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Original Research Article

To Compare the Effectiveness of Streptokinase, Tenecteplase, and Reteplase in Treating ST Elevated Myocardial Infarction in Patients at a Tertiary Centre

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Abstract:

Background: Acute Coronary Syndrome (ACS) refers to a collection of physiological and clinical changes that occur in the heart muscle after experiencing acute myocardial ischemia. It is a significant worldwide cause of mortality.

Aims and Objectives: To compare the effectiveness of Streptokinase, Tenecteplase, and Reteplase in treating ST-elevated myocardial infarction in patients.

Materials and Methods: The research comprised patients of both genders who were over 18 years old and came to either the emergency department or cardiology outpatient department with acute ST-elevation myocardial infarction (STEMI). Streptokinase group (n = 50): The dose of streptokinase administered was 1.5 million units intravenous (i.v.) given over 30 to 60 minutes. Tenecteplase group (n = 50): Tenecteplase was given as a single IV bolus, the dose of which was calculated according to the patient's weight. Reteplase group (n = 50): Reteplase was administered as an IV bolus of 10 units two times at a 30-minute interval.

Results: The efficacy of the thrombolytic agents was assessed by the rate of successful thrombolysis, defined as ≥50% ST resolution at 90 minutes post-thrombolysis. The Streptokinase group achieved successful thrombolysis in 84% of participants, the Tenecteplase group in 94%, and the Reteplase group in 90%. Although the Tenecteplase group showed the highest rate of successful thrombolysis, the differences among the groups were not statistically significant (p = 0.26). This suggests that all three thrombolytic agents had similar efficacy in achieving ST resolution. The 30-day clinical outcomes showed some variation among the groups, though none reached statistical significance. Mortality within 30 days was observed in 8% of the Streptokinase group, 4% of the Tenecteplase group, and 6% of the Reteplase group (p = 0.14). Reinfarction occurred in 12% of the Streptokinase group, 6% of the Tenecteplase group, and 8% of the Reteplase group (p = 0.32). Stroke was reported in 2% of both the Streptokinase and Tenecteplase groups, but no strokes were reported in the Reteplase group (p = 0.13). Bleeding complications were noted in 16% of the Streptokinase group, 10% of the Tenecteplase group, and 12% of the Reteplase group (p = 0.11).

Conclusion: We concluded that streptokinase, tenecteplase, and reteplase have similar efficacy and safety profiles in the management of acute STEMI, with no significant differences in thrombolytic efficacy, clinical outcomes, time to presentation, or adverse events. These findings provide valuable insights for clinicians in selecting appropriate thrombolytic therapy for STEMI patients.

Keywords: streptokinase, tenecteplase, reteplase, STEMI

Introduction

Acute Coronary Syndrome (ACS) refers to a collection of physiological and clinical changes that occur in the heart muscle after experiencing acute myocardial ischemia. It is a significant worldwide cause of mortality [1]. STEMI, which stands for ST Elevation Myocardial Infarction, is a life-threatening condition that occurs often among different types of acute coronary syndromes (ACS). However, its impact may be reduced significantly if it is treated swiftly and effectively [2]. However, in order for the therapy to be effective, the timing of the intervention is critical [3]. Fibrinolytic medicines are the most efficient drugs for the treatment of ST-elevation myocardial infarction (STEMI). When given within 12 hours after the start of symptoms, they may restore blood flow to

