Comparing the efficacy and safety of tenecteplase versus alteplase for acute ischemic stroke among South Indian patients: A prospective study from South India

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Comparing the efficacy and safety of tenecteplase versus alteplase for acute ischemic stroke among South Indian patients: A prospective study from South India

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Abstract:

Background: Acute ischemic stroke (AIS) requires efficient thrombolytic therapy to re-establish vascular permeability and mitigate tissue damage. Alteplase and Tenecteplase are eminent tissue plasminogen activators (tPAs) employed in this clinical scenario. This study presents a comparative overview of these two agents concentrating on their efficacy, safety profiles, time parameters, and re-hospitalization.

Objectives: Comparing the efficacy and safety of Tenecteplase versus Alteplase for Acute Ischemic Stroke among South Indian patients: a prospective study from South India.

Methods: At a single center we conducted a prospective, observational, non-interventional study of patients receiving thrombolytics Alteplase or Tenecteplase from November 2023 to July 2024, which included patients coming within a window period of 4.5 hours of symptom onset. The principal outcome of this study is to evaluate Early Neurological Improvement using the clinical assessment scales – the National Institutes of Health Stroke Scale (NIHSS) at baseline and 24 hours and the Modified Rankin Scale (mRS) at admission and 3 months while the secondary outcomes include the DTN (Door-To-Needle Time) and assessing the need for re-hospitalization. Data was scrutinized using a t-test and median Inter Quartile Range (IQR).

Results: The study group was divided into 32 patients each, treated with Alteplase and Tenecteplase, respectively. Statistical significance was found for the efficacy of the drugs (NIHSS post treatment p= 0.01 and mRS p = 0.002). The DTN and rehospitalization were found to be non-significant.

Conclusion: Both agents efficiently manage AIS, with Tenecteplase being more feasible than alteplase specifically regarding Early Neurological Improvement, Ease of administration, and cost-effectiveness.

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Keywords - Acute ischemic stroke, alteplase, Tenecteplase, NIHSS, hemorrhagic stroke.

INTRODUCTION

A Stroke is a medical emergency. The WHO estimated that around 15 million people every year suffer from stroke throughout the world [1]. Stroke is the second leading cause of death globally with annual deaths of around 6.5 million [2]. The current outlook represents that, Deaths resulting from stroke are projected to rise exponentially over the next 30 years due to an aging population and our challenges in managing risk factors effectively [3]. 85.5% of fatalities from strokes around the globe occur in lower- and middle-income nations in the Asia-Pacific region. Additionally, in these countries, the number of disability-adjusted life years (DALYs) is reported to be seven times greater than in high-income nations. In India, stroke fatalities have doubled over the last twenty years, with a nearly 100% rise in stroke incidence from 1970-1979 to 2000-2008 [5].

Currently, stroke ranks as the fourth leading cause of death and the fifth most common cause of disability in India [6]. The Global Burden of Disease estimates that there are approximately 1,175,778 new stroke cases in India. A recent systematic review, primarily based on cross-sectional studies, estimated the annual incidence of stroke in India to range between 105 and 152 per 100,000 people. [7].

METHODOLOGY

We carried out a prospective, observational, non-interventional study at a single center. The protocol received approval from the IRB and all patients or their legal representatives had been given the informed consent form. Patients who presented in the Neurology department ≥ 18 years of age, receiving Tenecteplase or alteplase for acute ischemic stroke. The study includes patients who present within 4.5 hours of symptom onset.

A Computed tomography (CT) or MRI was taken promptly, and the baseline characteristics {gender, Age, co-morbidities (Hypertension, Diabetes Mellitus, Dyslipidaemia, Hypothyroidism, Coronary Artery Disease, Chronic Kidney Disease, Atrial Fibrillations), social habits, TOAST classification, Door-To-Needle Time {DTN} along with baseline NIHSS and mRS were filled in a structured proforma. The study population was divided into two groups: Group A, which received Tenecteplase, and Group B, which received Alteplase.

