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Evaluation of Intravenous Thrombolytic Therapy in Patients with Acute Ischemic Stroke Presented within Window Period in a Tertiary Care Hospital

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ABSTRACT

The use of intravenous recombinant tissue plasminogen activator (rt-PA) for acute ischemic stroke (AIS) within 3 hours of onset was approved, and the therapy was later extended to 4.5 hours. The current Ambispective observational study was conducted at Krishna Institute of Medical Sciences (KIMS) in Hyderabad, India, to assess the outcomes of thrombolysis in patients with acute ischemic stroke who presented within the window period in a tertiary care hospital, which may decrease continual neurologic harm, death, and long-term disability. Between 2017 and 2018, AIS patients who received rt-PA 3-4.5 hours after onset in hospitals were included in the therapy group. Patients' names, ages, genders, body weights, lengths of stay, marital status, dietary habits, stroke type, stroke clinical features in hospital, discharge medicines (dosage, frequency), and condition at discharge were all recorded along with their NIHSS scores. There are 40 participants in the research. The current study's findings support the use of rt-PA in ischemic stroke patients within 3-4.5 hours of onset and under clinical monitoring as an effective and acceptable treatment for functional status after stroke.

Keywords: Intravenous thrombolysis, acute ischemic stroke, recombinant tissue plasminogen activator, mortality.

1. INTRODUCTION

The World Health Organization defines stroke as "rapidly acquired clinical symptoms of focal disruption of brain function lasting more than 24 hours or leading to death with no obvious cause other than vascular origin." Cerebrovascular incident, cerebral shock, brain infection, and stroke syndrome are all terms for the same thing.[1] Acute ischemic stroke is defined as a loss of blood circulation to a part of the brain, usually in a vascular zone, resulting in a loss of neurological function. It occurs more frequently than hemorrhagic stroke.[2] Stroke is the second biggest cause of death worldwide, despite growing mortality rates. 90% of all strokes in the world are linked to modifiable risk factors.

The developing world and post-Soviet countries have the highest incidence rates of ischemic

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stroke. During the last decade, the cumulative incidence of stroke ranged from 105 to 152/100,000 people each year, and the crude prevalence of stroke ranged from 4429 to 559/100,000 people in various sections of the nation. These figures outperformed those of high-income countries.[3,4]

In patients with acute ischemic stroke who reported within 4.5 hours of symptom onset, intravenous treatment of recombinant tissue type plasminogen activator (rt-PA) is the sole authorized therapy for reversing neurological impairment. The accumulation of real-world experience over the last 20 years has provided more knowledge on its safety and effectiveness in a variety of clinical scenarios that were previously regarded CIs for systemic thrombolysis.[5]

The literature on the use of intravenous tissue plasminogen activator in the treatment of acute ischemic stroke focuses on the proper use criteria and time window for delivery. In selected individuals, the rt-PA is beneficial when given up to 4.5 hours after the beginning of ischemic stroke symptoms; nonetheless, prompt administration is critical for achieving best therapeutic effects.[6,7] The third International Stroke Trial (IST-3) discovered that treating patients with rt-PA within 6 hours after AIS improved their functional result and did not raise the risk of mortality at sixth- and eighteen-month follow-ups. In studies conducted in China and Japan, there was no variation in functional outcome, prevalence of symptomatic intracerebral hemorrhage (SICH), or death rates between patients who received rt-PA between 3 and 3-4.5 hours after stroke start.[8]

Recommendations for the early therapy of AIS patients from professional organizations in the United States, Europe, Japan, and China have all strongly suggested that the intervention time be extended to 4.5 hours following the beginning of AIS. Although randomized control trials and related meta-analyses indicate the effectiveness of rt-PA within 3-4.5 hours of AIS start, there is limited information in the literature from research in Asian populations. The Food and Drug Administration (FDA) still has not authorized the use of rt-PA at 3-4.5 hours following the beginning of AIS.[9,10] As a result, the current study was designed to assess the effects of thrombolysis in patients with acute ischemic stroke who came during the window period in a tertiary care hospital, with the goal of reducing long-term brain damage, mortality, and disability.

2. MATERIALS & METHODS

2.1 Study Design

An Ambispective observational study was carried out in a tertiary care hospital, Krishna Institute of Medical Sciences (KIMS), Hyderabad, India. The Ethical Committee approval was obtained and the data was collected from Medical Record Department (MRD) for a period of 1.5 year from August 2017 to December 2018. Daily visits were done for the patients admitted in the Medical Intensive Care Unit (MICU) & emergency room (ER) wards to study the patient's condition at arrival and to check whether the patient was admitted within the window period so that thrombolysis can be initiated if needed, after the fulfillment of inclusion and exclusion criteria.

