

## Comparison of Safety and Efficacy of Streptokinase and Tenecteplase in Patients of Myocardial Infarction

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**Abstract:** Myocardial infarction is a major cause of mortality and morbidity worldwide. STEMI [ST segment elevation myocardial infarction] is a medical emergency condition. Reperfusion therapy like PCI [Percutaneous Coronary Intervention] is the gold standard for an early management of STEMI, which is better replaced by thrombolytic therapy. Thrombolytics available to treat STEMI include streptokinase (SK), urokinase (u-PA), alteplase (rt-PA), reteplase (r-PA), tenecteplase (TNK-tPA), lanoteplase.<sup>[3]</sup> Successful reperfusion therapy mainly depends upon the choice of thrombolytic agent. The aim of the study was to compare the safety and efficacy of Streptokinase and Tenecteplase in patients with acute ST segment elevation myocardial infarction. Time taken for drug administration after onset of symptoms and to assess the safety and efficacy of thrombolytics. Prospective observational study conducted for 6 months among 70 patients in cardiac care unit in Rajiv Gandhi Institute of medical sciences. Data was collected from the patients who are diagnosed with ST segment elevated myocardial infarction and who are prescribed either with streptokinase or tenecteplase. Microsoft excel was used for recording and analysing the data of recruited subjects. Descriptive statistics mean was used to calculate the average age and length of stay. Graph pad prism version 7.03(Chi-square test) was used to assess the level of significance between various parameters between the streptokinase and tenecteplase. Elderly patients more than 45 years and males were more prone to STEMI. As window period increases the thrombolytic efficacy decreases. The safety and efficacy were more for tenecteplase when compared to streptokinase. Hospital stay was increased for the streptokinase treated patients. Tenecteplase had minimum occurrence of ADR's, greatest ST segment resolution, better symptomatic relief when compared to streptokinase. So that streptokinase was completely replaced by tenecteplase, further studies may require in cost reduction.

Tenecteplase was the most safest and efficacious thrombolytic drug when compared to streptokinase in the treatment of STEMI. Co-morbidities did not affect the ST segment resolution in both thrombolytic drugs. The thrombolytic drug should be administered <2 hours of onset of symptoms for better resolution.

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### I. Introduction

Myocardial infarction is a major cause of mortality and morbidity worldwide. STEMI [ST segment elevation myocardial infarction] is a medical emergency condition.<sup>[1]</sup> Reperfusion therapy like PCI [Percutaneous Coronary Intervention] is the gold standard for an early management of STEMI, which is better replaced by thrombolytic therapy. Thrombolytics available to treat STEMI include streptokinase (SK), urokinase (u-PA), alteplase (rt-PA), reteplase (r-PA), tenecteplase (TNK-tPA), lanoteplase.<sup>[2]</sup> Successful reperfusion therapy mainly depends upon the choice of thrombolytic agent. The aim of the study was to compare the safety and efficacy of Streptokinase and Tenecteplase in patients with acute ST segment elevation myocardial infarction.

#### Objectives:

1. Time taken for drug administration after onset of symptoms
2. To assess the safety and efficacy of thrombolytics.

**Study design and study period:**

The present study was prospective observational study, conducted in Cardiology Department at Rajiv Gandhi Institute of Medical Sciences (RIMS), Kadapa for a period of 6 months i.e., from November 2016-June 2017.

**Source of data:**

All the data was collected in the previously designed data collection form. The data required for the prospective observational study was collected on daily basis for six months from cardiology care unit in a tertiary care teaching hospital.

**Sample size:** A total of 70 patients were included in the study.

**Inclusion criteria:**

We included all the subjects who satisfied the following criteria:

- Patients of either sex who were diagnosed with MI and treated with either streptokinase or tenecteplase would be included in the study,
- Patient admitted in the hospital  $\leq$  6 hours of onset of symptoms,
- Patient with co-morbidities other than specified.

