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Original Research Article

The impact of intravenous thrombolysis in acute ischemic stroke in National Medical College, Kolkata: initial experience

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ABSTRACT

Background: Acute ischemic stroke is a potentially treatable condition, if left untreated, lead to mortality and morbidity. This study was conducted to study clinical profile of patients with acute ischemic stroke receiving intravenous thrombolysis (r-TPA-alteplase) and to measure the outcome of thrombolysis.
Methods: Retrospective observational study of 54 patients who underwent thrombolysis for acute ischemic stroke at National Medical College, Kolkata over a period of one year.
Results: There was statistically significant improvement in NIHSS (p value-0.000) after intravenous thrombolysis.
Conclusions: IV thrombolysis is feasible for AIS in governmental hospital in India.

Keywords: Atherothrombosis, Cardioembolic, Dyslipidaemia, Ischemic stroke, Thrombolysis

INTRODUCTION

Stroke is one of the most common causes of morbidity, mortality, in developed as well as in developing countries. WHO defined stroke as "rapidly developed clinical signs of focal disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin". In 2008, the estimated deaths worldwide due to cerebrovascular disease was 6.1 million, equivalent to 10.8% of all deaths worldwide. In India, the prevalence of stroke is less compared to that of developed countries but the proportion of stroke in young population is significantly more in India than that of in developed countries. In India, the prevalence of stroke is about 1.54 per 1000 population. The total number of stroke cases estimated in the year 2004 were about 9.3 million with about 0.63 million deaths. Intravenous (IV) thrombolysis with Recombinant Tissue Plasminogen Activator (r-TPA) has assumed vital importance in the successful treatment of acute ischemic stroke. Conventionally, alteplase infusion has proved to be efficacious in improving the functional outcomes when given within 4.5 h (h) of the stroke onset.[1,2] Tenecteplase can also be used in AIS within 3 hours of stroke onset.

Present study was conducted with the objective to study clinical profile of patients with acute ischemic stroke receiving intravenous thrombolysis (r-TPA) and to measure the outcome of thrombolysis.

METHODS

This study is a retrospective analysis of 54 patients who underwent thrombolysis for acute ischemic stroke within the period of 13th May 2016 to 12th May 2017.

Study design and subjects was all the acute ischemic stroke patients were assessed by the stroke on call resident in medical emergency on a priority basis. Those

presenting within the window period for thrombolysis underwent a quick evaluation to rule out the contraindications to thrombolysis through medical history, blood pressure, pre-morbid mRS score and NIHSS score assessment. Simultaneously, capillary blood glucose estimation was done, and blood samples were withdrawn for other standard laboratory tests as mentioned in the exclusion criteria for thrombolysis.

Inclusion criteria

- Acute ischemic stroke with clearly defined time of onset (who could be treated <4.5 hours of symptom onset).
- Measurable deficit on the NIHSS.
- Baseline brain CT scan that showed no evidence of hemorrhage.

Exclusion criteria

- Another stroke or serious head injury within the preceding 3 months
- Major surgery within prior 14 days
- History of ICH
- SBP >185 mmHg or DBP >100 mmHg
- Rapidly improving or minor symptoms
- Symptoms suggestive of SAH
- GI or GU hemorrhage within the previous 21 days
- Arterial puncture at a non-compressible site within the previous 7 days
- Seizure at onset of stroke
- Use of anticoagulation:-patients receiving heparin within the 48 hours preceding the onset of stroke who have an elevated PTT, patients with a PT >15 seconds (or INR >1.6), patients with a platelet count <100,000
- Glucose level of <50 mg/dL or >400 mg/dL.

Soon after, patients were shifted for an urgent CT scan of the brain. The early sign of ischemia like hyperdense MCA sign (Figure 1), loss of grey white differentiation, insular ribbon sign was searched. The patients having no evidence of intracranial hemorrhage were thrombolyzed according to the treatment protocol. All the patients receiving r-TPA were closely monitored in either stroke unit or neurology ICU for heart rate, blood pressure, and oxygen saturation for initial 24 h. NIHSS scores were calculated at baseline, then hourly for 24 hours post-thrombolysis while mRS scores assessment was done at baseline and 90-day post-thrombolysis.

