia): Ischemic time as well as CPB time were the most two influencing factors to cause cTnT elevation with a

the 2 groups as regards reading 1 (preoperative reading) with z = - 0.089 and p = 0.46, NS. On the other hand, group 1 showed highly significant higher postoperative reading (reading 2) when compared to group II (z = - 5.749, p < 0.001, HS). The same applied to the next day's reading (reading 3) where z was - 3.438 with p < 0.001, HS.

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*Group II (Blood-enriched cardioplegia): Ischemic time as well as CPB time were the most two influencing factors to cause cTnT elevation with a

multiple r of 0.90 (r^2 = 0.81). The next important factor to be entered in step no. 2 (i.e. to influence the cTnT level) was the PAP which improved the linear correlation to a multiple r of 0.92 (r^2 = 0.83). The last variable to cause improvement in the linear correlation between the AUC-T and any other combination of them was the EF which yielded a multiple r of 0.93 with r^2 of 0. 84.

On the other hand, Multiple regression analysis between AUC - CK-MB (dependent variable) and the same variables showed the following:

Group I: The only variables which influenced the CK-MB level were the PAP and EF with a multiple r of 0.48 (r^2 = 0.23).

Group II: The only variables which influenced the CK-MB level were the ischemic time and CPB time with a multiple r of 0.45 and r^2 of 0.20.

Discussion

Perioperative myocardial damage remains the most common cause of morbidity and mortality following technically successful cardiac operations. As many as 90% of patients who do not survive the perioperative period show, at postmortem examination, varying degrees of gross, microscopic, or histochemical myocardial necrosis which is most severe in the subendocardium of the left or right ventricle (Buckberg et al., 1993). The many advantages of using blood rather than crystalloid cardioplegia have been extensively studied and proven (El Fiky and El Bokl, 1996, Kamlot et al., 1996 and Obadia et al., 1996). The major benefit of blood as a cardioplegic perfusate is related to its ability to buffer changes in pH thanks to its blood proteins, especially histidine imidazole groups. This helps to achieve a reasonable state of metabolism during hypothermia and thus optimizing the small energy output of anaerobic glycolysis during ischemia (Vander Woude et al., 1985 and Buckberg et al., 1993). A second advantage of blood cardioplegia is its ability to provide the appropriate osmotic conditions for myocardial cells. The erythrocytes of blood cardioplegia also contain abundant endogenous oxygen free radical scavengers such as superoxide dismutase, catalase, and glutathione which may reduce oxygenmediated injury. (Van Asbeck et al., 1985). The ability of blood-enriched cardioplegia to transfer oxygen to the tissues is, however, very questionable in hypothermic conditions due to unfavorable shifts in the oxyhemoglobin dissociation curve to the left with resultant impairment of oxygen unloading at the cellular level (Buckberg et al., 1993).

In this study, we tried to investigate the very simple method of using blood-enriched cardioplegia in the way explained before rather than using the costly disposable heat exchangers to deliver blood cardioplegia as classically described by Buckberg in 1989.

The results of our study have also demonstrated that blood-enriched cardioplegia offered better myocardial protection than crystalloid cardioplegia. Our methods to monitor evidences of myocardial injury were both clinical and biochemical. Clinical markers included the incidence of spontaneous defibrillation and hemodynamic recovery during reperfusion, incidence of the need of inotropic support in the postoperative period, and the ventilation time of each patient. Biochemical markers included the

monitoring of the level of CK-MB and Troponin T immediately after patients arrival in the ICU and 24 hours postoperatively.

Our clinical data showed that cold blood-enriched cardioplegia reduced the incidence of fibrillation during reperfusion with better hemodynamic recovery suggesting better myocardial protection than crystalloid cardioplegia. The significant increase in the incidence of need for inotropic support in the crystalloid group as well as significant longer ventilation time suggests the superiority of the blood-enriched cardioplegia as a myocardial protection technique.

The postoperative leakage of CK-MB and Troponin T is a reliable marker of myocardial tissue injury. The CK-MB represents a good index of the myocardial membrane integrity (De Leiris et al., 1978). However, minor tissue damage may be difficult to diagnose by CK-MB (Kaukoranta et al., 1997). Also, CK-MB is released predominantly but not exclusively from myocardium after cardiac surgery (Shell and Sobel, 1976). Caveats concerning the myocardial sensitivity and specificity of biochemical markers after cardiac surgery can be resolved by the measurement of troponin T, a highly specific myocardial isoform of the respective subunit of the troponin regulatory complex (Lee et al., 1996).

The biochemical markers assay have also confirmed the clinical findings. The use of crystalloid cardioplegia was associated with highly significant more release of cTnT both in timmediate postoperative period and 24 hours after surgery when compared with blood-enriched cardioplegia indicating more myocardial tissue injury with more leakage of cardiac enzymes. The same finding was found in the immediate postoperative reading of CK-MB. The area under the curve for cTnT was significantly bigger in group I. On the other hand, the area under the curve for CK-MB was bigger as well in group I but with no statistically significant difference when compared to group II.

The duration of ischemic time was the best explanatory variable to affect the release of both biochemical enzymes. The second most important explanatory variable for the release of the biochemical markers in both bivariate and multivariate analysis was the CPB where longer bypass time was associated with higher enzymatic release. To a lesser extent, lower preoperative ejection fraction as well as higher pulmonary artery pressure were significantly associated with more leakage of biochemical markers indicating more myocardial tissue injury.

The ischemic time, which was expected to be the strongest predictor of release of biochemical markers, correlated very strongly with the release of cTnT but more weakly with the release of CK-MB. Moreover, patients who needed inotropic support had statistically significantly higher cTnT but not CK-MB as compared to patients who did not need such support. Both clinico-biochemical findings were consistent with the increased sensitivity and specificity of the cardiac troponins. These findings were also reported by Taggart and associates in 1997. In a population undergoing vascular or spinal surgery, Adams et al in 1994 found that cardiac

troponins elevations occurred in all 8 patients who developed new abnormalities in left ventricular segmental wall motion (sensitivity = 100 %), but CK-MB elevations were detected for only 6 of these patients (sensitivity = 75%). Lee et al in 1996 also reported less specificity of CK-MB since its elevations were detected in 19% of patients without echocardiographic evidence of perioperative infarction in contrast to cardiac troponins which were slightly elevated in only 1% of patients without echocardiographic abnormalities.

In summary, this study demonstrates the beneficial effect of blood-enriched cardioplegia for myocardial preservation during open heart surgery. The simple nonexpensive technique used in this study proved to be easy and efficient. Our study also supports the sensitivity and specificity of troponin T as a marker of myocardial injury after cardiac surgery and defines the importance of ischemic time in determining its release. Cardiac troponins are useful for providing comparative data and will aid assessment of new myocardial protective strategies or other potentially therapeutic myocardial interventions.

References

1. Bigelow WG, Lindsay WK, Greenwood WF. Hypothermia. Its possible role in cardiac surgery. Ann Surg 1950; 132: 849-66.
2. Buckberg GD. Antegrade/retrograde blood cardioplegia to ensure cardioplegic distribution: Operative techniques and objectives. J. Card. Surg 1989; 4 (3): 216-36.
3. Baum H. Evaluation and clinical perfortnance of a second generation cardiospecific assay for Troponin T. Hossam El Okda, and Mona Mostafa Osman Clin Chem 1997; 43: 1877-84.
4. Wurburg U. Enzymatic assay for CK-MB. Clin Chem 1976; 54: 357-60.
5. Buckberg GD, Allen BS, Beyersdorf F. Blood cardioplegic strategies during adult cardiac operations. In Piper HM, Preusse CJ (eds): Ischemia-reperfusion in cardiac surgery. Kluwer Academic Publishers, Dordrecht 1993; 279-91.
6. El Fiky MM, El Bokl F. Randomized trial to compare cold crystalloid cardioplegia versus cold blood enriched cardioplegia in mitral valve replacement. J of Egypt. society of Cardiothoracic Surg. 1996, Vol. IV: 35-42.
7. Kamlot A, Bellows SD, Simkhovich BZ, Hale SL, Aoki A, Kloner RA, Kay GL. Is warm retrograde blood cardioplegia better than cold for myocardial protection? Ann Thorac Surg 1997, 63: 98-104.
8. Obadia JF, Ben Baoulai A, Maupoil V, Rochette L. Crystalloid versus cold blood cardioplegia in patients operated on for myocardial revascularization. The Journal Of Cardiovascular Surgery; 37: 45-51.
9. Vander Woude JC, Christlieb IY, Sicard GA. Imidazole-buffered cardioplegic solution: Improved myocardial preservation during global ischemia. J Thorac Cardiovasc Surg 1985; 90: 225-34.
10. Van Asbeck B, Hoidal J, Vercelloti GM et al. Protection against lethal hyperopia by tracheal insulation of erythrocytes: role of red cell glutathione. Science 1985; 227: 756-8.

11. De Leiris J, Opie LH. Effects of substrate and of coronary artery ligation on mechanical performance and on release of lactate dehydrogenase and creatinine phosphokinase in isolated working rat hearts. Cardiovasc Res 1978; 12: 585-96.

12. Kaukoranta PK, Lepojärvi MPK, Ylitalo KV, Kiviluoma KT, Peuhkurinen KJ. Normothermic retrograde blood cardioplegia with or without preceding ischemic preconditioning. Ann Thorac Surg 1997; 63: 1268-74.

13. Shell WE, Sobel BE. Biochemical markers of ischemic injury. Circulation 1976, 53 (Suppl): 198-106.

14. Lee TH, Thomas EJ, Ludwig LE, Sacks DB, Johnson PA, Donaldson MC, Cook EF, Pedan A, Kuntz KM, Goldman L. Troponin T as a marker for myocardial ischemia in patients undergoing major noncardiac surgery. am J Cardiol 1996; 77: 1031-36.

15. Taggart DP, Hadjinikolas L, Hooper J, Albert J, Kemp M, Hue D, Yacoub M, Lincoln JC. Effects of age and ischemic times on biochemical evidence of myocardial injury after pediatric operations. J Thorac Cardiovasc Surg 1997; 113: 728-35.

16. Adams JE, Sicard GA, Allen BT, et al. Diagnosis of perioperative myocardial infarction with measurement of cardiac troponin I. N Engl J Med 1994; 330: 670-4.

Extended Endartrectomy of the Left Anterior Descending Coronary Artery as an Adjunct to Coronary Revascularization, Early Results

ABSTRACT

We are reporting our experience in a group of 46 patients who underwent isolated coronary bypass surgery involving extended endarterectomy to the LAD from August 1996 to April 1998. The group includes 34 males and 12 females with a mean age of 52.6 ±14.4 years. All the cases had diffuse disease involving the LAD. Thirty patients (65.2%) had a history of myocardial infarction and 2 patients (4.3%) presented with unstable angina. The mean cross clamp time was 55±20 minutes, the mean length of LAD reconstructed was 7.2 ± 2.9 cm.

There was one hospital mortality (2.2%). There were no cases of perloperative MI. 7 cases (15.2%) required postoperative inotropic support including 2 cases that required intra-aortic balloon pump. All patients were free of chest pain on hospital discharge. The mean follow up period was 13.2±1.4 months. During follow up 5 patients (11.1%) experienced recurrent chest pain and were studied angiographically. In all 5 patients, the reconstructed LAD was nearly totally occluded by thrombus inspite of patent IMA. The other 40 patients (88.9%) remained pain free with improved myocardial wall motion in previously hypokinetic and dyskinetic segments.

We conclude from our study that extended endarterectomy of LAD could be done with acceptable early mortality and morbidity. However, it should only be done in diffuse LAD disease. Longer follow up period is needed for complete assessment of the long-term patency of the reconstructed LAD segment.

Gamal S. Mohamed MD, Wael Abdel-Aziz MD, Mostafa A. Abdel-Gawad MD, Ahmed El Kerdany MD and Ahmed Derwaza MD.

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INTRODUCTION

Coronary endarterectomy began as a treatment of atherosclerotic heart disease before coronary artery bypass grafting (CABG) became the gold standard {1}. However, the high risk of perioperative myocardial infarctions in the earlier studies made adjunctive endarterectomy a less attractive option to most surgeons {2}. On the other hand, both the current patient population with more complex coronary pathology in whom standard coronary bypass techniques are not sufficient alone for total revascularization, together with advances in cardiac surgery improving the safety and efficacy of the procedure have led some surgeons to call for the resurgence of coronary endarterectomy {3-6}.

Endarterectomy and reconstruction of the left anterior descending (LAD) coronary artery is a meticulous time consuming, and

Ain Shams University Hospitals, Department of Cardiothoracic Surgery

a technically challenging procedure. However, sometimes it may be the only therapeutic option for some patients whose condition is otherwise deemed inoperable {7-8}.

Here we report our recent experience with this technique and examine its safety and efficacy in modern cardiac surgical practice.

Patients and Methods

Between August 1996 and April 1998, 46 patients underwent extended endarterectomy to the LAD in conjunction with CABG by our group. This constitutes 15% of all patients who had CABG during this period. Excluded from this study are patients who underwent endarterectomies to arteries other than the LAD, patients with additional procedures such as valve repair or replacement, and patients with redo CABG.

The preoperative characteristics of patients in the studied group are summarized in Table (1).

Surgical technique

All operations were performed through standard median sternotomy and cardiopulmonary bypass. Patients were cooled to 27°C - 31°C. Endarterectomies and distal anastomoses were performed under aortic cross clamping and cardioplegic arrest. Myocardial protection was achieved by induction of antegrade cold blood cardioplegia infusion followed by replenishments every 30 minutes.

In 40 patients (87%) the decision to perform extended endarterectomy to the LAD was made intraoperatively. If the atherosclerotic process involved the distal LAD artery or obstructed the intermediate, or diagonal branches such that there was no suitable place to construct a conventional anastomosis, a long arteriotomy was made and extended until a good arterial lumen was reached.

The cleavage plane between the plaque and the vessel wall was reached. The atherosclerotic plaque as a whole was removed under direct vision without traction or counter-traction on the endarterectomy core and without the use of any special device. The septals and the diagonals were easily endarterectomized with tapered-feathered ends of the plaques (Figure 1).

It was deemed crucial to avoid residual dissecting layers and not to leave residual plaques with separated ends. After establishment of a smooth lumen free of atherosclerotic material, the LAD was reconstructed using a longitudinally opened saphenous vein graft of suitable length with a running 7/0 prolene suture with special care not to create a too patulous lumen. After reconstruction, the left IMA graft was anastomosed onto the saphenous vein patch. In 5 of our cases in whom the IMA was small or its flow was not satisfactory, a vein "patch-graft" was used and the IMA was anastomosed onto it.

Routine postoperative care was required for all cases. The electrocardiographic criteria for defining postoperative MI included new Q waves, persistent intraventricular conduction defects, or loss of R wave progression across chest leads. Also creatine kinase MB fraction levels greater than 10% were considered highly

Table (1): Preoperative characteristics of the 46 patients studied

Variable	Value
Age (years)	56.2±14.4
SEX (M:F)	34:12
RISK FACTORS	
Hypertension	37 (80.4%)
Smoking	34 (73.9%)
Diabetes	23 (50%)
Hyperlipidemia	10 (21.7%)
Obesity	12 (26%)
Family history	27 (58.7%)
ANGINA	
Grade I	5 (10.9%)
Grade II	9 (19.6%)
Grade III	20 (43.5%)
Grade IV	10 (21.7%)
Unstable angina	2 (4.3%)
HISTORY OF CHF	5 (10.9%)
HISTORY OF MI	30 (65.2%)
CHRONIC ARRYTHMIAS	2 (4.3%)
EJECTION FRACTION	0.45±0.15
NUMBER OF VESSELS AFFECTED	
Single vessel disease	2 (4.3%)
Double vessel disease	15 (32.7%)
Triple vessel disease	23 (50%)
Left main disease	6 (13%)

Table II: Operative Criteria of the studied cases

variable	Value
Cross clamp time (min)	55±20
Bypass time (min)	125±29
Number of grafts per patient:	
Single graft	1 (2.2%)
Two grafts	14 (30.4%)
Three grafts	22 (47.8%)
Four grafts	9 (19.6%)
Mean length of reconstruction (cm)	7.7±2.9

Table III: Early events following Extended LAD endarterectomy

Event	Value
Hospital mortality	1 (2.2%)
Perioperative MI	0 (0.0%)
Postoperative inotropic support	7 (15.2%)
Need for IABP	2 (4.4%)

suggestive of preoperative MI.

All patients were given aspirins 325-mg day indefinitely. Provided there was no excessive blood loss, anticoagulation using heparin was started 6 hours postoperatively in all patients. All patients were switched to warfarin after 3 to 4 days and continued indefinitely to maintain an international normalized ratio between 1.5-2.

Results

Early (In Hospital):

There were no intra-operative deaths. One patient (2.2%) died on the 26th day before hospital discharge. She was a 65 years old female who suffered delayed recovery after uneventful sugery and died from complications of prolonged ventilation.

There were no cases of perioperative myocardial infarction. 7 (15.2%) required postoperative intropic support, including 2 cases who required intraoartic balloon pump support.

Follow-up data:

Follow-up was complete in all 45 patients. The average follow-up period for these patients was 13.2 ± 1.4 months (range 6-17 months). All patients received follow-up examinations 3 months, 6 months after operation, and yearly thereafter. Patients (5)

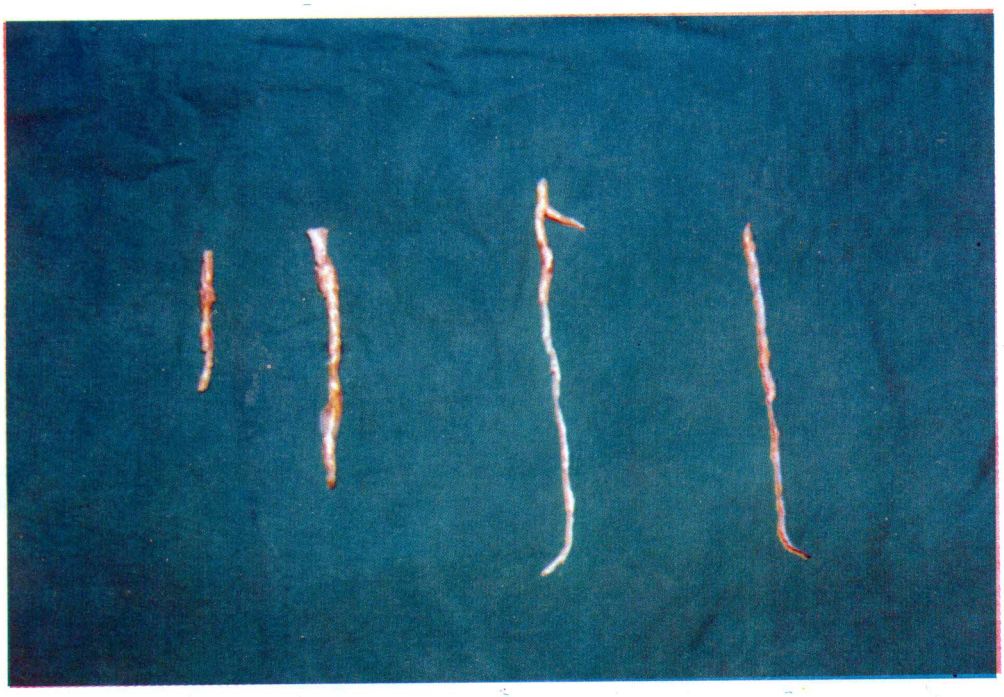

Figure (1):

who had recurrent chest pain were restudied angiographically.

All the patients were free of chest pain on hospital discharge.

During follow up, 40 patients (88.9%) remained angina free or in Canadian Cardiovascular Society (CCS) angina class I or II. Follow-up echocardiographic examination 3 months following operation revealed improved local wall motion in the previously hypokinetic or akinetic areas. The 5 patients who had recurrent anginal pains class III or IV (6-12 months) following surgery were studied angiographically. In all those patients (11.1%), the reconstructed LAD segment was nearly totally occluded with patent IMA graft. In all patients hypokinesia or akinesia of the anterior wall and septum was obvious.

Discussion

Postoperative infarctions after coronary endarterectomy are the main reasons for the increased morbidity and mortality. Infarctions can result from residual obstruction, intimal flaps, thrombosis or atheroemboli. The reported post operative infraction rates vary widely from 5% to 25% {5,9 and 11}.

However, there appears to be a trend toward lower rates of infarction and mortality in more recent studies {3,9 and 12}.

Djalilan and Shumway in 1995 for example, reported a 5% postoperative MI rate and a 3% mortality rate following endarterectomy. They also reported a higher incidence of infarctions in patients with left-sided endarterectomy because of the likelihood of blocking off small branches by a "Snow-plow" effect, thus making the right coronary artery anatomically more favourable for endarterectomy {12}.

However, extended endarterectomy as described by us and others, where a long arteriotomy is done to the LAD exposing the whole arterial lumen and origins of side branches containing the atherosclerotic occlusive material which is then removed under direct vision without traction or counter traction. This technique has the advantage of avoiding leaving residual material in LAD lumen or inducing dissections, both of which could cause early thrombotic or embolic occlusions leading to perioperative infarctions and/or early mortality.

Using this technique, we and other authors were able to achieve postoperative MI values ranging from 0-4% {8 and 13}.

It is to be noted that we have not used any special device or instrument for separation of the atheromatous core. Others have used special devices including laser, gas, or cardioplegic solution {14, 15 and 16}.

Two techniques are currently in use for reconstructing LAD following endarterectomy. Either using a vein patch or an IMA patch {8 and 13}. Some authors prefer the use of IMA patch, as they believe that it provides better match in diameter between the graft, the reconstructed segment and the native coronary artery with good flow characteristics. Moreover, the presence of muscle layer (media) in the IMA patch is associated with a lesser incidence of aneurysmal dilatations of the reconstructed segment with resultant stasis and thrombus formation {8}.

We used saphenous vein patch to reconstruct LAD. We were reluctant to use IMA patch as we believe that this may lead to unavoidable trauma to with resultant spasm and perioperative MI or endothelial injury with resultant jeopardy of its long term patency.

We consider complete removal of the atheromatous plaque from LAD as well as its septal and diagonal branches to maximize distal run off in addition to trimming of the saphenous vein patch so as not to create too patulous reconstructed LAD segment, are the most important factors to minimize the incidence of aneurysmal dilatation with attendant stasis and thrombus formation.

We implanted the IMA onto the patch to enjoy its superior hemodynamics, long term patency, and almost negligible incidence of atherosclerotic disease {17-20}.

In 5 of our cases {10.9%}, in whom the IMA size or flow was considered inadequate, a vein "patch graft" was put on the endarterectomized LAD, followed by implantation of IMA onto the vein patch in order to combine the benefit of good early vein graft flow with the long term patency of the IMA.

Increased operative risk, lower patency, and higher morbidity rates following coronary endarterectomy, limit its use only for cases with diffuse disease in whom the distal vessel is unsuitable to bypass alone {3,9,21 and 22}.

There are several reasons for the lower patency rates after endarterectomy than for conventional anastomoses. Because of the lack of endothelium, all the subendothelial material that can trigger the coagulation cascade as it's exposed to the blood flow. Also, some platelet aggregation and fibrin clot formation occur in all cases even if flow through the lumen is sufficient. With poor distal runoff, however, this clot formation progresses rapidly with resultant thrombosis of the lumen caused by stagnation of the blood {23}.

Another important factor is the absence of substances released from the endothelium, such as prostacyclin and nitric oxide, which prevent platelet adhesion and aggregation, and may further contribute to early occlusion {8}.

We maintain all our patients on long term antiplatelet and anticoagulation therapy. Still we have an 11.1% occlusion rate at a mean follow up of 13.2+1.4 months. Others show similar results. Djalilian and Shumway in 1995 reported 75% endarterectomy graft patency at 3 years compared with 80% in conventional grafts. Brenowitz, Kayser and Jhonson reported a 72.5% late patency rate after an average of 31 months after saphenous vein reconstruction of LAD through coronary endarterectomy. Tasdemir and colleagues, in 1996, reported a 79.1% patency rate at a mean follow up period of 5.7 years compared to a patency rate of 81.5% of grafts to LAD in the conventional bypass group (non significant difference).

Actuarial survival after CABG with left coronary endarterectomy was reported to vary between 46.5% and 92.5% at 5 years, depending on the risk factors {3}. Our median follow up period is short (around one year) and all our patients who were discharged are still alive with no single mortality. On the other hand, 88.8% of theses patients are in CCS anginal class I and II, and they are enjoying a reasonable functional capacity and working status. Naturally, these are only preliminary results and long-term follow up of these patients will enable us to conclude actuarial curves and estimates of survival and freedom from angina at subsequent reports.

Conclusion

We are seeing increasing numbers of patients with diffuse coronary artery disease. This -phenomenon is due to increasing numbers of elderly, females, diabetics or patients who present to us in a more advanced stages of the disease who underwent one or more percutaneous coronary angioplasty sessions.

By making ungraftable vessels suitable for grafting, adjunctive endarterectomy allows patients with diffuse disease to achieve the longterm clinical benefits of conventional bypass grafting.

Our results confirm the superiority of the extended of LAD over the conventional (limited) endarterectomy technique as it ensures total removal of the atheromatous plaque from LAD and all its diagonal and septal branches under direct vision.

Despite improved safety, the risks of extended endarterectomy should be weighed against its potential benefits. We and other authors advocate limiting this technique to patients in whom complete revascularization would otherwise be impossible.

Refrences

1. Bailey CP, May A, Lewman WM. Survival after coronary endarterectomy in man. JAMA 1957, 164: 641-6
2. Effler DB, Groves LK, Sones FM, Shirely EK. Endarterectomy in the treatment of coronary artery disease. J thorac. Cardiovasc. Surg. 1964, 47: 98-102.
3. Brenowitz JB, Kaiser KL, Johnson WD. Results of coronary endarterectomy and reconstruction. J thorac. Cardiovasc. Surg. 1988, 95: 1-10.
4. Shapira N, Lumina FG, Gottiener JS et al. Adjunct endarterectomy of the left anterior descending coronary artery. Ann Thorac. Surg. 1988, 46: 289-96
5. Parsonnet V, Gilbert L, Gielchinsky I, Bahaktan EK. Endarterectomy of the left anterior descending and mainstem coronary arteries: a technique for reconstruction of inoperable arteries. Surgery 1976, 80: 662-73.
6. Loop FD: Resurgence of coronary artery endarterectomy. J Am Coll Cardio 1988, 11: 712-3.
7. Ladowski JS, Schatzlein MH, Underhill DJ, Pearson AC. Endarterectomy, vein patch and mammary bypass of the anterior descending artery. Ann Thorac Surg 1991, 112; 1187-9.
8. Tasdemir O, Kiziletepe U, Karagoz HY, Yamak B, Karkmaz S, Bayazit K. Long-term results of reconstruction of the left anterior descending coronary artery in diffuse atherosclerotic lesions. J Thorac Cardiovasc Surg 1996, 112; 745-54.
9. Livasey JJ, Cooley DA, Hallman GA, Reul GL, Ott DA and Duncan JM. Early and late results of coronary endarterectomy. Analysis 3369 patients. J Thorac Cardiovasc Surg 1986, 92; 649-660.
10. Wallace E, Francine AJ, Claus RH, Armellini C, Steichen F and Stertzer SH. Manual coronary endarterectomy with saphenous bypass experience with 263 patients. Ann Thorac Surg 1981, 32; 451-7
11. Hochberg MS, Merrill WH, Michael's LL, Macintosh CL. Results of combined coronary endarterectomy and coronary bypass for diffuse coronary disease. J Thorac Cardiovas Surg 1978, 75; 38-44
12. Djalilian AR and Shumway SJ. Improved safety in modern cardiac surgery. Ann Thorac Surg 1995, 6; 174-954.
13. Sankar NM, Satyaprasad V, Rajan S, Bash VV, Sherin KL. Extensive endarterectomy, onlay patch and internal mammary bypass of the left anterior descending coronary artery. J Card Surg 1996, 11; 56-60.
14. Izzat MB, Angelini GD. How to do it. A modified battery powered toothbrush for coronary artery endarterectomy. J Cardiovasc Surg 1993, 34; 527-8.
15. Oliver JP, Gandjbakhch 1, Avrillier S, Delettre E and Cabrol C. Intraoperative coronary artery endarterectomy with exeimer laser. J Thorac Cardiovas Surg 1990, 100; 606-11.

16. Sawyer PN, Pasupathy CE, Fitzgerald J et al. Six-year follow-up study in the use of gas endarterectomy. Surgery 1972,72; 837-48.

17. Nassau M,, Takashi A, Akasaka T et al. Postoperative flow characteristics of the left internal thoracic artery grafts. Ann Thorac Surg 1995, 59; 154-62.

18. Fusejima K, Takahara Y, Suto Y et al. Comparison of coronary hemodynamics in patients with internal mammary artery and saphenous vein coronary artery bypass grafts; a non-invasive approach using combined two dimensional and Doppler echocardiography. J Am Coll Cardiol 1990. 15; 131-9.

19. Singh RN and Sosa JA. Internal mammary artery; a live conduit for coronary bypass. J Thorac Cardiovase Surg 1984, 87; 936-8.

Emergency Mitral Valve Re-replacement during Pregnancy

ABSTRACT

Valve re-operations still presents a challenge to the surgical group. Re-operations are technically more difficult and are not uncommonly performed on a functionally compromised group of patients who tolerate complications poorly. Emergency presentation compound the risks even further.

During the period from January 1993 till December 1997, 96 patients underwent emergency mitral valve replacement at Ain Shams University Hospitals. Twelve of these patients were pregnant women.

The aim of the study is to examine how pregnancy affects the surgical risk (outcome) for both the mothers and their babies and what is the most appropriate anti-coagulation policy to follow during pregnancy to avoid potential complications.

The mean age of group is 29 years. 7/12 were primigravida, and 7/12 shifted to heparin at some time during their pregnancy. The mean interval between first operation and emergency re-operation was 6.2 years. 7/12 presented through the last trimester.

Pre-operatively, all patients were in NYHA class 111 or IV. Diagnosis of valve thrombosis was confirmed by echocardlogtaphy with a mean valve gradient of 26 mmHg. Pre-operative fetal viability was not confirmed in 8/12 cases. Emergency valve re-replacement was performed via sternotomy except in 2 cases through right antro-lateral thoracotomy. 2 mothers died (16.6%) one due to myocardial failure and the other due to persistence of pre-operative acute renal failure. This mortality is not statistically significant (p=0.086) when compared to our overall emergency valve re-operation patient population. Fetal wastage was high (10/12).

The rate of 0.9 per patient year of valve thrombosis in our patient is very much in accordance with other reports from "Third world-Developing countries", all of which is double that reported from "Developed countries". This is related to the anti-coagulation policy with lack of standardization of PT test, failure of INR reporting, and poor patient education and compliance.

Also, this study illuminates the danger in the practice of shifting pregnant women to heparin in the first trimester, since this increases the risk of valve thrombosis to the mother without. reducing any of the risks subjected by the fetus.

Mostafa A. Abdel-Gawad MD, Ahmed El-Nori MD, Hossam F.El-Shahawy MD, Gamal S. Mohamed MD and Walla Saber MD.

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INTRODUCTION

Rheumatic fever still remains one of the most common health hazards in Egypt making cardiac valve surgery still constituting more than half our work load at Ain Shams University Hospitals.

Ain Shams University, Department of Cardiothoracic Surgery

During the period from January 1993 till December 1997, 168 underwent reoperations either for replacement of malfunctioning prosthesis, degenerated bioprosthesis or development of a new valve lesion. 96 (57%) patients were performed on emergency basis. Twelve of the latter were pregnant women, forming the base of this study.

The aim of this study is to examine if pregnancy increases the operative risk and outcome of such a sub-group and their babies. Also, in light of this study, will try to address the issue of anti-coagulation to pregnant women with prosthetic valves. Valve re-operations still presents a challenge to the surgical group. Re-operations are technically more difficult because of the adhesive processes around the heart, and the common association of pulmonary hypertension. Re-operations are not uncommonly performed on a functionally compromised group of patients who tolerate complications poorly. Emergency presentation compound the risks even further, and a mortality of 30-50% have been quoted (1-3) .