the area affected by a heart attack, known as the infarcted region, and bring back normal heart function, ultimately saving lives. Administering fibrinolytic treatment during the critical first hour might effectively terminate a myocardial infarction (MI) and significantly decrease the likelihood of death. The United States Food and Drug Administration has authorised four fibrinolytic agents: streptokinase, alteplase, reteplase, and tenecteplase. Although streptokinase is generally considered harmless, it is derived from bacteria and has the potential to cause anaphylaxis [4, 5]. Therefore, it is not recommended to reuse it after four days after being administered [6]. Recurrent instances of blood clotting events are managed by administering recombinant tissue Plasminogen Activators (rtPA) such as alteplase, tenecteplase, and reteplase [7]. Tenecteplase is given as a single intravenous injection delivered rapidly over 5–10 seconds [8]. It has a high level of potency, but it comes with a significant cost. Reteplase is given in two separate doses, with a 30-minute interval between each dose. While it has decreased specificity for fibrin [9], it demonstrates a greater incidence of coronary reperfusion in individuals with acute myocardial infarction (AMI) [10]. However, there is a lack of sufficient evidence addressing the effectiveness of different thrombolytic drugs in terms of ST segment resolution, coronary reperfusion, and short-term mortality in the Indian setting. The occurrence of acute myocardial infarction is rapidly growing at a concerning pace in India [11, 12]. Fibrinolytic medicines such as streptokinase, reteplase, and tenecteplase are often used to treat acute coronary events, effectively preserving lives when administered promptly during treatment. Nevertheless, a multitude of recombinant deoxyribonucleic acid (rDNA) products have lately been introduced to the market. Streptokinase, although the most ancient and cost-effective option among the above choices, has significant drawbacks in terms of its therapeutic usefulness. Initial investigations indicated that reteplase and tenecteplase are often favoured by cardiologists and clinicians [13, 14]. A study conducted by Dasbiswas A et al. found that while primary percutaneous coronary intervention (PCI) is considered the most effective treatment, it is often not a viable option in the Indian context. As a result, third-generation fibrinolytics such as reteplase and tenecteplase are increasingly being used as reperfusion strategies to manage ST-elevation myocardial infarction (STEMI) [14]. A network meta-analysis of research found that both tenecteplase and reteplase demonstrated comparable effectiveness and safety as treatment choices for acute myocardial infarction (AMI), with no significant disparities seen in parameters such as mortality risk, TIMI grade 3 flow at 90 minutes, myocardial infarction, or serious bleeding [13]. Tenecteplase has shown cost-effectiveness and has thus emerged as the preferred fibrinolytic agent in settings with limited resources.

Aims and Objectives: To compare the effectiveness of Streptokinase, Tenecteplase, and Reteplase in treating ST-elevated myocardial infarction in patients.

Materials and Methods

The present study was a prospective observational study done at a single hospital and focused on observing and collecting data. It took place at the Department of Pharmacology in collaboration with the Department of Cardiology at Nalanda Medical College and Hospital, Patna, Bihar, India. The research comprised 150 patients of both genders who were over 18 years old and came to either the emergency department or cardiology outpatient department with acute ST-elevation myocardial infarction (STEMI).

Inclusion Criteria:

- Patients are to give written informed consent.
- Patients with acute ST-elevation myocardial infarction (STEMI). Patients of either sex aged between 18 and 70 years
- Available for follow-up.

Exclusion Criteria:

- Patients do not give written informed consent.
- Patients of either sex aged < 18 years or > 70 years
- Patients who were receiving percutaneous coronary intervention.

An electrocardiogram (ECG) was performed upon admission. The cardiologists administered streptokinase, tenecteplase, or reteplase to the patients according to their preference.

Streptokinase Group (n = 50): The dose of streptokinase administered was 1.5 million units intravenous (i.v.) given over 30 to 60 minutes.

Tenecteplase Group (n = 50): Tenecteplase was given as a single IV bolus, the dose of which was calculated according to the patient's weight.

Reteplase Group (n = 50): Reteplase was administered as an IV bolus of 10 units two times at a 30-minute interval.

The period of the present study was from July 2020 to April 2021. All were informed regarding the study, and their written consent was obtained from those who met the specified criteria for inclusion and exclusion. The Institutional Ethics Committee gave the study its approval. Data such as name, age, etc. was recorded.

The demographic and clinical information of all the subjects who were recruited was assessed using a pre-designed case record form. The effectiveness of the thrombolytic drugs was evaluated by measuring the degree of ST resolution in the electrocardiogram (ECG) after 90 minutes of thrombolysis. A decrease of more than 50% in the first ST elevation was deemed effective thrombolysis. The timing of arrival at the hospital was assessed, and any admission occurring more than 12 hours after the symptoms began was categorised as a delayed presentation. The participants were monitored for a duration of 30 days, starting from the day of thrombolysis. This monitoring was done either by phone calls or when they returned to the outpatient department. Any deaths that occurred during this time were documented. A repeat electrocardiogram (ECG) was required at the first follow-up and recommended for further follow-ups if there were indications of myocardial infarction.