Treatment protocol

Intravenous r-TPA was administered in all eligible cases. The most suitable candidates were given full dose of intravenous r-TPA as 0.9 mg/kg body weight. 10% of the total dose was given as bolus and rest of the 90% was given over 1 hr. through infusion pump. Aspirin or appropriate anticoagulation was started after 24 hrs.

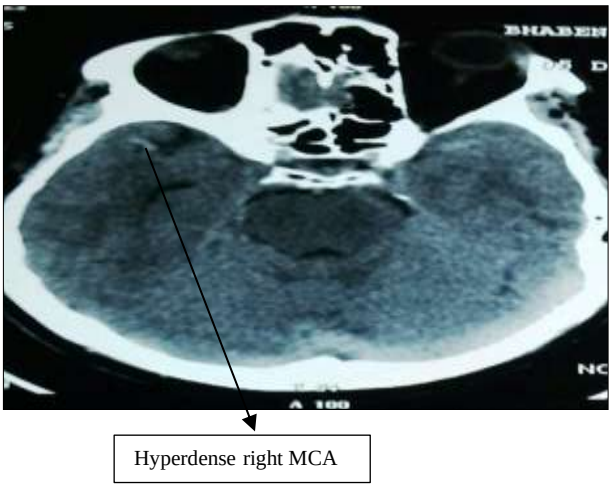

Figure 1: Hyperdense right MCA sign in NCCT head.

Follow-up brain imaging

Any patient who showed neurological deterioration with an NIHSS score decline of ≥4 points was made to undergo an urgent CT scan to rule out SICH. In addition, all the patients receiving r-TPA underwent CT or magnetic resonance imaging of the brain with MR angiography within 24-48 h post-thrombolysis.

Outcomes

Primary clinical outcome was defined as improvement in NIHSS score of 4 or more points after 24 h.[3] Secondary clinical outcome was disability assessment at 90 days based on mRS score, dichotomized as a favorable outcome (with a score of 0 or 1) or an unfavorable outcome (a score of 2-6).[2] The safety endpoints were death rate at 90 days and symptomatic intracranial hemorrhage (sICH), which is defined as any fresh intracranial bleeding resulting in clinical worsening with a decline of >4 points in score on NIHSS or death, as per European Cooperative Acute Stroke Study III study protocol.[2]

Statistical analysis

After collecting all the data, a grand chart was prepared using Microsoft Office Excel 2007 and statistical analysis was performed using SPSS -20 statistical software for analysis of data, p-value of <0.05 was taken as significant.

RESULTS

Intravenous thrombolysis on 54 patients during the period of 13th May 2016 to 12th May 2017 was done.

Demographic profile

Treatment of 37 male patients and 17 female patients were done. Median age of presentation was 67.00 yds, 40

patients came from urban area and 14 patients came from rural area.

The etiological factor and risk factor assessment were studied in all cases. Out of the 54 patients, 35(64.81%) had stroke due to atherothrombosis, 9(16.67%) patients had cardioembolic stroke and 10(18.52%) patients had stroke due to coagulopathy. Coagulopathy as a cause of stroke was present mostly (11.11%) in the young stroke cases. History of smoking was present in 30(55.56%) cases of stroke, out of them 28 were male and 2 were female. History of frequent alcohol intake was present in 14(25.93%) cases. Hypertension was present in 24(44.44%) cases, diabetes was present in 15(27.79%) cases and dyslipidemia was present in 23(42.59%) cases (Table 1). Family history of stroke was present in 7(12.96%) cases. Among the cardioembolic group, 7 patients had atrial fibrillation, 2 patients had rheumatic heart disease and one patient had dilated cardiomyopathy.

Table 1: Risk factors.

Risk factors	No of patients
Hypertension	24(44.44%)
Diabetes	15(27.79%)
Dyslipidemia	23(42.59%)
Atherosclerotic	35(64.81%)
Coagulopathy	6(11.11%)
Smoking	30(55.56%)
Cardioembolic	9(16.67%)
Alcohol	14(25.93%)

Time onset to needle time

Out of the 54 patients, 3(5.56%) patients came within 1 hr. of onset, 10(18.52%) patients came within 1 to 2 hrs. of onset, 11(20.37%) patients came within 2 to 3 hrs. of onset and 30(55.56%) patients came within 4.5 hrs. of onset. Average door to needle time for patients was 54 minutes.