The National Institutes of Health Stroke Scale is a valuable instrument for measuring neurological disability (NIHSS). The National Institute of Health Scale (NIHSS) is a 42-point scale. A score of 5 is frequently assigned to patients who have had mild strokes. A NIHSS score of >10 is associated with an 80% chance of proximal vascular blockage. NIHSS scores are linked to outcomes and can assist identify individuals who will benefit from reperfusion therapies as well as those who are more likely to suffer problems from the stroke and prospective reperfusion therapies. The NIHSS focuses on level of consciousness (LOC), visual function, motor coordination, perception and cognition, cerebellar function, and speech, which are the six primary areas of the neurologic evaluation. The patient's name, age, gender, body weight, duration of stay, marital status, dietary habit, stroke kind, stroke clinical features in hospital, discharge medicines (dosage, frequency), and condition at discharge were all documented in

the current study.[11] Patient distribution depending on afflicted body side was recorded in a socio-demographic profile form, and additional outcomes such as mortality and disability were tracked until discharge.

2.2 Study Criteria

2.2.1 Inclusion Criteria

- Age over 18 years old
- Symptoms of acute stroke with a clear onset time
- Thrombolysis can be administered within 4-5 hours of symptom onset

2.2.2 Exclusion Criteria

- Major surgery in last 14 days
- GI or UTI bleeding in last 21 days
- History of intracranial hemorrhage, intracranial malignancy or intracranial AVM
- Symptoms suggestive of subarachnoid bleed (even if CT head clear)
- BP > 185 systolic or >110 diastolic unresponsive to medical treatment
- Hyperglycemia (>20) or hypoglycemia (<3)
- Stroke or head injury in last 3 months
- Seizure at onset of symptoms
- Use of anticoagulants in last 24 hrs

2.2.3 Source of Data

- Out patient records, case sheets (in patients), lab reports, prescription.
- Communication with health care professionals.

Patients diagnosed with an AIS who were in the therapy and control groups were all under the age of 18. The diagnosis was made based on clinical examination and validated by in-charge neurologists and radiologists using proper diagnostic techniques. Both groups of patients did not take part in any clinical studies for the treatment of AIS. Patients in the therapy group received rt-PA within 3-4.5 hours after the beginning of the stroke. Patients who arrived at the ER between 2-4.5 hours after stroke start but did not get rt-PA at the same hospital were included in control group. Because they were unlikely to be able to undergo rt-PA therapy within 3 hours, the lowest limit of 2 hours was selected. Microsoft Excel 2007 Windows 10.1 was used to gather and evaluate the data.

2.3 Statistical Analysis

The data was analyzed using Microsoft excel. Descriptive statistics such as percentage was calculated for categorical variables.

3. RESULTS

From August 2017 to December 2018, a total of 40 eligible patients, of whom 30 (75%) were males and 10 females (25%), treated with rt-PA within 3-4.5 h after the onset of an AIS were enrolled in our study from Krishna Institute of Medical Sciences (KIMS), Hyderabad, India. The hospital in the study was a medical center and contributed patients in both treatment and control groups. The mean age of the patients in the present study was 45 years respectively. Among these patients 10 (25%) patients stayed less than 4 days in the hospital while 30 (75%) stayed more than 4 days. 37 (92.5%) of the patients diagnosed with the acute ischemic stroke while 7 (7.5%) diagnosed with recurrent stroke (Table 1). Various clinical features diagnosed in the study were face hemiplegia & aphasia, dysarthria, cognitive impairments, impaired motor coordination, loc, headache, vomiting, fever, linguistic problems, giddiness/drowsiness and weakness (Fig. 1). The mean NIHSS score was found to be higher in the patient group with minor stroke in 10 patients, moderate in 28, moderate to severe in 1 and severe in 1 (Table 2). The study's other outcomes included impairment in one patient after a CT scan revealed cerebral bleeding and death in one patient (Fig. 2 & 3).

