

STUDY OF INTRAVENOUS THROMBOLYSIS IN ACUTE ISCHEMIC STROKE IN THE SOUTHERN PART OF INDIA AND ITS OUTCOME, A SINGLE CENTER STUDY

Neurology

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ABSTRACT

Background: Stroke is one of the leading causes of morbidity and mortality. Intravenous thrombolysis by using tissue plasminogen activator (tPA) within 4.5 hours of onset of ischemic stroke is approved treatment. Though most of data available from developed nations, limited data are available regarding the intravenous thrombolysis from the developing countries like India. **Aim:** This study aims to enroll and analyze the patient characteristics and use of tissue plasminogen activator (tPA) in acute ischemic stroke patients in a tertiary care center in southern India. **Methods:** All acute ischemic stroke patients presenting within 4.5 hours of symptoms onset from JUNE 2021 to MAY 2023 were enrolled and analyzed. **Results:** A total of 87 acute ischemic stroke patients who are eligible for intravenous thrombolysis therapy were enrolled in the study. Out of 87 eligible patients, 62 were male and 25 were female. The National Institutes of Health Stroke Scale score at presentation was median of 11 (IQR 7-13) with window period of 2 hours and 46 minutes. Image studies shows 33% patients with small vessel infarct and 67% shows large vessel infarct. Improvement in National Institutes of Health Stroke Scale (NIHSS) at 1 week after treatment was seen in 50.5% of patients with mean score of 4 (IQR 4-13). 10 (11.4%) patients had hemorrhagic transformation of which 4(4.5%) patients have symptomatic intracranial hemorrhage, 15 patients had stroke related complications like sepsis, aspiration pneumonitis, deep vein thrombosis and 5 (5.7%) patients died during this study. **Conclusions:** Treatment with acute ischemic stroke with intravenous thrombolysis shows early improvement in the quality of life in patients in developing countries like India as measured by NIHSS score at 1 week post thrombolysis therapy. Earlier the treatment with intravenous thrombolysis can reduce stroke related mortality and morbidity.

KEYWORDS

Intravenous thrombolysis, tissue plasminogen activator(tPA), acute ischemic stroke and The National Institutes of Health Stroke Scale (NIHSS)

INTRODUCTION

Stroke is an increasing global health challenge worldwide causing significant physical disability in adults known to be as one of the leading causes of mortality and morbidity in the world¹. Most of the acute stroke is due to ischemic stroke and hemorrhagic stroke contribute minority of stroke. Intravenous thrombolysis by tissue plasminogen activator (tPA) is well approved treatment for acute ischemic stroke^{2,3}. But the thrombolysis by tPA is time bounded and need accessibility and awareness to achieve the expected success rate. The American Heart Association/American Stroke Association formed Stroke Performance Oversight Committee in 2011 to regulate the stroke treatment performance and quality measures and enabled health-care professionals to uphold the standard of care and continually improve stroke care facilities.

By then most studies describe the quality of care for stroke patients from developing nations⁴. India being a developing nation faces double challenge of communicable and non-communicable diseases with improving management especially stroke management^{5,6}. Since the dedicated stroke units are increasing in developing countries like India⁴, it is essential to study the characteristics of patients and effect of the therapy from developing countries like India. Some previous studies from India showed that only about 8-11% patients eligible for thrombolysis received the therapy with many barriers and delays preventing the timely intervention for stroke patients⁷. Though the modified Rankin Scale (mRS) at 3 months is the most commonly used primary outcome measure in stroke treatment trials which consume time and resources an alternative may be the National Institutes of Health Stroke Scale (NIHSS) within 1 week after treatment which could serve as a primary outcome measure for trials of acute treatment for ischemic stroke⁸. Our study aimed to analyze the patient characteristics and use of tissue plasminogen activator (tPA) in acute ischemic stroke patients in a tertiary care center in southern India and observe the NIHSS score at admission and at 1 week post thrombolysis.

METHODS

This prospective study was carried out in the tertiary care center in South India, from June 2021 to May 2023. The center is an academic teaching hospital with a well-established stroke treatment protocol, 24 h on-call neurologist, imaging (computed tomography [CT]), and thrombolysis facility. Onset time was noted as the time when the patient was last seen normal. Symptomatic intracranial hemorrhage (ICH) was defined as CT documented hemorrhage with deterioration in NIHSS of ≥ 4 within 36 h of thrombolysis. The dose of alteplase (tissue plasminogen activator) was 0.9 mg/kg for the study. For any patient suspected to have stroke, the on-call neurologist is alerted by the emergency medical officer. The neurologist examines the patient in ED, and after a quick assessment, the patient is transferred to imaging facility to rule out hemorrhagic stroke. If thrombolysis can be offered, consent is taken and patient is thrombolysed. All stroke patients who were given tPA during the study period were included in the study. NIHSS score was measured at admission and at 7 days post thrombolysis.

Statistical Analysis

Data are presented as mean $\pm$ standard deviation or median (interquartile range, [IQR]). The primary outcome measure was NIHSS score at 1 week post thrombolysis. IBM SPSS, version 21.0 Armonk, NY: IBM corp., was used for analyses.