At Ain Shams University Hospitals, reductions in the operative risks and postoperative morbidity have been made in the past few years, as the whole anesthetic and surgical team gained more experience to manage such a high risk group, together with implementing the concept involving " global or total " myocardial protection, most importantly the use of antegrade blood enriched cardioplegia with retrograde supplementation, more frequent and the early institution of partial femoral CPB in unstable patients to avoid and manage injury to the hypertensive right ventricle during re-operative sternotomy and decrease myocardial distention, thus reducing myocardial oxygen consumption (4).

Material and Methods

Mothers;

Mean age of the group 29 years ± 5.2 (21-32 years). 7/12 were primigravida. 4/12 had one or more living children born before their first valve replacement and one patient had 4 children, 2 of whom were born after placement of a prosthetic valve.

Eight of the patients were from outside Cairo, and only 6/12 presented for regular follow-up. A total of 7/12 women shifted to heparin at some time during their pregnancy. The mean interval between first operation and re-operation was 6.2 years ± 2.7. All patients presented either in NYHA -functional class 111 or IV, 3 patients had associated pulmonary edema necessitating pre-operative mechanical ventilation and one patient had preoperative acute renal failure.

Echocardiography confirmed the diagnosis in all the cases, earlier in the study was TTE (5/12), and lately using TEE (7/12). Mean mitral valve gradient was 26 mmHg, with limited mobility or total immobilization of the valve leaflets. Details of pre-operative variables Table 1;

Fetal status

could not prove preoperative viability in 8/12 cases, in the form of lost fetal kicks as reported by the mothers (12-36 hours before presentation), or failure to detect fetal heart sounds by echo-doppler.

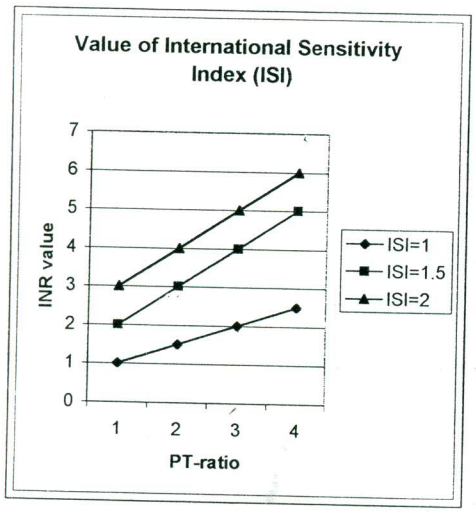

Figure (1):

Operation:

Re-entry was through median sternotomy with right pelvic tilt in 10/12 patients, using an oscillating saw for sternal division, and through right antro-lateral thoracotomy in the fourth intercostal space in two patients.

One re-entry injury to the right ventricle occurred necessitating early institution of femoro-femoral CPB. Another 3 patients required early femoro-femoral CPB for hemodynamic instability.

Inspite of inability to confirm fetal viability in 8/12 cases, we employed the benefit of the doubt and all handy measures to decrease the chance of fetal wastage was instituted; pelvic tilt to improve venous drainage and placental perfusion, keeping CPB flow rate > 2.5L/min/m2 to maintain a mean arterial pressure >70 mmHg and perfusion temperature not less than 32 Celsius (except for 2 patients at 28 Celsius) to avoid inducing uterine contracts and premature labor or abortion. No intraoperative measures (Doppler fetal heart sounds or vaginal ultrasound) were taken to monitor fetal well being.

Myocardial preservation was performed by infusion of cold (4°C) antegrade high potassium (20mEq/L) cardioplegia at a dose of 15-20 ml/kg body weight. Half of this dose was repeated every 20 - 30 minutes of cross clamp time. Blood enriched cardioplegia was used in the last 4 patients. The mean CPB time was 110 min (65135 min) and mean aortic cross clamp time was 73 min (49-93 min). Exposure of the mitral valve was through the previous left atriotomy in all patients except for 2 were trans-septal approach through the right atrium was used. Tricuspid annuloplasty was performed in 5/12 cases.

Examination of thrombosed valves showed that all but one was of the mono leaflet type (9 Omniscience, 2 Sorin and one Carbomedics). The main cause of obstruction was a fresh thrombus on the valve in 10/12 cases, while 2 showed evidence of an underlying pannus overgrowth and entrapment complicated by thrombosis.

Results

Mothers;

10/12 survival, 2 patients died, one on the second post-operative day from low cardiac output , the other on the fourth post-operative day from persistence of preoperative renal failure. Mean blood loss was 730±290 ml and blood transfusion was 4.3±2.2 units. Incidence of postoperative morbidity is reported in table 2. Mean hospital stay was 13 days.

Table (1):

Mean age	29 ±5.2 years
Adequacy of anticoagulation	
• Well controlled	5/12 (41.6%)
• Poorly controlled	5/12 (41.6%)
• Stopped taking oral anticoagulants	2/12 (16.6%)
Shift to heparin during pregnancy	7/12 (58.3%) total
• During first trimester	4/7 (57.2%)
• During last trimester	1/7 (14.2%)
• Throughout pregnancy	2/7 (28.6%)
Time of presentation	
• First trimester	2/12 (16.6%)
• Second trimester	3/12 (25%)
• Last trimester	7/12 (58.3%)
Echocardiographic diagnosis	
Valve gradient	26± 7.3 mmHg (mean)
LV function	
• Mildly impaired	3/12 (25%)
• Moderately impaired	7/12 (58.3%)
• Severely impaired	2/12 (16.6%)
RV pressure	89±16 mmHg (mean)

Fetus;

Fetal wastage was 10/12 through spontaneous abortion (24 hours - 3 weeks) after operation.

Two pregnancies continued to near full term at 36 and 37 weeks, resulting in one normal baby and the other was microcephalic.

Discussion

In contrast to the literature from developed countries, were the indications for valve reoperations are mostly due to

Table (2):

Table 2; post-operative morbidity	
Re-entry for bleeding	1(8.3%)
Superficial wound infection	1(8.3%)
Post-operative depression	1(8.3%)
Urinary tract infection	1(8.3%)
Low out-put syndrome	2(16.6%)
Prolonged mechanical ventilation	2(16.6%)
ICU stay more than 2 days	4(33.3%)

valve degeneration (-60%-70%), endocarditis (-10%- 15%), peri-prosthetic leak (-10%-15%), making valve thrombosis (-5%) one of the least common indications (4, 5). At Ain Shams University Hospitals almost half of our patients who come for re-operations present as emergency valve thrombosis.

The cause of such high incidence of valve thrombosis could be attributed to many potential factors including; age, sex, atrial fibrillation, atrial size, and surgical technique... ect. However, in our experience, we believe that the valve type (design) and adequacy of anticoagulation including patient compliance are the most important factors.

Regarding valve type., all but one of the explanted valves were of the mono-leaflet type (10/12), nine of which were of the Omniscience type. The higher incidence of valve thrombosis with mono-leaflet valves is in accordance with other local experience (6). For the past 5 years, we use bi-leaflet valves almost exclusively. Regarding adequacy of anticoagulation. The 0.9 per patient year incidence of valve thrombosis in our patients is very much in accordance with other reports from "third world" communities e.g. the 1.06% reported by Deviri et al, 1991 (7) and 1.3% reported by Hall et al, 1980 (8), both about the black sub-population in South Africa, which is almost double the incidence of valve thrombosis when compared to the white sub-population inspite of inserting the same valve types in the same hospitals.

Poor people are unable to travel long distance to follow up clinics; an unsophisticated patients who are in good clinical condition after valve replacement does not understand the need to attend a clinic, nor does they understand the need to undertake anticoagulants, since such medications makes no apparent difference to their health. This is apparent, since more than half of the patients (8/12,66%) were from outside Cairo, and (7/12, 58%) were poorly anti-coagulated. Continuos and persistent patient education is of paramount importance.

Another important aspect to achieve proper anticoagulation is standardization of PT test, which still remains the primary measurement for monitoring the efficacy of oral anticoagulation treatment.

The PT test, original described by Quick and co-workers, 1935 (9) is based on the tissue factor pathway of blood coagulation. The result of the PT test is strongly dependent on the nature of the tissue extract (thromboplastin), the strength of which varies considerably from one manufacturer to another and even from one batch to another by the same manufacturer.

Therefore, the usual reporting of PT test results as a percentage of prothrombin activity is neither adequate nor accurate in describing the status of the patient's anti-coagulation level, since it does not take into account the strength of the reagent used.

In 1985 (10), the WHO recommended a universal scale for the intensity of oral anti-coagulation, that is, "International Normalized Ratio" (INR). Each manufacturer should report the strength of its tissue reagent in relation to a standard reference i.e. "International Sensitivity Index"

Using the INR in reporting the PT test results should reduce the highly variable and sometimes confusing results reported by different labs, thus allowing better anti-coagulation control. Also, it facilitates compliance of the patients through decentralization, allowing the patients to perform the PT test in their respective geographical area and reporting it by phone to their physicians, without the latter having to worry about the quality of the PT test being reported and the strength of the reagent used.

The Egyptian Society of Cardiothoracic Surgery should take a leading role in the implementation of the WHO recommendations regarding reporting the PT test results.

It is generally accepted that maternal mortality on elective cardiac operations does not differ from that expected in the overall population according to the type of surgical procedure performed, and hence pregnancy should not influence the outcome in female patients requiring cardiac procedures. The review by Beeker in 1983 (11), of the experience of the members of The Society of Thoracic Surgeons revealed only one maternal death in 68 operations with cardio-pulmonary bypass, and that death occurred late and was due to hepatitis.

In our experience, this expectation could also be extended to re-do emergency operations, since, the 16% maternal mortality in this study is not statistically significant (0.083) when compared to the overall emergency operations conducted at our center.

Fetal wastage was high (10/12, 83%) when compared to other reports. For example, Rossauw GJ, in 1993 (5), reported their experience with 7 pregnant women, with no maternal mortality and one fetal loss. However, only 3 were re-do operations from failure of bio-prosthesis. None were on emergency basis. On the other hand, all the mothers in the study presented on emergency basis, and 8/12 fetuses were non-viable on presentation due to their mothers severe cardiac decompensation, low cardiac output, acidosis, hypoxia and placental hypo-perfusion.

There have been no comprehensive experimental studies on the effect of CPB on the fetus. Theoretically, non-pulsatile perfusion, hyper - oxygenation, heparinization and prolonged hypotension could adversely affect both placenta and fetus. Fetal heart monitoring has shown dysrythmias and bradycardia during perfusion (12). Bradycardia occurs at the onset of bypass, a finding suggesting it is possibly related to hypothermia and can be eliminated by an increase in perfusion rate. Thus high flow rates together with

normothermic perfusion have reduced fetal risk during bypass (13).

Although case reports and collective reviews suggest that fetal mortality has become progressively less likely during bypass, the general trend is that if the mother is 28 weeks pregnant or more, is to deliver the baby by cesarean section in the same sitting and before commencing CPB for the cardiac procedure. This with good modern neonatal care provides the baby with a better survival chance than taking the risk of carrying the pregnancy through CPB (14).

When urgent/emergency cardiac operation is required during the first and second trimester, there is little option other than to try to preserve the fetus. This was the case in one of the three patients who presented in the second trimester and who continued her pregnancy till time of delivery. The other two presented with nonviable fetuses and aborted later.

On the other hand, 7 patients presented in the last tri-mester, 3 of them had viable fetuses at the time of operation but only one continued till delivery of a living baby. The other two suffered intra-uterine fetal death.

This reveals that, inspite of taking CPB precautions to increase chances of fetal survival, they are still at definite risk especially under emergency conditions. Cesarean section before or immediately after commencing CPB would increase chances of survival. We do not expect excessive bleeding from the contracting uterus, provided that the abdomen is not closed till after heparin reversal to ensure complete homeostasis (14).

Controversy still exsists regarding the anti-coagulation policy for pregnant women with mechanical valves, the magnitude of the risks involved and on the choice of prosthesis for young women who are expected to have children. Oral anti-coagulants cross the placenta to the fetus where their anti-coagulant effect is very much greater than in the mother. This is because of the immature fetal liver and the inability of maternal liver enzymes to cross the placental barrier due to their large molecular size. The risk of teratogenicity is dose dependent. Most abnormal fetuses are aborted.

The old standard practice used to be through shifting pregnant women with mechanical cardiac prosthesis from oral anti-coagulants to heparin during the first trimester to avoid fetal embryopathy, then again in the last two weeks to avoid the risk of intra-cranial hemorrhage during delivery.

This concept was based on numerous reports from North America regarding complications of oral anti-coagulants, where anti-coagulation levels generally used for patients with prosthetic heart valves have been high for many years (INR 5 to 10). The reported high fetal loss rates in these series are fortunately not seen in the European series, in which a much lower levels of anti-coagulation have been used (INR 2.5 to 3.5), (8,15 and 16).

On the other hand, heparin with its large molecular weight, does not reach the fetus to harm it directly, it can still cause placental hemorrhage and separation leading to abortion, pre-maturity or still birth (Howie PW, 1986).

Also, the major defect with heparin is the difficulty in maintaining an acceptable anti-thrombotic effect without inducing

hemorrhagic complications. It is to be noted that, the dose of heparin required to prevent arterial thrombosis is much higher than that needed to prevent venous thrombo-embolism. Thus, with heparin use, maternal hemorrhage is a real risk and side effects are not uncommon.

Salazar and associates from Mexico, 1996 (17), reported 40 pregnancies in 37 women with prosthetic heart valves prospectively followed up. Subcutaneous heparin was administered from the 6th until the end of the 12th week and in the last 2 weeks of gestation with oral anti-coagulant in the interval in between. Heparin was given every 8 hours in the first 36 cases and every 6 hours in the last 4 cases, and the dose was adjusted to maintain activated PTT at 1.5 to 2.5 times the control levels. The incidence rate of spontaneous abortions was 37.5%, and there was one neonatal death (2.5%) due to cerebral hemorrhage.

No signs of coumadin induced embryopathy were found in any of the 16 live-born infants studied by geneticist. There were 2 cases of fatal mitral valve thrombosis while on heparin therapy. The study was interrupted after the second death. They concluded that the regimen of adjusted doses of heparin in this study was not effective to prevent thrombosis of mechanical valves during pregnancy and did not reduce the high incidence of fetal wastage associated with anti-coagulant therapy. They recommended the use of oral anti-coagulants throughout pregnancy.

In our study, 7 women used heparin at some time during their pregnancy and 5 (71.5%) presented with thrombosis while on heparin (2 in the 1" trimester and 3 in the last trimester). All these patients were under the supervision of either the obstetricians or the cardiologist.

This confirms the risk of shifting women to heparin, especially given through the intermittent subcutaneous route. It should be administered as a continues intravenous drip in a controlled hospital setting.

In another study by Caruso and colleagues from Italy, 1994 (18), reviewed the results of 21 pregnancies in 16 women with prosthetic mechanical valves. Again oral anti-coagulants were discontinued before conception or as soon as possible for subcutaneous heparin (8000-14000 IU every 8-12 hours) throughout the 1st trimester and again in the last period of pregnancy. The spontaneous abortion rate was 15%, pre-term delivery 30% and low birth weight babies (<2500 gm) was 35%. The majority of thrombo-embolic events (6/7) occurred during heparin regimen in 3 mothers, one of them subsequently died. No oral anti-coagulant embryopathy was observed and physical and mental development in the 16-surviving children was good.

They concluded from the study the following, 1) the increased rate of pre-term delivery and infants weighing less than 2500 gm, 2) increased risk of maternal thrombosis related to heparin use, and 3) the good follow-up in the surviving children.

In our study, the rest of the patients (7/12), presented with acute valve thrombosis while on oral anti-coagulants. Three were apparently well anti-coagulated, and their valve thrombosis could be related

to pannus overgrowth limiting valve leaflet. mobility with acute thrombus on top. Four patients were poorly anti-coagulated, and could have developed valve thrombosis any time in their life, however, pregnancy with its increased thrombotic tendency could have precipitated the event.

We did not try thrombolysis in any of our patients, which is against departmental policy. Reports of thrombolysis describe variable efficacy in relieving prosthetic obstructions. Reports of thrombolysis during pregnancy, were almost all complicated by severe uterine bleeding and abortion (19-22). Also, its not uncommon to develop valve re-thrombosis (-25%) requiring surgical interference.

From the above study and from reviewing the world's literature we can recommend the following;

1) Women with prosthetic valve and who already have children, should be strongly advised in favor of contraception or sterilization.

2) Oral anti-coagulants are to be continued throughout pregnancy, keeping the INR 2.5-3.0, until an estimated two weeks before delivery, the patient should be admitted to the hospital to receive continuous IV heparin in full anti-coagulation dose. While the mother and fetus are under close observation, any problem can be immediately recognized and delivery if necessary expedited. There is no need to reverse heparin before vaginal delivery because the contracting uterus reduces blood loss, the heparin effect wanes quickly, and to ensure that there is minimal break in continuity of anti-coagulation to the mother. Once the baby is delivered, oral anti-coagulants can be re-started and heparin continued until PT- INR is back to therapeutic range. In the case of surgical delivery, heparin can be briefly partially reversed immediately before cesarean section, then re-started and continued until oral anti-coagulant take over is completed.

3) The risks of thrombo-embolic events in pregnant women treated with well controlled oral anti-coagulates are no greater than reported in the non-pregnant population with mechanical heart valves. If the INR is maintained between 2.53.0, the chance of oral anti-coagulants damaging the fetus is small. Although, there is an increased risk of abortion (-25%) in women on oral anti-coagulants compared with (-15 %) in healthy women, but the risk of a damaged child being born is no more than 5%.

4) Young, poor and illiterate women with poor access to medical facilities and with intention to make families, the use of using bio-prosthesis should be considered inspite of the relatively rapid deterioration rate in such patients.

5) Patient compliance could be much improved by decentralization through anticoagulation management and standardization of PT test by INR reporting.

6) Communicating the hazards and limitations of shifting pregnant women to heparin in the 1st trimester to our colleagues in the obstetric and cardiology department.

References

1) Cohn LH, Aranki SF, Rizzo RJ, et al. Decrease in operative risk of re-operative valve surgery. Ann Thorac Surg 1993, 56 (1):15-20.

2) Kawachi Y, Matuzaji K, Tominaga R, et al. The risks of re-operation for

prosthetic valve dysfunction. Surg Today 1994; 25 (5)- 415-9.

3) Mustafa R, Philip I, Bohm G, et al. Thrombosis of heart valve prosthesis; favorable and prognostic factors based on a study of 41 patients. Ann Chir 1994; 48 (3): 243-7.

4) Westbay S, Parry AJ, and Forfar JC, et al. Reoperations foe prosthetic valve endocarditis in the third trimester of pregnancy. Ann Thorac Surg 1992; 53: 263-5.

5) Rossouw GJ, Knott-Craig CJ, Barnard PM, et al. Intracardiac operations in seven pregnant women. Ann Thorac Surg 1993;55:1172-4.

6) Abdel-Aziz W. Evaluation of the use of bi-leaflet versus tilting disc prosthetic valves in the mitral position. NW Thesis, Ain Shams University,1995.

7) Deviri E, Sareli P, Wisenbaugh T, et al. Obstruction of mechanical heart valve prosthesis; Clinical aspects and surgical management. J Al-n Coll Cardiol 1991; 17: 646-650.

8) Hall JG, Pauli RM, Wilson KM, et al. Maternal and fetal sequelae of anticoagulation during pregnancy. Am J Med 1980;68:122-140.

9) Quik AJ, Stanley-Brown M and Bancroft FW, et al. A study of the coagulation defect in hemophilia and in jaundice. Am J Med Sei 1935; 190:501-51.

10) WHO Expert Committee on Biological Standardization. Requirements for thromboplastins and plasma used to control oral anticoagulant therapy. Tech Rep Ser 687, Genava, World Health Organization, 1983;81-105.

11) Becker RM. Intracardiac surgery in pregnant women. Am Thorac Surg 1983; 36: 453-8.

12) Kohl KS, Friesen RM, Livingstone RA, et al. Fetal monitoring during maternal cardiac surgery with cardiopulmonary bypass. Can Med Assoc J 1975; 112: 1102-4.

13) Lamb NW, Ross K, Johnstone AM, et al. Fetal heart monitoring during open heart surgery. Two case reports. Br J Obestet Gynaecol 1981; 88:669-74.

14) Martin MC, Pernoll ML, Boruszak AN, et al. Cesarean section while on cardiac bypass; report of a case. Obest Gynaecol 1981; 57 (suppl): 415-55.

15) Hawkins DF. Drug treatment of medical disorders in pregnancy. In Hawkins DF (Ed): Drugs and pregnancy, 2d ed. Edinburgh, Churchill Livingstone, 1987: 90-114.

16) Howie PW. Anticoagulants in pregnancy. Clin Obest Gynaecol 1986; 13: 349-364.

17) Salzar E, Izaguirre R, Verdejo J, et al. Failure of adjusted doses of subcutaneous heparin to prevent thrombotic phenomena in pregnant patients with mechanical valve prosthesis. J Am Coll Cardiol 1996, 27 (7): 698-703.

18) Caruso A, De Carolis S, Ferrazzani S, et al. Pregnancy outcome in women with cardiac valve prosthesis. Eur J Obest Gynaecol Reprod Biol 1994; 54 (l):711.

19) Rajasekhar D, Balakrishnan KG, Venkitachalam CG,et al. Thrombolytic therapy for prosthetic cardiac valve thrombosis. Indian Heart J 1994; 46 (2): 1015.

20) Ramamurthy S, Talwar KK, Saxena A, et al. Prosthetic mitral valve thrombosis in pregnancy successfully treated with streptokinase. AM Heart J 1994; 127: 446-8.

21) Souto JC, Zuazu-Jausoro I, Mateo J, et al. Short-term treatment of thrombosis of heart valve prosthesis with high doses of streptokinase. Presentation of 5 cases. Med Clin (barc) (Abstract) 1991; 96 (7): 261-4.

22) Edmunds LH. Thrombolytic and bleeding complications of prosthetic heart valves (collective review). Arm Thorac Surg 1987;44:430.

23) Pansini S, Ottino G, Forsennati PG, et al. Reoperation on heart valve prosthesis; An analysis of operative risk and late results. Ann Thorac Surg 1990; 50: 590-6.

Transatrial Repair of Tetralogy of Fallot one Step Approach

ABSTRACT

Background: Tetralogy of Fallot (TOF) repair can be done by different techniques: transventricular repair, transatrial repair combined with transventricular and/or transpulmonary with or without transannular patch. In this study, we used transatrial approach alone for VSD closure, adequate resection of the infundibulum and pulmonary valvotomy.

Patients and Methods: Forty two patients with TOF were operated upon in the period from April 1997 to December 1998 at Cairo University hospitals. Nineteen patients (Group. A) with an age range from 18 months to 12 years, with pulmonary artery index (PAI) > 200 and a Z value >-3 and a Mc Goone ratio > 1.8, were operated upon using transatrial approach only. These patients were compared to 23 patients with TOF with comparable pathologies and age, using other combined approaches (Group B).

Results: During the period from April 1997 to December 1998 there were no moralities. Group A patients had a right ventricular to systemic pressure ratio (P RV /LV) ranging from 45% to 60% (mean 52%), the mean gradient across the right ventricular outflow tract (RVOT) ranged from 10 - 40 mmHg (mean 21 mmHg) . In Group B, P RV/LV ranged from 45% to 70% mean (58%) and the mean gradient across the RVOT was 10-48 mmHg (mean 27). Group A patients showed no significant difference in the RVOT obstruction and PRV/LV ratio, but had a significantly shorter clamp time, ventilatory support time and a lower dose of inotropic support compared to Group B patients

Conclusion: Transatrial approach can be done safely in properly selected patients with TOF. The results are comparable to conventional techniques.

Hesham A. Shawky, MD

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INTRODUCTION

Tetralogy of Fallot is a congenital cardiac malformation characterized by underdevelopment of the right ventricular infundibulum with anterior and leftward displacement of the infundibular (conal, outlet) septum and its parietal extension leading to big VSD and right ventricular outflow tract (RVOT) obstruction. This obstruction occurs in the form of isolated infundibular stenosis in 26% of cases (infundibular chamber), presents as infundibular and valvular stenosis with good sized pulmonary ring in 26%, as combined infundibular, valvular and annular stenosis in 16%, as diffuse RVOT hypoplasia (infants with severe cyanosis) in 27%, and finally, very rarely as valvular PS with no infundibualr stenosis in 5% of cases. [1]. As we can see that almost 50 -

Department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt.

60% of patients with TOF have good pulmonary annulus.

There are more than one surgical modality to treat patients with TOF such as transventricular incision either vertical or transverse with/or without transpulmonary approach, transatrial combined with transpulmonary and 1 or transventricular approach and transannular patch with and without a monocusp could be used in addition to other techniques. Transatrial approach alone or even transpulmonary alone is described .[2,3]

There are some factors that affect the surgical outcome like residual RVOT obstruction, P RV/LV and the size of the ventriculotomy. The smaller the ventriculotomy the better the prognosis. The outcome is poorer if the ventriculotomy exceeds one third of the size of the ventricle. [4,5,6] The RV function is much better in patients repaired by transatrial approach, and the ventricular arrhythmia is much less in comparison to the ventricular approach [7].

Patients and Methods

In this study 19 patients were operated through a transatrial approach only in the period between Jan 1997 - Dec 1998 Cairo University hospitals. (Group A). A matching group of 23 patients were chosen as control group to assess the efficiency of the technique (Group B), all patients had preoperative full Echo cardiograph, and cardiac catheterisation

Transatrial Approach technique

Selective bicaval cannulation is done, then the atrial incision is made parallel to the AV groove. The VSD and outflow are identified. The parietal band of the conal septum is divided 5-10 mm from the aortic valve. The Os ventricular is divided and as much as possible of the fibrous tissue is removed, muscle bands are divided in the direction of pulmonary artery, using a right angled instrument to separate the muscle band and cut it, this is to avoid going out the free wall of the RVOT. Visualization of the pulmonary artery is absolutely essential. Hegar dilators are passed one after the other through the atrium till a size is reached that passes snugly but not tightly. Another option is to use the Tubbs' dilator and try to open the pulmonary valve to the predicted Pulmonary Artery size and then use the Hegar to size it. The size of the Hegar is changed to a Z- value and if it is > -3, this is considered satisfactory at this stage. {fig. 1} [1,8] If the Z- value is < -3 an additional procedure will be done to the RVOT and the patient is excluded from the group. The VSD is then closed in the regular fashion. Re-warming is started and the aorta is unclamped.

At 33-34°C, the perfusionist is asked to go off pump shortly, the RV pressure is measured and if it is < 0.6 of aortic pressure re-warming is continued. If the P RV/LV is >0.6 cooling is re-started and further procedure is done for the RVOT and the patient is excluded from the group .

At the end of re-warming and after going off bypass for 30 minutes, P RV/ AO, PA pressure are measured. RVOT mean Gradient is measured.

In the postoperative period, the time the patient is kept on the ventilator is recorded the dose and the duration of the inotropic support is measured. Other parameters

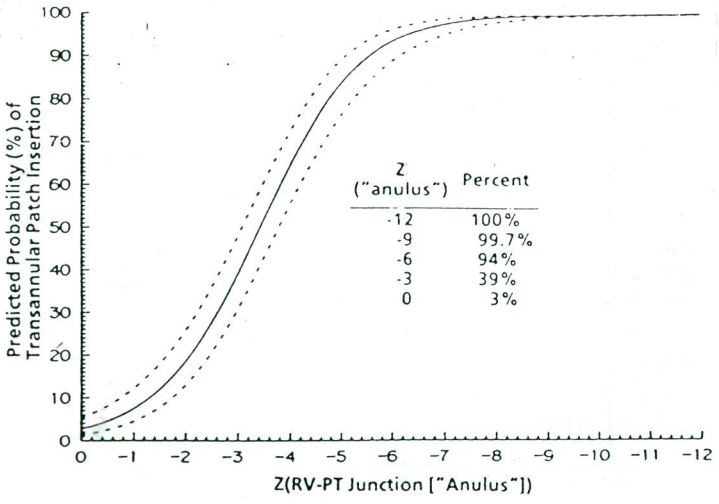

Figure (1): Nomogram indicating the predicted probability of transannular patch insertion during repair of tetralogy of Fallot with pulmonary stenosis, according to the dimension, expressed as Z-value, of the pulmonary valve "aulus" (see original paper for data and equation).

recorded were the amount of bleeding, and the length of the ICU and hospital stays.

Statistical analysis

The results of both groups were compared using the Student T-test

Results

In this study two groups of patients where compared, Gr. A 19 patients were operated through a single incision only in the right atrium with a fixed protocol described above, and Gr. B 23 patients chosen to have similar pathologies Table (1).

Gr. B comprised 23 patients operated in our department with other surgical technique by different surgeons during the same period of time. (table 2)

Surgical technique Evaluation:

The two groups of patients were compared. Group A patients had a significantly shorter clamp time and cardio Pulmonary Bypass (CPB) time. No significant difference was found as concerns P RV/LV. If P RV/LV exceeded 0.6, there was still the option to go again on bypass to do further surgical technique. However, these patients were then excluded from Group A. Table (3). (Five patients were crossed over to Gr. B because of having P RV/LV > 0. 6 and required a transpulmonary approach to complete the procedure).

The patients of group A left the operating room with smaller dose of inotropes, the dose of adrenaline did not

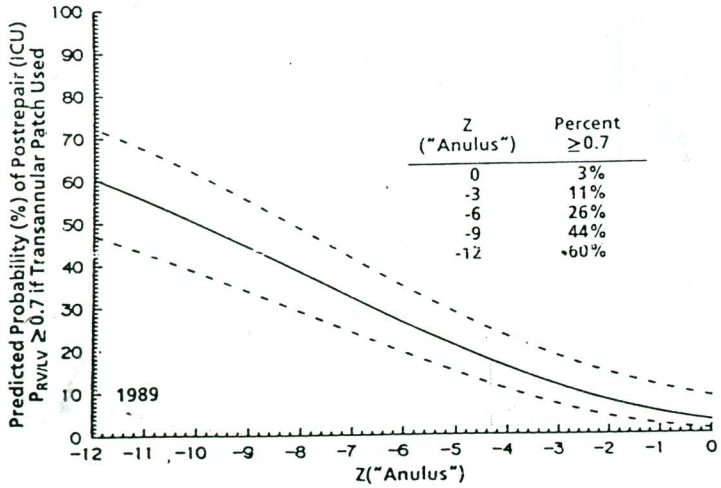

Figure (2): Nomogram showing the predicted probability of the postrepair PRVA (measured in the intensive care unit) being greater than 0.7 after repair that includes insertion of a transannular patch, according to the dimension, (expressed as Z-value) of the pulmonary "aulus" as detemined on the preoperative cineangiogram (see original paper for data and equation).

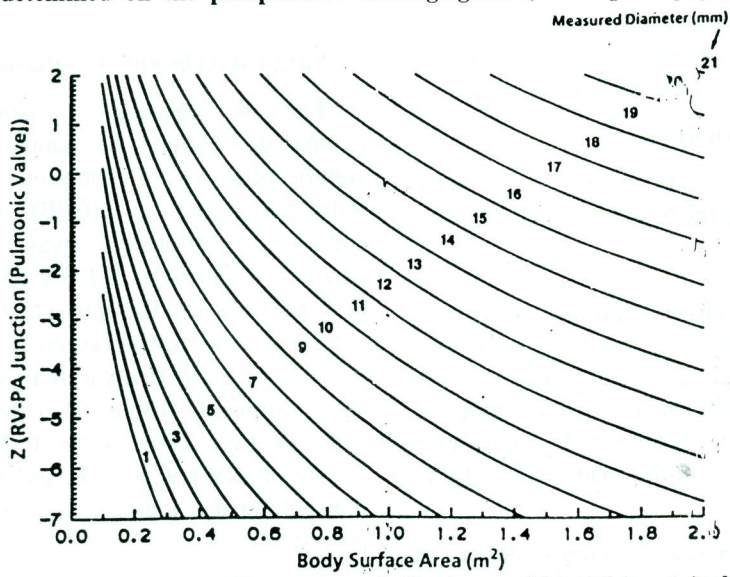

Fig. (3): Nomogram expressing the measured diameter of the right ventricular - puimonary artery junction, so-called r is," (isobars) in a patient of a given body surface area (horizontal axis) as the Z-value (vertical axis). The mean norr equation to calculate the Z-values were obtained form the publication of Rowlatt and colleagues.