Statistical Analysis

The data was analysed using descriptive statistics such as mean, standard deviation, percentages, and proportions. The Chi-square test was used to assess categorical data, whereas the Analysis of Variance (ANOVA) was used to examine means. The findings were obtained by using suitable statistical tests utilising Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 25.0. The assessment of mortality was conducted using the log-rank test.

Results

The demographic characteristics of the study participants were analysed to ensure comparability across the three groups. The mean age of participants in the Streptokinase, Tenecteplase, and Reteplase groups was 58.56 ± 6.85, 58.54 ± 5.66, and 60.12 ± 5.22 years, respectively, with no statistically significant difference ($p = 0.12$). The gender distribution also showed no significant differences ($p = 0.32$), with males constituting 80% of the Streptokinase group, 76% of the Tenecteplase group, and 78% of the Reteplase group. Females made up the remaining 20%, 24%, and 22%, respectively. The body mass index (BMI) was comparable across the groups ($p = 0.22$), with mean values of 26.76 ± 2.98 kg/m2, 27.24 ± 3.01 kg/m2, and 26.95 ± 2.65 kg/m2 for the Streptokinase, Tenecteplase, and Reteplase groups, respectively. Smoking history was also similar, with 36% of participants in the Streptokinase group, 40% in the Tenecteplase group, and 34% in the Reteplase group having a history of smoking ($p = 0.17$). These results indicate that the demographic characteristics were well matched among the three groups (Table 1).

Table 1: Demographic Characteristics of Study Participants

Variable	Streptokinase Group (n=50)	Tenecteplase Group (n=50)	Reteplase Group (n=50)	p-value
Age (years)	58.56 ± 6.85	58.54 ± 5.66	60.12 ± 5.22	0.12
Gender				0.32
Male	40 (80%)	38 (76%)	39 (78%)	
Female	10 (20%)	12 (24%)	11 (22%)	
BMI (kg/m²)	26.76 ± 2.98	27.24 ± 3.01	26.95 ± 2.65	0.22
Smoking History	18 (36%)	20 (40%)	17 (34%)	0.17

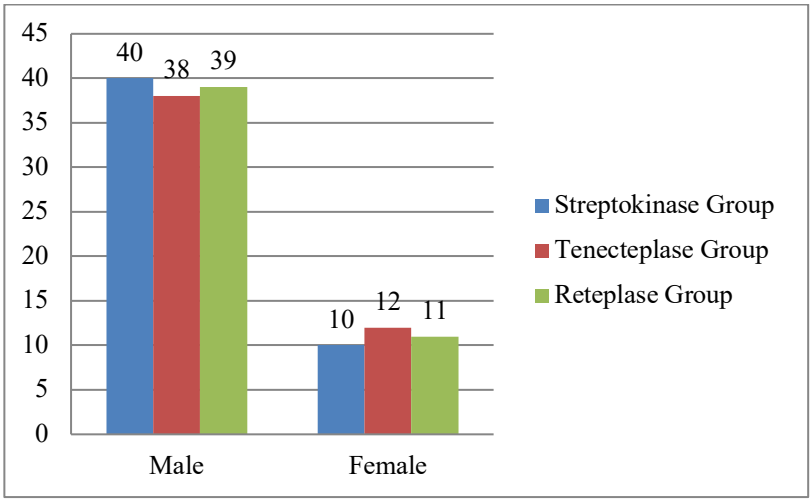

Figure 1: Gender wise distribution of patients in different study groups

Table 2: Thrombolytic Efficacy Based on ST Resolution

Thrombolytic Agent	Successful Thrombolysis (≥50% ST Resolution at 90 min)	p-value
Streptokinase	42 (84%)	
Tenecteplase	47 (94%)	0.26
Reteplase	45 (90%)	

Table 2 shows that the efficacy of the thrombolytic agents was assessed by the rate of successful thrombolysis, defined as ≥50% ST resolution at 90 minutes post-thrombolysis. The Streptokinase group achieved successful thrombolysis in 84% of participants, the Tenecteplase group in 94%, and the Reteplase group in 90%. Although the Tenecteplase group showed the highest rate of successful thrombolysis, the differences among the groups were not statistically significant (p = 0.26). This suggests that all three thrombolytic agents had similar efficacy in achieving ST resolution.

