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**Original Research Article**

# COMPARE INTRAVENOUS TENECTEPLASE WITH ALTEPLASE IN PATIENTS OF ACUTE ISCHEMIC STROKE

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## ABSTRACT

**Background:** Alteplase (TPA) and tenecteplase is the thrombolytic agent used for treatment of acute ischemic stroke (AIS), alteplase approved by the USFDA**.** Recently, there has been interest in the thrombolytic tenecteplase, because it is more safe and effective.

**Objectives:** The aim of the present study to compare the safety and efficacy of determine the intravenous alteplase and tenecteplase in acute ischemic stroke patients.

**Methods:** This was a prospective observational study**.** A total of 102 patients of acute ischemic stroke confirmed by MRI/CT with in window period of 3 hours admitted during the study period were enrolled**.** 56 patients received alteplase and 46 patients received tenecteplase. Alteplase and tenecteplase agents were given to the patients 3 hours after the onset of symptom. Various parameters were assed in terms of socio-demographic data, NIHSS score, ICH and mortality.

**Results:** Most of the patients were male in both the group. There is no significant difference in baseline NIHSS score among alteplase and tenecteplase group, whereas statistically significant difference on 24 hours and 7$^{th}$ day NIHSS score in both the group. Co morbidities like: Diabetes Mellitus, Hypertension and hyperlipidaemia was more in alteplase group. Intracerebral hemorrhage (ICH) and mortality was higher in alteplase group whereas functional outcome was better in tenecteplase group.

**Conclusion:** Tenecteplase has better functional outcome, safety and efficacy as compared to alteplase for treatment of Acute Ischemic Stroke

**Keywords:** tenecteplase, alteplase, acute ischemic stroke, functional outcome

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## 1. INTRODUCTION

Stroke is a serious global health problem. According to the World Health Organization, it is estimated that 16.5 million people suffer from stroke and 5.7 million people die as a result of stroke every year, accounting for 11.5% of the total number of deaths in the world [1]. The incidence of stroke is higher in developed countries than in developing countries, where stroke is the most common cause of death, but it is increasing faster in developing countries than in developed countries [2]. Current American Heart Association/Stroke guidelines recommend the use of alteplase for intravenous thrombolysis (IVT) in patients with acute ischemic stroke presenting within 4.5 hours of symptom onset [3-4]. Intravenous thrombolysis with alteplase (ALT) has been the standard of care for acute ischemic stroke (AIS) treatment for more than 25 years [5]. Despite that alteplase can dramatically increase the probability of a full recovery without handicap, it has some disadvantages. These include a low recanalization rate, intracranial hemorrhage (ICH) risk, and a short half-life, necessitating constant infusion [6–8]. Accordingly, increasing efforts have been made in recent years to develop new thrombolytic agents with an improved safety, superior efficacy, and a more convenient delivery [9].

Tenecteplase, a second generation modified recombinant tissue type plasminogen activator, is more fibrin specific, has a longer half-life and depletes less systemic fibrinogen than alteplase. Tenecteplase is also easier to administer as a single bolus over 5-10 seconds when compared to alteplase (bolus + 1 hour infusion), potentially facilitating faster treatment and transport of acute stroke patients within and between hospitals [10]. Multiple phase 2 studies and the recent large phase III Alteplase Compared to Tenecteplase (AcT) and Tenecteplase versus alteplase in acute ischemic cerebrovascular events (TRACE-2) randomized controlled trials show that intravenous tenecteplase (0.25mg/kg) is non-inferior to alteplase (0.9mg/kg) for IVT within 4.5 hours of symptom onset [11]. These results are therefore supporting a transition to tenecteplase as the thrombolytic agent of choice for treating acute ischemic stroke.

**Aims & objectives:** The aim of the study was to compare intravenous tenecteplase with alteplase in patients of acute ischemic stroke

## 2. MATERIALS AND METHODS

This was a prospective observational hospital based study conducted in the department of Neurology, Ramesh Cardiac Multispecialty Hospital in Andhra Pradesh from December 2018 to December 2019 (01 years). A total of 100 patients of acute ischemic stroke confirmed by MRI/CT with in window period of 3 hours admitted during the study period were enrolled.

**Inclusion criteria**

- Acute ischemic stroke with serious measurable deficit on NIHSS
- Patients Aged 18–75 years.
- Patient willing to provide written informed consent before participation

**Exclusion criteria**

- Patients of minor stroke symptoms, or major symptoms rapidly improving Intracranial hemorrhage on pretreatment, CT head suggesting subarachnoid hemorrhage
- Known case of bleeding diathesis or patients who had received heparin within 48 hours
- Major surgery or serious trauma within 14 days; serious head trauma within 3 months

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- Uncontrolled baseline hypertension (185/110 mm Hg)
- Clinical stroke within 3 months or history of intracranial hemorrhage
- Myocardial infarction in past 30 days
- Patients who not provide written informed consent

Patients with ischemic stroke who are eligible to receive thrombolytic agents to receive tenecteplase (at a dose of 0.2mg per kilogram of bodyweight; maximum dose, 20 mg) or alteplase (at a dose of 0.9 mg per kilogram; maximum dose, 90 mg) within 3 hours after symptom onset. The selection of thrombolytic agent as per patient preference

The primary outcome was reperfusion of greater than 50% of the involved ischemic territory or an absence of retrievable thrombus at the time of the initial angiographic assessment. Non inferiority of tenecteplase was tested, followed by superiority. Primary outcome was improvement of National Institutes of Health Stroke Scale (NIHSS) score of 4 or absolute 8 at 7 days and mRS of 0-2 at 90 days. Secondary outcomes included the modified Rankin scale score (on a scale from 0 [no neurologic deficit] to 6 [death]) at 90days. Safety outcomes were death and symptomatic intracerebral hemorrhage. Observation was performed with the use of hospital Stroke Proforma.

