

Original Research Article

Role of Tenecteplase in management of acute ischemic stroke: a knowledge, attitude, and practice survey among Indian neurologists

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ABSTRACT

Background: Tenecteplase, a third generation tissue plasminogen activator has important place in the thrombolytic therapy in acute ischemic stroke. The objective of present study was to understand the knowledge, attitude and practice (KAP) towards the usage of tenecteplase in daily clinical practice.

Methods: This was a prospective questionnaire based knowledge, attitude and practice survey with involvement of practising neurologists across the country. A specially designed validated questionnaire containing 18 questions was shared with neurologists and their anonymous inputs were captured and analysed in qualitative manner.

Results: Total Sixty-eight neurologists completed this questionnaire. The 73 percent of neurologist preferred tenecteplase in stroke patients arriving within 4.5 hours of onset of stroke symptoms. Almost 70% of neurologists preferred tenecteplase in patients <60 years of age with average NIHSS score between 5-15. The preferred dosage was 0.2 mg/kg by majority (78%). Bridging therapy was used up to 0-10% of patients by 70% neurologists which ultimately has lesser bleeding chances. 46% neurologists reported that no sICH after tenecteplase, while 30% reported in <1% patients. Almost 70% neurologists reported no allergic reaction noted with tenecteplase. Overall, 70% neurologists reported good to very good improvement in the patient's quality of life at 90 days after tenecteplase therapy.

Conclusions: The current KAP survey emphasized tenecteplase as a commonly preferred thrombolytic agent in acute ischemic stroke with better efficacy and safety, affordable cost with single bolus administration.

Keywords: Tenecteplase, Ischemic stroke, KAP survey, Questionnaire, Thrombolytic

INTRODUCTION

Stroke is defined as a neurological deficit attributed to an acute focal injury of the central nervous system (CNS) (i.e. brain, retina, or spinal cord) by a vascular cause.¹ There are two types of stroke one of most common which is ischaemic stroke due to abridged blood flow, generally resulting from arterial occlusion. The remaining 10-40% of stroke are haemorrhagic and result from the rupture of cerebral arteries. Globally there are 9.6 million acute

ischemic stroke (AIS) cases while 4.1 million haemorrhagic strokes (including intracerebral and subarachnoid haemorrhage) each year.²

Acute treatments for ischaemic stroke comprises Intravenous (IV) thrombolysis with recombinant human tissue plasminogen activator or mechanical thrombectomy aims to re-perfuse the ischaemic brain. Currently in India, Alteplase and Tenecteplase are the approved drugs for intravenous (IV) thrombolysis. They act by converting

plasminogen to plasmin, which can dissolve the thrombus that is causing the stroke.³ Tenecteplase is a genetically modified tissue plasminogen activator having 15-fold greater fibrin specificity and 80-fold more resistance to degradation by plasminogen activator inhibitor-1 (PAI-1) and a longer plasma half-life compared to Alteplase.⁴

At least five randomised clinical trial where Alteplase compared with tenecteplase in acute AIS and had shown no significant differences in the chance of neurological recovery or in mortality rates.⁵ In India, two randomised trials had shown that 0.2 mg/kg dose of tenecteplase in AIS patients administered within 3 hours of onset of symptoms seems to be effective and safe.⁶

Still there is lack of awareness and data about the use of tenecteplase in AIS. A knowledge, attitude, and practice (KAP) survey is a structured, standardized questionnaire which make an effort to understand knowledge, attitude, and practice of a group to a specific intervention. These surveys are accepted and commonly used because they apply fewer resources and tend to be more cost-effective than other social research methods and provide useful insights.⁷

There are limited data about the knowledge, perception, and routine clinical usage pattern of Tenecteplase among Indian neurologists. The present survey was undertaken to explore knowledge, perception, and usage of Tenecteplase in the real-life setting in India.

METHODS

This was a prospective, cross-sectional, observational, questionnaire-based survey conducted across India from October 2020 to December 2020. Registered medical practitioners with recognized qualifications in Neurology (DM/DNB Neurology) working in public and private clinics/hospitals participated in this survey. A specially designed, structured, self-completion survey questionnaire was filled in by neurologists, based on their prior clinical experience and knowledge of usage of Tenecteplase. The questionnaire was internally validated by Investigators. The survey assessed the knowledge, attitude, and practice toward the use of Tenecteplase in acute ischemic stroke in real-life scenario. The questionnaire consisted of 18 multiple-choice questions (MCQs), out of which 4 questions were pertaining to knowledge, 6 to attitude and 8 to practice about Tenecteplase usage in routine clinical practice.⁷

Knowledge related questions as follows: commonly used diagnostic tool, percentage of patients had successful recanalization after Tenecteplase therapy, percentage of patients who gets tenecteplase as bridging therapy before thrombectomy, frequency of adverse effects noted with Tenecteplase.

