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Original Article

An Observational Study on Assessing the Safety and Efficacy of Tenecteplase for Door-To-Needle Time Acute Ischemic Stroke Patients

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ABSTRACT

Background: Stroke is a significant burden in India which is a leading cause of death globally. This study aimed to evaluate the Safety and Efficacy of Tenecteplase for Acute Ischemic Stroke patients who arrived within 3.5 hr of symptom onset. **Materials and Methods:** The observational study was conducted from March 2023 to August 2023 at a multi-specialty hospital with 38 patients. Data were collected on demographics, medical history and various scales to assess stroke severity and recovery. Tenecteplase was administered at a dose of 0.4 mg per kg and patients were monitored clinically before and after thrombolysis, with follow-ups at 24 hr and 1 month. **Results:** The study found to have a higher incidence of stroke among males, with the age group being 56-65 years. Among the patients, most of the patients were smokers. Significant improvements were observed in the maximum number of patients, who scored 1-4 and 0 on the National Institute of Health Stroke Scale within 24 hr and 1 month respectively. The Modified Ranking Scale indicated that most of the patients reached the score of 2 and 0 within 24 hr and one month respectively. Muscle strength improvements were noted after 1 month using a Medical Research Council score. **Conclusion:** Tenecteplase shows a stronger safety profile and is efficacious in treating Acute Ischemic Stroke patients had 3.5 hr of symptom onset which highlights the effective treatment option, promoting better recovery and reducing morbidity and mortality rates.

Keywords: Neurological Outcomes, Stroke, Tenecteplase, Thrombolytic therapy, Tissue Plasminogen Activator.

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INTRODUCTION

Stroke is a critical medical emergency and a leading cause of mortality and adult disability globally. According to the World Health Organization (WHO) report, Stroke is the second leading cause of death worldwide. Stroke is a neurological condition caused by disruption of blood supply to the brain. About six million people die annually due to stroke.[1] Stroke turns out to be the fourth leading cause of death and the 5th leading cause of disabilities. The incidence of stroke in India ranges from 105 to 152 per 1, 00, 000 people per year. This proves that in the past decades, the burden of stroke has been increasing in India. However, the reliability of the available data is very sparse, since there are few available data and studies and available data collected even lacked uniform methods, this highlights the requirement for more comprehensive and standardized research on the stroke epidemiology of the country.[2] Stroke is broadly classified into two hemorrhagic and ischemic strokes where hemorrhagic is caused by rupture of blood vessels while obstruction of blood flow to the brain is the cause of most Ischemic strokes.[3] A thrombotic stroke, a subtype of an ischemic stroke, is caused by a blood clot that forms in the brain's arteries, preventing blood flow to the brain. Embolic stroke is another subtype that is caused by narrowing or obstruction of a vessel from the body elsewhere, usually in the heart or pulmonary arteries. Inadequate brain perfusion is a major feature in ischemic stroke, with atherosclerosis as a common cause. Additionally, ischemic strokes can result from conditions like arterial dissection and other rare vascular disorders.[4] Common risk factors identified were hypertension, prior stroke or transient ischemic attack, dyslipidemia, family history of stroke and smoking.[5] The primary and secondary prevention of

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stroke, focused on managing modifiable risk factors, is crucial for effective stroke management.[6] The essential treatment part of Ischemic stroke is the administration of fibrinolytic agents to dissolve the clot through thrombolysis. These agents induce the plasmin synthesis from the precursor plasminogen, resulting in clot breakdown. Tissue Plasminogen Activator (t-PA) is the primary agent used for thrombolysis, which induces fibrinolysis and breaks down thrombi. The modified t-PA derivative Tenecteplase (TNK) offers promising advantages in treating stroke. These properties include a longer duration of 24 min compared with 4-5 min for Altepase, greater fibrin specificity and stronger clot solubility. These properties contribute to faster artery recanalization, which promotes vascularization of the disease recovers quickly. TNK, developed using recombinant DNA technology, holds promise as a valuable intervention in managing Ischemic stroke, offering improved clinical outcomes and safety profile.[7]

The study aims to assess that tenecteplase is a safer and more productive drug for acute Ischemic stroke patients, presented at the hospital within 3.5 hr of symptom onset. The result of the study will provide a detailed description of better neurological outcomes through the National Institute of Health Stroke (NIHS) scale and the Modified Rankin Scale (MRS) and muscle strength through the Medical Research Council (MRC) Scale.