Table (1): Patient population in both surgical groups.

	GR A (n=19)	Gr. B (n=23)	
Age	1.5-6 yr.	1.5 - 8yr	p NS
Wt	>10 kg	>10 kg	p NS
Hb.	16 -21 gr.	17 - 22 gr.	p NS
McGoone	>1.8	>1.8	p NS
Nikata index	>200 (200 -330)	>200 (200- 340)	p NS
Z-value	1 - (-3)	1 -(-5)	p NS

Table (2): Group B Surgical technique.

8 PT	TRANSANNULAR PATCH (2 WITH MONOCUSP
10 pt	Transatrial and transpulmonary
5 pt	Transatrial ,transventricular, and transpulmonary

Table (3): *Due to different techniques used **If it is above 0.6 an additional technique is used, and the patient is excluded from the group

	GR. A	GR. B	
Clamp time	25-57 m(40 m)	27 -70 m (56m)*	p< 0.05
CPB	45-70 m(53 m)	45-100m (65m)*	p< 0.05
RV/AO	0.4-0.6 **	0.4-0.7	p NS
LVOT	Gr.15-45 mm Hg	15 -40 mm Hg	p NS

Table (4): Post operative evaluation.

	GR A	GR B	
Vent. time	0 -8 hr	4 - 24 hr	p< 0.001
Inotrops period	24 -36 hr	48 -72 hr	p< 0.01
Bleeding	100- 350 ml	100 -400 ml	p NS
ICU Stay	2- 5 days	2 -9 days	p< 0.01
Hospital stay	5-13 days	5 - 20 days	p< 0.01

exceed 0.05 microgram/kg/hr, as for group B the dose of adrenaline ranged from 0.03-0.32 microgram/kg/hour. On leaving the operating room, all Group B patients required a renal dose of dopamine as well as nitroglycerin

Post-operative Evaluation:

In the early postoperative period there was a significant difference in the period the patient spent on the ventilator (ventilator time). In Group A the time ranged from 0-8 hours. Three patients were extubated on table. In Group B the ventilator time ranged from 4-24 hours (m 12 +/-4). All our patients were kept on inotropic support for the first 24 hours with no attempt to wean them as a part of our protocol. All the patients in Group A were weaned smoothly over the next 12 hours, as for Group B patients were weaned over the next 24-72 hours. The above two factors lead to shorter I C U and hospital stays in Group A. Table (4).

Discussion

In 1992 the transatrial approach for repair of TOF was introduced at Kasr el Aini Since then around 400 cases were done, using a transatrial approach in combination with transpulmonary and / or trans-ventricular with or without a transannular patch . In this study we tried to evaluate the repair of some selected patients with TOF through a transatrial approach only and compared the results with other patients operated upon in our unit with other techniques.

Selection of patients is the key stone for the success of this surgical technique, which was attempted in all patients. The success depends on the intraoperative Z-value. As we can see from {figures 2,3}, [1,9,10] if we use a Z-value > -3 as a cut edge only 39% need a trans -annular patch, and only 11% will have a P RV/ LV > 0. 7 which is considered not acceptable for the repair of TOF . These figures also show that 89% will have a favorable outcome and a predicted lower P RV/LV. Taking this in account this study was designed to evaluate the efficiency of the repair of TOF by transatrial approach only.

It has been reported in the literature that the absence of the ventriculotmy and transannular patch influence the outcome markedly. Although no change in the operative mortality was reported [9, 11] in patients with ventriculotomy or transannular patch, there was significant depression in the RV function, response to exercise [10,12,13] and higher incidence of arrhythmia and sudden death [14,15,16]. In this study there was no long term follow up. However, in the absence of the ventriculotomy the better RV performance was reflected in the significantly smaller dose of inotropes in the operating room and the ICU. Using the transatrial approach only did not compromise the repair as evidenced by pressure measurements before complete re-warming (PRV/LV). The response of the heart to volume gives the surgeon the guide whether to continue re-warming or to go again for further resection or other surgical procedure. Accepting the upper limit of P RV/LV as 0.6 rather than 0.7 leads to a smoother postoperative course [10,13] . As for the postoperative period the patients stayed on the ventilator for a significantly shorter period in Group.

A (0-8 hours) with on table extubation

in comparison to 4- 36 hr. In Gr. B. Also the dose and the duration of inotropic support was significantly shorter.

Conclusion

Transatrial approach for TOF is simple technique which can be applied in a selected sub-group of our patients with good out come. This selection depends on:

1- Weight of the patient: We considered > 10 Kg as a suitable weight for our patient selection, as the size of the Hegar, and the Tubbs' dilators avaílable at present is too big to manipulate in hearts of smaller babies. 2-Favorable anatomy from the angiogram and Echocardiography with a McGoone ratio> 1.8 and Nakata index >200.3 - A Z-value of the pulmonary annulus > -3 at operation. Anti-clockwise rotation of the heart displaces the PA posteriorly and makes manipulation and visualization of LVOT difficult.

4- Orientation with the anatomy through this approach will need a learning curve from the surgical team.

In future, a larger number of patients should be studied for a longer period to evaluate merits and long term results of this technique. This approach should also be attempted in smaller children < 10 kg, and even in neonates [4,11,17].

Reference

1. Kirklin J, Barratt -Boyes B: Cardiac surgery second edition 1992 vol. 3 chapter 23, 886-979.
2. Stellin G, Milanesi O, Rubino M, Michielon G, Bianco R, Moreolo GS, Boneva R, Sorbara C, Casarotto D: Repair of Tetralogy of Fallot in the first six months of life: transatrial versus transventricular approach. Ann Thorac Surg 1995 Dec; 60 (6 Suppl): S 588-91.
3. Pacifico AD, Sand ME, Bargeron LM Jr, Colvin: Transatrial-transpulmonary repair of tetralogy of Fallot. J Thorac Cardiovasc Surg 1987 Jun; 93 (6): 919 .
4. Karl TR, Sano S, Pornviliwan S, Mee RB Tetralogy of Fallot: favorable outcome of neonatal transatrial, transpulmonary repair. Ann Thorac Surg 1992 Nov; 54 (5): 903-7.
5. Dietl CA, Torres AR, Cazzaniga ME, Favaloro RG Right atrial approach for surgical correction of tetralogy of Fallot. Ann Thorac Surg 1989 Apr;47 (4): 546-51; discussion 551-2.
6. Brizard CP, Mas C, Sohn YS, Cochrane AD, Karl TR Transatrial-transpulmonary tetralogy of Fallot repair is effective in the presence of anomalous coronary arteries. J Thorac Cardiovasc Surg 1998 Nov; 116 (5): 770-9.
7. Coles JG, Kirklin JW, Pacifico AD, Kirklin JK, Blackstone EH The relief of pulmonary stenosis by a transatrial versus a transventricular approach to the repair of tetralogy of Fallot. Ann Thorac Surg 1988 Jan;45 (l):7-10 .
8. Edmunds LH Jr, Saxena NC, Friedman S, Rashkind WJ, Dodd PF Transatrial repair of tetralogy of Fallot. Surgery 1976 Dec;80(6):681-8
9. ER Kirklin JK, Kirklin JW, Blackstone Milano A, Pacifico AD Effect of transannular patching on outcome after repair of tetralogy of Fallot. Ann Thorac Surg 1989 Dec; 48 (6): 783-9.
10. Miura T, Nakano S, Shimazaki Y,

Kobayashi J, Hirose H, Sano T, Matsuda H, Kawashima Y Evaluation of right ventricular function by regional wall motion analysis in patients after correction of tetralogy of Fallot. Comparison of transventricular and nontransventricular repairs. J Thorac Cardiovasc Surg 1992 Oct; 104 (4): 917-23.

11. Munkhammar P. Cullen S. Jogi P. de Leval M. Elliott M. Norgard G. Department of Pediatric Cardiology, University Hospital of Lund, Sweden. Early age at repair prevents restrictive right ventricular (RV) physiology after surgery for tetralogy of Fallot (TOF): diastolic RV function after TOF repair in infancy. Journal of the American College of Cardiology. 32 (4): 1083-7, 1998 Oct.

12. Singh GK. Greenberg SB. Yap YS. Delany DP. Keeton BR. Monro JL. Right ventricular function and exercise performance late after primary repair of tetralogy of Fallot with the transannular patch in infancy. American Journal of Cardiology. 81 (11): 1378-82, 1998 Jun.

13. Norgard G. Gatzoulis IM. Josen M. Cullen S. Redington AN. Does restrictive right ventricular physiology in the early postoperative period predict subsequent right ventricular restriction after repair of tetralogy of Fallot?. Heart. 79 (5): 481-4, 1998 May.

14. Paixao A. Oliveira M. Bernardino L. Kaku S. Ventricular arrhythmia after surgical repair of Tetralogy of Fallot]. [Portuguese] Revista Portuguesa de Cardiologia. 17 (2):169-71, 1998 Feb.

15. Gunal N. Tokel K. Kahramanyol O. Ozer S. Celiker A. Ekici E. Yurdakul Y. Kutsal A. incidence and severity of arrhythmias and conduction disturbance after repair of tetralogy of Fallot. Turkish Journal of Pediatrics. 39 (4): 491-8, 1997 Oct-Dec.

16. Fischlein T. Bouterwek S. Bohmer C. Klinner W.R Long-term survival in patients with repair of tetralogy of Fallot: 36-year follow-up of 490 survivors of the first year after surgical repair [see comments]. Journal of the American College of Cardiology. 30 (5): 1374-83, 1997, Nov 1.

17. Kesih. Rubino M. Michielon G. Bianco R. Moreolo GS. Boneva R. Sorbara C. Casarotto D. Repair of tetralogy of Fallot in the first six months of life: transatrial versus transventricular approach. Annals of Thoracic Surgery. 60 (6 Suppl): S588-91, 1995 Dec.

Transthoracie Approach to Liver Hydatid Cysts

ABSTRACT

In this study, 16 patients with liver hydatid cysts treated by the right transthoracic approach were presented. They were divided into two groups. Group I: included 9 patients having liver hydatid cysts only whether simple (5 patients) or with intrathoracic complications (4 patients). Group II: included 7 patients having both liver and pulmonary hydatid cysts,. simple (6 patients) or complicated (1 patient). One patient of group II had bilateral lung and liver cysts. The age ranged from 15-56 years (mean 43 years) and 10 patients (62.5%) were males. Of the 4 patients of group I presenting by intrathoracic complications of liver cysts; 3 patients had bronchobiliary fistulae and one patient had empyema thoracis. The patient of group II with complicated lung cyst presented with hydatidemesis from bronchial rupture of the cyst.

All the liver hydatid cysts of both groups were removed by the transthoracic approach and right phrenotomy. The lung cysts were removed by the Barrett's intact endocystectomy technique without prior aspiration of the cysts. For the complicated lung cyst of group II, atypical lung resection was done. For the three patients (18.75%) with bronchobiliary fistulae of group I right lower lobectomy was performed for two patients and atypical lung resection for one patient. Decortication was done for two patients (12.5%). The direction of drainage of the residual liver cavity was abdominal in 11 patients (68.75%) and thoracic in 5 (31.25%). Postoperative courses of mebendazole were given to 12 patients (75%).

No mortality was reported. Morbidity was in the form of prolonged air leak in one patient (6.25%) and prolonged biliary drainage in one patient (6.25%), both were treated conservatively. No recurrences of the cysts were reported during the period of follow up.

It was concluded from this study that a thorough search should be made in every patient with lung hydatid cyst for associated liver cyst. The transthoracic approach offered a suitable, safe and one-stage procedure to deal with liver cysts associated with right lung cysts and to deal with liver dome cysts.

Khaled Karara. MD

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INTRODUCTION

There are two forms of human hydatid disease; Echinococcus granulosus, which causes the classical cystic hydatid disease, and Echinococcus alveolaris or multilocularis which is a much rarer and more aggressive form in man (1). Ecllinococcus granulosus (Taenia echinococcus. Echinococcus cysticus or hydatidosus) is endemic in sheep and cattle rearing districts in Middle East, Greece, Yugoslavia, Australia and South American

Faculty of medicine, Alexandria University.

countries (1-3). The tapeworm lives in the intestine of its definitive host the dogs. The ova are ingested by the sheep, and occasionally humans, hatch in the stomach, penetrate the intestine and reach the liver with the portal vein radicals. Those escaping the liver reach the lungs, then to anywhere else in the body.

About two thirds of all hydatid cysts in man occur in the liver where they are solitary and in the right lobe in 80% of cases (1). The lung is the second most commonly affected organ after the liver (10-40%) (2-4.). The associated presence of liver hydatid cysts in patients with lung cysts varies from 4-25% (4,5).

In this study, the patients are presented for whom the transthoracic approach with right phrenotomy was used to deal with liver hydatid cysts with or without associated right lung cysts and with or without intrathoracic complications.

Material and Methods

The 16 patients included in the study presented to Alexandria Main University Hospitals in the period from January 1990 till December 1997. They were divided into two groups:

Group I: included 9 patients having liver hydatid cysts only. whether simple or with intrathoracic complications.

Group II: included 7 patients having both liver and pulmonary hydatid cysts, simple or complicated.

For each patient, thorough history taking and clinical examination were done. Laboratory tests included in addition to routine tests, complement fixation test for hydatid disease (Weinberg test), sputum and pleural fluid analysis, and bacteriological cultures. Plain X-ray chest and ultrasonography abdomen were done for every patient and CT scans chest and/or abdomen were done when required.

General endotracheal anaesthesia was routinely done using ordinary cuffed endotracheal tubes. However, in the cases of bronchobiliay fistulae, single lung anaesthesia was performed. During anaesthesia, the patients were carefully monitored for developing anaphylactic reactions and the drugs needed to counteract them were prepared beforehand. The head of the table was kept lower, so as when any accidental endobronchial rupture occurs, the fluid flows out along the trachea to be aspirated.

Surgery for Group I:

A right posterolateral low thoracotomy in 9h or 10th space was done for simple liver cysts. For cysts having intrathoracic complications, a higher thoracotomy in the 7th or 8th space was required to deal with the associated lung pathology. The diaphragm was inspected and the location of the liver cyst was identified. The pleural cavity on either side of the planned diaphragmatic incision was packed with saline pads. The diaphragm overlying the cyst was radially incised (4). The edges of the diaphragmatic incision were sutured to the edges of the skin incision creating a well in the bottom of which rested the liver cyst (Fig. 1). This was done with the aim of securing the pleural cavity from any possible contamination from the cyst. The pericyst was then incised and the main and daughter cysts were removed. The residual

cavity was sterilized using 0.5% cetrimide and chlorhexidine (Savlon®, 3% cetrimide) or 0.5% povidone-iodine (Betadine antiseptic solutions, 10% povidone-iodine) according to surgreon's preference. Any biliary leak was closed with fine absorbable sutures. A self-retaining mushroom catheter was placed in the cavity and brought out of the abdomen through a right loin stab. The diaphragm was then closed and the pleural cavity was drained by an intereostal tube under-water seal.

In complicated liver cysts with biliary bronchial fistulae, the cyst and diaphragm were disconnected from the lung. The cyst cavity was cleaned from the purulent remnants of the main and daughter cysts, the biliary leaks were closed, and thoracic or abdominal drainage was instituted and the diaphragm was repaired. A trial was made to preserve the pulmonary tissue, but if the right lower lobe was found to be grossly diseased, lobectomy was performed. In cases of empyema thoracis complicating infected liver hydatid, decortication together with cleaning of the liver cavity were done. Thoracic rather than abdominal drainage was done to avoid contamination of the peritoneal cavity.

Surgery for Group II:

The pulmonary cysts were dealt with by the transthoracic approach following the standard technique (2,6,7). For lower lung cysts, a posterolateral thoracotomy in the 7th or 8th space was done. For upper lobe cysts associated with liver cysts, double thoracotomy technique through a single skin incision was required. Thoracic exploration was then done, the cyst was identified as a tense grayish-white swelling on the surface of the lung with some filmy adhesions to the parietal pleura. The operative field around the cyst was isolated with saline pads for avoidance of spillage of cystic fluid in case of cyst rupture. Barrett's technique of intact endocystectomy was then used; where the endocyst was removed intact from within the pericyst without prior aspiration of the cyst to avoid contamination of the field (6,7). The free flaps of the pericyst were then excised and the margin was underrun with continuous absorbable suture. Bronchial fistulae were closed. Capitonnage was done to close the residual cavity by purse-string absorbable sutures starting from the bottom of the cavity (2-4). If the mouth of the cavity was found to be sufficiently wide and the cavity was shallow, it was left open to the pleura, marsupialized, especially so if the walls of the cavity were friable, not holding the sutures (8).

The liver hydatid cysts associated with lung cysts were removed through right phrenotomy following the measures mentioned above for simple liver cysts (3,4).

Results

Out of the 16 patients studied, 10 were males (62.5%) and 6 were females (37.5%). Their age ranged from 15-56 years (mean 43 years). All the patients were Egyptian citizens except one Libyan female patient. Two patients were working, outside Egypt during the period of their infestation, one in Iraq and one in Libya. All the patients, except two, were living in rural areas or oases where sheep rearing occurs. All were infected by Echinococcus granulosus.

Presentation:

As shown in table (1), 5 of the 9 patients of group I presented with simple liver cysts.

Table (1): Location and nature of the hydatid cysts.

	Simple	Complicated	Total n (%)
Liver	5	4*	9 (56.25%)
Liver + Rt. Lung	5	1#	6 (37.50%)
Liver + Both Lung	1	-	1 (6.25%)
Total n (%)	11 (68.75%)	5 (31.25%)	16 (100%)

*** Complicated liver cysts.** **# Complicated lung cyst**

Table (2): Presentation according to location.

	Liver	Liver+R1.Lung	Liver+Both Lungs	Total n (%)
Dyspnoea	4	6	1	11 (68.75%)
Pain	5	4	1	10 (62.50%)
Cough	4	3	-	7 (43.75%)
Asymptomatic	2	2	-	4 (25.00%)
Fcycr	31	1	-	4 (25.00%)
Hydatidemesis	3	1	-	4 (25.00%)
Bile stained spulum	3	-	-	3 (18.75%)
Empycma Thoracis	1	1*	-	2 (12.50%)

*** This patients had previous lung hydatid excision and empyema was a complication of that procedure.**

Table (3): Surgical procedures.

	n	%
Lung cyst excision	6	37.50
Atypical lung resections	2	12.50
Lobectomy	2	12.50
Decortication	2	12.50
Liver cyst excision	16	100
Preop. tube thoracostomy	2	12.50
Direction of drainage of liver cysts: Abdominal	11	68.75
Thoracic	5	31.25
Postop. tube thoracostomy	16	100

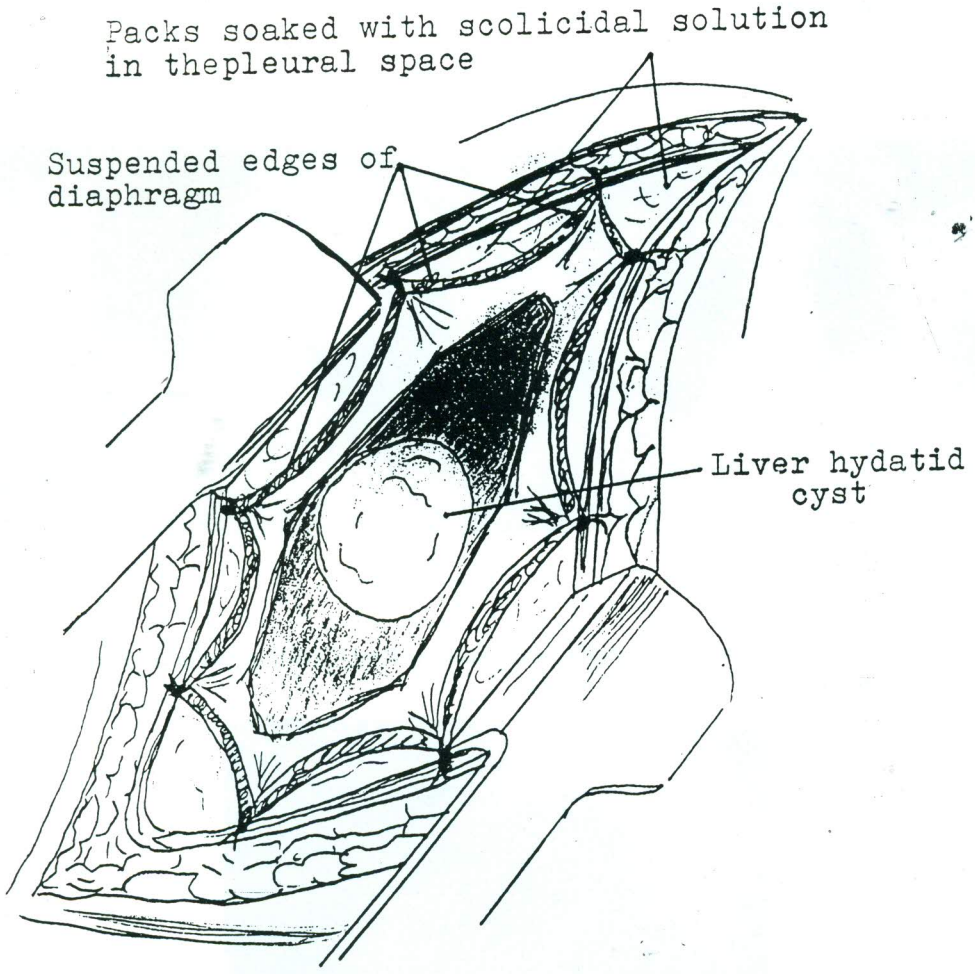

Fig. (1): transthoracic approach to isolated liver cysts: (a) Thotacotomy in the tenth space, the rib spreader in place. (b) The pleura protected by packs socked in scolecidal solution. (c) The diaphragm radially cut and suspended. (d) The liver cyst is seen on the liver surface.

The remaining 4 patients had liver cysts with intrathoracic complications; 3 patients with bronchobiliary fistulae and one with empyema. Of the 7 patients of group II, 5 had simple right lung and liver cysts, one with simple bilateral lung and liver cysts and one with complicated right lung cyst (bronchial rupture of the cyst) associated with liver cyst.

Table (2) shows that the commonest presenting symptoms were dyspnoea, pain and cough. The three patients with bronchobiliary fistulae stated that

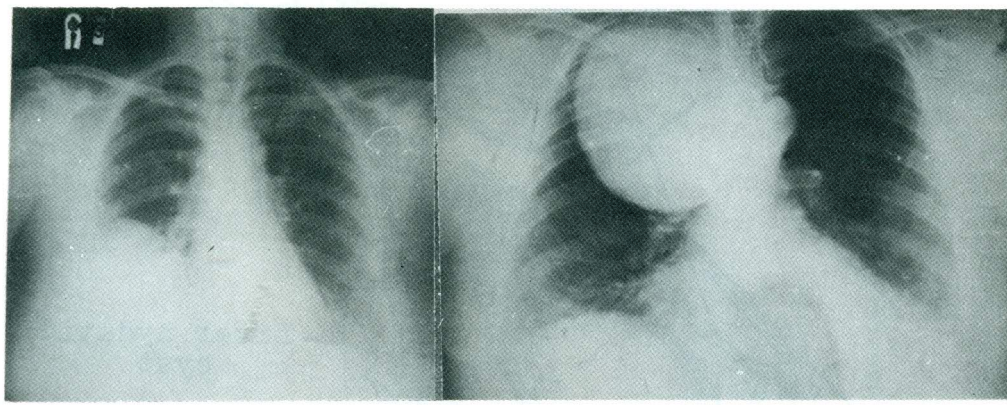

Fig. (2): (a & b) Plain chest radiographs demonstrating lung hydatid cysts, in the lower lobe (a-to the left) and the upper lobe (b-to the right).

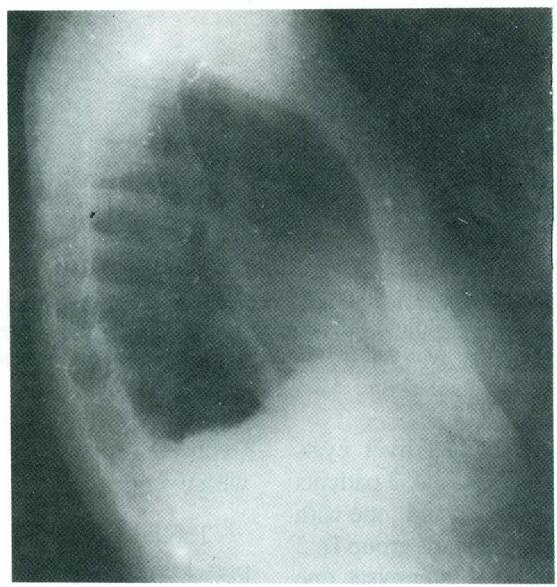

Fig. (3): Pain X-ray chest. lateral view-showing right lower lobe hydatid cyst with bronchial rupture exhibiting "water lily" sign.

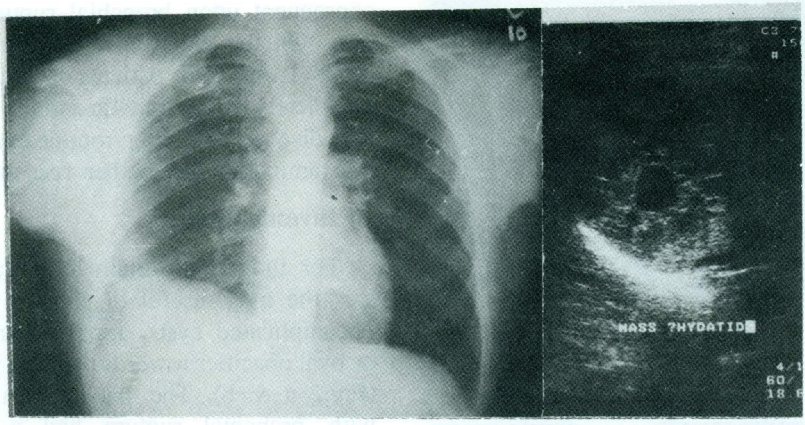

Fig. (4): (a & b). a-Plain X-ray chest showing elevated right diaphragmatic copula. b-Ultrasonography abdomen of the same patient demonstrating "liver dome" hydatid cyst.

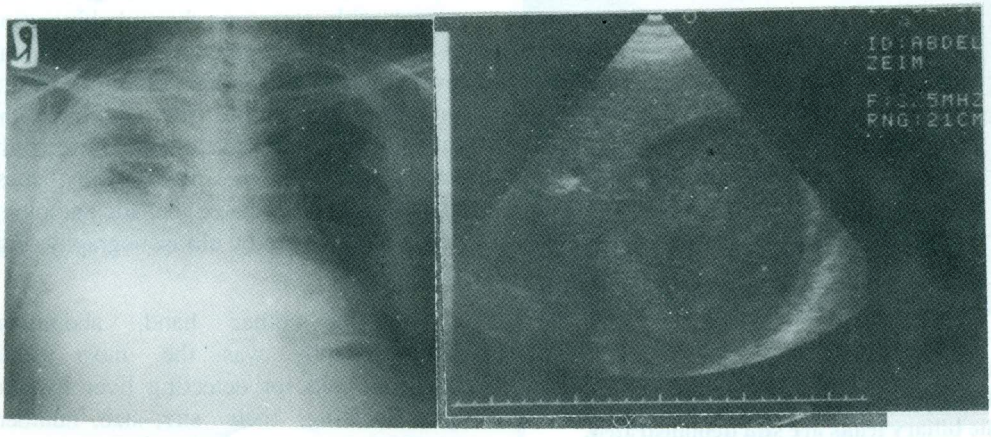

Fig. (5) (a&b). a-Plain X-ray chest of a patient presenting with empyema thoracis After tube insertion, the right diaphragmatic copula appears elevated. b-Ultrasonography abdomen of the same patient showing complicated liver hydatid cyst.

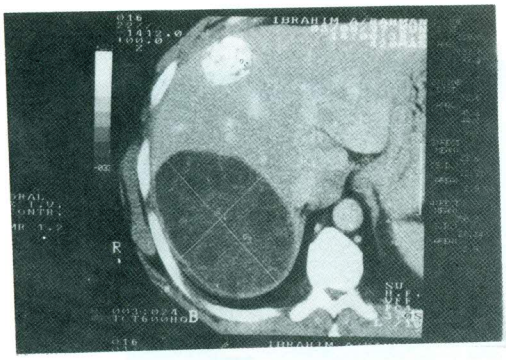

Fig. (6): CT-scan abdomen showing two hydatid cysts in the right lobe of the liver one is dead and calcified and the other is viable.

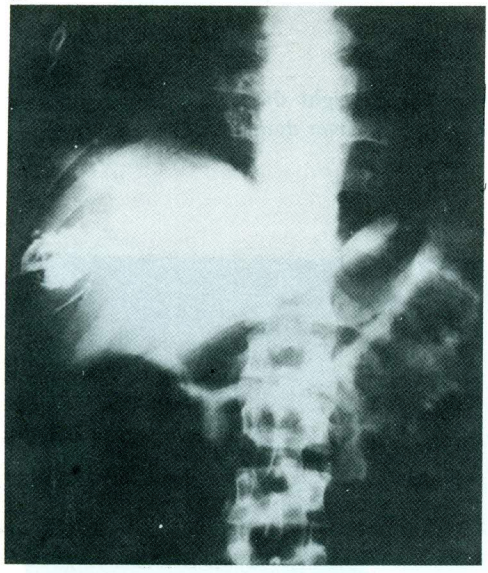

Fig. (7): A sinogram through a thoracic drainage tube placed in the residual cavity in the liver showing small residual cavity but the biliary leaks are still demonstrated.

expectoration was first watery in nature with occasional expulsion of grape skin-like material. Expectoration then became copious, offensive and bile-stained. One patient of group II had also hydatidemesis consequent upon bronchial rupture of the cyst. On the other hand, two patients of group I and two patients of group II were completely asymptomatic and the condition was discovered during, routine examination or examination for another reason.

Investigations:

For lung cysts, plain chest radiograph was the most useful diagnostic tool. The uncomplicated cysts appeared as spherical or oval opacities towards the lung periphery (Fig.2 a & b). The patient with lung cyst with bronchial rupture had a classical water-lily sign (also described as sign of camalote or iceberg sign, Fig. 3) (3,6,8). The commonest location of lung cysts was the right lower lobe, encountered in 6 patients (85.7%) of group II. In patients with liver cysts, raised right diaphragmatic copula may be encountered (Fig. 4a). The patient with empyema showed obliteration of the right costophrenic angle with rising level towards the axilla. After insertion of an intercostal tube for draining the empyema, the marked elevation of the right copula seen in the plain X-ray chest suggested an associated hepatic pathology which was proved by ultrasonography (Fig, 5a).

On the other hand, abdominal ultrasonography was the most useftd diagnostic aid for detecting liver hydatid cysts locating, their site, size, number, calcified or not and noting the presence of daughter cysts so differentiating hydatid cysts from amebic or pyogenic liver abscess and was important in postoperative follow up (Fig. 4b, 5b). CT scans of both the lungs and the liver added another accurate tool

for defining the nature, exact location, number of the cysts and gave more data about, parenchymal lung or liver damage (Fig.6). Sinogram through the thoracic drainage tube placed in the residual liver cavity was helpful in assessing the size of the cavity and the presence of biliary leaks (Fig.7). Immunological tests were not performed routinely for every patient. Casoni's skin test was performed in 7 patients and was positive in 4 of them (57.14%). Complement fixation test (Weinberg) was done for 4 patients and was positive in all of them.

