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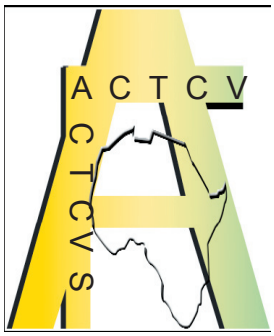

Chirurgie Cardiaque / Cardiac Surgery

THROMBOLYSIS FOR PROSTHETIC VALVE THROMBOSIS: A REPORT OF 6 CASES AND REVIEW OF THE LITERATURE.

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Summary

Objectives: To determine the outcome of thrombolysis in patients with Prosthetic valve thrombosis (PVT).
Design : A retrospective descriptive study.
Setting : The intensive care unit of the National Cardiothoracic centre, Korle-bu Teaching Hospital , Accra, Ghana.
Subjects: 5 consecutive patients who were thrombolysed for 6 episodes of prosthetic valve thrombosis.
Method: Over a 3-year period 5 patients underwent a total of 6 thrombolytic sessions. All the patients were symptomatic and diagnosis had been confirmed by echocardiography. Streptokinase was used in 5 of the sessions. 1.5 million International units (IU) was used in the adults and 750,000IU in the 13 year old. One patient had 2.0 IU of uroki nase. The inf usion was by the short course thrombolytic method over 90 Minutes.
Results: There were 6 episodes of thrombosis out of 142 (5.0%) valve replacements during the study period. The mean age was 29.5 + 11.2 years (range 13-48years). The time from insertion of prosthetic valve to thrombosis was 15.5 months (range 1 week – 2 years). The INR was sub-therapeutic in 5 (83 .3%) of the patients. Streptoki nase was used in 5 (83 .3%) and urokinase in 1 (16.7 %) of the patients. The overall success was 83.3%. Thombolysis was completely successful in 3 (50 .0%) and partially in 2 (33.3 %). There was no response to thrombolysis in one patient who died after 14 years.
Conclusion : Thrombolysis of prosthetic heart valves is not common from out series. Thrombolysis using streptokinase should be the first line management as it is cheap and relatively safe in the management of such cases.

Key words : Thrombosis - Thrombolysis - Prosthetic valve

Introduction

Prost hetic heart valve disease may be rarely complicated by thromboembolism, bleeding, endocarditis and valve dysfunction from pannus formation[1]. Of these thromboembolism of a mechanical prosthetic valve is the most serious as it leads to severe haemodynamic decompensation including shock and acute heart failure[1-3]. Thrombosis may also complicate pannus formation. Until recently the management of prosthetic valve thrombosis (PVT) was mainly by reoperation where a thrombectomy or replacement of the valve is done[2].
Re-operation is usually by cardiopulmonary bypass and because most of the patients are in i ntractable heart failure there is a high mortality[4-5]. Many workers have advocated thrombolysis as the first line management of PVT using the rapid inf usion or the slow infusion method[4-6]. The mortality of the PVT is related to the New York Heart Association (NYHA) class of heart failure at the time of presentation, with NYHA IV usually having a poor prognosis[6-7].
The intensive care unit of the Cardiothoracic Centre has for the past 3 years treated 5 patients who had 6 episodes of PVT. This study therefore looks at management of these cases as well the outcome in terms of morbidity and mortality.

Method

Using the intensive care, admissi ons and discharge register, the report books and the patients case notes, patients who had thrombolysis for prosthetic valve thrombosis between 1st January 2003 and 31st December 2006 were studied. The clinical presentation, NYHA Class of heart failure, the initial INR, and echocardiographic information were also looked for.

The patients were all thrombolysed in the intensive care unit of the Cardiothoracic Intensive Care unit. All the patients had invasive monitoring through a radial arterial and a central venous line. Inotropic support by dopamine and adrenaline infusions was started as part of the protocol for management of such cases. After pre- thrombolytic therapy of intravenous methyl-prednisolone 250mg and Promethazine 12.5mg, 5 patients were administered streptokinase and 1 urokinase. After a test dose of 20,000 IU units, each patient was administered 1.5 million units of streptokinase in the adults and 750,000 units in the adolescent. Two million units of urokinase was administered to one patient who had previously been administered streptokinase. All the thrombolytics were infused over a 90 minute period. Complete hemodynamic success was defined as return of the transvalvular gradient to normal. Partial success was defined as partial improvement in gradient without complete normalization of the valve movements. The data was analysed using SSPS (Microsoft 2003).