Post-treatment, after the first 24 hours the check CT was evaluated and NIHSS after 24 hours was noted. A significant clinical improvement was assessed by improvement in NIHSS by ≥4 points in the first 24 hours [8-9]. A follow-up after 3 months for the assessment of mRS was made, where 1 or 3 points improvement was considered a major improvement [10-11]. The severity of NIHSS was divided from mild to very severe [12] and mRS has become the most commonly used clinical outcome measure in stroke clinical trials [13-14].

The study criteria for our study are listed below in Table 1

Inclusion criteria	
○ All patients with AIS coming within the window period of 4.5 hours and conformed with CT scan ○ Age group 18-85 years ○ Willing patients/ informed consent	
Exclusion criteria	
○ Pregnant and lactating women ○ Pediatrics ○ Patients with venous thrombosis ○ Patients with infective stroke – sepsis ○ Presence of intracranial hemorrhage ○ Only Minor or quickly resolving stroke symptoms ○ Current internal bleeding (gastrointestinal or genitourinary bleeding within the past 21 days) ○ The patient, who has had heparin within the last 48 hours, presents with an increased APTT. ○ Recent administration of warfarin with increased PT/INR levels ○ Craniotomy, significant head injury, or a prior stroke within the last 3	○ Recent arterial puncture at an incompressible region ○ Recent lumbar puncture (within the past week) ○ A history of conditions such as intracranial hemorrhage, arteriovenous malformation, or aneurysm ○ Seizure observed at the onset of the stroke ○ Acute myocardial infarction occurring recently ○ Systolic blood pressure exceeding 185 mmHg or diastolic blood pressure surpassing 110 mmHg during treatment ○ Ongoing treatment with oral

months, as well as major surgery or severe trauma within the past 2 weeks.	anticoagulants o NIHSS score exceeding 25, indicating severe stroke o Previous history of stroke and diabetes

Table 1: study criteria

Statistical analysis

Statistical analysis is performed using IBM SPSS version 27.0 (SPSS Inc., Chicago, IL, USA). Data was represented as mean and standard deviation, median with IQR (interquartile range), or percentage, based on the appropriateness for describing the characteristics of the subjects. Statistical significance for the two groups being compared was found using an independent t-test of continuous variables. p-value <0.05 is taken as statistically significant.

RESULTS

In the study duration starting from November 2023 to July 2024, a combined total of 64 patients participated in the study. 32 being thrombolysed with Tenecteplase and the rest being thrombolysed with Alteplase. All the baseline characteristics are mentioned in Table 2. Patients in both groups have an almost similar mean and the p-value is 0.15 which is non-significant presenting that the groups being compared are similar and have no bias. The male population is greater than that of the female population, p-value for gender distribution is also non-significant p=0.10. the most found co-morbid condition is HTN with 62.5% of patients from both groups having this condition and all the co-morbid conditions are non-significant. Alcoholism was found the most in patients as a social habit. In both groups, patients came in with TOAST 3 which is a small vessel occlusion. The majority of patients in both sets arrived within 1.5 hours of DTN. From NIHSS vast majority came as mild to moderately severe conditions and baseline NIHSS is not significant. The post-treatment score of Group A and Group B have P = 0.01 (P<0.05) suggesting significance and difference of scores in both Groups. There is an adequate shift of patients from higher to lower scores of NIHSS in Group A moving from severe to mild NIHSS. While in Group B less of a shift is observed from severe to mild NIHSS, this indicates a faster improvement of the Neurological symptoms in participants of Group A thrombolysed with TNK. The MRS score improvement is likely in both groups. The safety assessment of both the groups provides evidence of ADR's being more

prevalent In Group B compared to Group A, the ratio of ADR occurrence of Group A and Group B in our study is 1:3 after a follow up 3 months post thrombolysis.

