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A Prospective Observational Assessment of the Results of Tenecteplase Treatment for Patients With Acute Ischemic Stroke

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ABSTRACT

The aim of the present study was to assess the outcome of acute ischemic stroke patients treated with tenecteplase. Patients with ischemic stroke who presented to the Basweshwar Teaching and General Hospital and Vatsalya Life Hospital Kalaburagi within a 3-hour window and were treated with tenecteplase were included in a prospective observational trial. The patients had to be 18 years old or older. The study comprised forty patients. All participants provided written informed permission and the research was approved by the institution's ethical committee. In the trial, 40 patients received tenecteplase IV stroke thrombolysis. The research had a mean age of 61.36±12.48 years, with 70% of participants being male. Hypertension predominated at 60%, followed by dyslipidemia at 50%. Most patients had major artery stroke subtype, with all 20 infarct regions in the middle cerebral artery. The mean time from symptom onset to medical emergency was (116±11.49) minutes, while the mean "door to needle" duration was (55±17.23) minutes. At baseline, the study individuals had a mean NIHSS score of (11±3.16) and a median mRS score of 5 (range: 3-5). Primary clinical efficacy outcome: NIHSS score improvement of 4 or more points at 24 h. The mean NIHSS scores at 2 and 24 hours were (10.48±5.16) and (9.34±5.23), respectively. We utilized "one-way repeated measures analysis of variance" to find a significant difference in baseline and 24-h NIHSS scores (p = 0.017). Tenecteplase is the safest, faster, and cheaper thrombolytic drug for acute ischemic stroke, and it works in rural and urban settings. More investigations on this innovative thrombolytic drug will show its superiority even in rural settings, reducing stroke epidemics, especially in this endovascular care era.

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Key Words

Acute ischemic stroke, alteplase, tenecteplase, thrombolysis

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INTRODUCTION

When it comes to treating acute ischemic stroke, intravenous (IV) thrombolysis with recombinant tissue plasminogen activator (rt-PA) has become crucial. The only rt-PA medication currently licensed for stroke thrombolysis is alteplase, which, when administered intravenously within 4.5 hours of the start of the stroke, has traditionally been shown to improve functional outcomes[1,2]. Recent randomized controlled studies (RCTs) comparing tenecteplase with alteplase for stroke thrombolysis found that tenecteplase was just as effective and safe, if not safer, than alteplase[3-5]. In addition, tenecteplase has a number of pharmacological benefits over alteplase. Its effects last longer and it is more selective to fibrin. In addition, it has the advantage of being easily administered as a single bolus injection, as opposed to alteplase, which requires a continuous infusion following the bolus dosage. The third-generation tissue plasminogen activator tenecteplase (TNK) was engineered by modifying alteplase at three sites genetically. This resulted in tenecteplase with improved fibrin specificity, resistance to plasminogen activator inhibitor 1 and simpler administration (by bolus injection)[6-9]. The safety and efficacy profile of TNK in treating patients with acute ischemic stroke (AIS) has been demonstrated by both data from randomized-controlled clinical trials (RCTs) and real-world data[10-14]. The latest accelerated guidelines from the European Stroke Organization (ESO) state that patients with acute ischemic stroke (AIS) within 4.5 hours after the start of symptoms may be treated with TNK at a dose of 0.25 mg/kg instead of alteplase. This advice is supported by excellent evidence[14]. Given the ease of administration with a single bolus dose, an expert's opinion implies that TNK may even be preferred to alteplase. However, 0.4 mg/kg of TNK is not recommended because it increases the risk of symptomatic intra cranial hemorrhage (sICH) without improving the effectiveness of the treatment[14]. The current evidence-based recommendations suggest that patients who meet specific neuroimaging criteria, such as a perfusion mismatch indicating the presence of significant salvageable tissue or a diffusion-weighted imaging/fluid-attenuated inversion recovery MRI mismatch, should undergo intravenous thrombolysis (IVT) with alteplase[15,16]. Examining the results of tenecteplase treatment for patients with acute ischemic stroke was the primary goal of this research.

MATERIAL AND METHODS

This study was a prospective observational study on a consecutive set of ischemic stroke patients over the age of eighteen who visited the Basweshwar Teaching and General Hospital and Vatsalya Life Hospital Kalaburagi within a three-hour time frame and received tenecteplase treatment. The study involved forty patients. A brain CT or MRI was obtained as soon as possible and all baseline features and NIHSS scores were recorded. Patient were thrombolysed with tenecteplase if there were no contraindications for thrombolysis. A check CT was done after 24 hours or earlier if there was clinical deterioration.

Clinical, epidemiological, imaging parameters, outcome measures including baseline NIHSS, NIHSS at 1 hour, 2 hours, discharge and mRS [modified Rankin Score] at 0, 1 and 3 months were filled in a structured proforma. The primary outcome measured was NIHSS at discharge and secondary outcome was mRS at 3 months. An NIHSS of 0 or 1 or a drop in NIHSS by eight scores was considered as major improvement[17] and decrease in scores by values of 4 and 2 were considered ,as moderate and mild improvement respectively[18,19]. A mRS of 0 or 1 or a three point improvement was considered as good functional outcome or a major improvement[17], two and single point improvement of mRS was used to indicate moderate and mild improvement respectively[18,19].