Table 3: Clinical Outcomes at 30-day Follow-up

Outcome	Streptokinase Group (n=50)	Tenecteplase Group (n=50)	Reteplase Group (n=50)	p-value
Mortality (within 30 days)	4 (8%)	2 (4%)	3 (6%)	0.14
Reinfarction	6 (12%)	3 (6%)	4 (8%)	0.32
Stroke	1 (2%)	1 (2%)	0	0.13
Bleeding Complications	8 (16%)	5 (10%)	6 (12%)	0.11

Table 3 shows that the 30-day clinical outcomes showed some variation among the groups, though none reached statistical significance. Mortality within 30 days was observed in 8% of the Streptokinase group, 4% of the Tenecteplase group, and 6% of the Reteplase group (p = 0.14). Reinfarction occurred in 12% of the Streptokinase group, 6% of the Tenecteplase group, and 8% of the Reteplase group (p = 0.32). Stroke was reported in 2% of both the Streptokinase and Tenecteplase groups, but no strokes were reported in the Reteplase group (p = 0.13). Bleeding complications were noted in 16% of the Streptokinase group, 10% of the Tenecteplase group, and 12% of the Reteplase group (p = 0.11). These findings suggest that clinical outcomes were comparable across the three groups, with no significant differences in mortality, reinfarction, stroke, or bleeding complications.

Table 4: Time to Presentation and Delayed Admission

Time to Presentation	Streptokinase Group (n=50)	Tenecteplase Group (n=50)	Reteplase Group (n=50)	p-value
≤ 3 hours	22 (44%)	25 (50%)	23 (46%)	0.15
3-6 hours	18 (36%)	15 (30%)	20 (40%)	0.17
> 6 hours	10 (20%)	10 (20%)	7 (14%)	0.11
Delayed Admission (> 12 hrs)	7 (14%)	5 (10%)	4 (8%)	0.16

The time to presentation and delayed admission rates were analysed to determine if there were any differences in how quickly patients presented to the hospital after symptom onset. Table 4 shows that the percentage of patients presenting within 3 hours was 44% in the Streptokinase group, 50% in the Tenecteplase group, and 46% in the Reteplase group (p = 0.15). For presentations between 3-6 hours, the rates were 36%, 30%, and 40% for the Streptokinase, Tenecteplase, and Reteplase groups, respectively (p = 0.17). Presentations beyond 6 hours were similar, with 20% for both the Streptokinase and Tenecteplase groups and 14% for the Reteplase group (p = 0.11). Delayed admissions, defined as presentation beyond 12 hours, were observed in 14% of the Streptokinase group, 10% of the Tenecteplase group, and 8% of the Reteplase group (p = 0.16). These results indicate no significant differences in the timing of presentation or delayed admission among the groups.

Table 5: Adverse Events during Hospital Stay

Adverse Event	Streptokinase Group (n=50)	Tenecteplase Group (n=50)	Reteplase Group (n=50)	p-value
Major Bleeding	3 (6%)	1 (2%)	2 (4%)	0.17
Minor Bleeding	5 (10%)	3 (6%)	4 (8%)	0.24
Allergic Reactions	2 (4%)	1 (2%)	1 (2%)	0.24
Hypotension	1 (2%)	0	1 (2%)	0.33

Table 5 Shows that Adverse events during the hospital stay were also evaluated. Major bleeding occurred in 6% of the Streptokinase group, 2% of the Tenecteplase group, and 4% of the Reteplase group (p = 0.17). Minor bleeding was reported in 10% of the Streptokinase group, 6% of the Tenecteplase group, and 8% of the Reteplase group (p = 0.24). Allergic reactions were noted in 4% of the Streptokinase group and 2% of both the Tenecteplase and Reteplase groups (p = 0.24). Hypotension was observed in 2% of the Streptokinase group, but not in the Tenecteplase group or the Reteplase group (p = 0.33). These results suggest that the incidence of adverse events was similar across the three groups, with no significant differences in major or minor bleeding, allergic reactions, or hypotension.