MATERIALS AND METHODS

Study Design

An observational study was conducted in a Multi-specialty hospital with 38 patients, to assess the Safety and Efficacy of Tenecteplase for door-to-needle time Acute Ischemic Stroke patients using NIHS, MRS and MRC scale. The study was done from March 2023 to August 2023, with a 6-month duration followed by the ethical research approval at the hospital with Registration No: ECR/319/Inst/TN/2013/RR-19.

Inclusion and Exclusion Criteria

Age above 35 of male and female patients, patients with co-morbidities and patients with Acute Ischemic Stroke with a serious measurable deficit on the NIHS, MRS and MRC scales were included in the study. Age below 35 of both male and female patients, patients who came after the stroke window period of above 3.5 hr and patients with recurrent Ischemic stroke, hemorrhagic stroke, seizure at stroke onset and Major surgery within 14 days were not included in the study.

Method of Data Collection

During our study, we collected all patients who met the inclusion criteria. Data was collected using a well-structured data collection proforma and checklist which includes the patient's demographics (Age, Gender, height and weight), Medical and medication history, Habits, Vital signs, Laboratory investigations, Time of onset of stroke, Activities of daily living, MRC Scale, MRS, NIHSS, Thrombolytic drug-Tenecteplase (Dose, Time of administration, Route of administration). Before thrombolisation, a Computed Tomography (CT) scan and Vital signs were monitored clinically. After thrombolisation, the patient's Blood Pressure was monitored for 24 hr and NIHSS, MRS and MRC scores were recorded for efficacy, A CT scan was monitored for the safety of the patients and collected 1-month review. Every difference in investigations that was found has been suitably recorded.

Data Analysis

The data were evaluated using percentage calculation to note the Safety and Efficacy of Tenecteplase for door-to-needle time Acute Ischemic Stroke patients.

RESULTS

From Table 1, the demographic study revealed a higher stroke incidence among males 25 (62.5%) compared to females 13 (37.5%). The largest proportion of patients 15 (39.5%) fell into the 56-65 age group, followed by 14 (36.8%) in the 46-55 ages, 3 (7.8%) aged 35-45 years and 6 (15.7%) aged 66-80 years. In terms of habits, 24 (58.3%) were smokers and 17 (44.7%) were alcohol consumers.

From 38 patients, the study showed that 26 (68.4%) of patients with an NIHS score of 1-4 considered as minor strokes and 27 (71.0%) of patients with a score of 0 resembling no stroke symptoms experienced notable improvements within the first 24 hr and one month after treatment respectively which were shown in Figure 1.

Based on the distribution of the Modified Rankin Scale, 15 (39.5%) attained a score of 2 having slight disability after 24 hr and 25 (65.8%) achieved a score of 0 specifies no symptoms for one-month post-treatment which is represented in Figure 2.

Of 38 patients, 21 were affected on the right side 9 (42.9%) were upper limbs and 8 (38.09%) were lower limbs within 24 hr. Whereas after 1 month 18 (85.7%) were upper limb 17 (81.0%) were lower limb achieved a score of 3 which is an active movement against gravity and 5 which resembles the normal power scale respectively showed in Table 2.

Of 38 patients, 17 were affected on the left side 8(47.1%) were upper limbs and 10 (58.9%) were affected by lower limbs within 24 hr. Whereas after 1 month 14 (82.4%) were upper limbs 14 (82.4%) were lower limbs achieved a score of 3 referred as an active movement against gravity and 5 indicating normal power scale respectively (Table 3).