Surgical procedures:

All patients were treated surgically by the right transthoracic approach.

In group II, one-stage procedure was done to remove the associated lung and liver cysts in 5 patients starting by the lung first. In one patient of this group, right thoracotomy was done to remove a lung cyst. As a complication of the procedure, localized empyema developed. Localized decortication was done together with removal of a liver cyst that was overlooked in the first operation. For the patient who had bilateral lung cysts mid liver cyst, a right thoracotomy was done to deal with the right lung and liver cysts. Six months later, the left lung cyst was removed through a left thoracotomy.

The level of the thoracotomy varied. In isolated simple liver cysts, a low thoracotomy in the 10th space was done for 5 patients. For complicated liver cysts with bronchobiliaiy fistulae, higher thoracotomy in the 8th was done to allow lobectomy and liver cyst excision to be done at ease. Double thoracotomy through a single skin incision was done for a patient of Group II having an upper lobe lung cyst and a liver cyst. For the remaining cases, thoracotomy in the 7th space was satisfactory.

As summarized in table 3, all the liver hydatid cysts of both groups were removed by the transthoracic approach and right phrenotomy following the previously described technique. In one patient of group I, a viable and a calcified cyst were present in the right lobe (Fig. 6). Only the viable one was attacked. The direction of drainage of the residual cavity, was abdominal in II patients and thoracic in 5. Preference of thoracic drainage was in complicated septic cases which already produced intrathoracic complications to avoid spreading the infection to the peritoneal cavity. In addition, these cases had already, dense adhesions between the diaphragmatic surface of the liver and the diaphragm making it difficult to attempt abdominal drainage. For simple liver cysts, the abdominal drainage of the residual cavity, was the preferred technique. The reason for that, since early in this series, thoracic drainage was found to be accompanied with more prolonged biliary leakage than abdominal drainage (Fig.7).

In patients with complicated liver cysts, for the patients with bronchobiliary fistulae right lower lobectomy was done for two patients with grossly damaged lobe, and atypical conservative resection to close the fistula in one patient. After cleaning the liver cavity and closing the biliary leak, the diaphragm was thoroughly closed in one patient with abdominal drainage of the cavity. In two patients, because of dense adhesions between the liver and diaphragm and friability of the edges, the cavity was left marsupialized to the pleura and thoracic

drainage was established. Decortication was done for the patient with empyema secondary to rupture of infected hepatic cyst and thoracic drainage of tile hepatic cavity was done (5a,b).

In group II, the Barrett's technique of intact endocystectomy without aspiration was done for the simple lung cysts in six patients. For the patient with complicated lung cyst by bronchial rupture, atypical lung resection was necessary to close the fistula.

Complications:

No mortality, was reported in this study. One patient (6.25%) had prolonged air leak for more than 10 days and was managed by prolonged tube drainage without reoperation. One patient (6.25%) had prolonged biliary drainage for more than 10 days. She had a thoracic drainage tube for her liver cyst for about three months, till finally the leakage decreased and the tube was removed (Fig.7). One patient (6.25%) developed empyema after the first operation for lung cyst. Decortication together with removal of all overlooked liver cyst was done later. Being a complication of the first operation-it was not considered as a complication of the transthoracic approach for liver hydatid cysts, the subject of this study.

Postoperative Follow-up:

12 patients (75%) were given postoperative medical treatment in the form of mebendazole, 20-40 mg/kg/day divided into three doses for the first 21 days of the month for three successive months. The follow-up period ranged from 6 months to five years for 13 patients (81.25%). 3 patients (18.75%) could not be contacted to come for follow up. No cases of recurrence of the cysts were reported in the study in the patients who submitted to follow up. Since it was not our routine to fill the liver cyst cavity with omentum, it was considered a normal finding to find a residual space after removal of the liver cyst that became smaller and smaller on ultrasonographic follow-up.

Discussion

Human cystic hydatid disease was already known to Hippocrates and Galen (1,3). Afler the World War II, great advances in the diagnosis and management of the disease were made (1). Thoracotomy, for dealing With lung cysts became a standard and safe technique (6,7). Thoracotomy was then used to deal with liver hydatid cysts with intrathoracic complications (9). From 1982, reports started to appear about the simultaneous attack of right lung and uncomplicated liver hydatid cysts through right thoracotomy and phrenotomy (4,5,10-15). This was probably because of the advances made by that time in abdominal ultrasonography, liver scintigraphy and CT scans, diagnosing, preoperatively the presence of liver cysts even if asymptomatic. A step further was taken by the simultaneous removal of bilateral lung, cysts via median sternotomy (16). More recently, one-stage surgical procedure for bilateral lung and liver cysts through midsternotomy along with phrenotomy or laparotomy was reported (17,18). The advances made in video assisted thoracoscopic surgery from the early nineties allowed the removal of dead hydatid cysts thoracoscopically (19). Transthoracic approach to deal with

uncomplicated cysts on the upper surface of the liver. "liver-roof or liver-dome cysts", without associated lung, cysts was recently documented (3).

The goals of surgery of simple lung hydatid cysts are to remove the parasite, to avoid contamination of the field and to deal with the empty lung cavity. To achieve these goals, two surgical principles are available; the conservative and the radical. The **conservative technique** can be performed as;1) Endocystectomy: a-with prior puncture-aspiration of the cyst followed (4) or not (8,18) by the instillation of a scolecidal solution, puncture-aspiration endocystectomy (8), this however carries the risk of contamination of the exposed tissues (2,6), and is better reserved for tense cysts more than 10cm in diameter (18), b-Barrett's technique of intact endocystectomy without prior aspiration, the technique that was utilized ill this study and preferred by many authors (2,6,7), 2) Pericystectomy, the Perez-Fontana's technique. where both the endocyst and the pericyst are excised (3). The fear of cyst rupture and contamination of the field should not, however, be over-estimated. True recurrences after documented cyst rupture during surgery occurs m only 10% of cases (7). The radical technique involves resection of lung parenchyma whether formal resections as segmentectomy or lobectomy, or atypical and wedge resections. It was our aim of surgery, as well as that of many other authors to preserve lung tissue as much as possible. The lung parenchyma around the cyst is compressed rather than infiltrated and destroyed, and will reniflate when the parasite is removed (2,3,6). In addition-when the patient returns back to the endemic area after surgery, re-infection may occur with the development of [illegible] cysts.

Isolated liver cysts can be approached by different ways depending on their location. A midline incision is suitable for left lobe cysts. Cysts on the anteroinferior aspect of the liver are approached through a right paramedian or subcostal incision. Cysts located on the lower part of the posterior aspect can be approached through the bed of the resected 12 th rib posteriorly, extrapleurally and after reflecting up the diaphragm. However, liver dome' or 'liver roof cysts located on the posterosuperior aspect of the liver towards the midline or laterally are better and safer to be approached transthoracically than abdominally, as evidenced in this study, and that of others (2.3). The transthoracic approach offers better visualization of the area with better evacuation of contents and dealing with biliary leaks. This area is also near the major hepatic veins and inferior vena caval fossa, and serious uncontrollable bleeding may result if the cysts are approached abdominally.

In this study, on dealing with the liver cysts transthoracically, the phrenotomy incision was made either peripherally and circumfrentially, or centrally and radially depending on the site of the cyst minimize the number of phrenic nerve fibers cut by the incision (20). in contrast to lung cysts, main hydatid liver cysts are found fragmented by the time of presentation, leaving a cavity walled up by a pericyst of compressed hepatic tissue containing remnants of the main cyst, daughter cysts and of the hydatid mud (1). Accordingly, intact endocystectomy technique for liver cysts is inapplicable. Surgery involves opening the pericyst, evacuating the cavity,

closing any leaking biliary duct, sterilizing the cavity and filling it with omentum whenever possible. No major hepatic resections are generally required (1-3). After dealing with uncomplicated liver cysts, it was our preference, and that of others, to prefer abdominal drainage of the residual space than draining it towards the thorax and to repair the diaphragm (11,17). Primary closure of the cavity of simple cysts, after sterilizing it, with neither abdominal nor thoracic drainage followed by repair of the diaphragm was also reported without complications (4,9,18). Other authors prefer thoracic drainage and do not repair the diaphragm but marsupialize the cavity towards the pleura by suturing the pericyst to the edges of the diaphragm (3). They claim that, by doing so, the peritoneal cavity is protected from spillage of hydatid contents (3). We disagree with this principle; they may be protecting the peritioneal cavity, but what about contaminating the pleural cavity? It is also not physiological not to repair the diaphragm and to transfer abdominal problems to the chest. In this study, thoracic drainage was accompanied with more prolonged biliary drainage than abdominal drainage (Fig.7).

The reason for that is probably with prolonged abdominal tube drainage the abdominal contents and the omentum, abdominal policeman, form a well formed track around the tube. Upon removal of the tube, the track will collapse by the positive intra-abdominal pressure stopping the residual leakage in absence of any distal biliary obstruction. In case of thoracic drainage, with no policeman as the omentum, such well formed tract takes more time to form, with the pssibility of leaving chest wall sinus or localized empyema that will need interference. Yet, thoracic drainage was done when we were obliged to do it, in cases of infected liver cysts with intrathoracic rupture or when there were dense adhesions between the liver and the diaphragm interfering with in sension of abdominal drains.

Liver cysts are known to produce a number of intrathoracic complications (fig.4,5). These include: elevation of the right diaphragmatic copula with right lower lobe compression, 'water pleural effusion', empyema thoracis, Iung abscess, bronchobiliary fistula, bronchopleural biliary fistula, pericarditis or mediastinitis (6,11). Pulmonary ruptures tend to be more common than pleural ruptures because of the pleural adhesions generally initiated by the cyst before rupture (6,11,21). In this study, enmpyema thoracis was reported in one patients and bronchobililary fistulae were reported in three-all were successively managed by the one-stage transthoracic approach. This approach avoided the need for the two-staged procedure previously recommended to deal with these complications (8).

As emphasized in this study and in others, search for associated liver hydatid cysts should be made in every patient with lung cysts, and when present a one-stage transthoracically procedure to deal with being of them was safe mid satisfactory (3-5, 10-15). A question comes when the associated liver cyst was in a location difficult to be approached transthoracically being for example on the anteroinferior aspect of the liver. This condition was not encountered in the present series. One of

three solutions were offered; a- to close the thoracotomy and to call the patient later for a second-stage laparotomy (4). b- to perform thoracoabdominal incision (11) or c- to perform a simultaneous laparotomy (18). A simultaneous laparotomy was also advised to perform common bile duct exploration for patients having associated cholestasis (11).

Different scolecidal agents could be utilized in surgery of hydatid cysts depending on the surgeon's preference including 10-20% hypertonic saline (3-0.5% cetrimide (1), chlorhexidine(l), hydrogen peroxide (11), 0.5% povidone-iodine (18) or 80-96% alcohol (1). Formalin (2-10%) was no longer utilized for its local reactions and systemic toxicity amounting to death (2-8, 11). However, reports about its use were still present ill the literature till the late eighties (4). No one of such agents should be utilized in completed cysts when bronchobiliary communications are suspected. Scolecidal agent are not required in the Barrett's technique of intact endocystectomy, (2-6,7). It is important here to note that some authors, using, even the puncture-suction technique that theoretically produces potential infection-do not inject any scolecidal agents after aspiration and were satisfied with proper isolation of the field with saline pads, for fear of toxic reactions (8,18).

Mebendazole was successively tried in the treatment of liver hydatid cysts (22,23). For lung cysts, its use without surgery is denied by several authors, exposing the patient to the risks of complicated cysts (8,11,17,18). However, its postoperative use gained a wide acceptance and is given with the aim of decreasing recurrences from probable contamination during operation or from re-infection (4, 11, 17, 18, 23). Albendazole was also used for the same purpose postoperatively (3).

In recent reports- the mortality, rate of lung and liver dome cysts was low varying from 0-4.21% (2-4,8,11). The overall early and late morbidity was also low ranging from 0.5-17% (2-4,8,11). During the follow up, the recurrence rate, or probably the onset of a new hydatid disease infection, varied from 0-5.9% (2-4,7). In this study, there were no mortality, morbidity occurred in 12.5?% in the form of prolonged air leak 1 and prolonged bile leak and no recurrences were reported during the period of follow up.

It was concluded from this study that a thorough search should be made in every patient with lung hydatid cyst for associated liver cysts. The transthoracic approach offered a suitable, safe and one-stage procedure to deal with liver cysts associated with right lung cysts and to deal with liver dome cysts. A public health program should be addressed to people in the endemic areas about the proper sanitary habits required to protect them from this preventable disease.

References

1. Kune GA. Hydatid disease, In Maingot's Abdominal Operations. 8th Edition. Volume III. Schwartz SI and Ellis (editors). Appleton-Century-Crofts. 1989, 1605-24.
2. Qian Z. Thoracic hydatid cysts: A report of 842 cases treated over a thirty-year period. Ann Thorac Surg 1988; 46-342-6.
3. Athanassiadi K, Kalavrouziotis G,

Loutsidis A, et al. Surgical treatment of echinococcosis by a transthoracic approach. 11th Annual Meeting of the European Association for Cardiothoracic Surgery, Copenhagen, Denmark, September 28-October 1, 1991.

4. Peleg H, Best L-A and Gaitini. Simultaneous operation for hydatid cysts of right lung and liver. J Thotac Cardiovasc Surg 1985. 90:

5. Rami-Porta R, Ais-Conde JG, Bravo-Bravo JL, et al. Treatment of synchronous pulmonary and hepatic hydatid cysts (Letter to the Editor). J. Thorac Cardiovasc Surg 1986. 92 (2)-314-5.

6. Barrett NR and Thomas D. Pulmonary hydatid disease. Brit J Surg 1952; 40: 222.

7. Lichter I. Surgery of pulmonary hydatid cyst-the Barrett technique. Thorax 1972- 27:529.

8. Burgos L, Baquerizo A, Munoz W, et al. Experience in the surgical management of 331 patients with pulmonary hydatidosis. J Thorac Cardiovasc Surg 1991; 102: 427-30.

9. Crausaz PH. Surgical treatment of hydatid cysts of the lung and hydatid disease of the liver with intrathoracic evolution. J Thorac Cardiovase Surg 1967; 53: 116-29.

10. Aubert M and Viard P.Etude statistique sur 1'hydatidose pleuropulmonaire dans le basin mediterraneen en 1982. A propos de 8,384 cas. Ann Chir. 1983; 37-74-7.

11. Freixiet JL, Mestres CA, Cugat E, et al. Hepaticothoracic transdiaphragmatic echinococcosis. Ann Thorac Surg, 1988. 45: 426.

12. Eren N and Ozgen G. Simultaneous operation for right pulmonary and liver echinococcosis. Scand J Cardiovasc Surg 1990, 24 (2): 131 -4.

13. Pomelov VS, Karimov ShI and Nishanov KhT. Surgical tactics in associated echinococcosis of the liver and the lung. Khirurgiia (Mosk) 1991. 11; 69-74.

14. Gomez R, Moreno E, Loinaz C, et al. Diaphragmatic or transdiaphragmatic thoracic involvement in hepatic hydatid disease: Surgical trends and classification: World J Surg 1995; 19 (5): 714-9.

15. Kir A and Baran E. Simultaneous operation for hydatid cyst of right lung and liver. Thorac Catdiovasc Surg 1995; 43 (1)- 62-4.

16. Cetin G. Dogan R, Yuksel M- et al. Surgical treatment of bilateral hydatid disease of the lung via median sternotomy. Experience in 60 consecutive patients. Thorac Cardiovasc Surg 1988; 36: 114-7.

17. Jakob H, Kohlhaufl M, Hurter T, et al. Echinococcal disease of both lung and liver: Successful simultaneous resection. J Thorac Cardiovasc Surg 1989. 9640-1.

18. Dhaliwal RS and Kalkat MS. One-stage surgical procedure for bilateral lung and liver hydatid cysts. Ann Thorac Surg 1997. 64: 338-41.

19. Hugh SP and David FB. Thoracoscopic

evacuation of dead hydatid cyst. J Thorac Cardiovasc Surg 1996. III: 6.

20. Douglas JM, Jr. Thoracoabdominal incisions. In: Atlas of Cardiovascular Surgery. Sabiston DC. Jr. (editor). 1st ed. Volume I.W-B Saunders Company. 1995.

21. Xanthakis DS, Katsaras E, Efthimiadis M, et al. Hydatid cyst of the liver with intrathoracic rupture. Thorax 1981- 36: 497-501.

22. Gil-Grande LA, Boixeda D, Garcia-Hoz F, et al. Treatment of liver hydatid disease with mebendazole: A prospective study of thirteen cases .Am J Gastroenterol 1983- 78 (9)-.584-8.

23. Khalaf SA, Abd El-Shahead M, Amr TA and El-Desouky ME. CT and surgical evaluation of pulmonary hydatid disease. J Egypt Society, Cardiothorac Surg 1996. 4 (3): 81-90.

Management of the Tracheobronchial Foreign Bodies

ABSTRACT

From January 1996 to December 1997, we performed rigid bronchoscopy in 119 patients in whom foreign body (FB) inhalation was suspected at the department of cardiothoracic surgery, Ain Shams University in Cairo.

In 99 (83%) of the cases, FB was identified in the tracheobronchial tree and successfully removed in 98 out of them (99%). In the remaining 20 cases (17%), the presence of FB was excluded.

There were 63 males (53%). The mean age was 4.6 years with the peak in the second year of life. X-ray is the sole investigation needed and being negative did not exclude the presence of FB. A wide variety of objects were recovered, most of them were organic in nature. The right main bronchus was the commonest site.

Bronchoscopy was required for treatment of FB. Inhalation and with suitable experience, this procedure is simple and safe.

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INTRODUCTION

The event of FB inhalation could turn into a fatal problem. Its incidence of the reported cases varies widely from place to another. The Children's Memorial Hospital in Chicago reported more than 5000 cases in more than 35 years (1), while John Hopkins Hospital only reported 234 cases in 52 years (2) .

This problem accounts for more than 300 deaths per year in the United States (3) (about 1:850,000). It was almost the same ratio when Datau reported the mortality of FB inhalation in France in 1981, with children under 2 years of age most commonly affected .

Although these were some of the reported mortality, we believe that the actual mortality rate is higher since some more victims die instantly before having the chance to reach to any hospital.

Patients and Methods

We reviewed the data of all patients admitted to the Thoracic Unit at the Department of Cardiothoracic Surgery at Ain Shams University Hospitals in Cairo with suspected FB inhalation from January 1996 to December 1997.

Our diagnosis of inhaled FB was based on one or more of, history of inhalation, symptoms, physical examination, and/or radiological evidence.

The clinical picture varied widely depending on the age of the patient, the nature, site, and size of the FB, and the presence or the absence of associated chest infection.

The main presenting symptom was one or more of the following, cough, persistent or recurrent chest infection, wheezes and/or, severe respiratory distress. In spite

of that, some patients were completely asymptomatic.

Physical signs ranged from totally normal patients up to respiratory arrest that necessitated intubation and ventilation before the bronchoscope.

X-ray was the only investigation we performed for most of the patients. In severe cases of respiratory distress, bronchoscope was performed depending only on clinical picture without waiting for an X-ray.

The urgency of performing the bronchoscope depended mainly upon the extent of symptoms and the age of the patients. Bronchoscopes were considered as elective if they were scheduled for the next operating list, they were considered as urgent if scheduled for the next morning, and were considered as emergency if they were done immediately once referred.

We considered any child below the age of two years as an urgent case if it is not an emergency due to the relative small diameter of his / her airway regardless the severity of symptoms.

Operative technique:

All the procedures were done under general anesthesia. Both the pulse and oxygen saturation were continuously monitored from induction till the end of the procedure. Patients were premedicated with 0.02 mg/kg Atropine. Induction was by Fentanyl 2 microgram/kg., Ketamine 1-2 mg/kg then maintained with Halothane 2 vol. % in 100% Oxygen. The introduction of the bronchoscope was usually facilitated by 1-2 mg/kg Succinylcholine.

We used the appropriate size of the Rigid Holinger Ventilating fiber optic bronchoscope and the suitable graspers. It is important to have a complete selection of endoscopes and extraction forceps before attempting any FB extraction.

We used to introduce the bronchoscope with the help of a laryngoscope in the infants and young children.

In most of the cases, extraction of the FB is done as a unit (the bronchoscope and the FB), while in some of the FB was removed through the bronchoscope.

In cases pins lying horizontally in the tracheobronchial tree with neither end could be seen. The bronchoscope is introduced down till it touches the pin. The forceps is then introduced and the pin is grasped firmly. Gradual traction is applied next on the middle of the pin till it starts to bend and the angled resulted from the constant traction goes into the lumen of the bronchoscope. No traction at all should be applied before the scope rests on the horizontal pin otherwise this might injure the tracheobronchial tree.

Once the FB, has been removed, reinspection is undertaken to rule out the presence of a second FB and to suck out the secretions accumulated behind it.

In the absence of chest infection, we used to give a single dose of a third generation Cephalosporin then oral antibiotics for 48 hours post operatively. We also used to give the infants Hydrocortisone after instrumentation for fear of laryngeal oedema for 24 hours if the procedure was prolonged or more the scope was introduced more than one time.

Table (1): The data of the 119 patients.

	Group 1	Group 2	p. value
Number patients	94	25	
Mean age	1.7	15.7	
Gender (M:F)	1.35:1	1:1.78	> 0.05
Mean elapse (day)	6.7	32	> 0.05
Median elapse (day)	2	3	
Symptomatic patients (%)	98%	28%	< 0.001
+ ve physical sings (%)	89%	20%	< 0.001
+ ve X-ray findings (%)	41%	72%	< 0.05
Central FB (%)	99%	48%	< 0.001
Negative beonchoscopes	17%	16%	> 0.05
Vegetative FB	90%	5%	< 0.05
Non vegetative FB	10%	95%	< 0.05
Emergency	27%	0%	< 0.001
PO ventilation	11%	0%	< 0.001
Mean hospital stay	1.6	1.4	> 0.05

Table (2):The main presenting symptoms

	Gp.1	Gp.2	total
Persistent or recurrent chest infection	29	3	32
Cough	22	5	27
Wheezes +/- stridors	21	0	21
Respiratory distress	20	0	20
Asymptomatic	2	17	19
Total	94	25	119

Table (3): The main physical signs.

	Gp.1	Gp.2	total
Difference in air entry between RT. & Lt. Lungs.	52	5	57
Wheezes +/- stridors	27	0	27
Mechanically ventilated	5	0	5
No physical signs	10	20	30
Total	94	25	119

Table (4): Radiological examination.

X- ray findings	Gp.1	Gp.2	total
Within normal limits	48	7	55
Collapse +/- emphysema	29	2	31
FB. Seen	5	16	21
X-ray was not done	12	0	12
Total	94	25	119

Table (5): Priority of performing bronchoscope.

	Gp.1	Gp.2	total
Elective	7	23	30
Urgent	62	2	64
Emergency	25	0	25
Total	94	25	119

For comparative purposes, we divided the patients into two groups depending on their age. Group 1 were those patients below the age of six (preschool age), and group 2 were those aged six or above.

Results

We performed 119 bronchoscopes for suspected FB inhalation. The scope

Table (6): Site of the inhaled FB.

	Gp.1	Gp.2	total
Trachea (T)	14	0	14
Right main bronchus (RMB)	47	7	54
Left main bronchus (LMB)	14	3	17
Right lower lobe bronchus (RLL)	1	4	5
Left lower lobe bronchus (LLL)	0	6	6
Right upper lobe bronchus (RUL)	0	1	1
Bronchus Intermedius	1	0	1
T & RMB	1	0	1
No FB.	16	4	20
Total	94	25	119

Table (7): Nature of FB removed

	Gp.1	Gp.2	total
Vegetative FB.	70	1	71
Non- vegetative FB.	8	20	28
No FB.	16	4	20
Total	94	25	119

Table (8): Nature of FB removed

Vegetative FB.	Gp.1	Gp.2	total
Pea-nut	20	0	20
Water-melon or sunflower seeds	36	0	36
Beans	2	1	3
Fish bone	3	0	3
Chicken bone	2	0	2
Orange seed	2	0	2
Maize seed	2	0	2
Piece of pop corn	1	0	1
Piece of sweet potato	1	0	1
Piece of carrot	1	0	1
Total	70	1	71
Non-vegetative FB.			
Pin	1	12	13
Safety pin	2	0	2
Nail	0	2	2
Toy piece	1	1	2
Peed	2	0	2
Pen	1	3	4
Piece of stone	0	1	1
Piece of earring	1	0	1
Milk tooth	0	1	1
Total	8	20	28

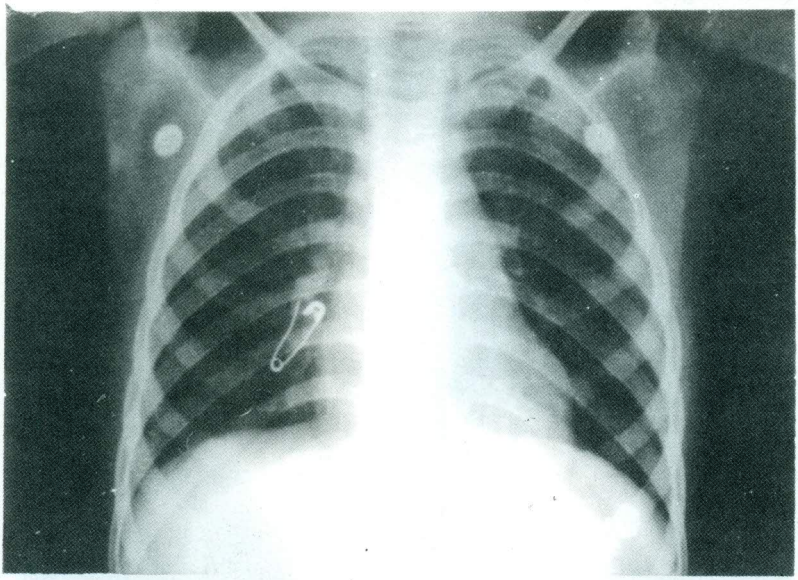

Fig. (1): An open Safety pin in the right lower lobe bronchus that needed a thoractomy to remove.

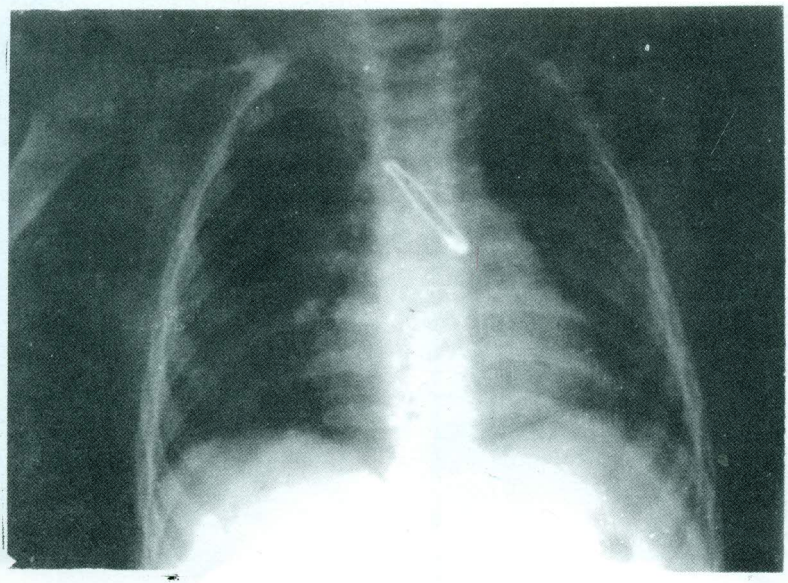

Fig. (2): Another closed safety pin removed from a 1 year old boy.

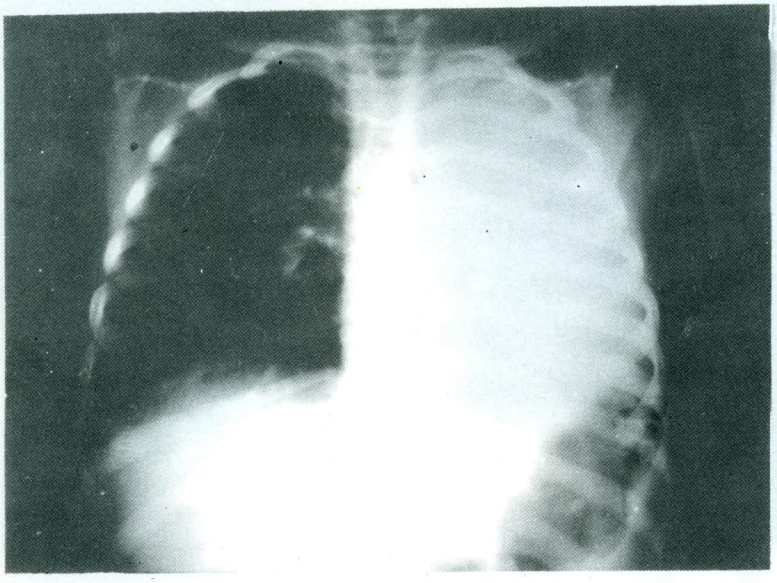

Fig. (3): Total collapse of the left lung due to inhaled a piece of plastic pen.

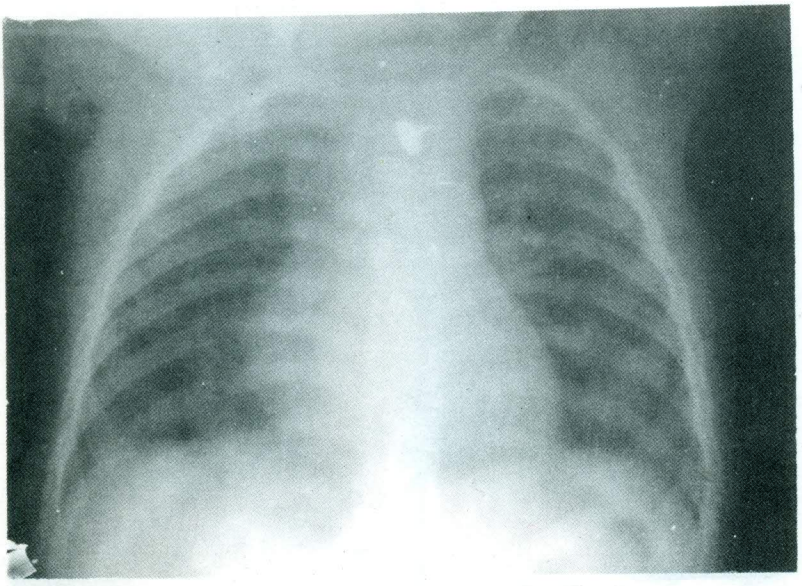

Fig. (4): Pin in the lower trachea of a 14 months old boy.

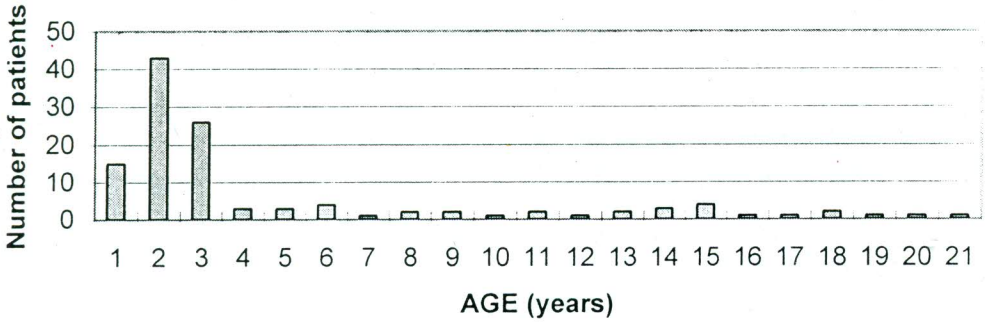

Fig. (5): Age of the patients.

confirmed the presence of FB in 99 cases (83%) and excluded the presence of FB in 20 cases (17%). We successfully removed 98 foreign bodies (99%) out of the 99 FB. Bronchoscopic removal failed in 1 (1%) patient who needed a thoracotomy and bronchotomy to remove it.