Results

There were 6 episodes of PVT in 5 patients out of a total of 142 valve replacements during the study period. The age range was 13-48 years (mean 29.5+11.2 years). There was a male to female ratio of 2:1. The mitral valve was involved in 5 (83. 3%) of the episodes with the aortic valve being involved in 1 episode. Five (83.3%) of the patients had sub-therapeutic INR. These are depicted in table 1 below. All the patients presented with pulmonary oedema, 3 (50. 0%) were hypotensive and 1 (16.7%) was in shock with multi-organ dysfunction. The mean time from insertion of the valve till thrombosis was 15.5+11.2 months with a range of 7 days to 24 months. Three (50.0%) of the patients were in NYHA IV and 3 (50.0%) in NYHA III.

Table 1 : Showing age, sex, age of valve, INR, clinical signs and NYHA class.

Age	Sex	Valve throboly-sied	Age of valve mouths	INR	Clinical signs of	NYHA Class
13	M	Mitral bileafleft	2	1,5	Pulmonary oedema	III
29	M	Mitral bileafleft	21	1,3	Pulmonary oedema Hypotension	II
29	M	Mitral bileafleft	24	1,7	Pulmonary oedema Hypotension	IV
31	F	Mitral bileafleft	22	1,2	Pulmonary oedema Hypotension	IV
27	F	Mitral bileafleft	24	2,0	Pulmonary oedema	III
48	M	Mitral bileafleft	0,25 (7 days)	1,5	Pulmonary oedema Shock Multi organ dys-function	IV

Streptokinase was used in 5 (83 .3%) of with urokinase in 1 (16. 7%) for thrombolysis.
Thrombolysis was successful in 3 (50.0 %) of the patients with a partial success in 2 (33.3%). The overall success rate was 83.3%.

The patients with partial success later had reoperation. The average time to improvement of haemodynamic signs was 4.4 + 2.2 hours with a range of 2-8 hours. These are seen in table 2.

Table 2 : Thrombolytic, time of improved function, success and outcome of thrombosis.

Valve thrombosed	Thrombolytic used	Times of improved function/ Hrs	Success of thrombolysis	INH A Class	Complications of thrombolysis	Outcome
Mitral	Streptokinase	2	Complete	III	Allergy Hypotension	Alive 3 years
Mitral	Streptokinase	6	Complete	III	Allergy	Re-thrombosed in 3 months
Mitral	Urokinase	8	Partial	IV	-	Re-operation died
Mitral	Streptokinase	5	Complete	IV	Allergy moderate moderate bleeding	alive 4 years
Aortia	Streptokinase	5	Partial	III	Allergy	Pannus re-operation alive
Mitral	Streptokinase	Did not improve	No response	IV	bleeding	Died after 14 hours

One of the patients who had a partial success from thrombolytic therapy from use of urokinase died during redo-surgery. The commonest complication was allergy (66.7 %) and this was from the use of streptokinase. The two patients who died were in NYHA class IV. Four of the patients who survived the management of their PVT are still alive 39-48 months after the thrombotic events.

Discussion

Prosthetic valve thrombosis though infrequent is usually dreaded by most physicians because of the severe haemodynamic complications. After PVT patients can present with hypotension, pulmonary oedema, embolic phenomenon or more seri ously cardiogenic shock[1-3]. The incidence of l eft si ded PVT is reported to be between 0.5 -8% but this increases to 20% in right sided valves especially in prosthetic tricuspid valves[7]. The institutional incidence of PVT in our study (5.0%) is within this range. Another study by Sivasubramanian who use the same Sorin bileaflet valves as our institution had an incidence of 6.7%[8]. Renzelli cited the most significant risk as tilting disc prostheses, prostheses without pyrocarbon coating, large prostheses, tilting disc prostheses with a small orifice posteriorly oriented, atrial fibrillation, enlarged left atrium and time from implant greater than 4 years[9]. The mitral valve from previous studies has been found to be more commonly involved in left sided PVT and this agrees with our finding of 83.3%[1,4-6]. The patient with the aortic valve had a cage-ball valve all the other patients had Sorin bileaflet valves. Rizzoli et al in their study

demonstrated that the relative risk of thrombosis was12 times higher for the tricuspid prosthesis and seven times higher for the mitral prosthesis[10]. Rizzoli and his colleague also showed that there was a 69% risk reduction if Sorin tilting valves were used and this risk reduced further to 83% with Sorin bileaflet valves, the common valve used in our institution.