DISCUSSION

This observational study on Tenecteplase for Acute Ischemic Stroke involved 38 patients, all of whom provided informed consent. Our study has reached the goal of assessing Tenecteplase

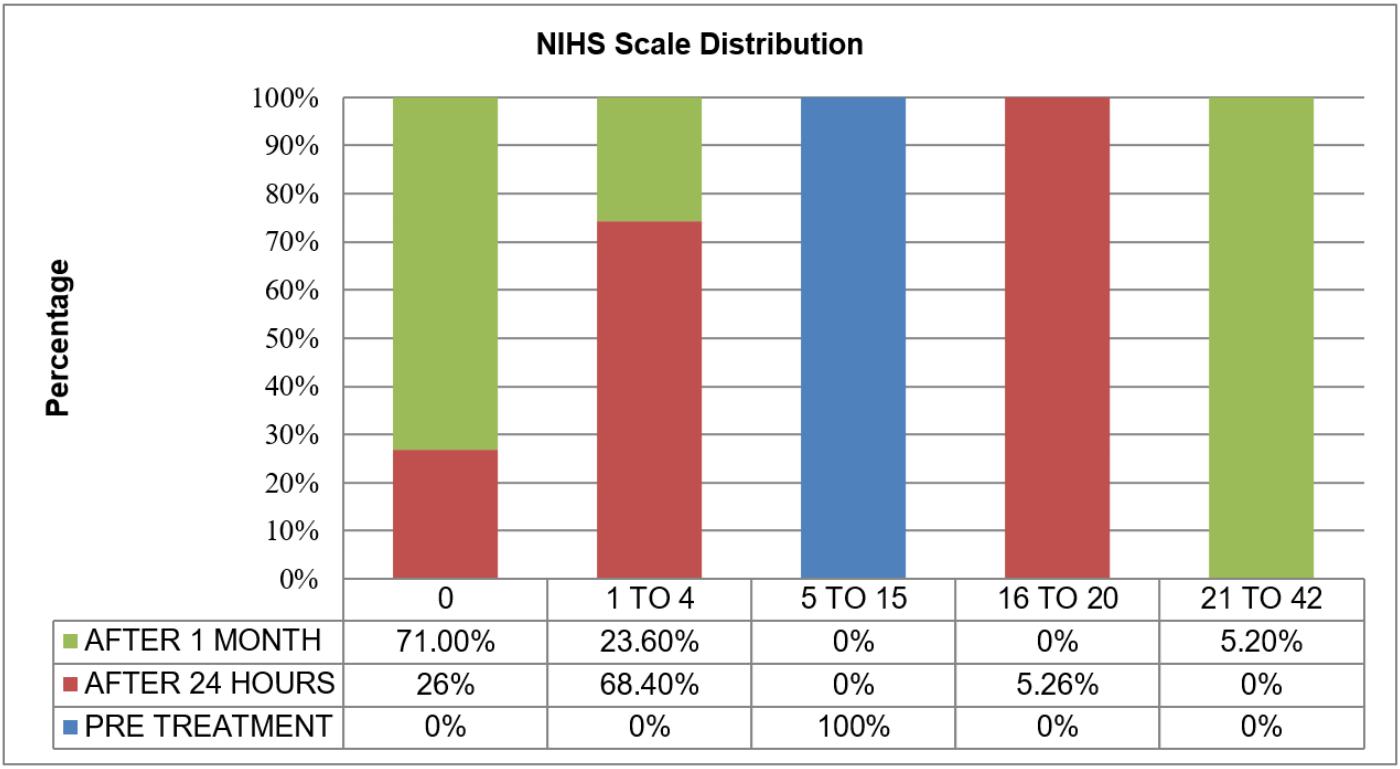


Figure 1: Overall Distribution Based on NIHS Scale. (Percentage distribution was mentioned in parenthesis [Eg: No of Patients (%)]).