Attitude related questions: patient age group do you avoid the use of Tenecteplase, optimum duration from the onset

of neurological symptoms up to which you use Tenecteplase, the change in Quality of Life in patients after 90 days since thrombolysis with Tenecteplase, the most common reason for less use of Tenecteplase, the critical factor for preferring Tenecteplase, considered using Tenecteplase after 3 hours.

Practice related questions included as follows: Preferred thrombolytic agent, the average time at which patients report to hospital after onset of stroke symptoms, preferred age group for Tenecteplase, average baseline National Institutes of Health Stroke Scale (NIHSS) score to use Tenecteplase in stroke, average reduction in NIHSS Score 24 hours after Tenecteplase therapy, preferred dose of Tenecteplase in stroke, percentage of patients developed symptomatic intra-cranial haemorrhage (sICH) after therapy with Tenecteplase, percentage of patients had developed allergic reaction to Tenecteplase.

Categorical data were summarized by number N and percentage (%) in each category, where N represents the total number of participants responding to each question. Data were summarized in frequency tables and graphs. This was observational survey and no patients related data was captured. Therefore, ethics committee approval was not necessary and not obtained.

RESULTS

Total 68 neurologists across India participated in the survey and their responses were evaluated and analysed. For the diagnosis of AIS, half (50%) of neurologists preferred to use Computed topography (CT) scan of brain, while 30% neurologists preferred both CT scan and magnetic resonance imaging (MRI) of Brain. Almost 61% neurologists reported that patients usually report in 3 to 4.5 hrs of onset of symptoms while 26% feels it is beyond 4.5 hours interestingly 13% neurologists do report of patient reaching within 1 to 3 hours (Figure 1).

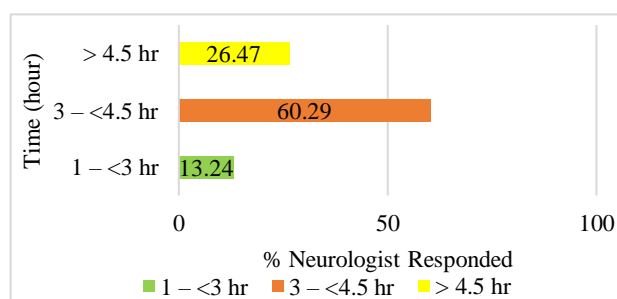


Figure 1: Average time at which patients report to hospital after onset of stroke symptoms.

Tenecteplase remains preferred choice of thrombolytic in 74% of neurologist while 24% preferred Alteplase (Figure 2). Tenecteplase is used in all age of patients and more than half neurologists uses this in age group of 41 to 60 years (54%) follows by 61 to 80 years (19%) and 41-60 years

(18%). Interestingly almost 9% neurologist prefer Tenecteplase in >80 years of patients (Figure 3).

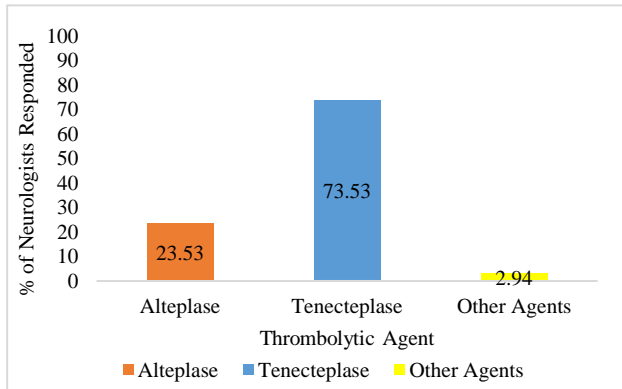


Figure 2: Preferred thrombolytic agent.

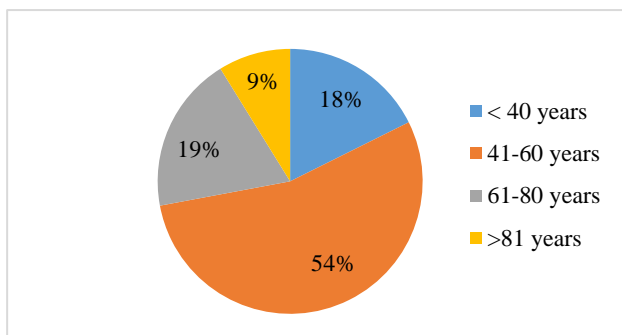


Figure 3: Preferred age group for Tenecteplase therapy.