RESULTS AND DISCUSSIONS

During the study, a total of 40 patients underwent IV stroke thrombolysis with tenecteplase. Mean age was 61.36±12.48 years with 70% of the study subjects being males. Hypertension was the commonest risk factor present in 60% of the cases, followed by dyslipidemia in 50%. Most of the patients had large artery stroke subtype, with the infarct region belonging to the territory of middle cerebral artery in all the 20 cases. The mean time from onset of symptoms to arrival at the medical emergency was (116±11.49) minutes (min) while mean “door to needle” time was (55±17.23) min. The study subjects had a mean NIHSS score of (11±3.16) and a median mRS score of 5 (range: 3-5) at the baseline. The primary clinical efficacy outcome with an improvement in NIHSS score of 4 or more points at 24 h. Mean NIHSS scores at 2 h and 24 h were (10.48±5.16) and (9.34±5.23), respectively. We used “one-way repeated measures analysis of variance” test and observed a significant difference between the NIHSS scores at baseline and 24 h ($p = 0.017$).

Recent randomized controlled studies (RCTs) comparing tenecteplase with alteplase for stroke thrombolysis found that tenecteplase was just as effective and safe, if not safer, than alteplase[20-5]. In addition, tenecteplase has a number of pharmacological benefits over alteplase. Its effects last longer and it is more selective to fibrin. In addition, it has the advantage of being easily administered as a single bolus injection, as opposed to alteplase, which requires a continuous infusion following the bolus dosage. In light of these benefits and the outcomes of the aforementioned randomized controlled trials, tenecteplase has just been authorized for the

Table 1: Baseline characteristics of patient's thrombolyzed with Tenecteplase

Variables	Values
Age (years, mean±SD)	61.36±12.48
Gender (Male)	28 (70)
Risk factors	
Hypertension	28 (70)
Dyslipidemia	20 (50)
Diabetes Mellitus	8 (20)
Smoking	8 (20)
Stroke subtype	
Large artery	28 (70)
Lacunar	12 (30)
Cereberal circulation	
Anterior cereberal artery	0
Middle cereberal artery	40 (100)
Posterior cereberal artery	0
Laterality	
Right hemisphere	24 (60)
Left hemisphere	16 (40)
Onset to door time (min, mean ± SD)	116±11.49
Door to imaging time (min, mean±SD)	36±16.54
Door to needle time (min, mean±SD)	55±17.23
Baseline NIHSS score (mean±SD)	11±3.16
Baseline Mrs score (median)	5

Table 2: Outcome analysis after tenecteplase thrombolysis

Variables	Mean±SD	p- value
	NIHSS score	
Baseline	13.87±3.75	
2 hours	10.48±5.16	0.066
24 hours	9.34±5.23	0.017
	mRS Score	
Baseline	5	0.001
90 days	1	

thrombolysis of ischemic strokes in India within three hours of the start of the stroke. Being accessible at a cost that is approximately half of alteplase, it also offers the added benefit of cheap price. Age, gender, race/ethnicity and regrettably, geographical geography and the urban-rural gap all play a role in the disparities in stroke risk and functional result[21]. Awareness of stroke symptoms, prehospital delays, ambulance service adequacy and most crucially, the expense of thrombolytic treatment are further variables impacting the rural-urban difference in India. Acute stroke care in rural areas is a significant barrier, however tenecteplase's lower cost compared to its predecessor helps overcome this.

Forty patients were enrolled in the study and administered tenecteplase intravenously for the purpose of stroke thrombolysis. The majority of the participants in the study were men, with a mean age of 61.36±12.48 years. In 60% of instances, hypertension was found to be the most common risk factor, followed by dyslipidemia in 50% of cases. The majority of the patients suffered from large artery stroke subtype, and in each of the twenty cases, the infarct location was located within the territory of the middle cerebral artery. On average, it took 116 minutes (±11.49 seconds) from when symptoms first appeared until the patient reached the medical emergency room, and the average duration from "door to needle" was 55 minutes (±17.23 seconds). The average NIHSS score for the study participants was (11±3.16) and their median mRS score was 5 (range: 3-5) when they started the study. Another single-arm research on tenecteplase for stroke found that in 77% (10/13) of cases, the NIHSS score improved by more than 4 points after 24 hours[22]. There has been no reporting of tenecteplase's efficacy in stroke thrombolysis in research involving patients from India. Nevertheless, our findings about the effectiveness of Tenecteplase align with the outcomes of earlier research from India concerning alteplase. According to research by Durai Pandian *et al*. of the All-India Institute of Medical Sciences, 65% of patients who took alteplase saw a four-point or higher improvement in their NIHSS score after 48 hours[23]. Consistent with the prior research on tenecteplase, we noticed a highly significant difference between the NIHSS scores at baseline and 24 hours[5]. At 24 hours, the major clinical efficacy metric is a four-point or higher improvement in the NIHSS score. At 2 hours and 24 hours, the mean NIHSS scores were (10.48±5.16) and (9.34±5.23), respectively. Using a "one-way repeated measures analysis of variance" test, we found that the NIHSS scores at 24 hours were significantly different from the baseline scores ($p = 0.017$). Consistent with the findings of Owais *et al*.'s study on juvenile stroke, our research demonstrated a favorable association between age and post-treatment scores, which were useful in predicting outcome[24]. The data imply that the trend of a declining responsiveness to tenecteplase with age is also valid in adults. One intriguing finding is that the mean mRS scores of the moderate stroke group improved significantly after delayed treatment with tenecteplase, in contrast to the higher degree stroke group, which actually showed mild worsening. This suggests that tenecteplase has a delayed but significant positive effect on the moderate stroke group. This study's population was comparable to others in that just one patient had sICH, which accounted for 5% of the bleeding risk[24].

CONCLUSION

Both urban and rural areas can benefit from tenecteplase since it is a safer, faster and more cost-effective thrombolytic drug for acute ischemic stroke. More research on this new thrombolytic drug will provide light on its efficacy, even in rural areas, reducing the likelihood of stroke epidemics and making it more suitable for individualized treatment in the modern era of endovascular medicine.

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