**Exclusion criteria:**

The study excluded

- Prior intracranial hemorrhage,
- Active bleeding or bleeding diathesis (excluding menses),
- History of internal bleeding in 2-4 weeks,
- Previous exposure or history of hypersensitivity to streptokinase,
- Pregnant women, lactating mothers,
- Active peptic ulcer,
- Current use of warfarin,
- Uncontrolled hypertension ( $>$  180/110 mm Hg),
- Major surgery,
- Stroke patients (within 6 months),
- Non compressable vascular punctures,
- Known malignant intracranial neoplasm.

**Parameters assessed:**

**Efficacy Monitoring Parameters:**

1. ST Segment resolution: ST-segment elevation resolution was calculated as the initial sum of ST-segment elevation (on pre-treatment ECG) minus the sum of ST-segment elevation on the second ECG (90 min after thrombolytic treatment) divided by the initial sum of ST-segment elevation and expressed as a percentage.
2. Symptoms relief: After initiation therapy with thrombolytic drugs, the symptoms decreased within 2 hours were considered as successful symptomatic relief.

**Safety Monitoring Parameters:**

1. Hypotension
2. Bleeding
3. Allergy
4. Fever and Chills

**Method of collection of data:**

A prospective observational study was conducted for a period of six months (November 2016-June 2017) in RIMS Kadapa, Andhra Pradesh. All the Patients who were diagnosed with STEMI, prescribed either with streptokinase or tenecteplase were included to participate. All the required data was collected from the self prepared data collection form, past medical and medication history, present medical and medication history, diagnosis, ECG, and interview of the subjects directly.

**Statistical analysis:**

- Microsoft excel was used for recording and analysing the data of recruited subjects.
- Mean was used to calculate the average age and length of stay.
- Graph pad prism version 7.03 (Chi-square test) was used to assess the level of significance between various parameters between the streptokinase and tenecteplase.
- *P* values of  $<$  0.05 were considered statistically significant.

## II. Results

In the present study, a total number of 70 patients who have been admitted with STEMI were included in which 30 were treated with streptokinase and 40 were treated with tenecteplase. Out of 70 members, 58 (82.5%) were male patients and other were females. Males were more prone to ST segment elevated myocardial infarction when compared to females.

Out of 70 patients, 54(77.14) were elder patients of age > 45 years which states that elders were more prone to ST segment myocardial infarction.

STEMI is classified depending upon the involved area of the myocardium. Here subjects suffered from the anterior wall MI were 39(55.7%) which was more than the Inferior wall MI (44.20%).

### Window period:

Window period is the time duration between the onset of Myocardial Infarction symptoms and the initiation of the thrombolytic therapy. The ST segment resolution >50% was more for the patients who were treated with in 2 hrs of onset of symptoms. Fisher's exact test was used to show the association between window period among the ST segment resolution of two drugs with the significant P-value of 0.0006. This is shown in table [1].

**Table 1.** Association between the ST segment resolution and window period

Window period	Number of subjects		P-Value
	ST segment resolution >50%	ST segment resolution <50%	
<2 hrs	16(35.55%)	2(8%)	0.0006
2-4 hrs	19(42.22%)	6(24%)	
4-6 hrs	10(22.22%)	17(68%)	
Total	45	25	

### Efficacy parameters:

**ST-Segment resolution:** ST segment resolution >50% were found in 14(46.6%) subjects treated with STK and 31(77.5%) subjects treated with TNK which represents the resolution of ST segment was more for tenecteplase than the streptokinase with the P-value of 0.0115 which was statistically significant. This is shown in table [2]. **Symptoms relief:** Thrombolytic drug which relieves the symptoms of patients with less time is having more effect than the other one. Symptoms relief within 2 hours were found in 13(43.3%) patients treated with STK and 29(72.5%) patients treated with TNK which results in TNK having more symptoms relief with statistically significant P- value of 0.0256. This is shown in table [2].