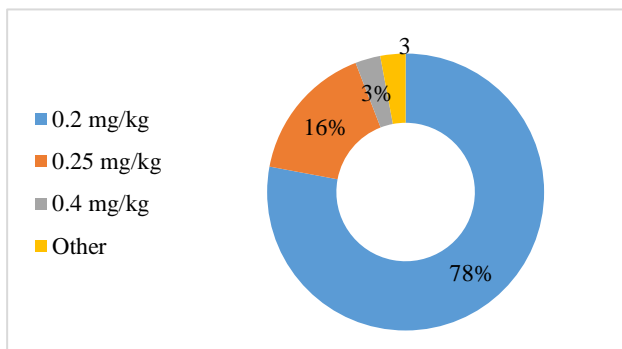


Figure 4: Preferred dose of tenecteplase in acute ischemic stroke.

Majority of neurologists (70%) are using tenecteplase where NIHSS Score was between 5-15, almost 25% are using where NIHSS Score between 0-4 and very few used in patients with NISS score of >15. Almost 78% of neurologists use 0.2 mg/kg while 16% use 0.25 mg/kg dose of tenecteplase in thrombolysis of acute ischemic stroke (Figure 4). Almost 44% neurologists had reported successful recanalization rates between 50-90% interestingly 7% had observed more than 90% recanalization rates (Figure 5).

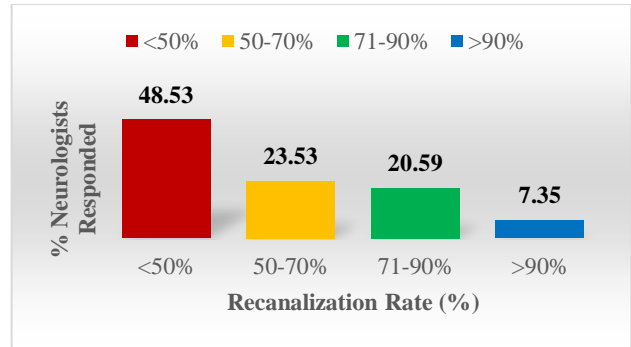


Figure 5: Percentage of patients with successful recanalization after Tenecteplase.

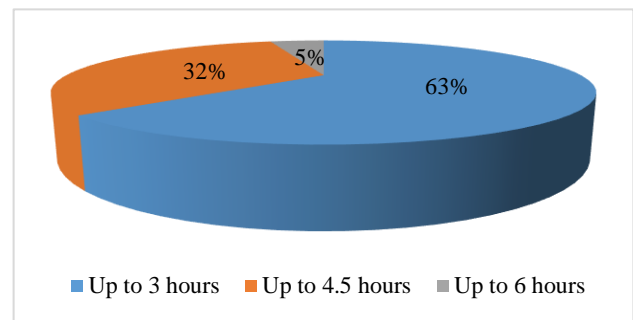


Figure 6: Duration from onset of neurological symptoms up to which Tenecteplase used.

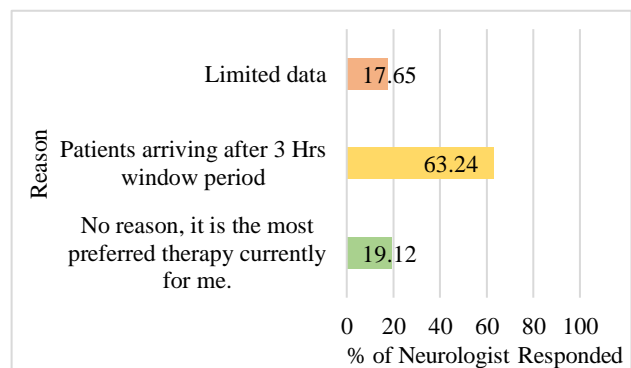


Figure 7: Reason for limited use of Tenecteplase.

Almost 90% of neurologist observed that the average 0-10 NIHSS reduction was observed after 24 hours after tenecteplase therapy. Approximately 70% of neurologists considered using tenecteplase in bridging therapy in 10% of their patients, while 22% neurologists considered in 11-15% of patients. Almost half (47%) of neurologists agreed that tenecteplase should be avoided in patients >81 years and taking anti-coagulants therapy, however 35 neurologists are responded that only patients taking anticoagulant should not receive tenecteplase therapy.

Interestingly 63% neurologists prefer tenecteplase up to 3 hours from the onset of symptoms of however 32% prefer to 4.5 hours. (Figure 6) Almost 28%, 60% and 10% neurologists responded that average, good and very good

improvement in the quality of life after 90 days of post-thrombolysis with tenecteplase. Nearly 63% neurologists observed that patients arriving after 3 hours of window period is the major restraining factor for tenecteplase use while inadequate data is limiting factor for 18% of neurologists (Figure 7).

