

Limitations to Intravenous Thrombolytic Therapy in Acute Ischemic Stroke in Our Settings

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ABSTRACT

Background: Stroke is the most common cause of disability and a leading cause of mortality worldwide. Though the incidence is falling in West but is rising in Asia. The burden of stroke risk factors in Pakistan is enormous e.g. by 2020 Pakistan will be 4th most populous country in terms of diabetic patients.

Aim: To determine the frequency of patients who present timely in the hospital and who can afford the thrombolytic therapy after acute ischemic stroke.

Methods: This cross-sectional survey was conducted in the Department of Emergency, Shaikh Zayed Hospital, Lahore from 3rd September 2013 to 3rd February 2014. Two hundred and seventeen patients with acute ischemic stroke were enrolled for this study. An informed consent was taken from patient's relatives. Patients were judged for the provision of thrombolytic therapy by focusing on the time of presentation and financial status. Outcome variables i.e. frequency of timely presentation and affordability were recorded as per operational definitions.

Results: The mean age of the patients was 60.4±14.2 years. There were 123(56.7%) male patients and 94(43.3%) female patients. There were 16(7.4%) patients who were presented to emergency department within 4.5 hours of onset of symptoms and 201(92.6%) patients were not presented. In the distribution of patients by affordability the thrombolytic therapy, there were 35(16.1%) patients had affordability and 182(83.9%) patients had not affordability.

Conclusion: It is concluded from this study that very few patients could reach emergency department within the due period to be eligible for thrombolytic therapy. In terms of affordability the situation is better but still less than the developed world. This is due to lack of awareness of thrombolytic therapy in stroke both among the patients and referring physicians, prehospital delays and lack of awareness of stroke symptoms.

Keywords: Acute ischemic stroke, thrombolytic therapy, affordability, timely presentation

INTRODUCTION

Stroke is the most common cause of disability and a leading cause of mortality worldwide. Though the incidence is falling in West but is rising in Asia. The burden of stroke risk factors in Pakistan is enormous e.g. by 2020 Pakistan will be 4th most populous country in terms of diabetic patients.¹ Estimated annual incidence is 250/100,000, translating to 350,000 new cases every year.²

Tissue plasminogen activator (tPA) for acute ischemic stroke was approved by the U.S. Food and Drug Administration (FDA) in 1996.³ In 1995 two studies by the NINDS showed that intravenous t-PA was superior to placebo in stroke patients when given in less than 3 hours from stroke onset. The recently published ECASS III study introduced new patient selection criteria and treatment between 3 and 4.5 hours.⁴ Treatment with intravenous rt-PA was associated with at least 30% increase in the chances

of achieving functional independence with complete or nearly complete neurological recovery at 3 months⁵. It is indicated that standard-dose IV-tPA (0.9mg/kg) is feasible and safe for treating acute ischemic stroke⁶. Although this therapy has demonstrated efficacy in improving outcomes, its use is often complicated by complex inclusion and exclusion criteria, risk of haemorrhage, requirement for intense patient monitoring, substantial cost, and the potential for devastating medication errors⁷.

The number of stroke patients receiving r-tPA in the developing world is extremely low. Pre-hospital delay, financial constraints, and lack of infrastructure are main barriers of thrombolysis therapy in developing countries. In an analysis, on stroke thrombolysis within developing countries, the percentage of stroke patients who reached the hospital within the 3-hour window period in Iran and India is 8% and 14.7%, respectively⁸.

In an Indian study where 641 patients were registered, 10% of the patients presented within 4.5 hours of stroke onset and 7.8% patients received

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thrombolysis. Among those not thrombolysed 80% of them were nonaffording⁹.

The rate of early stroke presentation in a Pakistani tertiary care facility is comparable to certain developed countries. To increase the proportion of patients who can benefit from thrombolytic therapy, programs need to be instituted to increase public awareness of treatment options for stroke and expedited referral by the primary care provider.¹⁰

PATIENTS AND METHODS

This cross-sectional survey was conducted in the Department of Emergency, Shaikh Zayed Hospital, Lahore over period of Six months from 3rd September 2013 to 3rd February 2014. All patients age between 18 to 80 years, both genders, diagnosis of ischemic stroke causing measurable neurological deficit as per operational definitions and neurological signs not clearing spontaneously were included. Patients who have hemorrhagic stroke on CT scan, taking oral anticoagulants are excluded regardless of the INR and history of stroke and hyperglycemia were excluded. Patients were judged for the provision of thrombolytic therapy by focusing on the time of presentation and financial status. Data was analyzed by using SPSS version 20.

RESULTS

The mean age of the patients was 60.4±14.2 years. There were 17(7.8%) patients in the age range of 20-40 years, 105(48.4%) patients in the age range of 41-60 years, 81(37.3%) patients in the age range of 61-80 years and 14 (6.5%) patients in the age range of 81-100 years (Table 1). In the distribution of patients by sex, there were 123(56.7%) male patients and 94(43.3%) female patients (Table 2). In the distribution of patients by presentation to emergency department within 4.5 hours of onset of symptoms, there were 16(7.4%) patients who were presented to emergency department within 4.5 hours of onset of symptoms and 201(92.6%) patients who were not presented to emergency department within 4.5 hours of onset of symptoms (Table 3). In the distribution of patients by affordability the thrombolytic therapy, there were 35 (16.1%) patients had affordability and 182(83.9%) patients had not affordability (Table 4).