## 3. RESULTS

A total of 102 patients were studied. 56 patients received alteplase and 46 patients received tenecteplase. The alteplase group had 41 males, 15 females (mean ages 57.95, 60.48). Baseline NIHSS score 10.55(Max-Min-20-3) and at 7 Days-1.67. mRS at 3 months-0-1(75%), 2-3(14%), 4- 5(3.5%), 6-(5.35%); Diabetes Mellitus 30(53%), Hypertension-46(82%), hyperlipidaemia- 13(23%) and smoking-9(16%). In the Tenecteplase group, males were 38 and 8 were female with mean ages 59.11 and 60.4 years respectively; Baseline NIHSS score-10.63, NIHSS at 7 Days-3.78, mRS AT 90 Days 0-1-(57.89%), 2-3-(23.68%), 4-5-(15.79%), 6-(2.63%), Hypertension- 25(54%), Diabetes Mellitus-20(43%), smoking-9(20%) and hyperlipidaemia-10(22%). 42 of 56 patients receiving alteplase recovered well. This compared favourably with Tenecteplase where 37 of 45 patients recovered well (p =0.067). There were 2 symptomatic and 3 asymptomatic Intracerebral hemorrhage (ICH) in alteplase group as opposed to 2 asymptomatic ICH in the Tenecteplase group. Three patients in the alteplase group and one patient in the Tenecteplase group died.

**Table 1: Comparison of baseline socio-demographic Characteristics of alteplase and Tenecteplase**

| **Baseline Characteristics** | **Alteplase** | **Tenecteplase** | **P value** |
|---|---|---|---|
| **Age in Year (Mean±SD)** | 67.4 ± 12.3 | 59.1±12.7 | 0.275 |
| **Gender** | | | |
| Male | 41 | 38 | |
| Female | 15 | 8 | 0.342 |
| **NIHSS Score:** Baseline | 10.5 ± 5.18 | 10.63±5.56 | 0.65 |
| 24 hours | 10.5 ± 5.18 | 6.4± 5.59 | **0.0002** |
| 7$^{th}$ Day of Discharge | 1.67 ± 3.2 | 3.78± 3.85 | **0.0032** |
| **Intracerebral hemorrhage** | | | |
| Symptomatic ICH | 2 | 0 | |
| Asymptomatic ICH | 3 | 2 | 1.00 |
| **Co morbidities or risk factors** | | | |

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| | | | |
|---|---|---|---|
| Hypertension, N (%) | 46 (82%) | 25 (54%) | 0.674 |
| Diabetes Mellitus, N (%) | 30 (53%) | 20 (43%) | |
| Hyperlipidemia, N (%) | 13 (23%) | 10 (22%) | |
| Smokers, N (%) | 9 (16%) | 9 (20%) | |

**Table 2: Comparison of outcomes among alteplase and Tenecteplase group**

| **Functional outcomes** | **Alteplase** | **Tenecteplase** |
|---|---|---|
| **mRS at 3 months** | | |
| 0-1 | 75% | 57.89% |
| 2-3 | 14% | 23.68% |
| 4-5 | 3.5% | 15.79% |
| 6 | 5.35% | 2.63% |
| **Recovery of patients** | 75% | 82.3% |
| **Patients death** | 5.4% | 2.2% |

## 4. DISCUSSION

Acute ischemic stroke is a leading cause of morbidity, mortality, and long-term disability worldwide. Alteplase is currently the only intravenous thrombolytic drug that is FDA approved, but its low recanalization rate, high risk of ICH, and short half-life necessitate continuous intravenous infusion. Tenecteplase is a new thrombolytic drug with a longer half-life and greater resistance to plasminogen activator inhibitors than alteplase. Intravenously administered tenecteplase for thrombolysis in patients with ischemic stroke has increasing attention in recent years [12-13].

Present study showed no significant difference between alteplase and tenecteplase in terms of mean age, whereas male was predominantly higher than female in both the group, our results comparable with the Li et al [14] and Huang et al [15].

The alteplase group in our study had significantly more patients with hypertension, diabetes Mellitus and hyperlipidemia compared to the tenecteplase group, in agreement with the Kobeissi H, et al [16] and Bivard A, et al [17].

There is no significant difference in baseline NIHSS score between alteplase and tenecteplase group ($p>0.05$), whereas on 24 hours and $7^{th}$ day of discharge NIHSS score was significantly differ among alteplase and tenecteplase group ($p<0.05$), similar finding also reported by M. Abuelazm, et al [18] and Menon BK, et al [19].

In our study Intracerebral hemorrhage was higher in the alteplase group as compared to the Tenecteplase group, our finding correlate with the many other studies: Chinniah, et al [20], Liang H, et al [21] and N Potla, et al [22].

Present study found functional independence (0-2) was good (82.2%) with tenecteplase group as compared to alteplase group, accordance with the Rehman et al [23] and Shen, et al [24].

Mortality rate was significantly more in alteplase group as compared to tenecteplase group, consistent finding observed by Haley EC, et al [25] and Katsanos et al [26].

## 5. CONCLUSION

We have concluded that intracerebral hemorrhage and mortality rate was more in alteplase. Early neurological improvement was better in both the groups. Functional outcome, efficacy and safety were better with tenecteplase as compared to alteplase.

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