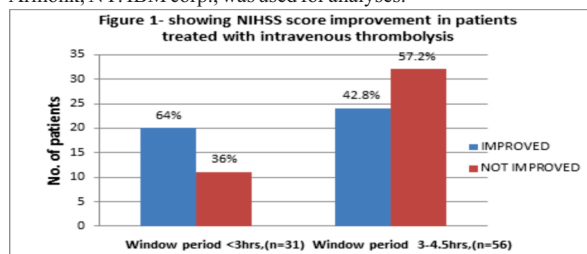


Table 1. Patient characteristics included in the study. NIHSS – National Institutes of Health Stroke Scale , IQR-Interquartile range

Mean age	57.1 years
Sex (male;female)	62;25
Hypertension	33(37.9%)
Diabetes mellitus	31(35.6%)
Coronary artery disease	11(12.6%)
Past cerebrovascular disease	9 (10.3%)
Smoking	27(31%)
Alcohol	31(35.6%)
Median NIHSS score at admission	11 (IQR 7-13)
Median NIHSS score at 1 week post thrombolysis	7(IQR 4-13)
Average window period	2 hrs 49 mins
Patients with large vessel stroke	29(33.3%)
Percentage of patients improved	44(50.5%)
Patients with CT hemorrhagic transformation	10(11.4%)
Patients with symptomatic intracranial hemorrhage	4(4.5%)
Number of patients died	5(5.7%)

RESULTS

In the study period, 87 stroke patients were eligible for thrombolysis. The mean age of thrombolysed patients was 57.1 (range 21–80) years, of whom 62 (71%) were men and 25(29%) were female. The median NIHSS at admission was 11 (IQR 7–13). Among total of 87 patients, the risk factors were hypertension (n = 33, 37.9%), diabetes mellitus (n = 31, 35.6%), coronary artery disease (n = 11, 12.6%), prior cerebrovascular disease (n = 9, 10.3%), smoking (n = 27, 31%), and alcohol (n = 31, 35.6%). The median NIHSS score was 11 (IQR 7-13) and the average window period in the study population was 2 hrs 49 minutes. Image studies shows 33% patients with small vessel infarct and 67% shows large vessel infarct (table 1). Primary outcome on improvement of NIHSS score at 1 week post thrombolysis achieved in 44 patients (50.5%). Among 87 patients undergone thrombolysis, 44(50.5%) patients showed improvement in NIHSS score of 4 or more. Patients (n=31) thrombolysed within window period of <3hrs showed improvement in NIHSS score in 20(64%) and patients (n=56) thrombolysed in window period of 3- 4.5 hrs showed improvement in 24(42.8%) patients at the 1 week post thrombolysis (figure.1). During the study period, 10 (11.4%) patients had hemorrhagic transformation in repeat CT brain and 4(4.5%) patients have symptomatic intracranial hemorrhage of which 2 patients needed decompressive craniotomy. 15 patients had stroke related complications like sepsis, aspiration pneumonia, deep vein thrombosis and 5 (5.7%) patients died during the study period.

DISCUSSION

Our study demonstrated that acute ischemic stroke patients treated with intravenous thrombolysis by tissue plasminogen activator have better outcome at 1 week post thrombolysis. This is shown by reduction of NIHSS score of 4 or more compared with admission. Though the modified Rankin scale was used as primary outcome, countries like India where resources are limited and needed a long follow up, it is less feasible as it is time consuming and lack of personnel will discourage the research. Hence as per Chalos V et al⁸, NIHSS score at 1 week of post treatment used as primary outcome for studies to determine the effect of thrombolysis therapy which is comparable to modified Rankin scale. Our study results are comparable to previous studies in terms of clinical improvement as outcome^{10,11}. Also the clinical outcomes were assessed 90 days in the NINDS study while our study can show the improvement in 1 week as earlier improvement further enhance favorable outcome as researched by ATLANTIS study¹² but this cannot be over emphasized here. The other finding of our study is that the symptomatic ICH rate was 4.5%, which is slightly higher than the expected. This can be explained by the fact that our study included majority of patients with window period from 3-4.5 hrs which is cautioned with higher hemorrhagic transformation by various studies in the past¹³. The longer window period would also explain for the higher mortality rate of 5.7 % in our study.

In India^{5,6} thrombolysis for stroke is being widely used across the country both in private and public sector hospitals. There has been an increase in the use of intravenous rtPA in the country. Because of the delayed hospital admission, thrombolytic therapy (recombinant tissue plasminogen activator (rtPA)) has been possible in only a very small number of acute ischemic stroke cases in India. Over the years, the utilization of rtPA has increased all across the country, but the use is

restricted only to urban centers. Stroke unit has a multidisciplinary team comprising medical, nursing, physiotherapy, occupational therapy, speech therapy, and social workers. Hence our focus is to target the earlier thrombolysis for more benefits with less complication rates. Many studies emphasizes that public awareness campaigns are effective in reducing the time taken for patients to arrive the hospital which can reduce the window period to start the thrombolysis therapy and improve the outcome⁹. It has been well demonstrated that patients treated in stroke units have substantially better outcome of acute stroke. Focus needed on early diagnosis, management, infrastructure, public awareness and capacity building at different levels of health care regarding stroke, so that early intervention like thrombolysis benefit the patient in terms of morbidity and mortality.

Limitations

This is a single-centered study which cannot be generalized to whole part of India with its varied culture and population. Small sample size might be another limiting factor.

CONCLUSION

Treatment with acute ischemic stroke with intravenous thrombolysis shows early improvement in the quality of life in patients in developing countries like India as measured by NIHSS score at 1 week post thrombolysis therapy. Earlier the treatment with intravenous thrombolysis can reduce stroke related mortality and morbidity

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Nil.

Conflicts Of Interest

There are no conflicts of interest.

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