The mean age of all the patients was 4.6+1-6.4 years (median 2 years, range 5 months to 37 years). They were 63 males (53%) and 56 females (47%).

13 (12%) of these patients had previous bronchoscope prior to admission to our department (10 patients had bronchoscope once, 2 patients had bronchoscope twice and one patient three times).

The mean elapse before bronchoscope was 12.1 +/- 50.1 days (median 3 days, range 4 hours to 1.5 years). Most of the results are summarized in table 1.

The main presenting symptoms, physical signs, radiological findings, and the urgency of doing the bronchoscope are summarized in tables 2, 3, 4, and 5.

We considered the trachea and both main stem bronchi as the central tracheobronchial tree, while any location distal to this, as peripheral.

In group I, we found that 77 (99%) of the 78 FB detected were central, while, only 10 (48%) of the 21 FB of group 2 were detected centrally.

The sites of FB in tracheobronchial tree are summarized in table 6. n. b. (water-melon and sunflower seeds are consumed as cheap nuts)

30 vegetative FB were fragmented during removal and 6 pins needed to be bend due to their horizontal position to facilitate their removal.

10 patients (8%) needed mechanical ventilation post operatively either due to subglottic oedema or severe chest infection. The mean period of mechanical ventilation was 32+/-57 hours (median 12 hours & range from 4 hours to 8 days).

One patient developed right-sided pneumothorax that was treated with an intercostal tube that lasted for 24 hours.

One patient died of hepato-renal failure. It was an accidental fall into the sewage. The patient had H2S poisoning. He was

comatose and had persistent consolidation of the right upper lobe inspite of intensive treatment with antibiotics. Fibro-optic bronchoscope was performed for suction, which revealed the presence of a FB in the right upper lobe bronchus. Rigid bronchoscope was performed and a piece of stone was removed from the right upper lobe bronchus. Although his X-ray improved and the right upper lobe was re-aireated, the patient died 5 days after bronchoscope due to hepato-renal failure as a complication of poisoning.

We failed to remove safety pin from the right lower lobe bronchus of a 5 years old girl.

She had a thoracotomy and removal of the pin and was discharged on the 7 th postoperative day.

105 patients (88%) were discharged home while the other 14 patients (12%) were referred to the pediatric department for the continuation their treatment. The mean hospital stay was 1.6+/- 1.6 days (median =1 & range from 1 to 14 days). 88 patients were discharged within 24 hours of the bronchoscope.

Discussion

We performed 119 bronchoscope for patients with suspected inhaled FB in 20 (17%) of them inhalation was excluded (-ve bronchoscope). The number of -ve bronchoscopes varied widely 3.4%, 2 0%3, 46%.

We believe that if suspicious is raised as regard FB inhalation, a bronchoscope should be performed to exclude it especially with the very low incidence of risk involved in this procedure. We also believe that the big gap between the reported -ve bronchoscopes is mainly due to the variable degree of suspicious between surgeons.

Infants and young children constitute the majority of our cases. 72 patients (61%) were below the age of three and the peak incidence was in the second year of life (43 patients (36%)). There was a steady decline in the numbers each year with slight increase towards teenage (Fig. 1).

The second year of life was the peak incidence in almost all of the reported series. 7,8,9

When gender was considered, males outnumbered females in group 1 while females outnumbered males in group 2. In both groups these differences were non-significant. Most of the reported series did not show significant difference between males and females (5,10).

The mean elapse between the event of inhalation and the bronchoscope reflect the severity of the inhalation event and the alertness of the parents.

In our patients, it was 12.1 +/- 50 days. This long time was mainly due to two patients who seek medical advice very late (7 and 18 months). Excluding these two patients brings the figure down to 6.2+/- 11.5 days.

Chest X-ray was the only investigation done for 107 of our patients (90%) and was found to be abnormal in only 52 (49%) of them.

The higher % of positive X-ray findings associated with group 2 compared with group 1 is due to the nature of the inhaled

FB. (76% of the inhaled FB in group 2 are radio-opaque compared with only 6.4% in group 1).

Even if no clinical signs are found, and radiography proves negative, one must always consider the possibility of a FB in the tracheobronchial tree particularly within the age range most at risk (under 3 years) in those having a highly suspicious clinical history.

We used rigid bronchoscopy in all our patients since it allows good visualization, manipulation through its wide lumen, and better suction.

Yeh and his colleagues considered that initial fibro-optic bronchoscopy is necessary to identify the site of the FB. 12 Donado and his colleagues suggested to use fibro-optic bronchoscopy in all patients and to keep rigid bronchoscopy only for very specific cases.10 We believe that this step is not necessary to minimize the maneuvers and manipulations and to minimize the operative time and trauma especially in young children.

In both our patients and other's experiences, the right-sided tracheobronchial tree continued to be the commonest site for the inhaled FB due to its anatomical characteristics.

The nature of FB was related to the surrounding environment in most of the cases, 71% of our FB were vegetative. Peanut, sunflower seeds, and watermelon seeds constitutes 57% of all FB we recovered. Peanut was the main FB recovered in most of the patients in nearly all reports (4,7,14) . Our second common FB inhaled was pins used to fix the hair cover and the risk group was teen-age girls since it is a new experience for them.

We did not experience problems or late complications with our antibiotic policy or the regimen of corticosteroids (a third generation cephalosporin for 1 to 3 days and corticosteroids for 24 hours in young children). Some other authors recommend antibiotics and corticosteroids for two weeks in cases of FB present in the tracheobronchial tree for longer than two weeks .

Thoracotomy rate varied from 1.5% 15 to 3 % 4 and resection was reported in 0.3% 5. Only one of our patients needed thoracotomy to remove an impacted safety pin. No resection was performed.

Procedure-related mortality varied from 0.5% 5 to 4.3% 13 We had one patient died of hepatorenal failure, a problem that was not related to the procedure itself.

At the end, every effort should be made to prevent of FB inhalation. Education should be directed to the target group like mothers, and child minders. Children should not be left unattended and they should not be given nut below the age of seven. Safety guidelines should be observed for toys of children younger than three years.

Experienced medical staff should be available in well-known centers around the clock to deal with any of these emergencies.

If peanut was not given to young children, three-quarters of inhaled FB could be avoided .

References

1. Lauren D. Holinger Management of foreign bodies of the tracheobronchial tree. Chapter 67 in General thoracic surgery by Thomas W. Shields Williams

& Wilkins fourth edition 1994.

2. Hughes CA., Baroody FM., and March BR. Pediatric Tracheobronchial foreign bodies: Historical review from John Hopkins Hospital Ann-Otol-Rhinol-Laryngol. 1996 Jul; 105 (7): 555 - 61.

3. Black RE., Johnson DG., and Matlak ME. Bronchoscopic removal of aspirated foreign bodies in children J. Pediatr. Surg. 1994 May 29 (5): 682-4.

4. Guy J. Datau, MD, Francois C. Bremont, MD, and Annie C. Sengelin, MD. Aerodigestive tract Foreign Bodies Chapter 15 in Pediatric thoracic Surgery, By Elsevier Science Publishing Co., Inc. 1991.

5. Senkaya I., Sagdik K., Gebitekin C., Yilmaz M., Ozkan H., & Cengiz M. Management of Foreign body aspiration in Infancy and children. A life threatening problem. Turk J Pediatr 1997 Jul. (3): 353-362.

6. Agostinho M.,Estevao HM., Boavida E., Pires J., Pato R., lsaac J B.. Coelho A., Barroso A. Foreign bodies in the tracheobronchial tree. 12 years experience Acta Med Port 1997 Feb; 10 (2-3): 151-155.

7. Burton EM., Brick WG., Hall JD., Riggs W Jr., and Houston CS. Tracheobronchial foreign bodies aspiration in Children South Med J. 1996 Feb. 89 (2): 195-8.

8. Sanchez-Echaniz J., Perez-Garcia J., Mintegui-Raso YS., Benito-FernandezJ., LopezAlvarez-Bunma F. Tracheobronchial aspiration of foreign bodies in children. An. Esp. Pediatr. 1996 Oct.45 (4) 365-8.

9. Cataneo AJ., Reibscheid SM., Ruiz Junior RL., and Ferrari GF. Foreign body in the tracheobroncheal tree. Clin. Pediatr. (Phlia) 1997 Dec., 36 (12): 701-706.

10. Donado Una JR., Miguel Poch E., Casado Lopez ME., and Alfaro Abreu JJ. Fiber optic bronchoscopy in extraction of tracheo-bronchial foreign bodies in adults Arch Bronconeumol 1998 Feb: 34(2): 76-81.

11. Carluccio F., and Romeo R. Inhalation of foreign bodies: Epidemiological data and clinical considerations in the light of a statistical review of 92 cases. Acta Otorhinolaryngol ltal. 1997 Feb; 17(l): 45-51.

12. Yeh Lc., Li HY., and Huang TS. Foreign bodies in tracheobronchial tree in children: a review of cases over a twenty-year period. Chang Keng 1 Hsueh 1998 Mar; 21(l): 44-49.

13. Yagi HI Foreign bodies in the tracheobronchial tree in Sudanese patients. J R Coil Surg Edinb 1997 Aug; 42 (4): 235-237.

14. Caversaccio MD., Zbaren P., Vischer M., Taschappeler H. Tracheobronchial foreign body in children. Is anamnesis alone enough to indicate tracheobronchoscopy? HNO 1996 Aug. 44 (8): 440-4.

15. Causey AL., Talton DS., MillerRC., & Warren ET Aspirated safety pin requiring thoracotomy: report of a case and review. Pediatr. Emerg.Care 1997 Dec.113'(6): 397-400.

Mohamed Attia, Magdy Mostafa and Morsy Amin

The use of Isuprel in the Perioperative Management of Right Ventricular Dysfunction in Patients with Pulmonary Hypertension

ABSTRACT

It is well known that progressive elevation of the pulmonary artery pressure resulting from long standing mitral valve stenosis or congenital heart diseases causing left to right shunt, leads to right ventricular dysfunction. The patients included in this study were 43 in number, 31 (72.1%) were males and 12 (27.9%) were females. 16 (37.3%) patient had mitral restenosis, 14 (32.5%) patients had calcific mitral stenosis, 8 (18.6%) patients had VSD and the last 5 (11.6%) patients had ASD. The ages of the patients with mitral valve disease ranged from 35 to 50 years, that of the patients with VSD ranged from 15 to 25 years and that of the patients with ASD were above 40 years. The preoperative pulmonary artery pressure ranged from 80 to 110 mmHg. In all of the studied patients, Tridil and nipride were tried firstly and separately, but on weaning from cardiopulmonary bypass the right ventricle distended and the heart arrested. Only after the use of Isuprel instead of tridil and nipride in a dose ranging from 80 to 120 nanograms/Kg it could be able to wean the heart from the bypass with suitable haemodynamics. The Isuprel is maintained for 48 hours postoperatively and then gradually weaned. The estimated pulmonary artery pressure at the end of the operation ranged from 65 to 95 mmHg and that estimated two weeks after the operation by Doppler's echocardiography ranged from 50 to 75 mmHg.

Conclusion: From the results of this study we conclude that Isuprel is beneficial in the management of right ventricular dysfunction in patients with pulmonary hypertension because of its inotropic effect vasodilator effect decreasing the preload of the heart and its suppressing effect on the pulmonary vascular resistance decreasing the afterload of the heart

Abbreviations: ASD: Atrial septal defect VSD: Ventricular septal defect

Mohamed Attia, MD.,Magdy Mostafa MD. Morsy Amin MD
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INTRODUCTION

Right ventricular, cardiac function is altered by abnormalities affecting primarily the- left-sided cardiac structures, the lungs or the right-sided cardiac structures themselves. The most common cardiac causes for right ventricular dysfunction are chronic left ventricular ischemia, left to right shunts and rheumatic mitral valvular disease. Common to all of these diseases is elevation of pulmonary vascular resistance with a commensurate increase in right ventricular pressure resulting in right ventricular hypertrophy (2). Pulmonary hypertension as a result of increased

Departement of Cardiothoracic Surgery, Ain-Shams University, Cairo, Egypt

pulmonary vascular resistance remains a significant problem in the treatment of patients undergoing surgical correction of such lessons. Such pulmonary hypertension is one of the most important determinants of preoperative morbidity and mortality and of long-term survival after cardiac, operations (3,4). The limited ability of right ventricular myocardium to function in the face of increased pulmonary resistance results in right ventricular dilatation, tricuspid regurgitation and ultimately right - ventricular failure. Therefore in this work we have studied the effect of isuprel in the perioperative management of right ventricular dysfunction in patients with pulmonary hypertension.

Patient and Methods

The patients included in this study (Table 1) were 43 in number, 31(72.1%) were males and 12 (27.1%) were females. All of them were operated upon at the department of cardiothoracic surgery in Nasr city Hospital of Insurance between Feb. 1996 and August 1997. 16 patients (37.3%) had mitral restenosis, 12 patients (27.7%) of them were males and 4 patients (9.2%) were females and their mean age was 41.7 years. The next 14 patients (12.5%) had calcific mitral stenosis, 11 patients (25.5%) of them were males and 3 patients (6.9%) were females and their mean age was 45.3 years. The next 8 patients (18.6%) had ventricular septal defect, 5 patients (12.3%) of them were males and 3 patients (6.9%) were females and their mean age was 20.3 years.

The last 5 patients had atrial septal defect, 3 patients (6.9%) of them were males and 2 patients (4.6%) were females and their mean age was 43.4 years.

Surgical Procedure

Routine monitoring of the vital data was done. All surgical procedures were done using general endotracheal anaesthia, the approach of choice was median sternotomy and after systemic heparinization cannulation of the aorta and both cavae was done.

Snaring of cavae was done in the cases in whome the right atrium was opened. Myocardial protection was done using cold blood cardioplegia given through aortic root cannula and repeated every 25 minutes together with moderate systemic hypothermia (28-30°c) and topical hypothermia using cold saline (4°c) applied into the pericardial cavity. The atrial septal defects were closed transatrially rising pericardial patches by contineous prolene stitches. The ventricular septal defects were also closed transatrially using Dacron patches by interrupted prolene stitches supported with teflon pledgets. Mitral valve replacement was done to patients with mitral valve disease using prosthetic St. Jude valves by interrupted ethibond stitches with teflon pledgets. It was done using left atriotomy approach in patients with calcific mitral stenosis and transseptal approach in patients with mitral restenosis.

Systemic rewarming was started after completion of replacement of the mitral valve or closure of the atrial or ventrianlar septal defects and after deairing of the heart declamping of the aorta was done. Inotropic support in the form of adrenaline in a dose of 100 nanogram was given and vasodilatation in the form of Nipride and tridil in the theraputic doses was also used.

Table (1): Clinical data of the studied patients

Diagnosis	Number of the patients	Mean age	Sex	
			Males	Females
Mitral restenosis	16 pts (37.3%)	41.7 years	12 pts (27.7%)	4 pts (9.2%)
Clacific mitral stenosis	14 pts (32.5%)	45.3 years	11 pts (25.5%	3 pts (6.9%)
VSD	8 pts (18.6%)	20.3 years	5 pts (12.3%)	3 pts (6.9%)
ASD	5 pts (11.6%)	43.4 years	3 pts (6.9%)	2 pts (4.6%)

On weaning from cardiopulmonary bypass the heart distended and arrested. Isoprel was used instead of them starting at a dose of 100 nanogram and then adjusted according to the response. The mean dose of isuprel used (Table 2) was 125.6 nanogram in patients with mitral restenosis, 117.8 nanogram in patients with calcific mitral stenosis, 90.0 nanogram in patients with atrial septal defects. After weaning from cardio pulmonary bypass, decanulation and completion of protamine administration, the pulmonary artery pressure is estimated using a needle inserted into the pulmonary artery through a purse-string stitch and connected through a pressure line into a transducer connected to the pressure module of the monitor. Postoperatively, the patients were maintained on the same intraoperative dose of isuprel for 48 hours and then gradually weaned over a period of 24 hours. On weaning from isuprel the patients were maintained on capoten at discharge from the hospital.

Doppler's echocardiographic assessment was done for all patients both preoperatively, and two weeks postoperatively. In addition to the full diagnostic data obtained, the pulmonary artery pressure was estimated.

Results

There was no single mortality among the studied patients. The heart in all cases recovred its power after the use of isuprel and it could be able to be weaned from cardiopulmonary bypass maintaining good haemodynamics. None of the patients showed signs of right ventricular failure till discharge from the hospital two weeks after the operation. The estimated pulmonary artery pressure (Table 3) showed significant reduction from the preoperative value. Whereas (Fig. 1) in patients with mitral

Table (2): The dose of isuprel used in the studied patients

Group of patient	Mean dose of isuprel used
Mitral restenosis	125.6 nanogram
Clacific mitral stenosis	117.8 nanogram
VSD	90.0 nanogram
ASD	80.0 nanogram

Table (3): The estimated pulmonary artery pressure

Group of patient	Mean preoperative pulmonary pressure	Mean intraoperative pulmonary pressure	Mean postoperative pulmonary pressure (2 weeks)
Mitral restenosis	103.8 mmHg	87.8 mmHg	68.4 mmHg
Clacific mitral stenosis	104.5 mmHg	82.3 mmHg	65.3 mmHg
VSD	84.7 mmHg	68.0 mmHg	53.8 mmHg
ASD	80.5 mmHg	65.0 mmHg	51.8 mmHg

N.B.: VSD Ventricular septal defect
ASD Atrial septal defect

restenosis the mean pulmonary artery pressure dropped from preoperative value of 103.8 mmHg to 87.8 mmHg intraoperatively and 68.4 mmHg postoperatively. In patients with calcific mitral stenosis, it dropped from preoperative value of 104.5 mmHg to be 82.3 mmHg intraoperatively and 65.3 mmHg postoperatively. In patients with ventricular septal defects, it dropped from preoperative value of 84.7 mmHg to be 68.0 mmHg intraoperatively and 53.8 mmHg postoperatively. In patients with atrial septal defects, it dropped from preoperative value of 80.51-g to 65.0 mmHg intraoperatively and 51.8 mmHg postoperatively

Discussion

The right ventricular dysfunction secondary to pulmonary hypertension remains a major problem in the surgical

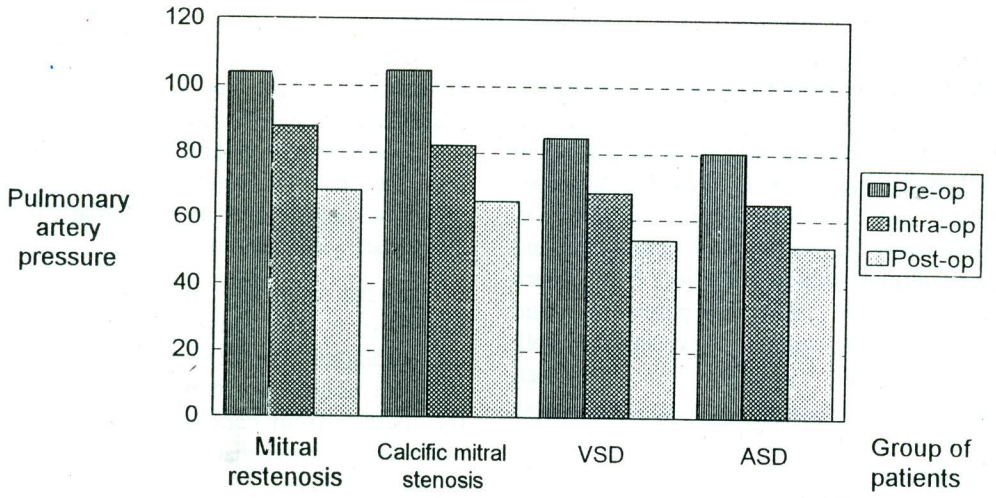

Fig. (1)

management of patients with left to right shunts and long standing mitral valve disease. Therefore every effort is directed towards lowering the pulmonary artery pressure to improve the surgical outcome of such patients.

The net pulmonary vascular tone results from the balance of the mecahnisms of pulmonary vasorelaxation and vasoconstriction. In the normal lung, the low pulmonary vascular smooth muscle tone may at least in part be due to the basal endothelial release of the vasodilator nitric oxide (5). Endothelium-derived nitric oxide lowers pulmonary vascular tone by stimulating guanylate cyclase in subjacent vascular smooth muscle cells to generate cGMp, which produces pulmonary vascular smooth muscle relaxation (6) .

If the mechanisms of pulmonary vasorelaxation are impaired, the net pulmonary vascular tone may be tipped in favor of pulmonary vasoconstriction. In addition, impairment of the mechanisms of pulmonary vasorelaxation may result in an exaggerated pulmonary vasoconstricting response to circulating or local vasoconstricting agonists (5). In addition to cGMp-mediated relaxation, the other principal intracellular mediator of pulmonary vasorelaxation is cAMP7 . Both cGMp and cAMp mediated mechanisms of pulmonary vasorelaxation become dysfunctional in the setting of a left to right shunt.

The structural changes produced in the pulmonary circulation as a rsult of chronic high pulmonary arterial flow have been well characterized. In 1958, Heath and Edwards (9) described the progresssion of changes begaining with the reversible changes of intimal hyperplasia and medial hypertrophy and progressing to the irreversible changes of angiomatous malformation and fibrinoid necrosis.

The mechanisms by which these

changes are produced remain unclear. Most current theories invoke endothelial cell injury by high pulmonary flow and pressure as an inciting event. Endothelial cell injury may result in release of proteases into the subendothelium, leading to destruction of the basement membrane and extracellular matrix proteins. This in turn may trigger both hypertrophy and hyperplasia of pulmonary vascular smooth muscle cells, leading to increased muscularization of small vessels (8). These structural changes have been clearly associated with progressively increasing pulmonary arterial pressure.

At least three pathophysilogic mechanisms contribute to the pulmonary hypertension seen in long standing mitral valve disease (1) increased left atrial pressure transmitted on a retrograd basis into the arterial circulation, (2) vascular remodeling of the pulmonary vasculature in response to chronic obstruction to pulmonary venous drainage (fixed component), (3) pulmonary arterial vasoconstriction (reactive component)

The clinical management of chronic pulmonary hypertension is challenging and despite the introduction of several therapeutic measures, no single treatment is universally recommended . For lowering of the pulmonary artery pressure in the studied patients, we tried first Nipride and Tridil but because of the severe degree of pulmonary hypertension, high doses of these drugs were required which markedly lowered the systemic pressure and we were unable to wean the heart from cardiopulmonary bypass. This is compatible with the Fullerton's (12) findings who stated that these drugs produce vasodilatation of both systemic and pulmonary circulation. Such non selective vasodilatation may be hazardous in patients with pulmonary hypertension, significant hypotension may result if the degree of systemic vasodilation exceeds that of the pulmonary vasodilation.

On the contrary, when we used the isuprel in a dose ranging between 80 and 125 nanogram in the studied patients with different diagnosis we were able to wean the hearts from cardiopulmonary bypass maintaining good haemodynamics and the pulmonary artery pressure dropped from a preoperative value of (80.5 to 103.8 mmHg) to 9, an intraoperative value of (65.0 to 87.8 mmHg) and furtherly dropped to a postoperative value of (51.8 to 68.4 mmHg). This means that the pulmonary artery pressure has decreased intraoperatively by about 20% and this is due to the beneficial effect of the use of isuprel and can not be considered to be owing to valve replacement or closure of the shunts since the increased pulmonary vascular resistance does not immediately return to the normal range following relieve of the elevated left atrial pressure by the surgical procedure. Several days to weeks may be required. In addition to its vasodilating effect reducing the pulmonary and systemic vascular resistance, the isuprel has a positive intropic effect improving contractility of both ventricles and overcoming its vasodilating effect on the systemic circulation. It also has a positive chrontropic action which increases the minute blood flow improving right ventricular filling capacity.

Oohata and associates (14) reported that after continuous infusion of prostaglandin E

l at low dose, the pulmonary vascular resistance decreased quickly, the right ventricular ejection fraction increased and the stroke volume index also improved. These hemodynamic changes are the result of the potent vasodilating effect of prostaglandin E l that especially could decrease selectively the pulmonary vascular resistance and increase the preload of the left ventricle. However, this benficial effect of prostaglandin E l has been concluded after its use in a case of acute right heart falire which resulted from the intrinsic right ventricular dysfunction.

Fullerton and coworkers (15,16) stated that adenosine may be used clinically as a selective pulmonary vasodilating agent to optimize pulmonary hemodynamic indices without adverse systemic hemodynamic effects in patients with pulmonary hypertension having cardiac operations. It may be particularly valuable in patients with right heart dysfunction by selectively lowering right ventricular after load.

Many reportes (17-23) recommended the use of nitric oxide by inhaltion which rapidly difuses directly into the pulmonary vascular smooth muscle cells where it leads to incerases in the concentration of guanylate cyclase which results in relaxation and vasodilation of the pulmonary vascular smooth muscle. Once nitric oxide diffuses through the smooth muscle cell into the vessel lumen, however, it reacts quickly with haemoglobin. Haemoglobin nitric oxide and prevents it from causing any systemic vasodilation. In this way, the vasodilating actions of inhaled nitric oxide are focused on the pulmonary circulation with virtually no systemic effets. These properties offer a significant advantage for nitric oxide as a selective pulmonary vasodilator.

However, Bocchiand and his coleagues (24) stated that inhalation of nitric oxide may precipitate pulmonary edema in a patient with stable heart failure. Of particular concern in patients undergoing cardiac operations is the possibility that inhaled nitric oxide may depress myocardial contractility.

Conclusion

We can conclude that the commonly used vasodilator drugs are not selective for the pulmonary vascular bed and in addition to lowering pulmonary vascular pressure, their use is also associated with significant decrease in the systemic mean arterial pressure and this may limit their use in the management of right ventricular dysfunction secondary to pulmonary hypertension. In contrast, the selective pulmonary vasodilators, irrespective of their possible minor complications, have no significant effects on the systemic circulation. The use of isuprel in the treatment of right ventricular dysfunction, inspite of its non selective pulmonary vasodilator effect, has produced satisfactory results because in addition to lowering the pulmonary vascular resistance, it has a positive inotropic effect improving the ventricular function and positive chronotropic effect improving the right ventricular filling capacity. This encourages its use for management of such cases as an alternative to the selective pulmonary vasodilators particularly when they are not available.

Referrences

1. Boxt LM. MR imaging of pulmonary hypertension and right ventricular dysfunction. Magn-Reson-Imagin-Clin-N.Am. 1996 May, 4 (2): 307-25.

2. Davila RVG, Waggoner AD, Hopkins WE and Barzilai B. Right ventricular dysfunction in low output syndrome after cardiac operations: assessment by transesophageal echocardiography. Ann Thorac Surg 1995, 60 (4):1081-6.

3. Cartmill T, Dushane JW and McGoon DC. Results of repair of ventrcular septal defect. J Thorac Cardiovasc Surg 1966, 52: 486-99.

4. Clarkson PM, Neutze JM and Wardill JC. The pulmonary vascular bed in patients with complete transposition of the great arteries. Circulation 1976, 53:539-42.

5. Mcintyre RC, Harken AH and Fullerton. Mechanisms of pulmonary vasomotor function in normal and injured lung. Surgery 1994, 115: 273-5.

6. Rabinovitch M. Problems of pulmonary hypertension in children with congenital cardiac defects. Chest 1988,93:119-26.

7. Fullerton DA, Hahn AR, Banerjee A and Harken AH. Pulmonary vascular smooth muscle relaxation by cGMp versus cAMp mediated mechanisms. J Surg Res 1994, 57: 259-63.

8. Fullerton DA, Mitchel MB, Jones DN Maki A and Mcintyre RC. Pulmonary vasomotor dysfunction is produced with chronically high pulmonary blood flow. J Thorac Cardiovasc Surg 1996, lll,:190-7.

9. Heath D, and Edwards JF. The pathology of hypertensive pulmonary vascular disease. Circulation 1958, 18:533-7.

10. Rabinovitch M, Keane JE, Fellows KE, Castaneda AR and Reid L, Quantitative analysis of the pulmonary wedge angiogram in congenital heart defects: Correlation with hemodynamic data and morphometric findings in lung biopsy tissue. Circulation 1981, 63:152-64.

11. Rabinovitch M, Keane JF, Norwood WI, Castaneda AR and Reid L. Vascular structure in lung biopsy corrected with pulmonary hemodynamic findings after repair of congenital heart defects. Circulation 1984,69:655-67.

12. Fullerton DA, Jaggers J, Piedalue F, Grover F and Mcintyre R. Effective control of refractory pulmonary hypertension after cardiac operations. J Thorac Cardiovasc Surg 1997, 113:363-70.

13. Chen E, Bittner H, Tull F, Craig D, Davis R and Trigt P. Nitric oxide improves pulmonary vascular impedance, transpulmonary efficiency and left ventricular filling in chronic pulmonary hypertension. J. Thorac Cardiovasc Surg 1997, 113:849-57

14. Oohata H, Ueda N, Hashimoto T, Akamatsu S, Shimonaka H and Dohi S. Prostaglandin E1 at low doses improved right ventricular ejection fraction in anesthetic management for CABG. Masui, 1996 Oct, 45(10):1272-7.

15. Fullerton DA, Jones SD, Grobver FL and Mcintyre RC. Adenosine effectively controls pulmonary hypertension after cardiac operations. Ann-Thorac Surg 1996 Apr, 61(4):1118-23.

16. Fullerton DA, Kirson LE, Jones SD and McIntyre. Adenosine is a selective

pulmonary vasodilator in cardiac surgical patients Chest. 1996 Jan, 109 (l): 41-6.

17.Bello N, Saulnier F, Drault JN, Onimus T, Pruvot FR, Lafitte JJ, Durocher-A and Wattel F. Inhaled nitric oxide test for patients with stable chronic obstructive pulmonary disease: Value and feasibility. Rev-Mal Respir. 1996, 13 (l):37-42

18.Fullerton DA, Jones SD, Jaggers-J Piedalue F, Grover FL and MCIntyre RC. Effective control of pulmonary vascular resistance with inhaled nitric oxide after cardiac operation. J Thorac Cardiovasc Surg. 1916 Apr, 111(4):753-62

19.Morita K, Ihnken K, Buckberg GD, Sherman MP and Igliarro LJ pulmonary vasoconstriction due to impaired nitric oxide production after cardiopulmonary bypass. Ann Thorac Surg 1996, Jun, 61 (6): 1775-80.

20.Cirard C, Fargnoli JM, Godin RD, Dutheil V, Maitrasse B, Girardet P and Arvieux CC. Inhaled nitric oxide: Effects on hemodynamics, myocardial contractility and regional blood flow in dogs with mechanically induced pulmonary artery hypertension . J. Heart lung transplant. 1996 Jul, 15 (7): 700-8.

21.Goldsren DJ, Dean DA, Smerling A, OZMC, Burkhoff D and Dickstein M. Inhaled nitric oxide is not a negative inotropic agent in a porcine model of pulmonary hypertension. J Thorac Cardiovasc Surg 1997, 114:461-6.

22.Koelling TIY, Kirmse M, Disalvo T, William G, Xapol VM and Semigran MJ. Inhaled nitric oxide improves exercise capacity in patient with severe heart failure and right ventricular dysfunction. American Journal of Cardiology 1998, vol 81:1494-97.

23.Hillman ND, Cheiletz IM, Craig DM, Smith PK, Ungerleider RM and Meliones JN. Inhaled nitric oxide, right ventricular efficiency and pulmonary vascular mechanics: selective vasodilation of small pulmonary vessels during hypoxic pulmonary vasoconstriction 1 Thorac Cardiovasc Surg 1997, 113-.1006-13.