Table 1: Distribution of patients by age (n=217)

Age (Years)	No.	%
20-40	17	7.8
41-60	105	48.4
61-80	81	37.3
81-100	14	6.5
Mean±SD	60.4±14.2	

Table 2: Distribution of patients by sex (n=217)

Sex	No.	%
Male	123	56.7
Female	94	43.3

Table 3: Distribution of patients by presentation to emergency department within 4.5 hours of onset of symptoms (n=217)

Presentation within 4.5 hours	No.	%
Yes	16	7.4
No	201	92.6

Table 4: Distribution of patients by affordability (n=217)

Affordability	No.	%
Yes	35	16.1
No	182	83.9

DISCUSSION

Stroke is the third most common cause of death and the first leading cause of disability in developed and developing countries¹¹. According to World Health Organization estimates, 5.5 million people died of stroke in 2002, and roughly 20% of these deaths occurred in South Asia.¹² The new South African national stroke guidelines recommend tPA as treatment for acute ischaemic stroke within 4.5 hours of symptom onset¹³. However, there are no published data on the use of thrombolysis in Africa. Although this therapy has demonstrated efficacy in improving outcomes, its use is often complicated by complex inclusion and exclusion criteria, risk of haemorrhage, requirement for intense patient monitoring, substantial cost, and the potential for devastating medication errors⁷.

In the present study the mean age of the patients was 60.4±14.2 years. As compared with the study of Wasserman and Bryer¹⁴ the mean age of the patients was 62 years, which is comparable with our study.

This study showed that there were 56.7% male and 43.3% female patients. As compared with the study of Wasserman and Bryer¹⁴ there were 54.8% male and 45.2% female patients, which is comparable with our study.

In my study 7.4% patients were presented to emergency department within 4.5 hours of onset of ischemic stroke. As compared with the study of Kurhade and Murthy⁹, 7.8% patients presented within 4.5 hours of stroke onset, which is comparable with our study.

In our study 16.1% patients had affordability of thrombolytic therapy. As compared with the study of Kurhade and Murthy⁹, 20% patients had affordability of thrombolytic therapy, which is comparable with our study.

CONCLUSION

The few patients could reach emergency department within the due period to be eligible for thrombolytic therapy. In terms of affordability the situation is better but still less than the developed world. This is due to lack of awareness of thrombolytic therapy in stroke both among the patients and referring physicians, prehospital delays and lack of awareness of stroke symptoms.

REFERENCES

1. Khealani BA, Hameed B, Uzma U. Stroke in Pakistan. *Mapari J Pak Med Assoc* 2008;58(7):400-3.
2. www.pakstroke.com. An official website of Pakistan Stroke Society. Last accessed on 2008.
3. Zivin JA. Acute stroke therapy with tissue plasminogen activator (tPA) since it was approved by the U.S. Food and Drug Administration (FDA). *Ann Neurol* 2009;66(1):6-10.
4. Hemmen TM, Rapp KS, Emond JA, Raman R, Lyden PD. Analysis of the National Institute of Neurological Disorders and Stroke tissue plasminogen activator studies following European Cooperative Acute Stroke Study III. patient selection criteria. *J Stroke Cerebrovasc Dis* 2010;19(4):290-3.
5. Fugate JE, Giraldo EA, Rabinstein AA. Thrombolysis for cerebral ischemia. Published 29: 2010.
6. Sharma VK, Tsivgoulis G, Tan JH, Wong LY, Ong BK, Chan BP, et al. Feasibility and safety of intravenous thrombolysis in multiethnic Asian stroke patients in Singapore. *J Stroke Cerebrovasc Dis* 2010;19(6):424-30.
7. Weant KA, Baker SN. New windows, same old house: an update on acute stroke management. *Adv Emerg Nurs J* 2012; 34(2):112-21.
8. Ghandehari K. Barriers of thrombolysis therapy in developing countries. *Stroke Res Treat* 2011;2011:1-4.
9. Kurhade D, Murthy J. Thrombolysis in acute ischemic stroke: The barriers and delays: A study from South India. *Am Acad Neurol* 2012;78:05-215.
10. Kamal AK, Khealani BA, Ansari SA, Afridi M, Syed NA. Early ischemic Stroke presentation in Pakistan. *Can J Neurol Sci* 2009; 36:181-6.
11. Feigin VL. Stroke epidemiology in the developing world. *Lancet* 2005; 365: 2160-61.
12. World Health Organization (WHO). The Atlas of Heart Disease and Stroke 2009. http://www.who.int/cardiovascular_diseases/resources/atlas/en/
13. Bryer A, Connor M, Haug P. South African guideline for management of ischaemic stroke and transient ischaemic attack 2010: a guideline from the South African Stroke Society (SASS) and the SASS Writing Committee. *S Afr Med J* 2010;100 Pt 2:747-778.
14. Wasserman S, Bryer A. Early outcomes of thrombolysis for acute ischaemic stroke in a South African tertiary care hospital. *S Afr Med J* 2012; 102:54-44.