4. DISCUSSION

The development of intravenous alteplase recombinant tissue plasminogen activator (rt-PA) as a reperfusion therapy has resulted in a significant shift in the treatment of acute ischemic stroke. The procedure was simple and clear: alteplase was given as a bolus dose of 0.9 mg/kg body weight (10% of total dose), followed by an infusion of the remaining dose over 1 hour.[12]

Table 1: Summary of the demographics of patients admitted in the hospital

Sociodemographic Parameters	No. of Patients	Percentage
Age Range		
15-49 Yrs.	10	25
50-74 Yrs.	29	72.5
>75 Yrs.	1	2.5
Gender		
Male	30	75
Female	10	25
Height (cm)		
141-150 cm	8	20
151-160 cm	13	32.5
161-170 cm	14	35
>170 Cm	5	12.5
Weight (Kg)		
31-40 Kg	1	2.5
41-50 Kg	0	0
51-60 Kg	13	32.5
61-70 Kg	11	27.5
>70 Kg	15	37.5
Length of Stay		
< 4 Days	10	25
> 4 Days	30	75
Marital Status		
Married	39	97.5
Unmarried	1	2.5
Dietary Habits of Patients		
Veg	1	2.5
Non-Veg	24	60
Mixed	15	37.5
Based on Stroke Subtype		
Acute Ischemic Stroke	37	92.5
Hemorrhagic Stroke	0	0
Cryptogenic Stroke	0	0
Recurrent Stroke	3	7.5
Based on Body Side Affected		
Left	19	47.5
Right	19	47.5
No Effect	2	5

Table 2: Patients with NIHSS scores

Scaling	Stroke Severity	No. of Patients (%)
0	No stroke symptoms	0 (0)
1-4	Minor stroke	10 (25)
5-15	Moderate stroke	28 (70)
16-20	Moderate to severe stroke	1 (2.5)
21-42	Severe stroke	1 (2.5)

Fig. 1: Clinical features of stroke in patients admitted in the hospital

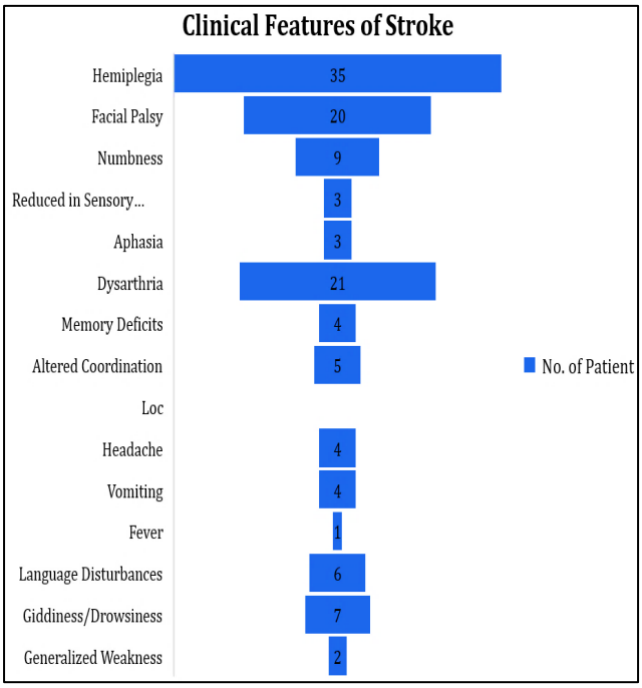


Fig. 2: No. of mortalities of patients after the administration of test

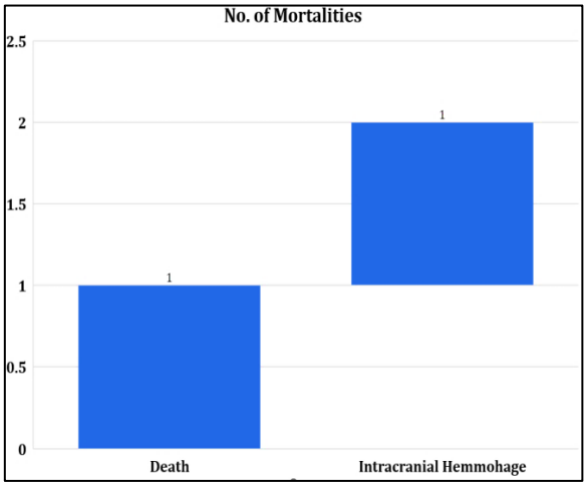
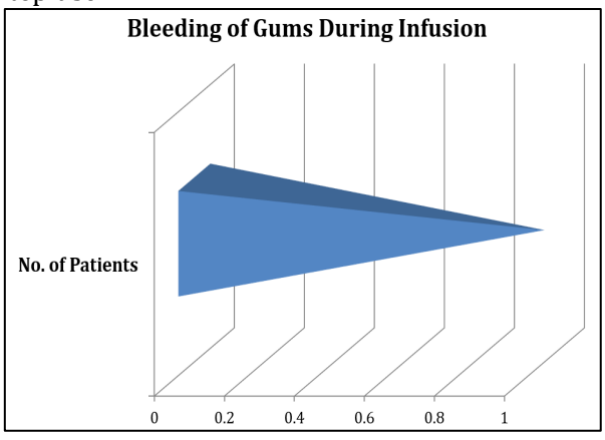


