Indian Heart Journal xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Articles

Tenecteplase versus streptokinase thrombolytic therapy in patients with mitral prosthetic valve thrombosis

D. Kathirvel[a,*], Gnanaraj Justin Paul[b], Gorijavaram Prathap kumar[c], G. Palanisamy[b], Ganesan Gnanavelu[b], G. Ravishankar[b], N. Swaminathan[b], Sangareddi Venkatesan[d]

[a] Postgraduate in cardiology, Institute of Cardiology, Madras Medical College - Rajiv Gandhi Govt General Hospital, Poonamalliee High road, Chennai – 3, India
[b] Professor of Cardiology, Institute of Cardiology, Madras Medical College - Rajiv Gandhi Govt General Hospital, Poonamalliee High road, Chennai – 3, India
[c] Senior Assistant Professor of Cardiology, Institute of Cardiology, Madras Medical College - Rajiv Gandhi Govt General Hospital, Poonamalliee High road, Chennai – 3, India
[d] Associate Professor of Cardiology, Institute of Cardiology, Madras Medical College - Rajiv Gandhi Govt General Hospital, Poonamalliee High road, Chennai – 3, India

ARTICLE INFO

Article history:
Received 29 March 2017
Accepted 26 October 2017
Available online xxx

Keywords:
Prosthetic valve thrombosis
Thrombolytic therapy
Tenecteplase
Streptokinase

ABSTRACT

Objective: Prosthetic valve thrombosis (PVT) is a dreadful complication of mechanical prosthetic valves. Thrombolytic therapy (TT) for PVT is an alternative to surgery and currently making a leading role. This study compares TT with tenecteplase (TNK) and streptokinase (SK) head to head in patients with mitral PVT.

Methods: In this single center, observational study, patients with mitral PVT diagnosed by clinical data, transthoracic echocardiography, transesophageal echocardiography, and fluoroscopy were included. After excluding patients with contraindications for thrombolysis, they were randomly assigned to receive either SK or TNK regimen. Patients were monitored for success or failure of TT and for any complications.

Results: Among 52 episodes (47 patients with 5 recurrences) of mechanical mitral PVT, 40 patients were thrombolysed with SK and 12 patients were thrombolysed with TNK. Baseline characteristics including demographic profile, clinical and echocardiographic features, and valve types were not statistically significant between the groups. Complete success rate was 77.5% in SK group and 75% in TNK group ($p = 0.88$). Partial success rate, failure rate, and major complications were not statistically significant between the two groups. Within 12 h of therapy, TNK showed complete success in 33.3% of patients compared to 15% in SK group (p-value <0.02). Minor bleeding was more common in TNK group.

Conclusion: Slow infusion of TNK is equally efficacious but more effective than SK in the management of mitral mechanical PVT. 75% to 77.5% of PVT patients completely recovered from TT and it should be the first line therapy where the immediate surgical options were remote.

1. Background

Prosthetic valve obstruction by thrombosis is a rare but serious complication which occurs in 0.5% to 8% of the left-sided mechanical prosthetic valves [1]. In India, the incidence of prosthetic valve thrombosis (PVT) is high, with 6.1% in the first 6 months after replacement of the valve [2]. High mortality rate was reported with urgent surgery in certain subsets of patients of PVT compared with thrombolytic therapy (TT) [3]. Intravenous thrombolytic treatment for prosthetic valve thrombosis has been used as an alternative to surgical treatment and currently making a leading role in the management of PVT [4]. Thrombolytic regimens of common thrombolytic agents used in previous studies showed different outcomes and various degree of safety in the treatment of PVT. However, comparative study of thrombolytic regimen of tenecteplase (TNK) with streptokinase (SK) was not done in patients with PVT. This study was done to compare the efficacy and safety of TNK thrombolytic regimen with SK thrombolytic regimen in the management of patients with mechanical mitral PVT.

2. Methods

This study was done in a tertiary care hospital during August 2014 to October 2016 after getting ethical committee approval. 47

* Corresponding author at: 19/3, VDM Main road, Mangalampet village, Vridhachalam taluk, Cuddalore district – 606104. Tel: 9943375533.
E-mail address: maestrokathir@yahoo.com (D. Kathirvel).

https://doi.org/10.1016/j.ihj.2017.10.014

patients with 52 episodes (5 recurrent PVT) of mitral PVT diagnosed by clinical data, transthoracic echocardiography [TTE], transesophageal echocardiography, and fluoroscopy in whom surgical treatment was not possible were included in this study after obtaining informed consent. A detailed history of presenting symptoms and their duration, time of mitral prosthetic valve replacement, drug compliance, and frequency of INR monitoring were enquired and analysed. Clinical examination was done for the presence of prosthetic valve click, murmur and lung signs.

Echocardiography:

- Thrombus was recognized as soft and homogeneous, mobile or fixed echo densities located at the valve occluder and/or valve struts. Thrombus mobility and dimensions were measured. Patients with thrombus size of $>1\,cm^2$ were excluded.
- Pressure gradient (PG) across the prosthetic valve was compared with previous baseline value. False causes of increased PG [e.g. increased flow across the valve due to tachycardia, anemia, and regurgitation) were excluded by measuring pressure half-time ($P^1/_2T \geq 150$ msec was considered as obstructed valve).
- If baseline value was not available, then the Doppler mitral valve area of $\leq 1.5\,cm^2$ and prosthetic mitral valve mean gradient of ≥ 10 mmHg were taken as prosthetic valve occlusion [5].