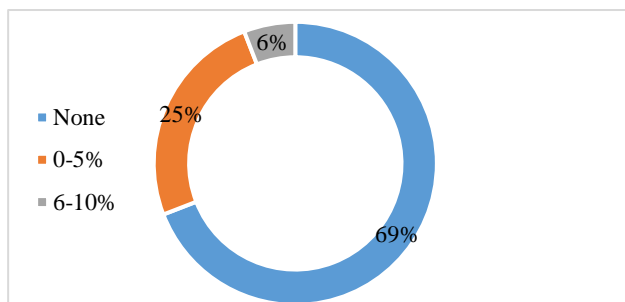


Figure 8: Percentage of patients had allergic reaction to Tenecteplase.

About 50% neurologists agreed that all the mentioned factors are considered while using tenecteplase in AIS. 59% of neurologists considered using tenecteplase beyond 3 hours. Clinical efficacy, ease of administration, better safety profile and affordable costs are the critical factors for preferring tenecteplase in AIS (Table 1).

Table 1: Critical factor for preferring Tenecteplase in AIS.

| Factors to prefer use of Tenecteplase | No. of neurologists responded (n=68) | Percentage of neurologists responded |
|---------------------------------------|--------------------------------------|--------------------------------------|
| Clinical efficacy | 2 | 2.94 |
| Ease of administration | 22 | 32.35 |
| Patient safety | 2 | 2.94 |
| Therapy cost | 8 | 11.76 |
| All of above | 34 | 50.00 |

Table 2: Symptomatic intra-cranial haemorrhage after therapy with Tenecteplase.

| Symptomatic intra-cranial haemorrhage (sICH) | No. of neurologists responded (n=68) | Percentage of neurologists responded |
|--|--------------------------------------|--------------------------------------|
| Not experienced | 31 | 45.59 |
| Yes experienced <1% | 20 | 29.41 |
| Yes experienced 1 - 2% | 17 | 25.00 |

Almost 46% of neurologists reported no symptomatic intra-cranial haemorrhage (sICH) noted after tenecteplase therapy; almost 30% reported in less than 1% patients and

25% reported in 1-2% patients (Table 2). Almost 69% neurologists responded that there was no allergic reaction with tenecteplase while 25% neurologists said that its seen in 1-5% of patients (Figure 8). No adverse effects were seen to 34% of neurologists while 41% neurologists observed rare (1 in 10000 people) with tenecteplase therapy.

DISCUSSION

Tenecteplase was developed as a plasminogen activator with greater fibrin specificity and reduced clearance compared with Alteplase, allowing single-bolus administration. It was approved in India for acute ischemic stroke with dose of 0.2 mg/kg single bolus injection.8 There are limited clinical data on the usage of tenecteplase in AIS in real-life scenario in India. Therefore, the present survey was taken to understand the current knowledge, attitude, and practice (KAP) related to tenecteplase. A KAP survey are used to explore the current behaviour of health care practitioners towards specific situation.7

In present KAP survey, Tenecteplase was the most commonly preferred thrombolytic agents in AIS as the reason behind it may be factors like ease of administration, clinical efficacy and low therapy cost. As mentioned in the literature the cost effectiveness, ease of administration was the factors which influence the use of tenecteplase.9

Patients reporting hospital between 3 to 4.5 hours and beyond 4.5 hours are the limiting factors for the thrombolytic therapy in AIS. Thrombolytic therapy in low NIHSS score patients leads to increase in therapeutic efficacy and overall average 0-10 NIHSS reduction. Studies suggest that low NIHSS score increases chances better prognostic outcomes in patients with acute ischemic stroke.10,11

Most of the neurologists prefer Tenecteplase for thrombolysis in patients with age below 60 years who has NIHSS score between 0-15 which ultimately gives better clinical outcome of therapy. Literature found that advanced age, male gender and co-morbidities were lead to worst outcome in AIS patients after thrombolytic or endovascular therapy.11

Maximum neurologist aware that the recommended dose of tenecteplase is 0.2 mg/kg which gives more than 50% recanalization rates in acute ischemic stroke patients. Interestingly, 70% of neurologist use the tenecteplase in up to 10% of patients as bridging therapy, which might result in lesser chances of bleeding complications. Thrombolysis with tenecteplase reduces the average NIHSS up to 0-10 in most of the patients with good to very good improvement in quality of life. Considering safety parameters of tenecteplase, three fourth of neurologists observed no allergic reaction or any major adverse effects including symptomatic intra-cranial haemorrhage (sICH). These findings are matches with reported in evidence where less adverse effects were seen with tenecteplase.12

This KAP survey was conducted across the country with renowned experienced neurologist responding to questionnaire. In spite of limitations like close ended questions, recall bias, this survey has highlighted interesting facts about the usage of tenecteplase. There may be further need of clinical evaluation of these facts.

CONCLUSION

Current survey emphasised that tenecteplase is most commonly used thrombolytic agent in acute ischemic stroke with ease of administration clinical efficacy and favourable safety. Reporting to the hospital within window period may increase the recovery as well as quality of life after thrombolytic therapy.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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