Table 1: Demographic Data.

Demographic details	35-45	46-55	56-65	66-80
Age	3 (7.8%)	14 (36.8%)	15 (39.5%)	6 (15.7%)
Male	0 (0%)	10 (26.3%)	13 (34.2%)	2 (5.3%)
Female	3 (7.9%)	3 (7.9%)	3 (7.9%)	4 (10.5%)
Smoker	1 (2.6%)	9 (23.7%)	10 (26.3%)	4 (10.5%)
Alcoholic	0 (0%)	8 (21.0%)	7 (7.9%)	2 (5.3%)

(Percentage distribution was mentioned in parenthesis [Eg: No of Patients (%)]).

for door-to-needle time Acute Ischemic Stroke patient's safety and efficacy, using NIHS, MRS and MRC scales. The patients were administered Tenecteplase at a dose of 0.4 milligrams per kilogram within 3.5 hr of symptom onset. The study found that the 56-65 age group had the highest prevalence of Acute Ischemic Stroke, followed by the >45 age group, similar to findings by Aswin *et al.*, This suggests that the risk of Acute Ischemic Stroke increases significantly for patients over 45 years of age.[8] Out of 38 patients, male patients were higher due to higher rates of lifestyle changes which is in contrast to the study by Yoon CW *et al.*, where the risk of stroke and worse outcomes is higher in females compared to men. This denotes that lifestyle changes can trigger the risk of Acute Ischemic Stroke in males.[9] In this study, maximum patients were smokers when compared with an alcoholic which is equivalent to the study conducted by Gorelick PB *et al.*, which ensures that smoking causes an independent risk for Acute Ischemic Stroke than alcohol.[10] Patients who came to the hospital within 3.5 hr underwent intravenous thrombolisation therapy using Tenecteplase where 26 (68.4%) achieved the score 1-4 within 24 hr and 27 (71.0%) took the score 0 which showed a massive improvement in effectiveness to the patients. This is comparable to a study conducted by Belkouch *et al.*, who arrived at the hospital within 4 hr and 30 min which implies that patient improvement of 77.0% more than 4 points was noticed within 2 hr and 24 hr of thrombolisation therapy using Tenecteplase.[11] As per Kheiri B *et al.,* study Tenecteplase expressed a significant improvement with excellent recovery has been noted through MRS when compared to Altepase which is correlated to this observational study with Tenecteplase where in MRS scale of 15(39.5%) achieved the score 2 within 24 hr, 25 (65.8%) attained the score of 0 at 1 month. This is spelled to have increased neurological outcomes with Tenecteplase for acute ischemic stroke patients.[12] Based on the MRC Scale, we have found that Tenecteplase shows significant improvement for 21 patients affected on Right limb values of 3 and 4 in maximum patients within 24 hr of thrombolisation. A score of 5 has been observed for 18 (85.71%) and 17 (81.0%) of

Table 2: Overall Distribution Based on the MRC Scale of the Right Limb.

Scale	Pre-Treatment		Post Treatment			
			After 24 Hr		After 1 Month	
	RUL*	RLL*	RUL	RLL	RUL	RLL
0	10 (47.6%)	11 (52.4%)	0 (0%)	0 (0%)	1 (4.8%)	1 (4.8%)
1	7 (33.3%)	4 (19.0%)	1 (4.8%)	1 (4.8%)	0 (0%)	0 (0%)
2	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	0 (0%)	0 (0%)
3	1 (4.8%)	3 (14.3%)	9 (42.9%)	8 (38.1%)	0 (0%)	0 (0%)
4	2 (9.52%)	2 (9.5%)	9 (42.9%)	6 (28.6%)	2 (9.5%)	3 (14.3%)
5	0 (0%)	0 (0%)	1 (4.8%)	5 (23.8%)	18 (85.7%)	17 (81.0%)

