



A Review on Thrombolytic Therapy used in Myocardial Infarction (Streptokinase vs Tenecteplase)

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Received: 03-05-2017; Revised: 12-07-2017; Accepted: 28-07-2017.

ABSTRACT

The most severe form of Acute Coronary Syndrome is ST elevation myocardial infarction which requires immediate therapy. Thrombolytic agents are the medications that are used widely for the treatment of myocardial infarction. Now day's different types of thrombolytic drugs recurrently available in market: alteplase, anistreplase, urokinase, streptokinase, tenecteplase. Thrombolytic therapy should be given with maintaining proper safety in order to minimize the risk of clinically important bleeding as well as enhance the chances of successfully thrombolysis of clot. Beside proper knowledge of contraindication, evolutionary factor and combination of drug is essential for successful thrombolytic therapy. And also should know which drug may produce more efficacy in thrombolytic therapy. Streptokinase may produce more bleeding complications and less resolution of st-segment when compared to tissue-plasminogen activators such as tenecteplase. The mortality rate is very high in acute myocardial infarction. So, this can be reduced by providing tissue plasminogen activator within the time.

Keywords: streptokinase, tenecteplase, myocardial infarction, safety, efficacy.

INTRODUCTION

A blood clot (thrombus) develops in the circulatory system which consolidates a mechanism in human body to repair the injured blood vessel. If thrombus is formed when it is not needed, this can produce significant consequence like embolism, ischemia, heart attack, stroke¹ and thrombus is formed due to exposition of the lipid-rich core after atherosclerosis plaque rupture / erosion into the arterial lumen triggers the formation of unstable platelet aggregates, which may lead to intermittent reduction in coronary flow and Acute coronary thrombosis resulting in total occlusion of a coronary artery leads to ST segment elevation myocardial infarction (STEMI).² Myocardial infarction is mainly treated by percutaneous coronary intervention and thrombolytic therapy. In India, PCI centres are not available in all hospitals. Due to this unavailability of PCI, the use of thrombolytics are increased. So there is need to know the safety and efficacy of thrombolytics in the patients of myocardial infarction.

Thrombolytic therapy classification

Thrombolytic drugs are also called "plasminogen activators" and "fibrinolytic drugs."³

Thrombolytics Used in Clinical Practice

Streptokinase

Streptokinase is a non-fibrinogen-specific fibrinolytic agent and is a protein which is derived from group a streptococci having a molar mass of 47 kDa and is made up of 414 amino acid residues. The protein exhibits its maximum activity at a pH of approximately 7.5 and its isoelectric pH is 4.7. Among thrombolytics, this indirect fibrinolytic agent is the most commonly used and studied due to its availability and lower cost in comparison to other agents in this pharmacologic class. It has a short half-life and is delivered in a continuous infusion over 1 hour (administered both intravenously or intra coronary).

Table 1: Classification of Thrombolytics

Generation of thrombolytic drug	Fibrin specific	Non fibrin specific
First	-	Urokinase Streptokinase
Second	Recombinant tissue plasminogen activator (t-PA) Alteplase	Prourokinase (scum-PA) Sk-plasminogen activating complex (APSAC)
Third	Tenecteplase (TNK-tPA) Reteplase Monteplase Lanoteplase Pamiteplase	-



Patients may develop antibodies following administration of this agent. If a patient has antibodies, they are at increased risk of an allergic reaction (including the most severe form, anaphylaxis) to streptokinase. Alternatively the presence of antibodies may diminish the thrombolytic effect of streptokinase. These effects mean that streptokinase is used only once in any given patient, and repeated administration is discouraged. In some areas, up to 50% of patients presenting with AMI have already received streptokinase once and are therefore not suitable for this drug.⁴⁻⁷

Dose: 1.5million units over 60 minutes.

Administration

Dilute two 75,000 unit vials of streptokinase with 5ml dextrose 5% in water each, gently swirl to dissolve.