The primary outcome was assessed by noting NIHSS both before and therapy. Average NIHSS before thrombolysis was 8.54±6.459 point and one hour after thrombolysis was NIHSS 6.24-±6.515 point (p value 0.000). In all cases MRI brain and MR angiography brain was done. Five large vessel occlusion cases (9.25%) did not recanalize (Figure 2).

The secondary outcome was measured by assessing mRS point during follow up at 3 months. Out of the 54 patients, 27(50.00%) patients achieved mRS 0-1, 8(14.81%) patients achieved mRS 2, 5(9.26%) patients achieved mRS 3, 10(18.52%) patients were mRS 4, 5(9.26%) patients were mRS 5, and 2(3.70%) patients died (mRS 6).

Haemorrhagic complications in 6(11.11%) cases were observed. Out of them, 3(5.56%) patients had intracranial hemorrhage corresponding infarct site and one patient had nonrelated site bleeding, 2(3.70%) patients had gum bleeding.

Figure 2: Non-recanalized left M2 segment.

DISCUSSION

The current status of modes and prospects of acute ischemic stroke care in India is witnessing a sea change. Day by day understanding of etiopathogenesis of stroke is getting better. Intracranial atherosclerosis is far more common in Indian population than the western population. This study also suggests the same findings.

Median age of stroke presentation in Safe Implementation of Thrombolysis in Stroke -Monitoring Study (SITS-MOST) study was 68 yrs. and in SITS-Non-European union World (SITS-NEW) was 64 yrs.[4] Similar findings are noted in this study.[5]

Hypertension, diabetes, dyslipidemia, use of tobacco and alcohol are the potential risk factors for stroke.[6] A retrospective study of 177 young adult ischemic stroke patients from South India showed most common etiologic subtype was atherothrombotic stroke (24%), followed by cardioembolic stroke (17%).[7] Higher rate of atherothrombotic (64.81%) stroke but almost similar rate of cardioembolic (16.67%) stroke cases was observed.

Intravenous thrombolysis in AIS is feasible to be performed in public hospitals, and particularly in regions of the country. The median DNT was 54 min. The possible causes for the result of this indicator are emergency service, delay in prioritization, delay in the evaluation by neurologist, delay in the taking of neuroimaging.

The 5.56% of symptomatic intra-cerebral hemorrhages (sICH) observed in series are comparable to that reported in national and foreign studies. SITS-MOST, SITS-NEW, J-MARS (Japan Post-Marketing Alteplase Registration Study) studies showed sICH rate as 1.7, 1.9 and 3.5% respectively.[8]

Not all thrombolysed patients access the intensive care unit and complete 24-48 h of observation in the emergency service, being later hospitalized in the internal medicine service. The developing world carries the highest burden of stroke mortality and stroke-related disability. Secondary outcome measured as 3 month mRS score 0-2 in this study was 64.81% which is similar to SITS-NEW study (62.5%), 3 month mortality rate was 11.3% in this study which is similar to SITS-MOST (11.3%) study and slightly lower than SITS-NEW(12%) study.

Number of patients treated for ischemic stroke at government hospital is very high, but a few of them is treated by intravenous r-TPA. This discrepancy is mainly due to late referral to higher center, financial constraints and delayed identification of stroke symptoms.[9] Stroke thrombolysis service is offered in very few centers in developing countries. Most of them are private setups.[10] But, recently most of the Indian states are providing r-TPA free of cost in governmental hospital.

CONCLUSION

Intravenous thrombolysis with alteplase is approved therapy for AIS. It should be offered to all eligible candidates within 4.5 hrs. of stroke onset. Door-to-needle time should be less than 90 minutes for better outcome. Though, in large vessel occlusion, re-canalization rate is very less for intravenous thrombolysis. Still it should be offered to all eligible candidates.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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