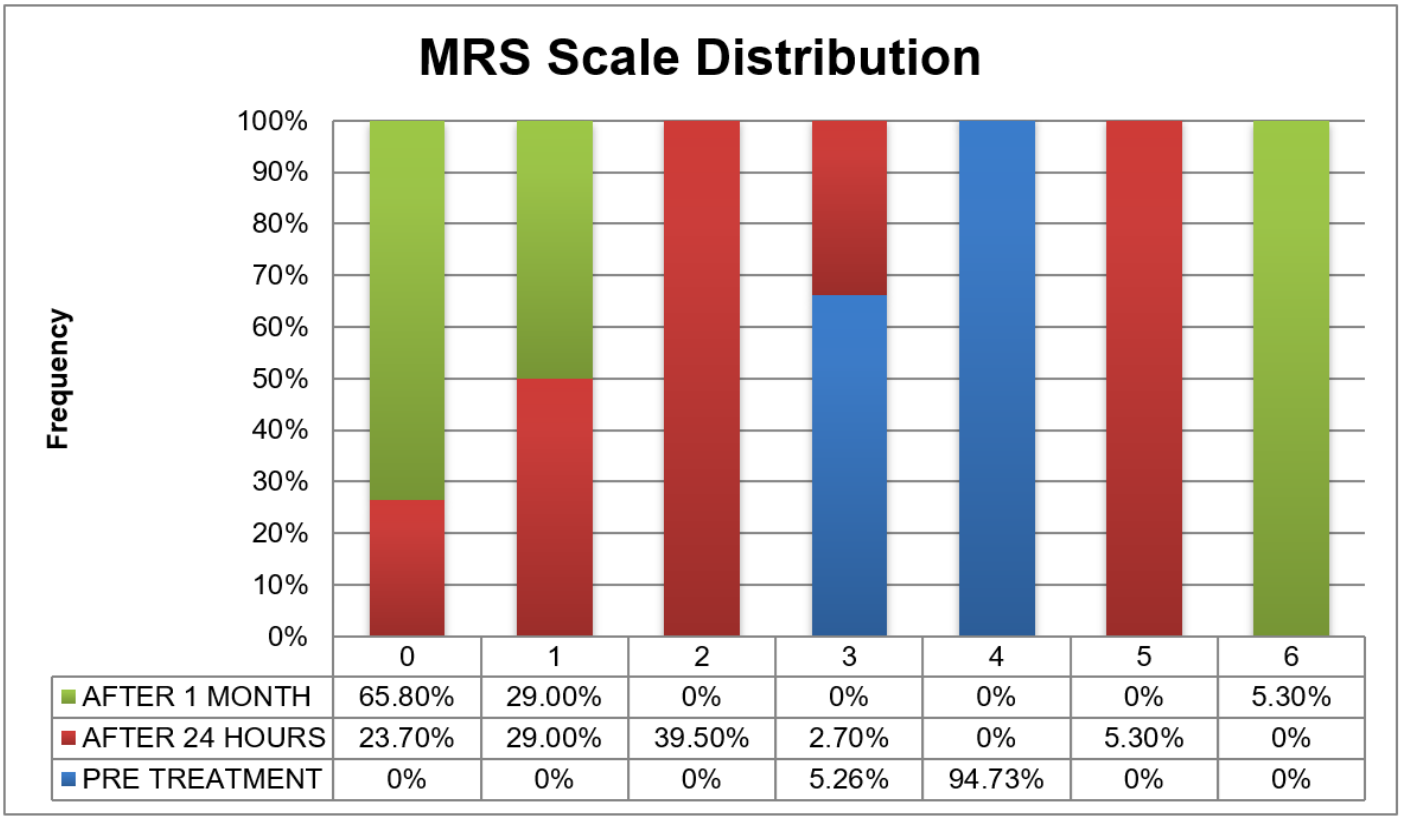
RUL*: Right upper limb; RLL*: Right Lower limb.