Add this dose of the 1.5 million units to 150ml dextrose 5% in water.⁸

Tenecteplase

Tenecteplase is the sixth thrombolytic to gain approval for manufacturing and marketing by the Food and Drug Administration (FDA) . Is an altered form of human tissue plasminogen activator (tPA)), a third-generation thrombolytic recently manufactured in India since 2007 is

indicated for the reduction of mortality associated with acute myocardial infarction (AMI). TNK-tPA is a 527 amino-acid glycoprotein derived by molecular modification of the native human t-PA. It has a prolonged half-life, increased fibrin specificity and increased resistance to inhibition by plasminogen activator inhibitors and the only thrombolytic agent that can be administered as a single bolus injection over 5 seconds. Tenecteplase is currently listed as a black triangle drug indicating that the Committee on Safety of Medicines is monitoring it to assess the frequency of adverse reactions.^{6,9,10}

Dose: The dose is adjusted according to body weight.⁸

Table 2: Doses of Tenecteplase according to body weight

Sl.No	Patient body weight	Dose
1	<60kg	30mg
2	60-69kg	35mg
3	70-79kg,	40mg
4	80-90Kg	45mg
5	>90Kg	50mg

Mechanism Of Thrombolytics:⁸

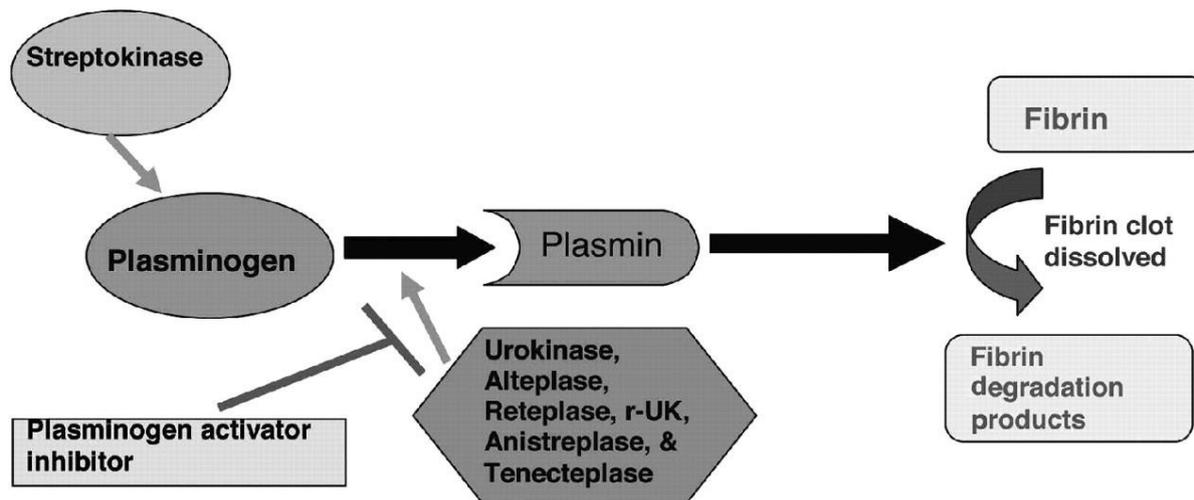


Figure 1: Mechanism of Thrombolytics

Contraindications to thrombolytic therapy

Absolute contraindications

- Prior intracranial hemorrhage (ICH)
- Known structural cerebral vascular lesion
- Known malignant intracranial neoplasm
- Ischemic stroke within 3 months
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed head trauma or facial trauma within 3 months
- Intracranial or intraspinal surgery within 2 months
- Severe uncontrolled hypertension (unresponsive to emergency therapy)
- For streptokinase, prior treatment within the previous 6 months

Relative contraindications

- History of chronic, severe, poorly controlled hypertension
- Significant hypertension on presentation (systolic blood pressure >180 mm Hg or diastolic blood pressure >110 mm Hg)
- Traumatic or prolonged (>10 minutes) cardiopulmonary resuscitation (CPR) or major surgery less than 3 weeks previously
- History of prior ischemic stroke not within the last 3 months
- Dementia
- Recent (within 2-4 weeks) internal bleeding
- Noncompressible vascular punctures
- Pregnancy
- Active peptic ulcer¹¹

How Thrombolytic Aare Administered

- ❖ Thrombolytic drugs are given intravenously, and they should be given as soon as possible after the patient develops the signs and symptoms of STEMI; the sooner they are given the better.
- ❖ The American College of Cardiology and the American Heart Association recommend that in order for the thrombolytic drugs to be most effective, they should be given within 30 minutes of the patient's arrival at the hospital.
- ❖ The most important factor determining patient survival is the time it takes to reperfuse the myocardium. However, fibrinolytics can be beneficial when given up to 12 hours after the onset of symptoms. Fibrinolytics can be also be given by emergency medical services (EMS) personnel in the field.¹²

Adverse Effects of Thrombolytics

- Being a foreign protein a streptokinase is antigenic and is responsible for a variety of allergic reactions such as urticaria, rashes(1-10%) angioneurotic oedema(<1%), hypotension(>10%), bronchospasm(1-10%), and fever(1-4%) may develop. The most common complication of streptokinase is bleeding.
- Risk of noncerebral bleeding may be lower with tenecteplase, but cranial bleeding incidence (22%) is similar, hematoma (12%), genito urinary bleeding (4%), stroke(2%)^{8,13,14,15}

How to Know that the Thrombolytics Are Working

Have to depend on indirect markers to determine if the ischemic area of the heart has been reperfused and the therapy has been successful.