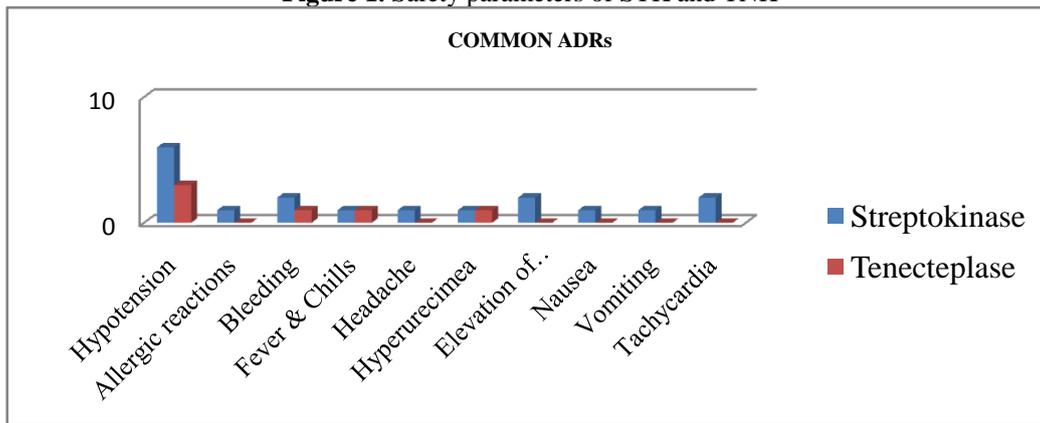
**Table 2.** Efficacy parameters of streptokinase and tenecteplase

Efficacy parameters		Number of subjects (%)		P-Value
		Streptokinase	Tenecteplase	
ST Segment resolution	>50%	14(46.6%)	31(77.5%)	0.0115
	<50%	16(53.3%)	9(22.5%)	
Symptom relief	within 2 hours	13(43.3%)	29(72.5%)	0.0256
	after 2 hours	17(56.6%)	11(27.5%)	

### Safety parameters:

In order to assess the safety of STK and TNK, we monitored patients and reported ADR's to peripheral Pharmacovigilance center. STK associated ADR's were 18(60%) and TNK were 6(15%). Most commonly reported ADR's with STK were hypotension, bleeding, elevated liver enzyme levels, tachycardia and TNK were hypotension, bleeding as shown in figure [1].

**Figure 1.** Safety parameters of STK and TNK



Fisher’s exact test was used to show the association between safety among the two drugs which was statistically significant with the P-value of 0.0001. This is shown in table [3].

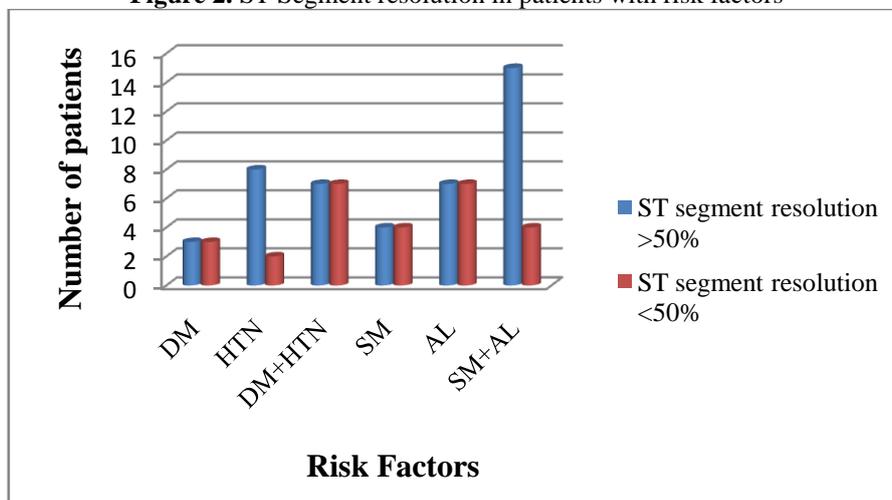
**Table 3.** Number of ADRs occurred in all patients treated with thrombolytic drugs