Many studies have shown a correlation between PVT and sub-therapeutic INR. Most of the patients with PVT in reported studies had INR below 2.0[1,4-6]. Of the 6 episodes of PVT 5 (83.3 %) had INR less 2.0. The main cause of sub- therapeutic INR in these patients was noncompliance in the taking of their coumarin drugs. The patient with the aortic PVT who had an INR of 2.0 had in addition extensive pannus formation around and in the cavity of the valve. Pannus formation, in addition to having an obstructive effect may also predis pose to the formation of extensive thrombi which was present in this particul ar patient[10]. Other causes of thrombotic events are associated coagulation disorders including protein C, Protein S and antithrombin III deficiencies 11.

Kontos, while investigating the clinical signs of PVT list ed exertional dypnoea, from pulmonary oedema as one of the main features[2]. He indicated that the presence of shock usually indicated a poor prognosis during management. This finding has also been confirmed in other studies[1,4-5]. All the patients in the present study had pulmonary oedema at presentation. Although hypotension was present in 66.7% of the cases only one was in shock with multi - organ dysfunction. All the patients were in NYHA class III-IV at the time of presentation. Roudant et al in their study of 127 cases had 90% of their cases in NYHA III-IV[12]. It has been categorically proven that a NYHA class of III-IV is associated with a high mortality rate no matter the mode of management. However workers have advocated thrombolytic therapy for these groups of patients[12-13]. Thrombosis can occur if the administration of heparin is not done early. There was an early thrombosis in our study of 7 days postoperatively. The early thrombosis in this patient was because of sub-therapeutic heparin administration 24-28 hours postoperatively. Talwar and his colleagues in a study on causes of early valve thrombosis found out that 6.1% of their patients developed significant thrombosis in 9 days if heparin therapy was not aggressive enough while warfarin was sub-therapeutic which has been confirm ed by other workers[13-15]. Streptokinase (SK), urokinase (Uk) and tissue plasminogen activator (rTPA) have all been used for thrombolys is with relatively good result s[11-17]. Roudaut et al in their study found out that SK and rTPA were more effective than Uk for thrombolysis. The other factors that may affect the choice of thrombolytic would be, the side-effects of streptokinase, the non-availability of urokinase and the expense of rTPA[6,7,12,16,17]. Some workers have used the prolonged or short course infusion protocols for thombolysis depending on the haemodynamic condition of the patients. However there is no clear advantage of one protocol over the other in terms of resul ts and the protocol adopted may depend on individual or institutional preferences[6,12,14,16-18]. Our inst itution uses the short course protocol which is much cheaper than the prolonged course infusion technique.

The short course protocol has the advantage in that clinical improvement is seen early in the management of the cases. Thrombolytic therapy was however not repeated during the thrombotic episodes in our study. Studies have shown increased success rate with repeated doses or prolonged infusion of thrombolytics during a thrombotic episode[6,12,16-18]. Overall success rates of thrombolysis cited in the literature have been between 70-90% and these have been independent of the thrombolytic used[12,16-18]. Our success rate of 83.3% falls within range. The overall success rate increases with repeat thrombolysis or if continuous prolonged infusion of the thrombolytics is used. However thrombolysis in patients presenting in NYHA class III-IV is less successful than in patients in class I-II. It has become evident that transoesophageal echo-cardiography (TEE) has become invaluable in the diagnosis and the proper management of patients with PVT. The thrombus size is significant in the determination of the clinical outcome and the complications that occur during thrombolysis . A study by Tong and his colleagues gave the best cu-off area of thrombus for predicating complications as 0.8cm2 [7]. Many workers use TEE to follow the progress of thrombolysis in these patients and also to assess the success to thrombolysis[12,13,16-19]. Complications cited in the literature include embolic phenomenon, strokes, transient ischaemic attacks, bleeding and allergy especially to SK[2,12,14,16-18]. Complications during thrombolysis are more common in patients with shock, tachycardia, hypotension, previous stroke, extension of thrombus beyond the valve margins and the thrombus area[7]. Our study had a high proportion of allergy to SK (60%) because of the suspected high incidence of streptococcal sore throats in developing countries. Studies have given a complication rate of 12-24%[7,17]. Surprisingly there were no embolic phenomenon and also no strokes in our study. Strokes which are common in some studies are usually associated with small thrombus rather than large thrombi[7]. It is now evident that thrombolysis has a lower mortality for all classes of NYHA functional

class from PVT as compared to open heart surgery. The ACC/AHA current recommendations advice thrombolysis for most cases of PVT[19]. There is also a high mortality in patients presenting with PVT and shock. Gupta and his colleagues recorded a mortality of 78% of patients who presented with PVT and shock[17]. One patient in out study died during thrombolys is and his presentation was shock and multi organ dysfunction.

In conclusion, thrombosis of prosthetic heart valves is not common from out series. Thrombolysis using streptokinase should be the first line management as it is cheap and relatively safe in the management of such cases.

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