Characteristics		Tenecteplase (n=32)	Alteplase (n=32)	P value
Age (years, Mean ± SD)		57.2±10.32	60.3±12.26	0.15
Gender	Male	21 (65.6%)	16 (50%)	0.10
	Female	11 (34.3%)	16 (50%)	
co morbidities	HTN*	28 (87.5%)	29 (90.6%)	0.33
	DM**	20 (62.5%)	20 (62.5%)	0.5
	DLP§	13 (40.6%)	15 (46.8%)	0.30
	Hypothyroidism	3 (9.3%)	2 (6.2%)	0.33
	CAD‖	6 (18.7%)	4 (12.5%)	0.5
	CKD┼	1 (3.1%)	1 (3.1%)	0.5
	AF¶	0	0	-
Social habits	Smoker	4 (12.5%)	2 (6.25%)	0.21
	Tobacco	5 (15.6%)	1 (3.1%)	0.05
	Alcoholism	5 (15.6%)	8 (25%)	0.18
TOAST	1	10 (31.2%)	8 (25%)	0.26
	2	10 (31.2%)	11 (34.3%)	
	3	11 (34.3%)	11 (34.3%)	
	4	0	0	
	5	1 (3.1%)	2 (6.2%)	
DTN╗	<1 hour	2 (6.25%)	0	0.04
	1-2 hours	7 (21.8%)	4 (12.5%)	
	2-3 hours	13 (40.6%)	12 (37.5%)	
	>4 hours	10 (31.2%)	16 (50%)	
NIHSS♯ – Baseline	<5	0	0	0.20
	5- 10	20 (62.5%)	17 (53.1%)	
	11-20	11 (34.3%)	15 (46.8%)	

	>20	1 (3.1%)	0	
NIHSS – After 24 hours	<5	11 (34.3%)	1 (3.1%)	0.01
	5- 10	18 (56.2%)	30 (93.7%)	
	11-20	3 (9.3%)	1 (3.1%)	
	>20	0	0	
Mrsb – Baseline	(median IQR)	1	2	0.41
mRS – After 3 Months		1	1	0.002

*Table 2: baseline characteristics

HTN*- Hypertension DM**-Diabetes Mellitus LP§-Dyslipidaemia CAD‖-Coronary Artery Disease CKD┼-Chronic Kidney Disease AF¶-Atrial fibrillation DTN╗-Door-To-Needle Time NIHSS♯-National Institutes Of Health Stroke Scale mRS ♭-Modified Rankin Scale IQR- Inter Quartile Range

DISCUSSION

The study presents the efficacy and safety of Tenecteplase and alteplase for its use in AIS. The average age of the study population was determined to be 59 years which turned out to be lower than the average age in other stroke studies and may be linked to an increase in the frequency of risk factors such as alcohol consumption, cigarette smoking, and HTN [15]. Out of all the subjects, 89% had HTN, which aligns with the literature as being a well-documented modifiable risk factor [16].

As for the TOAST classification, the majority of patients came with small vessel occlusion which lies as a primary risk factor for HTN [17]. Of 64 patients 39 came within 2-3 hours of symptom onset Demonstrating improved in-hospital care with the establishment of an efficient stroke protocol and stroke code. Post-treatment improvement for both primary and secondary outcomes was comparable with results from other studies [18].

In our study, Early neurological improvement (improvement in NIHSS by ≥4 points in the first 24 hours of thrombolysis), was seen as 71.8% and 28.1% in TNK and alteplase groups respectively. From the analysis done by Kheiri et al., the percentages of ENI were 64% and 36% for TNK and alteplase groups respectively [19].