Fig. 3: Bleeding of gums during infusion of alteplase



The aim of the study was to evaluate the outcomes of thrombolysis in stroke patients, to determine the socio-demographic characteristics of patients in neurology unit and to determine the other outcomes of the stroke and goals of treatment includes to reduce ongoing neurologic injury and to decrease mortality and long-term disability, to prevent complications secondary to immobility, neurologic dysfunction and to prevent stroke recurrence. During the study period, it was analyzed that patients admitted for the treatment of AIS presented within window period from data obtained from Medical Record Department (MRD) for previously admitted patients (August 2017 to December 2018) and daily visits were made in MICU & ER ward to study patient's conditions; approximately collecting 40 cases from MRD, MICU & ER wards respectively to find the outcomes of the study and was analyzed accordingly. 40 cases were collected from neurology department from MRD, MICU & ER wards respectively. The NIHSS results revealed that at least 25% of patients were admitted with stroke severity of minor stroke scaling from 1-4 followed by 70% of patients with moderate ranging from 5-15 whereas 2.5% of patients was with moderate to severe stroke severity of 16-20% and 25% of patients with severity of severe stroke of 21-42 scale grading respectively.

The socio-demographic profile of patients was analyzed providing 75% male population & remaining 25% female population with height ranging from 141-150cm (20%), 151-160cm (32.5%), 161-170cm (35%), &>170 (12.5%) and weight 31-40kg (2.5%), 51-60kg (32.5%), 61-70kg (27.5%) and above 70kg (37.5%) respectively. The length of the stay of patients was recorded <4 days (25%) and >4 days (75%) with marital status of married – 97.5% and unmarried – 2.5% suggested with their dietary habits of vegetarian – 2.5%, non-vegetarian – 60% & mixed type – 37.5% along with the stroke type of acute ischemic stroke – 92.5% and recurrent stroke – 7.5% with basics of distribution of body side affected on left side – 47.5%, on right side – 47.5% and no effect on either side of the body – 15% presented with clinical features in hospital like hemiplegia (87.5%), facial palsy (50%), numbness (22.5%), reduction in sensory and vibratory sensation (7.5%), aphasia (7.5%), memory deficits (10%), altered movement coordination (12.5%), loc, headache and vomiting (17.5%), fever (2.5%), language disturbances (15%), dysarthria (52.5%), giddiness or drowsiness (17.5%) and generalized weakness (5%). The other outcomes of this study included disability reported in 1 patient of CT scan showing intracranial hemorrhage and death reported in 1 patient.

The stroke results may vary widely depending on the size and location of the lesion causing dysfunction in parts of brain that are being damaged resulting in disability which might have an adverse effect on the quality of life of people affecting them physically, mentally and emotionally.[13] However, the stroke occur can be treated only if the patient is brought within the window period of 3-4.5 hours of stroke symptom onset by thrombolysis and only after CT scan has ruled out hemorrhagic stroke via recanalization strategies of using intravenous rt-PA, alteplase which has ability to burst the clot that has been dislodged in the cerebral arteries occluding the blood vessel and restoring the blood flow that can mitigate the effects of ischemia only if performed quickly. The only way to get rid of stroke reoccurrence is to avoid the conditions that dispose to have further stroke and disabilities by managing blood pressure, diabetes, diet by avoiding taking cholesterol and fatty substances containing food, quitting tobacco and alcohol use, drug use and maintaining a healthy weight by exercising regularly etc.[14]

5. CONCLUSION

In a real-world setting, the current study confirmed the efficacy and safety of rt-PA for patients 3–4.5 hours following the beginning of AIS. To summarize, the findings of this study suggest the use of rt-PA for ischemic stroke patients within 3-4.5 hours of the beginning of the stroke and while under clinical observation as an

effective and comfortable treatment for functional recovery after stroke. Only thrombolysis can be used to treat a stroke if it occurs within the window of 3-4.5 hours following the beginning of symptoms and only when a CT scan has ruled out hemorrhagic stroke.

Ethical Statement: The Institute Review Board of the Bharat Institute of Technology, Hyderabad, India examined and authorized the research involving human volunteers. To participate in this research, the patients submitted their written informed consent.

Conflict of Interest: The authors stated that there were no commercial or financial affiliations that may be interpreted as a possible conflict of interest when conducting the study.

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