24.Bocchi EA, Bacal F, Auler J, de Corvalho MJ, Belotti G and Pileggi F. Inhaled nitric oxide leading to pulmonary oedema in stable severe heart failure. Am J Cardiol 1994, 74: 70-4.

Video-Assisted Thoracoscopic Versus Bilateral Supraclavicular Upper Dorsal Sympathectomy in Management of Primary Palmar Hyperhidrosis

ABSTRACT

Primary palmar hyperhidrosis is defined as sweating above and beyond physiological needs. Upper dorsal sympathectomy is considered the treatment of choice. This could be achieved either by open techniques or through endoscopic measures. The purpose of this study is to evaluate the efficacy of the video-assisted thoracoscopic approach for upper dorsal sympathectomy in comparison with the standard, supraclavicular approach. Patients were randomly allocated into 2 groups of 20 each, one with the supraclavicular technique as described by Telford and the other with the transthroacoscopic approach with the patient under general anaesthea using double human endotracheal intubation. The extent of supraclavicular sympathectomy varied from interganglionic devision between first and fourth ganglion (n=10), to devision between first and third (n =5), to resection of first and second ganglion (n =5), on the other hand extent of thorocoscopic sympathectomy varied from resection of second and third ganglion (n=5), to division from second to fourth (n=10), to division between second and fifth ganglion (n =5). The mean age was 22.8 and 23.6, there was positive family history in 5 and 3 patient, medical treatment tried in 18 and 12 patients respectively. Effects on plamer prespiration, postoperative complications, operative risk, patient satisfaction on short term follow up were examined. All operations achieved dry hands. The spraclavicular approach was more difficult, less cosmetic and associated with higher morbidity as regards the incidence of Horner's syndrome (3 vs.0). The main problem in both groups was compensatory hyperhidrosis, which was located mainly at the trunk, thigh and buttock in 55% and 45% of patients.

From our study we conclude that, both techniques achieve equally the target of dry hands, but videoassisted thoracoscopic sympathectomy has the added advantage of excellent exposure, being simple technique with less morbidity and minimal postoperative discomfort and shorter hospital stay (2 vs 1 day), and shorter operative time (37 vs 22 minutes for unilateral procedure).

Moustafa El Hamami (M.D.)[1], Mohamed Sherif Zaki (M.D.)[2], Nagy El Masri (M.D.)[3].

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INTRODUCTION

Primary hyperhidrosis may be loosely defined as sweating above and beyond physiological needs. Given the normal person-to-person variance of sweat production, it is difficult to be exact about a definition. Subjectively, hyperhydrosis occurs when sweating, is clinically noticeable under conditions where it would not normally be expected, or is excessive in

1-Departments of Cardiothoracic Surgery,
2-General Surgery
3-Anaesthesiology, Faculty of Medicine, Alexandria University

response to heat or emotional stimuli (1). The etiology is unknown. Excessive sweating usually affects the palms, axillae, and soles and in some cases the face groin and legs (2,3). Epidemiological data are rare, although it has been suggested that the incidence may be as high as 0.6% - 1% (3). Not only can it cause psychological and social problems, it may also result in occupational and educational difficulties. Symptoms usually appear at puberty and gradually improve after marriage, but in certain patients symptoms persist throughout adult life (4). It is important to distinguish primary or idiopathic hyperhidrosis from secondary hyperhidrosis due to underlying systemic illness as diabetes and hypoglycemia, thyrotoxicosis, pheochromocytoma and carcinoid. It could be a symptom of central nervous system disorders with irritative lesion of the hypothalamus and hyperpitutarism. It is therefore important to exclude any underlying condition when evaluating a patient with hyperhidrosis.

Medical treatment is effective only in milder cases. It includes the use of topical astringents or absorbing powders (5). Electrophoresis can provide temporary relief (6) plastic wrap in association with aluminum salts (5), and systemic anticholinergic drugs e.g. atropine have poorly tolerated side effects such as dry mouth and loss of accomodation (3).

Palmar hyperhidrosis is best treated by sympathetic ganglionectomy that is the only satisfactory and lasting surgical option (7). The sympathetic innervation of the eccrine glands of the palm and axilla lies in the ganglia T2 through T4 (28-31). It is these ganglia that must be ablated at operation. There are at least six open surgical approaches to these ganglia described, all of which carry a significant morbidity rate. These include the anterior supraclavicular approach of Telford (10), the posterior paravertebral approach of Adson (11), posterior midline (12), anterior transthoracic (13), axillary transthoracic approach of Atkins (14), and the axillary extra-thoracic with first rib resection (15).

Minimally invasive approaches include percutaneous radio-frequency ablation (16) and endoscopic axillary transthoracic sympathectomy.

The thoracoscopic access was introduced in 1942 by Goetz and Marr (17) and used on a large number of cases by Kux as early as 1951 (18). Since the introduction of video-endoscopic systems in 1986, various endoscopic procedures have been developed. This system provides excellent illumination and good magnification of the operative field via a minimally invasive approach and allows surgical teamwork in performing a delicate operation (1). In 1989, Koa developed the technique of video transthoracic endoscopic sympathectomy to treat palmar hyperhidrosis and it was soon proven to be a simple and effective therapy for palmar hyperhidrosis (19-21).

Surgical techniques vary from one-lumen endotracheal tube anaesthesia (4.22), double lumen endobronchial anaesthesia (23,24,25), one skin incision (4,22), two skin incisions (36,24,25), three skin incisions (26), room air pneumothorax (27), carbon dioxide pneumothorax (24,35,25,26,22), video-assisted

endoscopy (19.26), non video assisted endoscopy (24,23,25), destruction of the second (T2), the third (T3), and the fourth (T4) sympathetic ganglia (23,24.26) or destruction of the T2 ganglion alone (41).

The aim of this study is to evaluate the video-assisted thoracoscopic approach for upper dorsal sympathectomy in the management of palmar hyperhidrosis comparing this relatively new minimally invasive technique with the standard supraclavicular approach. Comparison includes the easiness of the technique, operative time, complications, hospital stay and effectiveness of the approach to achieve its goal, of postoperative dry hands, and to find the best thoracoscopic maneuver that lessens the postoperative complications, (as regards) extent of sympathectomy, method of destruction of the sympathetic ganglia either by electro-coagulation or surgical excision.

Patients and Methods

Forty patients with palmar hyperhidrosis presented to the Alexandria Main University Hospital during the period between January 1995 to January 1998, were subjected to bilateral upper dorsal sympathectomy (T2-3 and in most cases T4 ganglionectomy). Patients were randomly allocated into two groups, 20 patients in each group. In the first group, patients were accessed through supraclavicular approach as described by Telford (10), whereas in the second group patients were accessed thoracoscopically. The two groups matched as regards their ages, 22.8 (17-34 years) in the supraclavicular group and 23.6 (16-36 years) in the thoracoscopic group. There were 13 males and 7 females in the first group, while in group two there were 11 and 9 respectively. There was a positive family history of palmar hyperhidrosis in 5 (25%) in the first group and 3 (15%) in the second group. In the first group one patient had palmar hyperhidrosis only, 12 had palmar and planter hyperhidrosis, and 7 had palmar, planter and axillary hyperhidrosis i.e. 19 patients had concomitant planter hyperhidrosis, while 7 patients had axillary hyperhidrosis as well. In the second group 3 patients had palmar hyperhidrosis only, 3 had palmar and planter hyperhidrosis, 8 had palmar, planter and axillary hyperhidrosis and 6 had palmar and axillary hyperhidrosis i.e. 11 patients had concomitant planter hyperhidrosis while 14 patients had axillary hyperhidrosis (Fig. 1). Eighteen patients in the first group and 12 in the second group had sought medical and topical treatment for their condition without any success . In the first group 6 patients had palmar hyperhidrosis severe enough to affect their ability to write, five were affected in their ability to shake hands, four affected in their ability to write and shake hands, five were affected in their work. In the thoracoscopic group, there were 7, 4, 5, and 4 patients in each category respectively (Fig. 2). In most of the patients (75% and 80% respectively) coldness of the hands was the main associated symptom, while cyanosis was present in 30 and 60 % respectively. The main provoking stimulus for sweating in both groups was mental and emotional stress (75% and 80% respectively).

Patients were excluded if they had secondary hyperhidrosis or if subjected to previous sympathectomy operation with recurrence or if they had lung adhesions or pleural thickening previewed by plain x-ray chest.

Preoperatively all patients were subjected to a thorough history taking with

emphasis on location of sweating, associated hand manifestations, provoking stimuli, family history, past history of Diabetes Mellitus or thyrotoxicosis and history of previous attempts to medical, topical or surgical treatments. Routine investigations were done, and in 5 patients of group 1 and 3 patients in group 11, thyroid function tests were done to exclude the possibility of underlying thyrotoxicosis. Plain x-ray chest was done to every patient to exclude any underlying pathology especially that which might predispose to lung adhesions and to exclude pleural thickening. Supraclavicular sympathectomy was performed as described by Telford (32) with exposure and excision of the lower third of the stellate ganglion, T2,T3, and T4 if the axilla was affected.

In the thoracoscopic group, bilateral procedures were performed in all patients. The patient was placed in a supine position under general anesthesia with a double lumen endotracheal tube or Robert-Shaw tube. Palm temperature electrodes were placed to monitor the temperature of the palm during the procedure. The upper limb of the patient was abducted at 80°, the opposite arm was tucked to the patient's side until it was necessary to abduct it for avoidance of thoracic outlet compression of brachial plexus. Arterial pressure, heart rate, electrocardiogram, pulse oximetry, end-tidal CO2 pressure, were monitored during the operation. The lower part of the axillary hair was shaved and the skin was prepared from the upper part of the neck to well below the nipples. It was helpful to flex the operating table at the hip so that camera scope or operative instruments can be easily manipulated, this position allows the intercostal spaces to open wider allowing easier placement of trocers in the interspaces and presumably less pressure on the intercostal nerve while the trocar is in place.

Three ports of entry were required, one for the telescope and two for the hand instruments. A 1.5 cm incision was made in the skin crease of the fifth intercostal space mid-axillary line. A standard 10 mm open flexible trocar was passed through the wound. Once the initial troacer has been placed, a telescope was introduced through it. All further trocars were placed under direct vision in the thoracic cavity to avoid inadvertent injury to thoracic structures. The second troacar was usually placed in the fourth intercostal space in the posterior axillary line, and the third in the third space in the anterior axillary line.

The Video Endoscopic Procedure

The partially collapsed lung comes into view first. The upper sympathetic chain was then easily visualized and located about 0.3 cm lateral to the head of the ribs. The second, third, and fourth sympathetic ganglia could be identified along the sympathetic chain. The stellate ganglion is located above the apex of the pleural cavity and is usually covered by a yellow fat pad. Identification of these structures could be assisted by palpation using a probe. The endoscope was guided along the second rib from the lateral to the medial direction and the T2 ganglion will be found at the neck of the rib.

The techniques adopted was sharp sympathetic trunk dissection technique, to dissect the sympathetic chain, the parietal pleura was opened along the main trunk using diathermy over the third sympathetic

Table (I): Patient demography.

Parameters	Supraclavicular	Thoracoscopic
Age Mean (range)	22.8 (17-34)	23.6 (16-36)
Gender Male	13	11
Female	7	9
+ve family history	5 (25%)	3 (15%)
Medical treatment	18	12

ganglia exposing it and its rami communicantes which were dissected with a Maryland dissector and the trunk and rami were transected using scissors. Upward dissection towards the T2 ganglia was performed and the rami were transected first followed by the trunk above the ganglion. No diathermy was used to prevent any diathermic injury to the stellate ganglion. The chain was removed en bloc. If SpO^2 fell below 90% during the procedure, temporary inflation of the lung with pure oxygen was done to prevent hypoxemia. The endoscope was partially withdrawn and the anesthetist was asked to inflate the lung slowly so as to minimize the risk of reflex pulmonary edema. As the lung expands gradually, the endoscope and the sleeve were further withdrawn until the tip of the sleeve was just outside the intercostal muscles. A thoracostomy tube was inserted through the 10-mm troacer and connected to an underwater seal after the lung was reinflated. When the lung was fully expanded, the anaesthetist keeps the patient in an end inspiratory state and the surgeon removes the sleeve and the endoscope altogether. Artificial ventilation with positive pressure was resumed and the thoracostomy tube was removed at the end of the procedure, then the wound was closed by a subcuticular purse-string stitch with 4/0 chromic catgut. The procedure was repeated on the other side of the chest. The patient receives 5 mg of dexamethasone intravenously at the conclusion of operation. 0.5% Marcaine was injected at the port sites to relieve post-operative pain in the first 24 hours. Patient was watched to be sure that the lung was fully inflated at the end of the procedure. A chest X radiogram was taken a few hours after the operation exclude intrathoracic complications. The patient was discharged from the hospital the next morning.

Results

Operative data: All patients in both groups were subjected to bilateral sympathectomy (80 procedures), all bilateral procedures were performed in one session. In the supraclavicular group a low arch of the subclavian artery was observed in seven out of 40 procedures (17.5%). The arch of the subclavian artery was higher than normal in six operations (15%), Sibson's fascia was observed to be replaced completely by muscle fibers in two

Table (2): The Length of operative time (min), Intraoperative complications and Hospital stay (days) in the studied groups

	Supraclavicular	Thoracoscopic
Length of operative time (min) (unilateral procedure)	37 ± 8.1	22 ± 10.2
Intraoperative complications	0	0
Hospital stay (days)	2 ± 1	1

Table (3): Intraoperative monitoring of palmar skin temperature before and following sympathectomy in the studied groups.

	Supraclavicular	Thoracoscopic
Before induction	28.1 ± 2.9	28.3 ± 2.3
After induction	29.3 ± 3.1	29.4 ± 2.4
Before Sympathectomy	29.9 ± 3.7	29.8 ± 3.5
After sympathectomy	32.9 ± 2.5	32.7 ± 2.3

Table (4): The extent of sympathetic chain resection in the studied groups

Level of dissection	Supraclavicular	Thoracoscopic
T1 –T4	10 (50%)	0
T1 –T3	5 (25%)	0
T1 – T2	5 (25%)	0
T2 – T3	0	5 (25%)
T2 – T4	0	10 (50%)
T2 – T5	0	5 (25%)

Table (5): Effect of upper dorsal sympathectomy on hyperhidrosis

Site	Supraclavicular				Thoracoscopic			
	No of patients	Dry	Diminished	Wet	No of patients	Dry	Diminished	Wet
Hand	20	20 (100%)	0	0	20	20(100%)	0	0
Foot	19	15(78.9%)	2(10.53%)	2(10.53%)	11	8(72.73%)	1(9.09%)	2(18.18%)
Axilla	7	6(85.7%)	0	1(14.3)	14	13(92.8%)	0	1(17.14%)

Table (6): Effect of the level of supraclavicular sympathectomy on the treatment of hyperhidrosis.

Level of resection	Group	Site	No	Response		
				Dry	Diminished	Wet
T1- T4	A	Hand	10	10 (100%)	0	0
	B	Feet	9	8 (88.8%)	1(11.1%)	0
	C	Axilla	6	6 (100%)	0	0
T1- T3	D	Hand	5	5(100%)	0	0
	E	Feet	5	4(80%)	1(20%)	0
	F	Axilla	0	0	0	0
T1- T2	G	Hand	5	5(100%)	0	0
	H	Feet	5	3(60%)	0	2(40%)
	I	Axilla	1	0	0	1(100%)

Z test value between all groups shows non significant difference in the level of sympathectonl on palmer and planter hyperhidrosis while it is significant between C and I cases. =2. 646

operations (5%) enlarged scalene lymph nodes observed in a single operation (2.5%), medial deviation of the brachial plexus was observed in a single case (2.5%) which was retracted without any problems on performing the operation.

In the thoracoscopic group the second rib in the 20 patients was parallel to the third rib. In 9 patients, the first rib was not readily visible just below the dome of the pleura, but was palpable with the diathermy probe. The first rib of the remaining 11 patients was readily visible but was not parallel to the second rib as the third rib was.

The operative duration for a unilateral

Table (7): Effect of the level of thoracoscopic sympathectomy on the treatment of hyperhidrosis.

Level of resection	Group	Site	No	Response		
				Dry	Diminished	Wet
T2- T4	A	Hand	10	10 (100%)	0	0
	B	Feet	7	5 (71.42%)	1(14.8%)	1(14.8%)
	C	Axilla	8	8 (100%)	0	0
T2- T3	D	Hand	5	5 (100%)	0	0
	E	Feet	2	2 (100%)	0	0
	F	Axilla	1	0	0	1 (100%)
T2- T5	G	Hand	5	5 (100%)	0	0
	H	Feet	2	1 (50%)	0	1 (50%)
	I	Axilla	4	4 (100%)	0	0

Z test value between all groups shows non significant difference in the level of sympathectonl on palmer and planter hyperhidrosis while it is significant between C and F = 2.. 645 and F and I = 2.645.

Table (8): Post operative complications in the studied groups.

	Supraclavicular	Thoracoscopic
Surgical emphysema	0	3 (15%)
Pneumothorax	3 (15%)	3 (15%)
Mild	2 (10%)	3 (15%)
Severe	1 (5%)	0
Haemothorax		
Mild	1 (5%)	1 (15%)
Moderate	0	1 (10%)
Severe	0	0
Atelectasis		
Mild	0	3 (15%)
Severe	0	
Horner's syndrome	1 (15%)	0
Transient	1 (15%)	
Permanent	0	
Neuralgia	2 (10%)	1 (5%)
Compensatory Hyperhidrosis	1 (55%)	9 (45%)
Infection	1 (5%)	1 (5%)
Phantom sweat	1 (5%)	1 (10%)
Chest pain for One week	1 (5%)	8 (40%)*

* **Significant**

Table (9): The correlation between compensatory hyperhidrosis and the extent of chain resection.

Group		Level of resection	No of patients	Incidence of compensatory hyperhidrosis
1	A	T1-T4	10	7 (70 %)
	B	T1- T3	5	2 (40%)
	C	T1- T2	5	2 (40%)
11	D	T2-T4	10	4 (40%)
	E	T2- T3	5	1 (20%)
	F	T2 –T5	5	4 (80%)

Z test value A,B = 1.118 n.s.
A.C= 1.118 n.s
B,C = 0 n.s
D,F = 2.11 s

n.s= non significant
s = significant
D,E = 1.005 n.s
E,F = 1.98 s

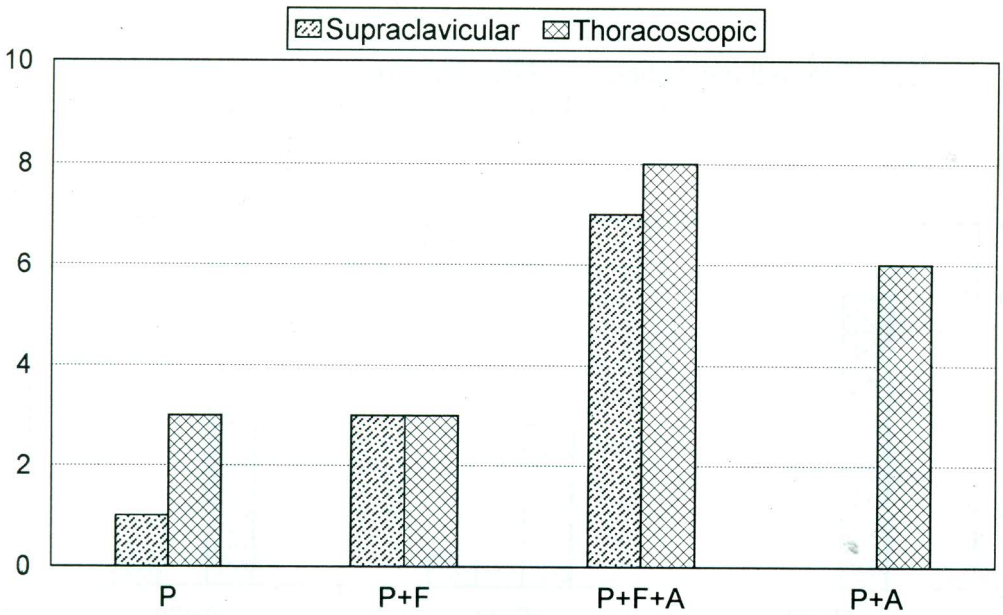

Fig. (1): Concomitant planter and axillary hyperhidrosis.
P = palm F = Feet A = Axillay

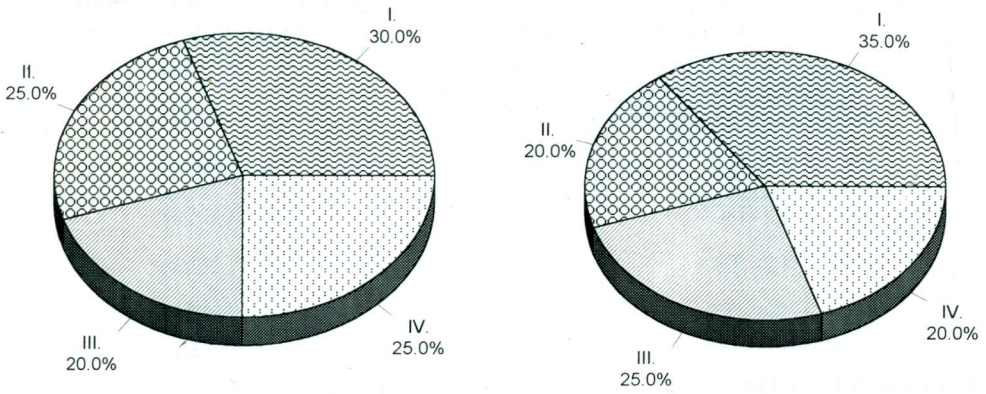

Fig. (2): Indication for sympathectomy.
I. Sweat affect ability to write
II. sweat affect ability to shake hands
III. Sweat affect ability to write and shake hands
IV. Sweat affect ability to work

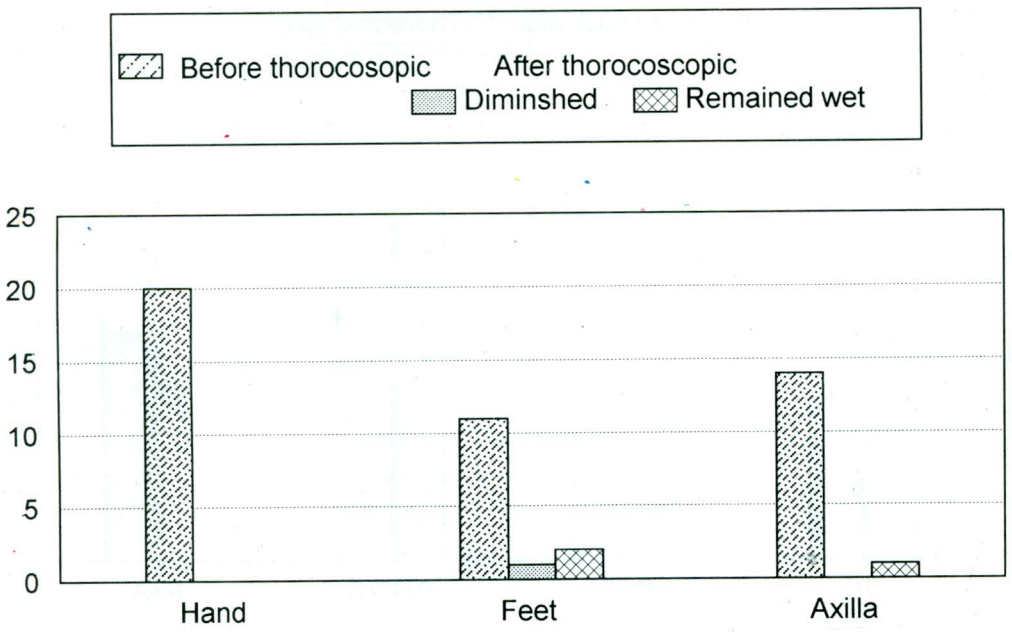

Fig. (3): Sweat production at different sites before and after thorocosopic sympathetomy

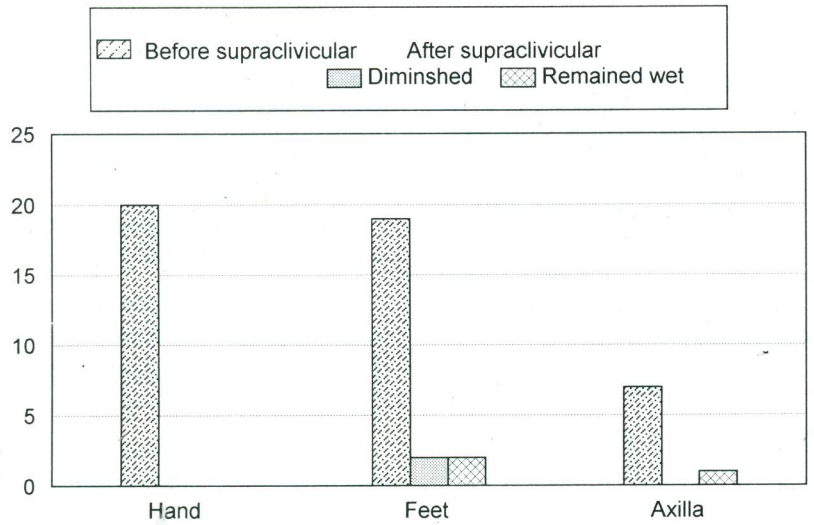

Fig. (4): Sweat production at different sites before and after supracilicicular sympathetomy

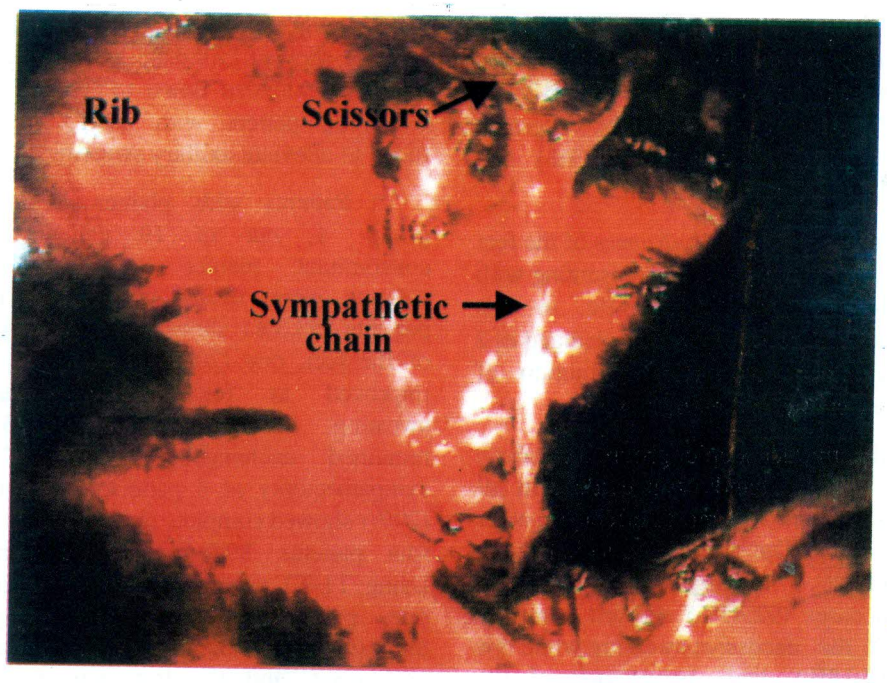

Fig. (5): The specimen in the T2, T3 and T4 ganglia is transected

cervical sympathectomy varied from 30-45 minutes with a mean duration of 37 minutes. On the other hand unilateral thoracoscopic sympathectomy varied from 15-30 minutes with a mean duration of 22 minutes. There were no intraoperative complications in both groups. Palm temperatures changes were recorded in both groups as shown in table (3) .

Effect on hyperhidrosis: (Table 5)

In the supraclavicular group, all patients showed complete dryness of both hands at the end of the procedure on each side. Hands were dry, red, hot, and showed venous dilatation markedly noted on the dorsum of the hand. other immediate sudomotor effects of supraclavicular sympathectomy on other parts were:

*Out of seven patients with concomitant axillary hyperhydrosis, six cases (85.7%) showed complete relief of the excessive sweating while one case (14.3%) had persistence of the sweating.

*There was complete dryness of the feet in 15 out of the 19 cases presenting with hyperhidrosis plantaris, while in the remaining. 4 cases it was unchanged in 2 patients and remarkable diminution of planter sweating in the other two.

In the thoracoscopic group, immediate drying of the hands was evident in all patients. Other sudomotor effects on other parts were: * Out of fourteen patients with concomitant axillary hyperhydrosis, thirteen cases (92.85%) showed complete relief of the excessive sweating while one case (7.14%) had persistence of the sweating. * There was complete dryness of the feet in 5 patients of the 11 presenting with concomitant planter hyperhidrosis, 5 patients (45.45%) remained unchanged and one showed remarkable diminution of planter sweating.

Effect of level of sympathectomy on the treatment of hyperhidrosis:

a) Palmer hyperhidrosis: All patients were completely and immediately relieved of their annoying palmer hyperhidrosis regardless of the level of the resection.

b) Patients with concomitant axillary hyperhidrosis showed complete relief in six out of seven in group 1, the level of resection extended down to the fourth thoracic ganglion, while the remaining case T1-T2 resection failed to alleviate excessive axillary sweating. On the other hand, in group 2 thirteen out of the 14 patients showed complete relief where the resection extended down to T4 or T5, the remaining patient with T2-T3 resection failed to alleviate axillary sweating.

c) Patients with planter sweating in group 1, out of 19 patients with concomitant planter hyperhidrosis, 9 patients were treated with T1-T4, three patients (33.3%) showed complete dryness of the feet, one (20%), one patient (11.1) improved as regards the excessive sweating, while 5 patients (55.6%) remained unchanged. On using T1-T2 sympathectomy in 5 patients, one patient (20%) showed complete dryness of the feet, four patients 80% remained unchanged. Using T1-T3 sympathectomy in 5 patients, one patient (20%) showed complete dryness, 3 patients (60%) remained unchanged and the last patient (20%) showed some improvement. In group 11, out of the 11 patients with concomitant

planter hyperhydrosis, 7 patients were treated by T2-T4 resection technique where five (71.42%) showed complete dryness of the feet and one (14.8%) showed diminution of the sweating and one (14.8%) showed no change Adopting the T2-T5 resection technique on two patients, one (50%) showed complete dryness and the other showed no improvement. Adopting the T2-T3 resection technique on two patients, complete dryness was observed in both (100%) hyperhidrosis

There were no deaths or major morbidities in both groups. Complications are listed in table (8) which shows that mild surgical emphysema was encountered in only 3 patients in group 2 that resolved spontaneously within 48 hours. Pneumothorax occurred in 3 patients in the supraclavicular group due to accidental pleural tear, one of them was severe and necessitated insertion of an intercostal tube for 3 days. In the thoracoscopic group, there were three mild cases of surgical emphysema that resolved spontaneously. Haemothorax was encountered in one patient in group 1 and in 5 patients in group 2, two (10%) of them needed needle aspiration. Horner's syndrome was observed in 6 cases, five were transient while one showed persistence of the condition. The level of resection of the chain in those affected patients was T1 -T2 in five patients and T1 -T3 in one patient. On the other hand Homer's syndrome was not detected in the thoracoscopic group. Arm neuralgia was detected in two patients (10%) and one patient (5%) in group 1 and 2 respectively. Pain was along the medial aspect of the forearm and hand, and was controlled by analgesics and relieved in 3 months. Compensatory hyperhidrosis was observed in 11 patients in the first group and in 9 in the second group. It was located mainly in the truck, loin and ventral aspect of the thigh. The stimulus to this hyperhidrosis was thermal.

(In more extensive resection T1-T4 and T2-T5 there was high incidence of compensatory hyperhidrosis).

Chest pain lasting for more than one week was noted in one case (5%) in the supraclavicular group while in the thoracoscopic group 8 patients (40%) presented with chest pain that decreased their subjective satisfaction.