TEE was used whenever TTE images were inadequate. Fluoroscopy was used as an additional tool to diagnose prosthetic valve thrombotic obstruction. Reduced or fixed mobility of leaflets was documented. (Examples: Figs. 1–6)

Patients presenting with cardiogenic shock with multi-organ dysfunction, prosthetic valve obstruction by pannus and contra-indications to use of thrombolytic therapy like, active internal bleeding, history of haemorrhagic stroke, recent cranial trauma or neoplasm were excluded. Prothrombin time (PT) and International Normalised Ratio (INR) were measured on the day of admission. Blood culture and sensitivity with other routine blood investigations were done.

Patients were randomly assigned to receive either SK regimen (2.5 lakh IU intravenous bolus for 30 min followed by 1 lakh IU/hr intravenous infusion for 24 h) [6] or TNK regimen (0.5 mg/kg as intravenous infusion over 24 h) [7] and thrombolysis was repeated up to 3 times (72 h) in SK regimen and 2 times (48 h) in TNK regimen for obtaining normal or near normal reduction of mitral valve pressure gradient. Patients were monitored for success or failure of hemodynamic improvement by serial TTE for every 6 h and for any complications. Routine blood investigations along with PT, INR, and culture and sensitivity for patients with fever were done at the time of admission. Complete success was defined as normal or near normal transvalvar gradient and restoration of normal leaflet motion on fluoroscopy without any major complications [6]. Partial success was defined as reduction of $>50\%$ of transvalvar gradient from the baseline or complete hemodynamic response with major complication or restricted movement of prosthetic valve leaflets on cinefluoroscopy even though the transvalvar gradients completely normalized [6]. Failure of TT is defined as no hemodynamic response even with extended

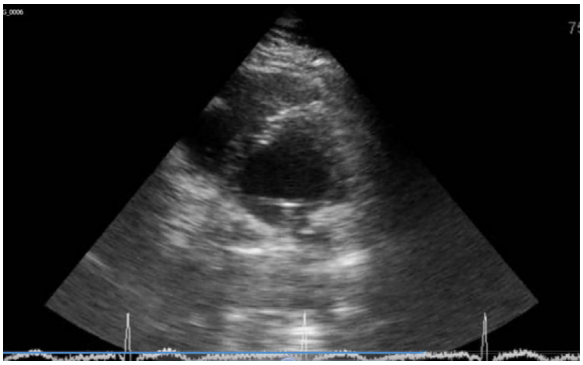

Fig. 1. A patient with obstructive mitral PVT. TTE of parasternal short axis view showed medial leaflet of mitral bileaflet valve was stuck in closed position and lateral leaflet was moved to open position during diastole.

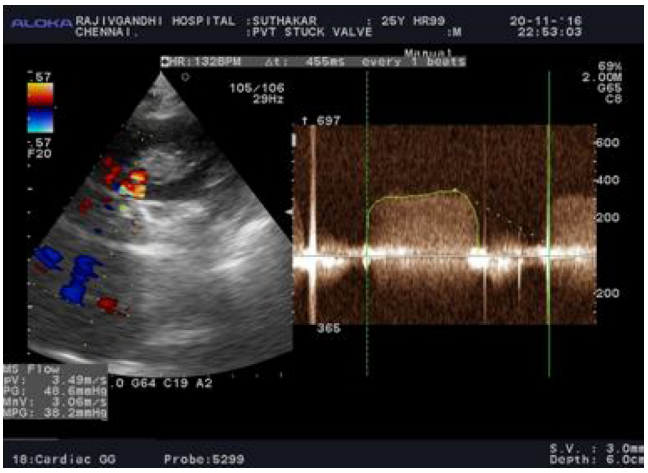

Fig. 2. Continuous Doppler across the mitral prosthesis of patient shown in Fig. 1: Peak PG was 48.6 mmHg and mean PG was 38.2 mmHg.

Fig. 3. Fluoroscopy showed the same leaflet was immobile in RAO caudal view of patient shown in Fig. 1 before TT.

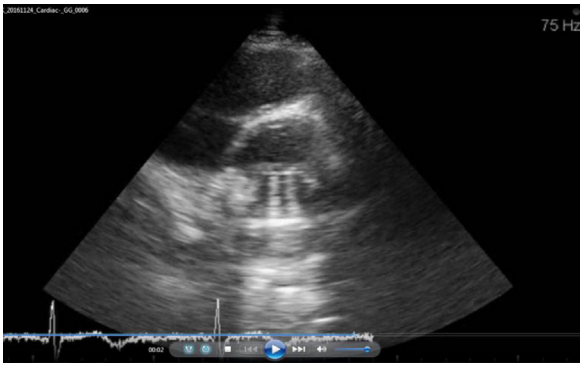

Fig. 4. After thrombolytic therapy of patient shown in Fig. 1, TTE parasternal short axis view showed both leaflets of mitral PV in open position during diastole.

Please cite this article in press as: D. Kathirvel, et al., Tenecteplase versus streptokinase thrombolytic therapy in patients with mitral prosthetic valve thrombosis, Indian Heart J (2017), https://doi.org/10.1016/j.ihj.2017.10.014