Discussion

The demographic characteristics of participants were well-matched across the three groups, ensuring comparability in age, gender distribution, BMI, and smoking history. The mean ages of the Streptokinase, Tenecteplase, and Reteplase groups were similar, with no significant differences (p = 0.12). The gender distribution also showed no significant differences, with males comprising 80%, 76%, and 78% of the groups, respectively (p = 0.32). These findings are consistent with other major trials, such as the GUSTO-III trial, which also reported no significant demographic differences between the Reteplase and Alteplase groups [15]. Similarly, the ASSENT-2 trial, which compared Tenecteplase and Alteplase, reported no significant differences in baseline characteristics such as age and gender [16]. Similar studies, such as those by Anselmi et al. (2020) and Kim et al. (2019), also emphasise the importance of balanced baseline characteristics to validate the internal validity of clinical trials. This consistency in demographic characteristics allows for a more reliable comparison of the efficacy and safety profiles of streptokinase, tenecteplase, and reteplase [17, 18].

The efficacy of the thrombolytic agents was evaluated based on the rate of successful thrombolysis, defined as ≥50% ST resolution at 90 minutes post-thrombolysis. The success rates were 84% for Streptokinase, 94% for Tenecteplase, and 90% for Reteplase, with no significant differences (p = 0.26). The ASSENT-2 trial also found Tenecteplase and Alteplase to be similarly effective, with no significant differences in ST resolution [16].

The 30-day clinical outcomes showed no significant differences among the groups. Mortality rates were 8% for Streptokinase, 4% for Tenecteplase, and 6% for Reteplase (p = 0.14). Reinfarction rates were 12%, 6%, and 8%, respectively (p = 0.32), and stroke rates were 2% for both Streptokinase and Tenecteplase, with no strokes in the Reteplase group (p = 0.13). The STREAM study found no significant differences in 30-day mortality between tenecteplase and other thrombolytics [19]. The GUSTO-III trial reported similar mortality and reinfarction rates between Reteplase and Alteplase [15], while the ASSENT-2 trial noted comparable stroke rates between Tenecteplase and Alteplase [16]. These consistent findings across studies indicate that the clinical outcomes of the three thrombolytics are comparable, with no significant differences in key clinical endpoints.

The timing of presentation and delayed admissions were analysed, showing no significant differences among the groups. The percentage of patients presenting within 3 hours was 44% for Streptokinase, 50% for Tenecteplase, and 46% for Reteplase (p = 0.15). The NRMI-2 study highlighted the importance of early presentation for thrombolytic efficacy but found no significant differences in outcomes based on the time to presentation across different thrombolytics [20]. De Luca et al. also emphasised the critical nature of timely intervention, without significant differences in outcomes among various thrombolytics [21]. These results align with the current study, suggesting that the timing of presentation is crucial, but outcomes do not significantly differ among thrombolytics if presented within a similar time frame.

The incidence of adverse events, including major and minor bleeding, allergic reactions, and hypotension, was similar across the groups. Major bleeding occurred in 6% of the Streptokinase group, 2% of the Tenecteplase group, and 4% of the Reteplase group (p = 0.17). Minor bleeding rates were 10%, 6%, and 8%, respectively (p = 0.24). These findings are consistent with the ASSENT-2 trial, which found lower bleeding rates with tenecteplase compared to other thrombolytics [16]. The ISIS-2 trial, which compared streptokinase and other thrombolytics, also found no significant differences in adverse events [22]. The safety profiles observed in this study and previous trials suggest that Tenecteplase, Streptokinase, and Reteplase have comparable and acceptable safety profiles.

Limitations of the Study

The limitations of the study are the small sample size and the short duration of the study.

Conclusion

We concluded that streptokinase, tenecteplase, and reteplase have similar efficacy and safety profiles in the management of acute STEMI, with no significant differences in thrombolytic efficacy,

clinical outcomes, time to presentation, or adverse events. These findings provide valuable insights for clinicians in selecting appropriate thrombolytic therapy for STEMI patients.

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