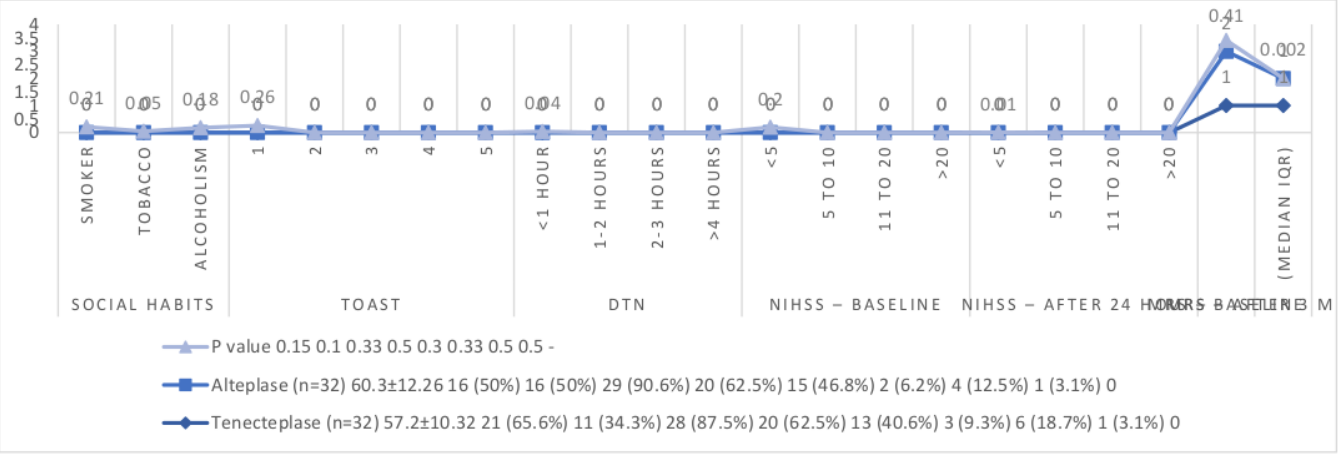

Figure 1 - Scatter chart

An interesting significant observation found in our study is the median mRS score after 3 months is 1 and 1 in the group of TNK and alteplase respectively, showing non-inferiority of TNK over alteplase. In one of the studies by Emily J et al., the median mRS of both groups had no significant difference [20]. Thus, the findings are similar to previous studies.

In our study, the 3-month follow-up mortality rate was 3% (1 death) in TNK and 9% (3 deaths) in alteplase. In a trial of Tenecteplase versus alteplase for acute ischemic stroke, 15.4% and 11.4% mortality occurred in 3 months of follow-up of TNK and alteplase respectively [21]. Thus, the studies done previously demonstrate similar findings as seen in our study.

Thus, Tenecteplase (TNK) has demonstrated superior outcomes concerning early neurological improvement (ENI) compared to Alteplase. Additionally, TNK shows comparable results in terms of the Modified Rankin Scale (mRS) at 3 months of follow-up, indicating similar functional outcomes between the two treatments. Importantly, TNK has presented reduced mortality rates and presents a safer drug profile, suggesting a lower risk of adverse effects compared to Alteplase. Other advantages of TNK over alteplase noted clearly during the study were the ease of administration and cost-effectiveness of TNK which saved time in drug administration and was accessible. Some of the limitations of our study were small sample size

and a short study period.

CONCLUSION

Based on the evidence and analysis, TNK (Tenecteplase) shows clear superiority over alteplase in several key areas.

Its ability to achieve faster and sustained restoration of blood flow in blocked arteries, along with a more favorable safety profile and lower incidence of bleeding complications, highlights TNK's advantage as a thrombolytic treatment for acute ischemic stroke.

Additionally, TNK's simpler administration process and potential for improved patient outcomes further establish it as a preferred therapeutic choice.

In summary, TNK presents itself as a promising alternative to alteplase, offering improved efficacy, safety, and convenience in the management of acute ischemic stroke patients.

Authors' contributions:

All authors contributed to the study's conception and design.

Data collection and analysis were carried out by Iqra Jahan, Syeda Noor Fatima, Yumna Fatima, and Mir Wajahath Ali.

The study idea, design, and supervision were provided by Dr. Maryam and Dr. Sandhya Manorenj.

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Conflict of interest:

The authors confirm that they have no competing interests.

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