DRUGS	ADRs	NO ADRs	P-value
Streptokinase	18 (60%)	12 (40%)	0.0001
Tenecteplase	6 (15%)	34 (85%)	
TOTAL	24 (34.28%)	46 (65.72%)	

**Risk factors:**

Figure [2] represents the success rate of thrombolysis was not found to be different among diabetic/ non diabetic population and hypertensive/non hypertensive patients and also smoking and alcoholism did not affect the outcome of thrombolysis. Fisher’s exact test was used to show the association between risk factors among the two drugs. The difference in outcome was statistically not significant with the P-value of 0.2820.

**Figure 2.** ST Segment resolution in patients with risk factors



**Length of stay:**

Table [4] shown that the length of hospital stay decreases with the effective thrombolytic drug with less adverse effects. Length of hospital stay of patients who received streptokinase therapy is more when compared to the tenecteplase treated group.

**Table 4.** Length of stay of Thrombolysed STEMI patients

Drug	Mean ± STD deviation for length of stay	P-Value
Streptokinase	7.5 ± 2.079	0.0002
Tenecteplase	5.8 ± 1.68	

Unpaired t test was used to show the association between length of stay among the two drugs. The obtained P-value was 0.0002 which was statistically significant.

### III. Discussion

Fibrinolytic therapy has become the main stay of treatment for AMI.<sup>[3]</sup> A comparative study was conducted to assess the efficacy and safety of fibrinolytic drug therapy (Streptokinase, Tenecteplase) for 70 patients with acute STEMI. Streptokinase was administered for 30 patients and Tenecteplase for 40 patients for fibrinolysis.

In our study streptokinase treated group had more ADR's than tenecteplase which was statistically significant. It shows hypotension, bleeding, elevated liver enzymes, tachycardia were the commonest side effects produced by Streptokinase, which was supported by Gruppo Italiano 1986, in PIT (Pulse Infusion Thrombolysis) patients with both a systolic pressure of less than 100 mm Hg and a heart rate exceeding 100 beats/min were also at high risk of death,<sup>[3]</sup> Gore JM, Granger Cb et al. thrombolytics especially Streptokinase has several side effects and limitations, higher rate of stroke and intracerebral hemorrhage is seen.<sup>[4]</sup>

Based on efficacy monitoring parameters, ST segment resolution of >50% and symptomatic relief were less for streptokinase than the tenecteplase.

The onset of symptoms and time of initiation of thrombolytic therapy is an important predictor of MI size and patient outcome. Rate of reperfusion is directly proportional to time of drug administration which is supported by Boersma E et al. a positive correlation was found between time to treatment and reperfusion rate, suggested that early thrombolysis produced better outcome.<sup>[5]</sup>

In our study, the co morbidities did not affect the ST segment resolution which was statistically not significant supported by Girish Ronad et al. success rate of thrombolysis was not found to be different among diabetic/non diabetic population and hypertensive/non hypertensive, smokers/non smokers, alcoholic/non alcoholic it was statistically not significant.<sup>[6]</sup>

As per our study length of stay was increased in patients who are treated with Streptokinase than Tenecteplase.

### IV. Conclusion

Tenecteplase was most safest and efficacious thrombolytic drug when compared to streptokinase. Tenecteplase had minimum occurrence of ADR's, greatest ST segment resolution, better symptomatic relief when compared to streptokinase. So that streptokinase was completely replaced by tenecteplase in centres where PCI is not available, further studies may require in terms of cost reduction.

Co-morbidities did not affect the ST segment resolution in both thrombolytic drugs. The length of stay for tenecteplase is less than the streptokinase.

The thrombolytic drug should be administered <2 hours of onset of symptoms for better resolution. Future research might see the development of optimal thrombolytic strategy with ability of maximal reperfusion and with minimal complications.

### References

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