Discussion

A new surgical method should be evaluated by the achievement of its goal, in short and long term and by the attending surgical complications. The vast experience accumulated with the different "open" surgical methods make their results the golden standard against which thoracoscopic sympathectomy should be compared.

The main goal of this operation is to achieve dry hands. This study and others (28.29,30,31,2) have shown that in 95% to 100% of the patients a satisfactory surgical result can be achieved no matter what approach has been used. Although some authors reported better visualization of the sympathetic trunk by open surgical procedures (30). Others stated a high success rate with endoscopic procedures as well (2-23,24), and endoscopic resection is gaining popularity day by day.

Different techniques have been described to perform video-assisted thoracoscopic sympathectomy. Some authors have reported their experience using only one single trocar and disrupting

the connections from the sympathetic chain to the brachial by thermocoagulation or laser coagulation. Although only one incision is necessary in these cases, intraoperative histologic confirmation of the sympathetic ganglion is not possible (32). There is some anatomical variability of the upper thoracic sympathetic chain (33), thus this technique may result in higher rates of failure and recurrence (3.26). Other disadvantages using one port technique reported by Lee et al (32), include the surgeons inability to deal with pleural adhesions hampering access to the chain, difficulty in controlling hemorrhage from intercostal and azygos vessels near or crossing the chain, and problems dissecting and separating the chain from other neural structures and vessels. Although the use of one skin incision is cosmetically superior to two or three skin incisions Wong (14) found that the latter approaches provide more room for safer manipulations of instruments in cases with pulmonary adhesions. Ablation of the sympathetic chain could be conducted with laser (19) electrocautery (36, 24, 22, 27) or use of microscissors and forceps to excise the chain precisely (26). Our technique using three small ports achieved good cosmetic results, and no patient was unhappy with small unidentifiable scars after the operation. We were able to excise the sympathetic chain, precisely dissect and lift the chain off adjacent blood vessels , retract under deflated lung to improve access and excision of the sympathetic chain and control of bleeding. it is possible that less incidence of postoperative intercostal neuralgia is encountered with the use of laser than with electrocautery, in which the spread of the electric current may damage the nearby intercostal nerve along the lower border or the inner surface of the rib (36) . Hederman (36) stated that, the use of laser is expensive and not yet shown to have any great advantage. On the other hand, unipolar diathermy instruments are cheaper and are readily available in most centers, it is also possible to diminish the severity of the postoperative intercostal neuralgia by centering the area of electrocautery on the individual ganglion. Hashmoni (28) prefers to use scissors to resect the sympathetic chain that allows histological confirmation. Although resection using the thoracoscope is more complicated than simple electrocautery, and it requires the use of a third access port, prolongs the operation and may result in a higher rate of complications, we and others (37) prefer to divide the sympathetic chain with scissors without diathermy to prevent diathermic injury of the stellate ganglion or intercostal nerve, and to avoid any possibility of recurrence especially that data of late recurrence after the use of diathermy or laser are still unavailable.

Intraoperative testing for completeness of sympathectomy could be achieved by palpation for moisture that may not always be reliable, or by precise temperature measurement or plethysmography or digital laser blood flow methods (36). Some authors (38.32) suggest that elevation of the palm temperature of approximately 1-3°C indicate the achievement of an adequate sympathectomy for a long lasting therapeutic effect for palmar hyperhidrosis. Wong et al (34) recommended to place a bag of ice beneath the dorsum of the hand to help in observing the changes of palm temperature. We found that in both groups

a successful outcome could be expected when there is a temperature rise of 1-3°C after the procedure. Placing an ice bag beneath the dorsum of the hand does not appear acceptable to us as excessive cooling may cause peripheral vasoconstriction to such an extent that the hand does not react properly to changes in temperature and it may abolish the rise in palm temperature despite proper sympathectomy. The extent of sympathetic chain destruction or excision should ensure success and avoid recurrence and at the same time minimize the incidence of compensatory hyperhydrosis, this varies from T2 ganglionectomy (23) to the destruction of T2-T3 and T4 ganglia (24,23,26) and sometimes the lower part of the stellate ganglion. Wong and others (24.34,26,27) suggest that the therapeutic effects of destruction of T2 and T3 ganglia are as good as those of destroying more sympathetic ganglia. Hederman (36) noted that the wider the sympathectomy, while preserving the stellate ganglion, the more likely would it be to obtain a good primary result. However, the incidence of compensatory hyperhidrosis of the waist was as high as 64%. He reduced the extent of electrocoagulation to the second dorsal ganglion alone, the portion of the chain between it and the two adjoining ganglia. This has reduced the incidence of compensatory hyperhidrosis to about 24%. Limiting the extent of sympathectomy is supposed to reduce operative time, intraoperative bleeding and the incidence of Horner's syndrome (37) .

Edmondson (24) found that extending thoracoscopic sympathectomy to involve T4 and T5 gave better results in reducing concomitant axillary hyperhidrosis (80% complete dryness and 20% partial dryness) . On the other hand using supraclavicular approach in which ablation of the T4 ganglion is relatively inaccessible yielding results of only 8% complete dryness and 78% partial dryness of the axilla. We found that T2-T4 sympathectomy is the level of choice as it entirely avoids the unpleasant sequelae of Horner's syndrome. It produces a sympathetic denervation as adequate as the more radical operation, e.g. T1-T5, it denervates the axilla and it seems to prevent any earlier return of sympathetic activity than T2-T3. Difficulty of removal of the fourth sympathetic ganglion through the supraclavicular approach illustrates a very important advantage of the thoracoscopic approach over the supraclavicular one.

All patients in both groups suffering of palmar hyperhidrosis were relieved of their excessive hand sweating, coldness and cyanosis by sympathectomy irrespective of the level of resection. This emphasizes the value of upper dorsal sympathectomy for treatment of primary palmar hyperhidrosis whatever the surgical approach used. However Adar (3) had 97% gratifying results through the supraclavicular approach while (12) through the posterior approach it was 92% by Cloward Inability to identify the sympathetic chain during the operation, either through the supraclavicular or posterior approach, is the commonest cause of failure in these approaches.

An interesting finding concerning the sweaty feet deserves comment and discussion. Preoperatively 19 (95%) of patients in group 1 and 11 (55%) in group 11 suffered from concomitant planter hyperhidrosis. Following surgery, feet were

completely dry in 15 (78.9%) in group 1 and in 5 (72.73%) in group 11, diminished sweating in 2 (10.53%) and 1 (19.09%) respectively and remained wet in 2 (10.53%) and (18.18%) respectively (Fig. 3,4). This observation, which can not be explained on the basis of our present knowledge of anatomy and physiology, could be explained by a theory postulated by Cloward (12) where 22% of his cases showed complete dryness of the feet, while many more showed considerable improvement. He claimed that the sudomotor function is located in the sharply demarcated area in the cerebral cortex representing various parts of the body similar to the motor cortex. Individual motor fibers from each of these areas may descend in the spinal cord, sympathetic chain, or both. In hyperhidrosis it is known that the lesion responsible for the excessive sweating is central rather than peripheral probably a congenital cortical anomaly involving the hand and foot areas. So, if the tract from these areas descends entirely in the sympathetic chain, surgical resection of the chain could explain the postoperative paralysis of sudomotor pathways to the remainder of the body descend in the spinal cord, and then pass to the sympathetic ganglion in the usual manner. Our results show that there is no influence of the more extensive resection of the chain nor the surgical approach of sympathectomy on that phenomenon.

Most immediate complications after operation were reversible, self limiting, not severe, and had no permanent clinical impact. Pneumothorax encountered in only 3 cases in the endoscopic group, and in 3 cases of the supraclavicular group, one of them was severe and necessiated insertion of intercostal tube. Other series showed 2% of pneumothorax that needed chest drainage after endoscopic sympathectomy (24,2), and 4% to 6% after supraclavicular operation (3,9). Chest physiotherapy including breathing exercises, encouragement of cough and early ambulation of patient seems to be of value in helping a rapid and complete resolution. Chest drains were not routinely used at the end of the thoracoscopic procedure and this has not caused any increased patient morbidity. The simple maneuver to inflate the lung during closure of the wound with removal of the chest tube at the end of the closure was enough to ensure complete lung expansion in most cases.

Surgical emphysema should not be considered as a complication since it gives rise to no troubles and requires no treatment. It usually disappears spontaneously within few days. Lung atelectasis manifested in 15% of our cases, could be considered as a non specific complication in patients undergoing surgery rather than a specific one to the thoracoscopic approach. The blame in such cases is usually put on the anaesthetic technique. Postoperative atlectasis can be largely prevented by early mobilization, frequent change in position and encouragement to cough. Clearing of the airway is sufficient by chest percussion, coughing, and nasotracheal suction.

Horner syndrome, which the patient always dislikes is the major complication after supraclavicular sympathectomy. It differs from other compllications by being irreparable, possibly permanent, and it

causes severe functional and aesthete disturbances to the patient. It is one of the main advantages of the endoscopic approach in its debate with the supraclavicular one. The incidence of temporary Horner Syndrome in our supraclavicular group was 15%, others reported up to 43% with permanent symptoms occuring in 2% to 8% (3,9) . The excellent results obtained by the endoscopic technique is due to the fact that, the stellate ganglion is well protected by the dome of the pleura and sometime covered by a fat pad. Also, the excellent exposure of the chain, and hence careful protection of the stellate ganglion is another factor (4). It was suggested that, the high incidence of Homer's Syndrome in open operation is due to anatomic variance. This is unlikely because none of the transaxillary approaches carry an equivalent risk, and other studies have shown a decrease in the Horner's with operative experience (24). Direct injury of the stellate ganglion has been implicated as being responsible for Horner's Syndrome. Violent manipulation and excessive dissection of the sympathetic chain damaging efferent fibers from the upper part of the stellate ganglion, ascending current from diathermic transaction is propably another cause of this complication rather than resection of T_1 portion of the ganglion (17). So this major complication could be avoided by non use of electrocautery in severing the chain and by avoidance of dissection of the stellate ganglion, by achieving T_2-T_4 sympathectomy which produces a very sufficient sympathetic denervation without producing Horner's Syndrome.

Compensatory hyperhidrosis is the most often reported side effect of sympathetic trunk resection in hyperhidrosis, it occured in 55% and 45% in group I and II respectively, which is similar to the incidence reported by other authors ranging from 37% to 85% (2.3.19). The cause of this Compensatory sweating is considered as compensatory response and serves a thermoregulation function (40,41,42). Bonjer et al (17) suggested that the incidence of compensatory sweating is related to the extent of sympathectomy, and this was also the case in our study where more extensive resection resulted in increased incidence of compensatory sweating. Compensatory hyperhidrosis, however, was only a minor inconvenience to most patients compared with the original problem, yet nearly all preferred this to their original complaint.

Postoperative neuralgia reported by Hashmonai (21) in 3 patients (out of 24) after cervical sympathectomy, and in 1 patient (out of 24) after tharcoscopic sympathectomy. In our series, there was 2 (10%) in supraclavicular group and 1 (5%) in thoracoscopic group.

The complication is explained by brachial pleuxus contusion from pressure by retractors which usually involves the lower trunk in supraclavicular sympathectomy, while in the thoracoscopic group it was attributed to hyperabduction of the uppper limb during surgery.

Phrenic nerve damage was recorded in 1-2% after supraclavicular sympathectomy (9,30), on the other hand this complication was not recorded after thoracoscopic sympathectomy as phrenic nerve could easly be identified away from the sympathetic chain.

The cosmetic result contrasts markedly using the two approaches, as more patients

(29%) reported dissatisfaction after cervical supraclavicular approach.

In conlcusion, hyperhidrosis is essentially a benign condition and any operation must keep morbidity to minimum, with minimal disruption of normal tissue, and should be acceptable cosmetically and functionally. Both supraclavicular and thoracoscopic approaches achieve effectively and equally the target of dry hands. The endoscopic transaxillary approach seems to fulfil all the above criteria and its results compare favorably with those from all other open tehniques. It has the added advantage of excellent exposure to the sympathetic chain, and simple access to T4 which is important in the control of axillary sweating. The risk for neural damage, including Horner's Syndrome is virtually absent. It offers minimal postoperative discomfort and excellent cosmetic results with short hospital stay and early return to work. The technique is easily learned , and requires no additional capital outlay in hospital already performing routine laparoscopy. Patients should be warned of the potential side effects of compensatory sweating, but they may be reassured that the vast majority of patients find these symptoms only a minor inconvenience in comparison with their original complaint.

Until long term results of electrocauterization are published, scissors dissection is considered by us the method of choice in destroying the sympathetic chain to lessen the chance of recurrence. There should be no controversy about the level of sympathetic chain resection, as T2-T4 ganglionectomy can achieve the target of dry hands and axilla with minimal accepted morbidity.

References

1. Ming-Chien, Kao, Yi Long Chen, Jue-Yi Lin, Chung-Szu Hsich, and Jui-Chang Tsai.Endoscopic sympathectomy treatment for craniofacial hyperhidrosis. Arch Surg 1996, 131: 1091-94.

2. Kux M. Thoracic endoscopic sympathectomy in palmar and axillary hyperhidrosis. Arch Surg 1978; 113: 264-66.

3. Adar R, Kurchin A, Zweig A, Mozes M. Palmar hyperhydrosis and its surgical management. Ann Surg 1977; 186.34-41.

4. Hang-Jung Chen, Din-Yuan Shih, and Si-Tun Fung. Transthoracic endoscopic sympathectomy in the treatment of palmar hyperhidrosis. Arch Surg 1994; 129: 630-33.

5. Shelly WB, Hurley HJ. Studies on topical antiperspirant control of axillary hyperhidrosis. Acta Derm Venereal 1975; 55: 241-260.

6. Midtgaard K.A new device for the treatment of hyperhidrosis by iontophoresis. Br J Dermatol 1986; 114: 485-88.

7. Moran KT, Bradly MP. Surgical management of primary hyperhidrosis. Br- J Surg 1991; 78: 279-283.

8. Hyndman OR, Wolkin J. Sympathectomy of the upper extremity. Evidence that only the second dorsal ganglion needs to be removed for complete sympathectomy. Arch Surg 1942; 45: 145-55.

9. Greenhalgh RM, Rosengarten DS,

Martin P. Role of sympathectomy for hyperhidrosis. BMJ 1971; 1: 332-34.

10. Telford E. The technique of sympathectomy. Br J Surg 1935.121: 113-10.

11. Adson AW, Brown EF. Raynaud's disease of the upper extremities: Successful treatment by resection of the sympathectomy cervicodorsal and second thoracic ganglia and the intervening trunk. JAMA 1992; 92. 444-49.

12. Cloward R. Hyperhidrosis. J Neurosurg 1969; 30. 545-51.

13. Palmbo L. Anterior transthoracic approach for upper thoracic sympathectomy. Arch Surg 1982; 72: 659-66.

14. Atkins HJB. Sympathectomy by the axillary approach. Lancet 1954; 1: 538-39.

15. Roos D. Experience with first rib resection for thoracic outlet syndrome. Ann Surg 1971; 17-1-429.

16. Wilkinson H. Radiofrequency percutaneous upper thoracic sympathectomy. N Engl J Med 1984. 311: 43 -36.

17. Goetz RH, Marr JAS. The importance of the second thoracic ganglion for the sympathetic supply of the upper extremity-two new approaches for its removal, Clin Proc 1944; 3: 102-14.

18. Kux E. The endoscopic approach to the vegetative nervous system and its therapeutic possibilities especially in duodenal ulcer, angina pectoris, hypertension and diabetes. Dis chest 1995; 20: 139-47.

19. Kao MC. Videoendoscopic sympathectomy using fiberoptic CO2 laser to treat hyperhidrosis. Neurosurgery 1992; 30: 131-35.

20. Kao MC, Tsai JC, Lai DM, Hasio YY, Chin MJ. Autonomic activities in hyperhidrosis patients before, during, and after endoscopic laser sympathectomy. Neurosurgery 1994. 34: 262-68.

21. Kao MC, Lee WY, Yip KM, Hasio YY, Lee YS, Tsai JC. Palmar heperhidrosis in children: treatment with video endoscopic laser sympathectomy. J Ped Surg 1994.129. 387-91.

22. Eothberg E, Claes E, Drott C. Electrocautery of the upper thoracic sympathetic chain: A simplified method. Br J Surg 1993; 80: 862.

23. J Bayne, TN Walsh, and WP Hederman. Endoscopic transthoracic electrocautery of the sympathetic chain for palmar and axillary hyperhidrosis. Br J Surg 1990, 77, 1046-1049.

24. Edmandson RA, Banerjee Anjan, and John Rennie. Endoscopic trnasthoracic sympathectomy in the treatment of hyperhidrosis. Arm Surg 1992. 215: 289-93.

25. Jedeikin R, Olsfanger D, Shachor D, Mansoor K. Anaesthesia for transthoracic endoscopic sympathectomy in treatment of upper limb hyperhidrosis. Br J Anaesthesia 1992; 69: 349-51.

26. Robertson DP, Simpson PK, Rose JE, Earza JS. Video assisted endoscopic thoracic ganglionectomy. J Neurosurg 1993; 79: 238-40.

27. Herbst F, Plas EG, Fugger R, Fritsch A. Endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limbs. A critical analysis and long term results of 480 operations. Arm Surg 1994; 220: 86-90.

28. Moshe Hashmonal, Doron Kopelman, and Moshe Schein. Thoracoscopic versus open supraclavicular upper dorsal sympathectomy. A prospective randomised trial. Eur J Surg 1994; Suppl 572: 13-16.

29. Drott C, Eothberg E, Elaec E. Endoscopic procedures of the upper thoracic sympathetic chain. Arch Surg 1993; 128: 237-41.

30. Hashmanac M, Kopelman D, Kein O, Schein M. Upper thoracic sympathectomy for primary hyperhidrosis of the upper limbs. World J Surg 1982; 6: 458-6.

31. Sternberg A, Brickman S, Kott I, Reiss R. Transaxillary thoracic sympathectomy for primary hyperhidrosis of the upper limbs. World J Surg 1982; 6: 458-63.

32. Kheng Hin Lee, Peter YK Hwang. Video endoscopic sympathectomy for palmar hyperhidrosis. J of Neurosurgery 1996; 84: 484-486.

33. Von Rhede Von der Kloot E, Drukker J, Lemmens NAJ. The high thoracic sympathetic nerve system-its anatomic variability. J Surg Res 1986, 40: 112-19.

34. Cheuk-Wah Wong. Transthoracic video endoscopic electrocautery of sympathetic ganglia for hyperhidrosis palmaris: Special reference to localization of the first and second ribs. Surg Neural 1997; 47:224-30.

35. WP Hedrman. Presented future trends in thoracoscopic sympathectomy. Eur J Surg, 1994.1572: 17-19.

36. Dominique Gossat, Sylvie Fritsch, and Michel Celerier. Thoracoscopic sympathectomy for upper limb hyperhidrosis: Looking for the right operation. Ann Thorac Surg 1997; 64:975-8.

37. HJ Bonjor, JF Hamming, and H Van Urk. Advantages of limited thoracoscopic sympathectomy. Surg Endosc 1996; 10. 721:23.

38. Ming-Chien, Kao. Transthoracic endoscopic sympathectomy in the treatment of palmar hyperhidrosis. Arch Surg; 1995 130: 1244.

39. Adar R. Compensatory sweating after upper dorsal sympathectomy. J Neurosurg 1979.151: 424-5.

40. Eutmann L. Distribution of disturbances of sweat secretion after extirpation of certain sympathetic cervical ganglia in man. J Anat 1940, 74: 537-49.

41. Monro PAE. Sympathectomy, Anatomical and physiological study with clinical applications. London: Oxford, 1959: 290,

42. Shelly WB, Florence R. Compensatory hyperhidrosis after sympathectomy. NEJM, 1960; 263: 1056-8.

Evaluation of Intra-Aortic Protamine Infusion Versus Peripheral Venous Infusion in Patients with Severe Pulmonary Hypertension in Open Heart Surgery

ABSTRACT

For many years protamine have been given intravenously to neutrilize heparin at the end of C.P.B. It has been well documented that in some patients IV protamine injection is associated with unpredictable haemodynamic changes as systemic hypotension, pulmonary hypertension and lastly right ventricular failure and myocardial depression. Prospective human studies on the cardiovascular effects of protamine vary in their methods with respect to the dose of protamine, rate of injection, route of administration, pre-operative physical status of the patients, anaesthetic management and lastly the haemodynamic variables that were measured. The objective of this study is to evaluate the haemodynamic changes of intravenous versus intra-aortic protamine sulphate (P.S) infusion at the end of CPB to reverse action of heparin in open cardiac surgery. This study was done in cardiothoracic surgical department at Alexandria Main University Hospital on 40 adult patients. (24 Male and 16 Female) admitted for elective open heart surgery, 20 of them with preoperative normal average pulmonary artery pressure (19.53±1.3 mmHg) [Group I] and other 20 with moderate to severe pulmonary hypertension (31.2±3.5 mmHg) [group II]. In each group, P.S injected intravenously in 10 patients and intra-aortic in other 10 patients. Parameters recorded were, HR, Lead II ECG, MABP, CVP, Cardiac Index, SVR, MPAP, PAOP, and PVR. In the present study, we detect no significant difference concerning the haemodynamic changes following P.S administration by intravenous versus intra-aortic route in group I. On the other hand, the decrease in ABP, SVR were statistically significant when P.S given by I.V versus intra-aortic route in group II. But the decrease in MABP and SVR and the increase in CVP, PAP and PVR that's occur when PS injected IV versus IA in G II were statistically significant. These observation strongly indicated that induction of haemodynamic changes is initiated in the lungs and there is a rapid mixing of protamine with blood when protamine infused by intra-aortic route, because the relatively small volume of protamine, compared with cardiac output, would mix quickly and completely with fast flowing blood that circulates, Protamine will reach the coronary and pulmonary circulation after it has been mixed thoroughly with blood and possibly after neutralization process is completed. On the basis of these findings, it would seem safer to give P.S into the aorta in patients with impaired right ventricle or preexisting pulmonary hypertension.

Abbreviation: PS: Protamine sulphate, CPB: Cardiopulmona byrpass, ACT: Activated clotting time, IV: Intra venous, IA: Intra-aortic, MABP: Mean arterial blood pressure, CVP: Central venous pressure, CI: Cardiac index, PAP: Mean pulmonary artery pressure, PAOP: Pulmonary artery occluded pressure, PVR: Pulmonary vascular resistance, mmHg: Mille mitter mercury, cm H2O: Centemeter water, GI:Group one, GII: Group two, BSA: Body surface area, MVR: Mitral valve replacement, AVR: Aortic valve replacement, DVR: Doublvalve replacement, *:Significant, C.O.P: Cardiac output.

Moustafa Elhamami[1], MD, Hesham Fouad Shabaan MD, Maha Hegazi[3] MD

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1-From Cardio-thoracic Surgery deparement, 2-Anaethesia Deparemt, 3-Physiology Deparement, Faculty of Medicine, Alexandria University

INTRODUCTION

For many years protamine have been given intravenously to neutrilize heparin at the end of C.P.B. Protamine is a sulfated polycationic peptide, it is a highly alkaline compound obtained from fish. Heparin is a highly sulfated polyanionic mucopolysaccharide, when protamine is added to heparinized blood, a tight ionic bonding forms between heparin and protamine and coagulation returns to normal state. (1)

It has been well documented that in some patients IV protamine injection is associated with unpredictable haemodynamic changes as systemic hypotension due to decrease in systemic vascular resistance (SVR), pulmonary hypertension and lastly right ventricular failure and myocardium depressions Kim et al attributed the haemodynamic changes to histamine release or rarely to anaphylaxis to heparin protamine compound.

Prospective human studies on the cardiovascular effects of protamine vary in their methods with respect to the dose of protamine, rate of injection, route of administration, pre-operative physical status of the patients, anaesthetic management and lastly the haemodynamic variables that were measured.

Many human protamine reactions can be avoided by slow infusion (10 mg/minute), but if haemodynamic changes were avoided by extremely slow protamine infusion, a cost-benefit analysis would be required to determine whether the blood loss sustained during 30 minutes of persistent anticoagulation would outweigh the benefits of avoiding the consequences of this adverse drug interaction. (3)

On the other hand, a strategy of prophylactic adminstration of histamine receptor blockers prevents some of the adverse haemodynamic effects associated with heparin-protamine reaction as HI receptor blocker plus H2 receptor blocker (Avil plus tegamet. (5)

Since 1981 some reports have claimed that the systemic hypotension following protamine administration can be prevented by giving protamine directly into the ascending aorta or the left atrium. This route of injection would prevent the exposure to the lung circulation is which considered the main source of histamine release in response to protamine during its first pass in pulmonary circulation.

These studies were not controlled, and methods varied with respect to selection of patients, dose of protamine and monitoring of the cardiovascular responses. (6)

The purpose of the present study was to evaluate the role of intraaortic administration of protamine in patients with normal preoperative pulmonary pressure and patients with pre-operative moderate to severe puilmonary hypertension in prevention of protamine-related adverse haemodynamic reactions.

Patients and Methods

This study was done in cardiothoracic surgical department at Alexandria Main University Hospital on 40 adult patients (Table 1,2). (24 Male and 16 Female) admitted for elective open heart surgery. 20 of them with pre-operative normal pulmonary artery pressure (group I) and 20

of them with moderate to severe pulmonary pressure (group II). Patients were excluded if they had a history of diabetes mellitus (and were receiving protamine containing insulin). If they had respiratory disease or low cardiac output (Ejection fraction EF< 50%). In each group 10 patients were given protamine into peripheral venous line and 10 patients with protamine into the ascending aorta.

Premedication consisted of 0.15 mg/kg diazepam plus 10 mg morphine sulphate IM 1 hour pre-operatively. Pulmonary artery catheter (Swan Ganz) was inserted through right internal jugular vein, and the radial artery cannulation was done under local Anaesthesia. In addition ECG, naso-pharyngeal temperature probe, and urinary catheter applied.

Anaesthesia was induced with sufentanyl 15/μg/kg, midazolam 5mg and pipecuronium 0.10 mg/kg and maintained with 0.5-1.5%. Isoflurane to maintain arterial blood pressure. All patients received heparin 3mg/kg before bypass. The bypass prime solution consisted of Hartmann solution, manitol and heparin. Additional heparin was given to obtain activated coagulation time > 480 second. Mild systemic hypothermia (28°C) was employed and cold (4°C) crystalloid cardioplegia supplemented by topical cooling with cold saline was used for myocardial protection. All operations were performed by the same surgical team. Before termination of C.P.B 300μg sufentanyl plus 2mg pipecuronium were injected. Patients with low cardiac output after weaning from C.P.B were excluded from our study.

When the patients were haemodynamically stable, requiring just pharmacological dose of inotrope, and with no surgical bleeding point, baseline haemodynamic data were obtained. No volume and inotrope was added during the registration peroid except when M-ABP or CVP or CI or PAP decrease or increase up to 40% than base line data.

Protamine hydrochloride 1.3mg for every 100 unit heparin, diluted in 100CC saline was administered continuously over 5 minutes by infusion pump in peripheral vein in 10 patients and into the ascending aorta using 18 gauge needle in other 10 patients in each group.

-Heart rate and ECG (lead II) pattern.

-Invasive mean arterial blood pressure (IMABP) (mmHg).

-Centeral venous pressure (CVP) (cmH_2O).

-Cardiac Index (CI) ($Lm\text{-}^1m^2$) by thermodilution method.

-Mean pulmonary artery pressure (PAP) (mmHg).

-Pulmonary artery occluded pressure (PAOP) (mmHg).

-Systemic vascular resistance (SVR) (dyne Scm^{-5}) can calculated by equation.

$$SVR = \frac{MABP\text{-}CVP}{C.O.P} \times 80$$

-Pulmonary vascular resistance (PVR) (dyne S cm^{-5}) can calculated by equation

$$PVR = \frac{PAP\text{-}PAOP}{C.O.P} \times 80$$

-Activated clotting time (ACT) (second).

These data were recorded just before

Table (I): Demography of the patients.

Variables	GI	GII
Age/year	21 ± 2.7 (15 - 28)	25.5 ± 3.2 (16 – 32)
BSA/m^2	1.512 ± 0.21 (1.47 – 1.62)	1.515 ± 0.23 (1.46 – 1.66)
Sex	13 Male 7 Female	11 Male 9 Female
Surgery	AVR 16 MV repair 4	MVR 9 MV ring 3 DVR 8

Table (II): Changes in Heart rate/ mint.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean SD t	98.8 8.121	106.8 3.011 0.05	105.4 4.221 0.1	107.4 4.325 0.09
GI IA	Mean SD t	97.6 7.705	103.2 7.004 0.053	104 5.734 0.074	104 4 0.0657
t		0.374	0.0793	0.0871	0.0229
GII IV	Mean SD t	97.3 246.8	107.6 18.61 0.186	108.8 12.007 0.189	111 7.557 0.197
GII IA	Mean SD t	97.6 7.705	103.2 7.005 0.053	104 5.73 0.084	104 4 0.075
t		0.098	0.491	0.406	0.443

protamine administration (A) as base line data, after 1/2 dose of protamine adminstration (B), after full dose of protamine administration (C), and lastly 1 0 minute after protamine administration (D). The data B, C, D compared with base line data (A).

ACT measurement before heparin, after heparin and after protamine administration.

Results

Heart rate (Table II Fig. 1)

In group I and II the mean heart rate was insignificantly changed all over the time of measurement compared to that before protamine injection.

MABP (Table III Fig. 2) Group I

In GI: There was significant decrease in

Table (III): Changes in M.A.B.P/mmHg.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean	79.2	69	69.4	74.1
	SD	4.467	5.597	3.534	6.118
	t		0.0001*	0.018*	0.0237
GI IA	Mean	77.6	67.2	66.6	71.8
	SD	5.719	5.181	4.005	7.269
	t		0.0002*	0.008*	0.031*
t		0.247	0.232	0.057	0.226
GII IV	Mean	77.4	58.4	57.8	62
	SD	9.901	3.747	3.047	2.981
	t		0.001*	0.008*	0.007*
GII IA	Mean	75.3	65.8	62.9	66.8
	SD	8.124	7.685	6.045	4.442
	t		0.007*	0.0005*	0.004*
t		0.0301*	0.0312*	0.046*	0.039*

Table (IV): Changes in C.I/Lm^{4}m^2.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean	2.88	2.84	2.85	2.95
	SD	0.181	0.259	0.295	0.222
	t		0.346	0.393	0.225
GI IA	Mean	2.91	2.81	2.86	2.97
	SD	0.233	0.303	0.267	0.245
	t		0.209	0.3305	0.2909
t		0.3758	0.4073	0.468	0.425
GII IV	Mean	2.8	2.605	2.6	2.6
	SD	89.283	0.325	0.316	3.235
	t		0.164	0.164	0.173
GII IA	Mean	2.705	2.61	2.6	2.66
	SD	0.123	0.246	0.115	0.142
	t		0.145	0.052	0.2305
t		0.089	0.219	0.217	0.144

MABP after 1/2 dose, full dose and 10 minutes after, IV and IA protamine adminstration, but there was insignificant difference concerning the degree of hypotension following IV versus IA protamine administration.

In GII: There was significant decrease in M-ABP at 1/2 dose, full dose and 10 minutes after IV and IA protamine injection, but the decrease in P following IV was significantly more than following IA over all the time of measurement.