Table 3: Overall Distribution Based on the MRC Scale of the Left Limb.

Scale	Pre-Treatment		Post Treatment			
			After 24 Hr		After 1 Month	
	LUL*	LLL*	LUL	LLL	LUL	LLL
0	12 (70.7%)	14 (82.4%)	0 (0%)	0 (0%)	1 (5.9%)	1 (5.9%)
1	2 (11.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2	0 (0%)	1 (5.9%)	3 (17.7%)	3 (17.7%)	0(0%)	0 (0%)
3	3 (17.6%)	1 (5.9%)	8 (47.1%)	10 (58.8%)	0(0%)	0 (0%)
4	0 (0%)	1 (5.9%)	6 (36.0%)	3 (17.6%)	2 (11.8%)	2 (11.8%)
5	0 (0%)	0 (0%)	0 (0%)	1 (5.9%)	14 (82.4%)	14 (82.4%)

LUL*: Left Upper Limb; LLL*: Left Lower Limb.

patients after 1 month. Simultaneously 17 patients were affected on a left limb value of 3 in most patients within 24 hr. A score of 5 was achieved for 14 (82.5%) patients within one month. This shows that Tenecteplase improves muscle strength significantly for Ischemic Stroke patients parallel to the study conducted by Putranto TA *et al.*, using Intra Arterial Heparin Flushing in chronic stroke patients with decreased muscle strength.[13] Based on the study done by Parsons M *et al.*, Tenecteplase has better reperfusion and clinical outcomes than Alteplase in patients with stroke who were selected based on CT perfusion imaging that is parallel to this observational study with Tenecteplase where 94.7% of patients have advanced the better functional outcomes and found to have no symptomatic intracerebral hemorrhage after treatment. This indicates that Tenecteplase has enhanced its safety.[14] Tenecteplase which is a cost-effective thrombolytic drug in the market when compared to other thrombolytic agents which are discussed in the study conducted by Nguyen CP *et al.*, ensures that even a commoner can get effective treatment.[15] Hence, future recommendations of Tenecteplase appear to be efficacious along with its safety with less expensive therapy for Acute Ischemic Stroke patients while assessing with other thrombolytic agents.



	0	1	2	3	4	5	6
AFTER 1 MONTH	65.80%	29.00%	0%	0%	0%	0%	5.30%
AFTER 24 HOURS	23.70%	29.00%	39.50%	2.70%	0%	5.30%	0%
PRE TREATMENT	0%	0%	0%	5.26%	94.73%	0%	0%

Figure 2: Overall Distribution Based on MRS.

STUDY LIMITATIONS

The study duration was only six months so the patients involved in the study were limited and difficult to score the patients after 30 days of treatment as they did not adhere to the follow-up, so the accurate mortality rate was found to be difficult. The patients were contacted via phone call to obtain their scores one month later.

CONCLUSION

Based on the findings of our study, Tenecteplase emerges as a highly promising thrombolytic treatment for patients with Acute Ischemic Stroke. A remarkable safety profile verified through CT scans and impressive efficacy to the patients within 24 hr and 1 month using NIHSS and MRS scales. Tenecteplase stands out as a game-changer. Its longer half-life, ease of administration and cost-effectiveness enhance its appeal. The treatment not only significantly boosts safety by extending lifespan but also leads to dramatic improvements in muscle power through the MRC scale, contributing to reduced morbidity and mortality rates. Therefore, Tenecteplase is a cutting-edge and transformative thrombolytic treatment for acute ischemic stroke patients.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

ABBREVIATIONS

MRS: Modified Ranking Scale; **MRC:** Medical Research Council; **NIHSS:** National Institute of Health Stroke Scale; **TNK:** Tenecteplase; **RUL:** Right Upper Limb; **LUL:** Left Upper Limb; **RLL:** Right Lower limb; **LLL:** Left Lower Limb; **CT:** Computed Tomography; **t-PA:** Tissue Plasminogen Activator.

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