- Decrease in and/or resolution of ST segment elevation appears to be a reliable indirect marker

for the success of thrombolytic therapy. If the ST segment elevation has decreased by $\geq 50\%$, this is associated with a higher rate of coronary artery reperfusion. The available research has clearly shown that the more the ST segment is decreased, the greater the improvement in mortality rates. Other indirect markers of reperfusion such as the presence/absence of chest pain, myoglobin levels don't appear to be very sensitive or reliable¹⁶

CONCLUSION

Streptokinase may produce more bleeding complications and less resolution of st-segment when compared to tissue-plasminogen activators such as tenecteplase. Now-a-days mortality rate is very high in acute myocardial infarction. So, this can be reduced by providing tissue plasminogen activator within the time.

REFERENCES

1. Md.Ramjan Ali, Mohammad Salim Hossain, Md.Arifullslam, Md.Saifullslam Arman, Golam Sarwar Raju, Prianka Dasgupta, and Tasnim Fariha Noshin, Aspect of Thrombolytic Therapy: A Review. The Scientific world journal, 2014, 1-8.
2. Ajay Suri, Sophia Tinney, Syed Ahsan and Pascal Meier, Novel Strategies in Ischemic Heart Disease, Intech, 2012, 123-134.
3. KD Tripathi, Essentials of MEDICAL PHARMACOLOGY.7th edition, apee brothers medical publishers, New Delhi, 2013, 626-627.
4. Anirban Banerjee, Yusuf Chisti, U.C Banerjee, Streptokinase—a clinically useful thrombolytic agent, Biotechnology Advances, 22, 2004, 287–307.
5. Ava Mansouri, ShimaTasharoe, SaeidehJavidee, Mona Kargar, Maryam Taghizadeh-ghehi, MoloukHadjibabaie, Kheirollah Gholami, StreptokinaseAdverse Reactions: A Review of Iranian Literature, J Pharm Care, 2, 2014, 120-129.
6. A Boland, Y Dundar, A Bagust, A Haycox, R Hill, R MujicaMota, T Walley, and A Dickson. Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation, Health Technology,7, 2003, 69-75.
7. Saira Afzal, Muhammad Arif Khan , Hafiz Muhammad, Ayesha Ashraf, Maria Afzal, Psychosocial risk factors of myocardial infarction and adverse effects of streptokinase in public sector hospitals, Pak J Medical Sciences, 31, 2015, 821-826.
8. Charles F.lacy, Loral. Armstrong, Drug information hand book international, 13th edition, lexi-coms, United states, 2005.(1468-1469),(1506-1507).
9. Nannette M Turcasso and Jean M Nappi,Tenecteplase for Treatment of Acute Myocardial Infarction, The Annals of Pharmacotherapy, 35, 2001, 1233-1239.
10. I Sathyamurthy, KN Srinivasan, K Jayanthi, D Vaidiyanathan, Efficacy and Safety of Tenecteplase in Indian Patients with ST-segment Elevation Myocardial Infarction, Indian Heart Journal, 60, 2008, 554–557.



11. Thrombolytic therapy, Available at: <http://emedicine.medscape.com/article/811234-overview> (accessed on 01/4/17).
12. Dana Bartlett et al. Thrombolytics and Myocardial Infarction.
13. KV Krishna das, Text book of medicine, 5th edition, Jaypee brothers medical publishers, New delhi, 2008, p.852-853.
14. Richard A. Helms, David J. Quan, Text book of therapeutic drugs and disease management, 8th edition, Lippincott Williams and Wilkins, Philadelphia, 2006, p.604-610.
15. Joseph T. Dipiro, Robert L. Talbert, Pharmacotherapy: A pathophysiologic approach, 7th edition, McGraw Hill, New York, 2008, p.250-251.
16. Rana Kishore Pelluri, Vanitha Rani N, M. Ramesh, G. Kannan and P. Thennarasu, Safety and efficacy of streptokinase and tenecteplase in patients with acute ST elevated myocardial infarction in an intensive cardiac care unit of a tertiary care teaching hospital, International Journal of Pharma and Bio Sciences, 5, 2014, 29-38.

Source of Support: Nil, Conflict of Interest: None.