Table (V): Changes in S.V.R dyne/S cm^{-5}.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean	1327.7	1172	1182	1244.2
	SD	87.339	111.95	66.164	115.21
	t		0.001*	0.0002*	0.042*
GI IA	Mean	1295.7	1176.7	1122.1	1183.1
	SD	111.577	117.02	98.753	140.16
	t		0.015*	0.0008*	0.031*
t		0.242	0.463	0.0642	0.1505
GII IV	Mean	1298	897	853.3	964.4
	SD	198.03	77.91	99.42	61.566
	t		0.001*	0.008*	0.008*
GII IA	Mean	1208.8	1074.3	1011.4	1061.6
	SD	161.006	158.02	128.8	80.74
	t		0.03*	0.003*	0.009*
t		0.0467*	0.012*	0.011*	0.023*

Table (VI): Changes in CVP / cmH_2O.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean	11.2	10.4	10.4	10.2
	SD	1.584	2.590	2.1705	2.043
	t		0.02*	0.01*	0.01*
GI IA	Mean	11.2	10.5	11.7	10.4
	SD	1.229	2.758	2.869	2.716
	t		0.02*	0.03*	0.02*
t		0.5	0.46	0.134	0.427
GII IV	Mean	12.5	15.2	15.9	16.6
	SD	2.592	4.638	3.478	2.319
	t		0.03*	0.01*	0.007*
GII IA	Mean	12.05	13.4	14.4	14
	SD	1.95	3.893	3.373	1.69
	t		0.01*	0.03*	0.04*
t		0.38	0.412	0.46	0.06

CI (Table IV Fig. 3). In group I,II. There was insignificant changes in CI over all the time of measurement compared to that before protamine infusion.

SVR (Table V Fig. 4): GI and GII

There was significant decrease in SVR after IV and IA protamine infusion over all the time of measurement compared to that

Table (VII): Changes in PAP/mmHg.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean	19.8	19	21.1	19.8
	SD	2.25	3.299	2.99	1.475
	t		0.08	0.143	0.5
GI IA	Mean	19.3	20.5	20.1	20.5
	SD	2.66	4.089	3.87	6.041
	t		0.1	0.29	0.28
t		0.328	0.189	0.263	0.363
GII IV	Mean	31.3	38.1	40.1	36.7
	SD	4.34	5.23	3.956	1.567
	t		0.002*	0.003*	0.005*
GII IA	Mean	31	35.6	35	34
	SD	5.27	3.627	2.624	1.66
	t		0.01*		0.14
t		0.028*	0.026*	0.045*	0.04*

Table (VIII): Changes in PAOP/mmHg.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean	11	12	11.8	11.3
	SD	2.054	2.828	3.96	2.869
	t		0.18	0.28	0.39
GI IA	Mean	11.6	12.9	12	13.4
	SD	2.796	4.175	3.59	6.501
	t		0.212	0.39	0.286
t		0.295	0.289	0.453	0.181
GII IV	Mean	21	23.2	23.6	23.8
	SD	2.44	3.43	3.83	2.788
	t		0.001*	0.0008*	0.0002*
GII IA	Mean	19.9	21.9	20.9	21.6
	SD	1.96	2.718	1.91	1.44
	t		0.03*	0.04*	0.04*
t		0.361	0.04*	0.04*	0.048*

before protamine infusion, but we detected no significant differences concerning the degree of decrease in SVR following protamine by IV versus IA in GI, whereas in GII there was significant decrease in SVR following IV protamine administration than following IA administration all over time of measurement.

C.V.P (Table VI Fig. 5)

In group I there was insignificant decrease in CVP all over the time of measurements when protamine injected IV and IA. We detected insignificant

Table (IX): Changes in PVR/dyne/S cm^{-5}.

Group		Base line A	½ dose B	Full dose C	after 10 m D
GI IV	Mean	147.5	160	166	163.4
	SD	47.39	16.32	34.05	59.74
	t		0.2	0.16	0.25
GI IA	Mean	163.2	163.9	161.7	155.9
	SD	52.04	53.38	55.62	31.77
	t		0.48	0.47	0.35
t		0.244	0.413	0.418	0.36
GII IV	Mean	206	318.9	300.7	291.4
	SD	59.66	45.22	31.05	71.343
	t		0.008*	0.001*	0.004*
GII IA	Mean	206	256.9	278.8	270.2
	SD	94.535	55.33	43.84	93.9
	t		0.03*	0.16	0.19
t		0.11	0.038*	0.03*	0.04*

difference concerning degree of decrease in CVP following.

IV versus IA protamine adminstration, whereas in GII there were significant increase in CVP during all time for measurement following protamine injection either IV or IA.

PVR, PAP and PAOP: (Table VII,VIII,IX Fig. 6,7,8).

In GI: There was insignificant changes in, PVR, PAP and PAOP all over the time of measurements when protamine was injected IV and IA. In GII: There was significant (Increase in PVR, PAP and PAOP, after IV and IA protamine adminstration all over the time of measurements, but the increase in PVR, PAP and PAOP was significantly increased following IV than IA administration during all time of measurement.

ACT was higher than normal in 5 patients after IV administration in (GI and GII) whereas it still high in 2 patient after IA administration in both groups. We in fused 50-100 mg of protamine after 15 minute from the initial dose.

Discussion

The effects of protamine given after CPB are unpredictable the most common effect is a decrease in arterial pressure and SVR especially if protamine is given rapidly to patients with poor ventricular function. (2) A few clinical hemodynamic studies have yeilded conflicting data. There are probably two main reasons for these conflicting results. First, it is difficult to attribute any haemodynamic change as solely caused by protamine at a time when the cardiovascular system recovering from CPB. Second, all of these studies have different experimental methods, including variation in dosage of protamine, rate of injection and route of administration. (1)-

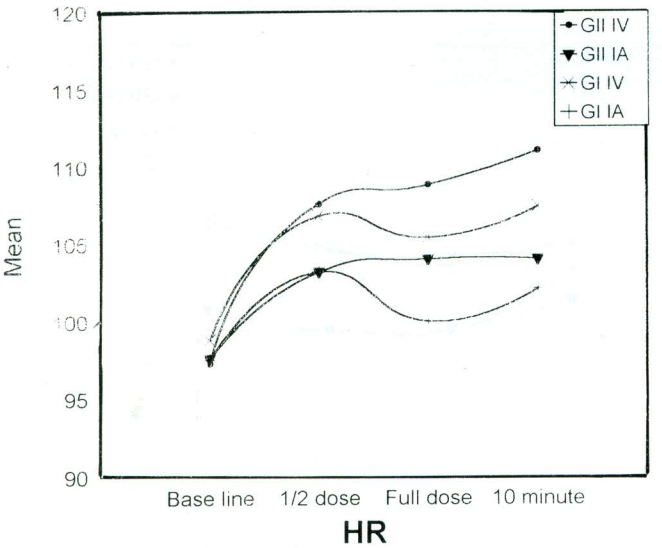

Fig. (1): Changes in Heart rate / mint.

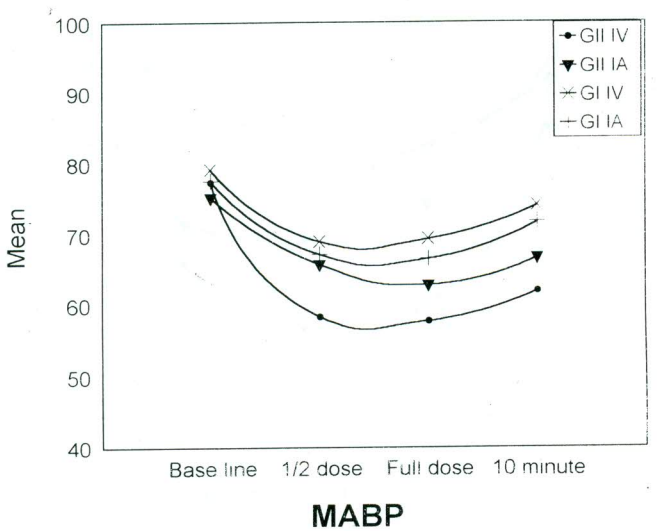

Fig. (2): Changes in M.A.B.P/mmHg.

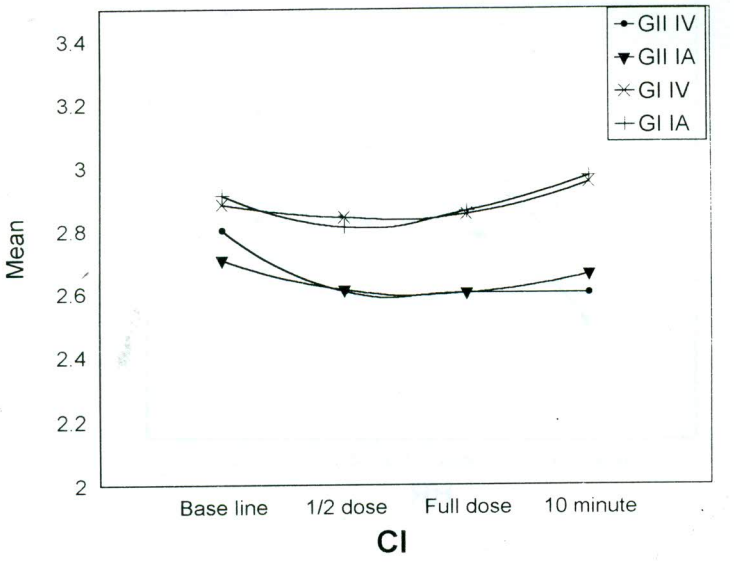

Fig. (3): Changes in C.I./Lm m.

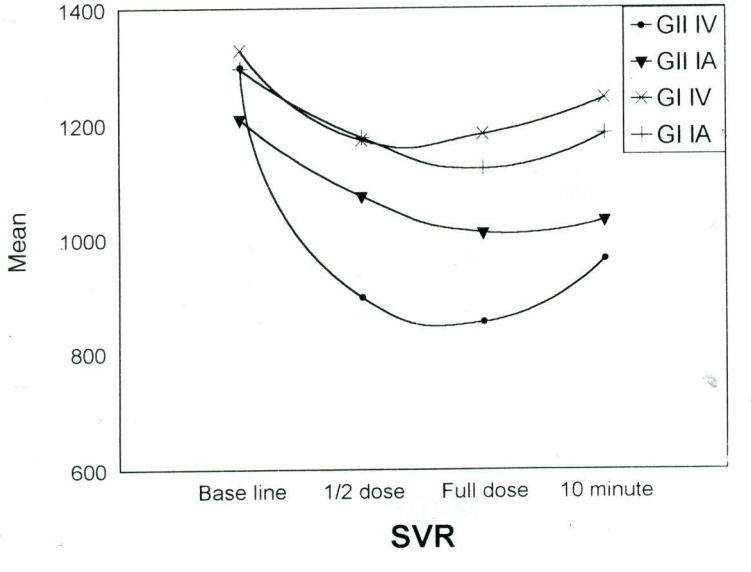

Fig. (4): Changes in S.V.R dyne/S cm.

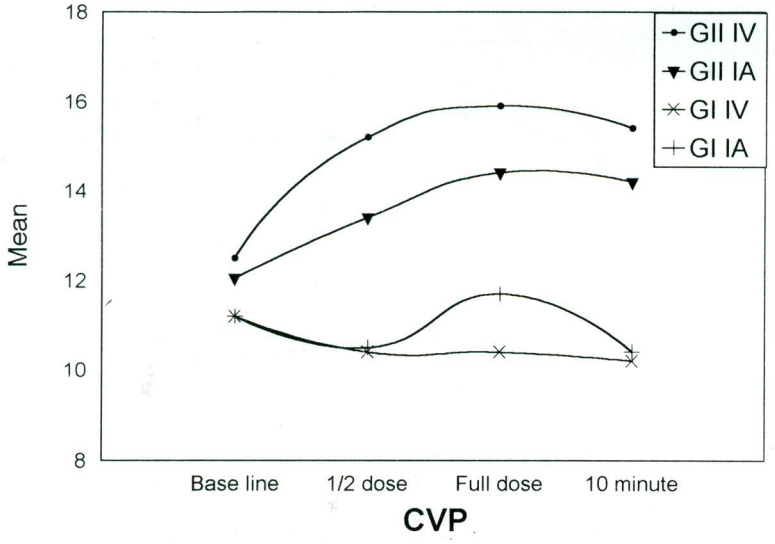

Fig. (5): Changes in CVP / cm H O.

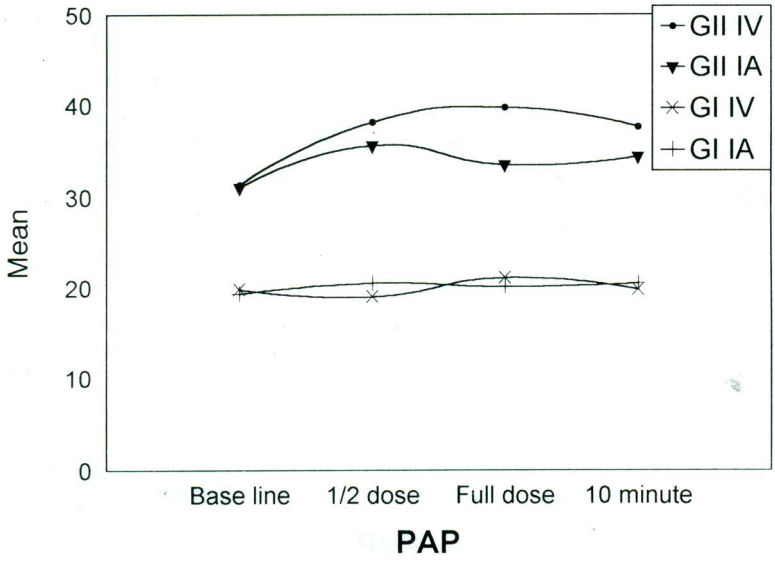

Fig. (6): Changes in PAP/mmHg.

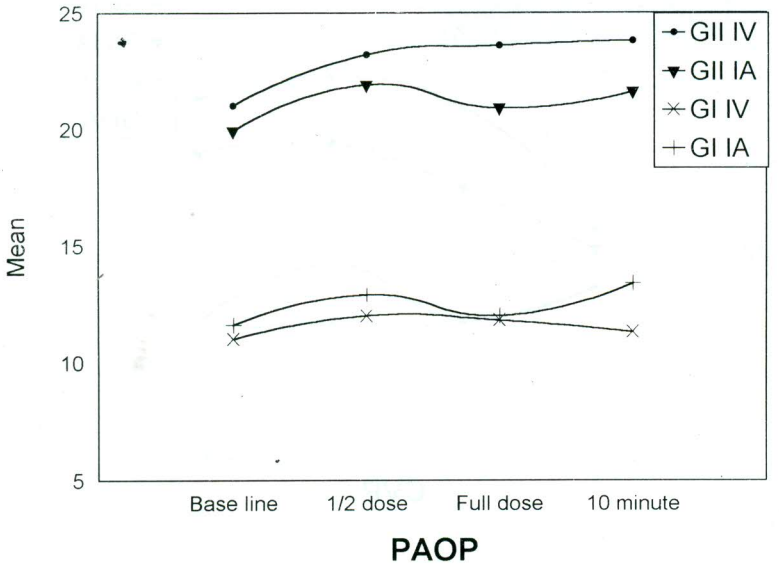

Fig. (7): Changes in PAOP/mmHg.

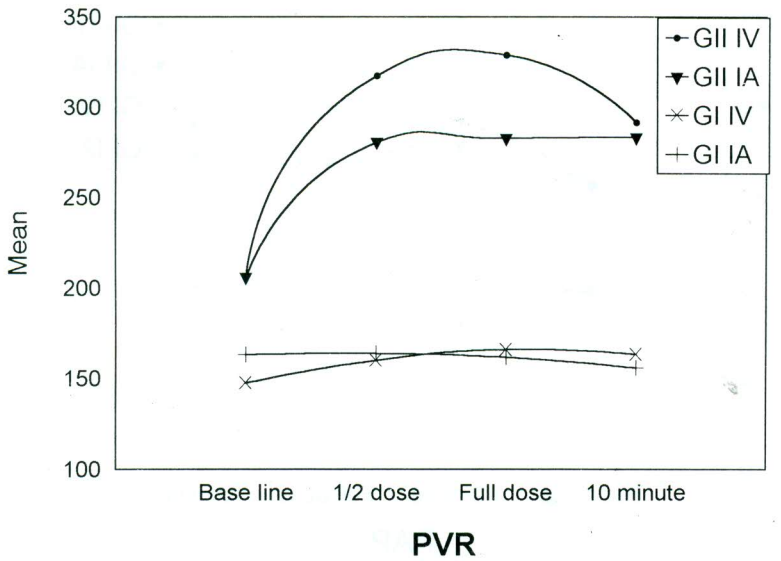

Fig. (8): Changes in PVR/dyne/S cm.

The present work was designed to study the haemodynamic effects of IA and IV protamine infusion in patients with pre-operative normal and moderate to severe pulmonary tension.

-Panca AL et al state that there is rapid mixing of protamine with blood when protamine is infused by intra-aortic route, because the relatively small volume of protamine, compared with cardiac output, would mix quickly and completely with fast flowing blood that circulates through the narrowest conduit of the systemic circulation. Protamine will reach the coronary and pulmonary circulation after it has been mixed thoroughly with blood and possibly after the neutralization process is completed. It is conceivable that platelet aggregation in the lungs, found by some investigators, would be minimized, and also if protamine heparin complex has a vasoconstrictive effect on pulmonary blood vessel directly or through toxic substance release by the lung itself, the effect would be minimized. (7)

In the present study when protamine was infused IV or IA in patient with pre-operative normal pulmonary pressure, we detected significant hypotension and decrease in SVR, whereas there was insignificant change in CI, pulmonary artery pressure and PVR in both groups and there were no significant differences concerning degree of systemic hypotension following protamine administration by the intra aortic versus intravenous route. Our results in GI are supported by the study done by Harrow JC et al who concluded that mild hypotension associated with protamine adsminstration whatever the route of injection (IA or IV) are not due to a generalized decrease in vascular resistance but to volume sequestration perhaps in the splanchnic area which appears by decrease in C.V.P. (8)

Most animal studies have shown that protamine produces an increase in pulmonary arterial pressure, pulmonary vascular resistance and decrease in cardiac output and vascular resistance but human studies have shown more variable effects some, have shown an increase PAP and some a decrease in PAP, while others have shown no changes in pulmonary haemodynamics. (9)

Michaels and Barash found a significant decrease in SVR and significant elevation in PAP and PVR in patient with pre-operative poor ventricular function; they postulated that pre-operative low cardiac output. valvular heart disease, preexisting pulmonary hypertension, diabetes mellitus and faster protamine infusion (less than one minute) have all been suspected to be a risk factor for protamine reaction but not confirmed. (10)

In our study when protamine was injected in patients with preoperative pulmonary hypertension there was significant decrease in SVR, MASP and significant increase in CVP, PAP, PAOP and PVR but the haemodynamic changes, however, were considerably more pronounced and significantly elevated when protamine infused by intravenous than intra-aortic route. These observation strongly indicate that induction of haemodynamic changes is iniated in the lungs. Lowerstein E et al described five patients who sustained precipituns life-Threatning cardiovascular changes associated with IV administration of protamine to reverse heparin anticoagulation. The primary event

appeared to consist of severe pulmonary vascular constriction, leading to right ventricular failure and pulmonary oedema. Because of the preponderance of patients with mitral valve disease, they speculate that underlying pulmonary vaso-disease may predispose to protamine-induced pulmonary vasoconstriction. Three of the cases occurrd in 1 month. They were unable to define an incidence and they suspected that pulmonary vasoconstriction is not a rare occurrence.(11) In our study, in patients with pre-operative pulmonary hypertension 4 patients after IV and one patient after IA protamine infusion showed marked increase of PAP, PAOP, PVR more than 30% than pre-protamine administration which need isoprenaline infusion to control pulmonary hypertension.

In conclusion, we detected no significant changes in haemodynamic variables following protamine adminstration by IV versus IA route in patient with pre-operative normal pulmonary tension, but a pronounced and significant elevation in CVP, PAP, PAOP and PVR when protamine injected IV rather than IA in patient with preoperative moderate to severe pulmonary pressure.

On the basis of these finding, it would seem safer to give protamine into the aorta in patients with pre-operative moderate to severe pulmonary hypertension.

References

1. Horrow JC. Protamine. A review of its toxicity. Anaesthesia Analgesia 1985; 14: 384-361.

2. Shapira N, Schaff HV, Piephler JM. Cardiovascular effects of protamine sulfate in man. J Thorac Cardiovascular surgery 1982; 84: 505-514.

3. Kim LF, Morel DR, Costabella PM: Adverse cardiopulomonary effects and increased plasma thromboxane concentration following the neutralization of heparin with protamine in man. Anaesthiology 1990; 73: 413-422.

4. Gravlee GP, Rogers AT, Dudas LM, Roy RC. Heparin management protocol for cardiopulmonary bypass, influences. Anaesthiology. 1992. 76: 393-401.

5. Kambam J, Merrill W, Smith BE. Prophylactic administration of histamine, and histamine, receptor blockers in the prevention of protamine related haemodynamic effects. Canadan J Anaesthesia. 1990; 37: 420-422.

6. Rogers K, Milne B, Salerno TA, Marim NA: Haemodynamic effects of intraaortic versus intravenous protamine administration after cardiopulmonary bypass in man. Scand J Thor Cardiovascular Surgery 1992-, 26: 113-118.

7. Panca AL, Grafam JE, Hudspeth AS. Haemodynamic effects of intraortic administration of protamine. Annals of Thoracic Surgery 1982, 35: 637-642.

8. Harrow JC, Rogers K, Salerno TA. The haemodynamic effects of intra-aortic versus intravenous administration of protamine for reversal of heparin. J Thorac Cardiovascular Surgery 1983; 85: 851- 855.

9. Hakim TS, Picone A, Oleary CE. Protamine-Induced pulmonary

venoconst-riction in heparinized pigs. Anaesthesia. Analgesia 1995, 581: 38-43.

10. Michaels M, Barash P. Protamine reactions, explaine mediator release and pulmonary vasoconstriction. Anaestheiology 1990; 73: 373-375.

11. Lowenstein E, Johnston WE, Lappas DG. Catastrophic pulmonary vasoconstriction associated with protamine reversal of heparin. Anaesthesiology. 1985; 59: 470-473.

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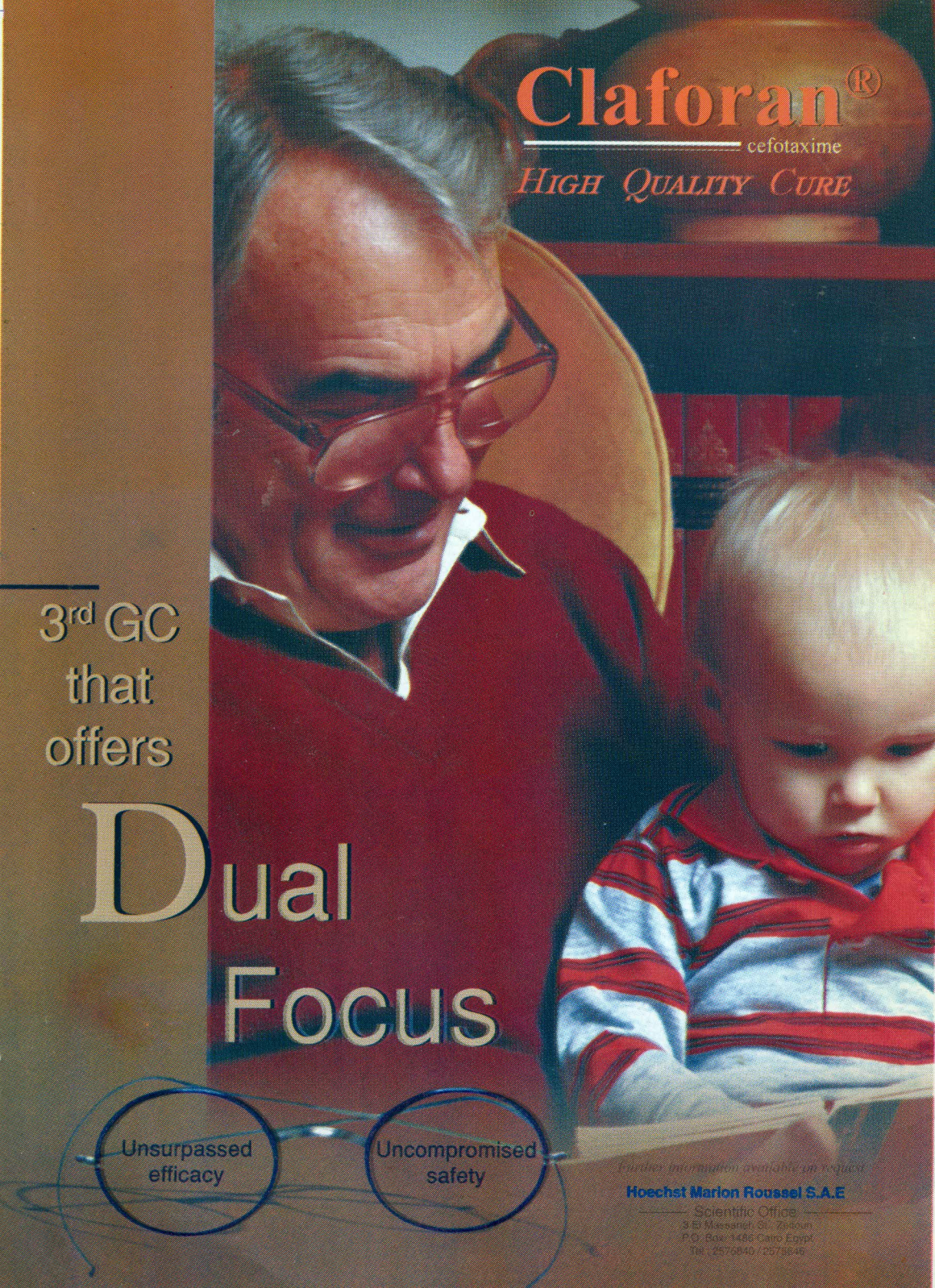
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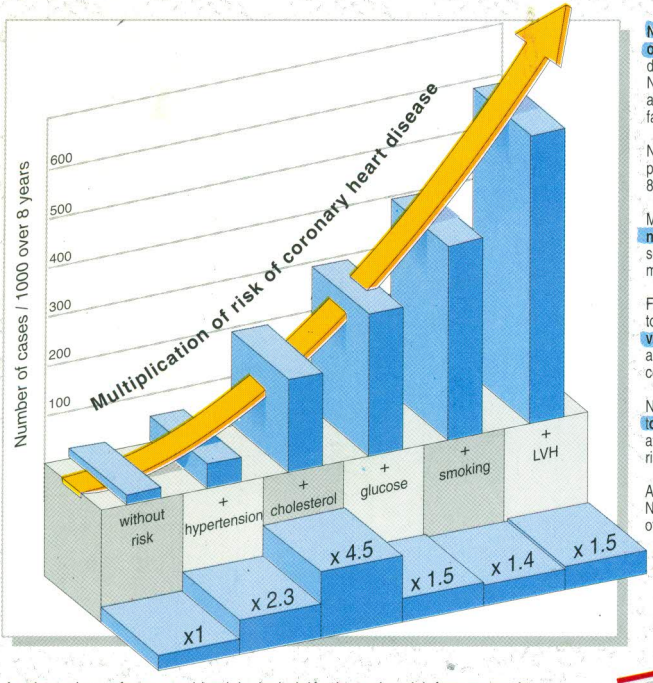

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1. Abbou CB et al. *Curr Med Res Opin.* 1985; 9 (7): 494-499.
2. Leonetti G et al. *Am J Cardiol.* 1990; 65 (17): 67-71.
3. Raggi U et al. *Hypertension.* 1985; 7 (6) (Part II): 157-160.
4. Raftery EB et al. *J Cardiovasc Pharmacol,* 1993; 22 (suppl 6): 106-110.
5. Flack JR et al. *J Cardiovasc Pharmacol.* 1993; 22 (suppl 6): 75-77
6. Kannel WB. *Am J Hypertens.* 1991; 4: 283-287

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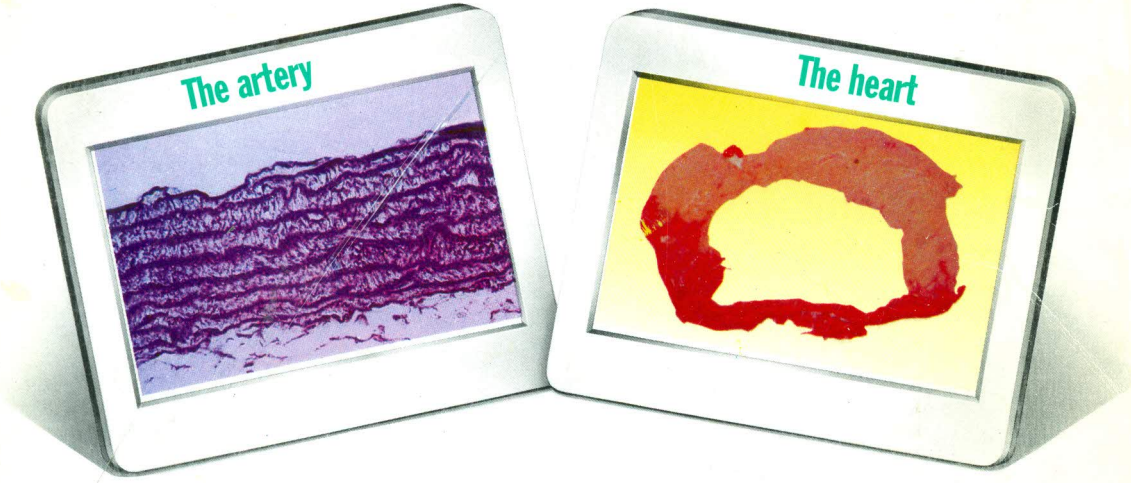

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1. SIHM I et al. *Eur Heart J.* 1993; 14(suppl) : 63 - 2. LEVY BI et al. *Circ Res.* 1988; 63 : 227-239 - 3. ASMAR RG et al. *J Hypertens.* 1988; (suppl 3) : S33-S39 - 4. MICHEL JB et al. *Circ Res.* 1988; 62 : 641-650
5. MORGAN TO et al. *Am J Hypertens.* 1993; 6 : 116 A - 6. MAC FADYEN RJ et al. *Br Heart J.* 1991; 66 : 206-211.

Coversyl is a long-acting ACE inhibitor. **International nonproprietary name** : Perindopril. **Indications :** Essential hypertension. Congestive heart failure (adjunctive therapy). **Dosage and administration :** *Hypertension* : 4 mg once a day in the morning. If necessary, the dose may be increased to 8 mg after one month of treatment. Coversyl should be taken before food. *Congestive heart failure* : Coversyl should be started under close medical supervision at a starting dose of 2 mg in the morning. This may be increased to 4 mg once blood pressure acceptability has been demonstrated. *Elderly patients* : start treatment at 2 mg daily. **Contraindications :** Children. Pregnancy. Lactation. Patients with a history of hypersensitivity to Coversyl. **Precautions :** Assess renal function before and during treatment where appropriate. Renovascular hypertension. Surgery/Anesthesia. Renal insufficiency : the dose should be cautiously adjusted in accordance with the creatinine clearance *(refer to complete data sheet)*. Symptomatic hypotension is rarely seen, but is more likely in volume-depleted patients, those receiving diuretics, or with the first two doses. In diuretic-treated patients, stop the diuretic 3 days before starting Coversyl. A diuretic may later be given in combination if necessary; potassium-sparing diuretics are not recommended. Combination with neuroleptics or imipramine-type drugs may increase the hypotensive effect. Serum lithium concentrations may rise during lithium therapy. **Side effects :** Rare and mild, usually at the start of treatment. Cough, fatigue, asthenia, headache, disturbances of mood and/or sleep have been reported. Less often, taste impairment, epigastric discomfort, nausea, abdominal pain, and rash. Reversible increases in blood urea and creatinine may be observed. Proteinuria has occurred in some patients. Rarely, angioneurotic edema and decreases in hemoglobin, red cells, and platelets have been reported. **Composition :** Each tablet contains 4 mg of the tert-butylamine salt of perindopril. **Presentation :** Packs of 30 tablets of Coversyl 4 mg (scored). *Refer to data sheet for complete prescribing information.*

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