

Thrombolysis in Stroke Patients; Problems and Limitations

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Abstract

Thrombolysis for stroke is being used in some developing countries. This study was designed to evaluate the problems of thrombolysis therapy in Iran. During January-July 2008, all patients with ischemic stroke admitted to Ghaem Hospital, Mashhad, northeast Iran, were enrolled in a prospective observational study. Ghaem Hospital is a tertiary care hospital that includes infrastructure for thrombolysis with tissue plasminogen activator (tPA). The stroke onset to hospital entrance time, hospital entrance to completed investigation time, contraindications of thrombolysis, and the capability of the patients to afford the treatment costs by their own were recorded. Of the 625 patients with ischemic stroke, 50 (8%, 30 men, 20 women) arrived at hospital within a 3-hour time window. About 44% of these early arrived stroke patients remained within the 3-hour time window to complete computed tomography and laboratory tests. About 30% of these patients were capable to pay tPA cost by themselves. Contraindications of thrombolysis by tPA were found in 58% of these early arrived stroke patients. Seven patients (five men, two women) were eligible for intravenous thrombolysis. The major hurdles in implementing the treatment are the high cost of the drug and the lack of priority for triage and investigation of hyperacute stroke patients.

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Keywords • Thrombolysis • tissue plasminogen activator • Iran

Introduction

Most health care systems in developing countries cannot afford the high expenses of thrombolysis therapy in public hospitals.¹ Patients must pay the costs using their own personal savings or not receive the treatment. In a study in south India, all seven patients eligible for thrombolysis therapy were from a lower socio-economic group of rural area and could not afford the treatment fee.² Intravenous tissue plasminogen activator (tPA) has been approved by health insurance companies in only a few of the developing countries for the use in acute ischemic stroke.² Medical centers with infrastructure for thrombolysis in stroke patients are very limited in developing countries, however stroke units are available in some developing countries including Iran.¹ This clinical study was conducted to assess the limitations and problems of thrombolysis therapy for patients with hyperacute stroke in a tertiary care center in Iran.

Patients and Methods

A prospective observational study was done on all patients

with ischemic stroke admitted to Ghaem hospital, Mashhad, northeast Iran during January-July 2008.

Ghaem Hospital is a tertiary care hospital and a referral neurology center in northeast Iran. Ghaem Hospital contains neurology, emergency neurology, and neuro-intensive care unit (ICU) divisions. Eight neurologists including two stroke neurologists are working in this center. Brain computed tomography (CT), magnetic resonance imaging (MRI), MR angiography, conventional angiography, emergency team, emergency laboratory, residents of neurology and neurosurgery are available in Ghaem Hospital in a 24/7 mode. Duplex sonography of neck arteries, transcranial Doppler, transthoracic and transthoracic echocardiography are available in this center 6 hours per day.

Patients demographics, stroke onset to hospital entrance time, hospital entrance to completed investigations time, and method of patients transportation to the hospital were recorded in a data bank considering the previous reports.³ Selection of the patients' transportation method had been made by their own or their relatives. In Khorasan Razavi province where Mashhad is the center, the paramedic teams do not have special training for thrombolysis therapy in stroke patients. There is no priority for triage of stroke patients in the emergency department of our hospital.

Contraindications for intravenous thrombolysis with tPA based on the standard protocols were evaluated in stroke patients who arrived at the hospital within a 3-hour time window after stroke onset.⁴ The patients arrived at hospital in the 3-hour time window were asked for their financial capability for payment of 1400 USD for a vial of tPA. Stroke was defined as presence of ischemic focal neurological deficit lasting more than 24 hours. Stroke onset to hospital entrance time, hospital entrance to completed investigations time and presence of

contraindication to tPA therapy were evaluated in patients. The cause of prolonged stroke onset to hospital entrance time was investigated in this group of patients. The present study was approved by the Ethics Committee of Ghaem Hospital and a signed informed consent was obtained from the patients or their first degree relatives.

Results

Of the 625 patients with ischemic stroke (344 men, 281 women) with mean age of 62.1 ± 10.7 years, 50 patients (8%, 30 men, 20 women) arrived at the hospital within a 3-hour time window.

Of these, 50 patients with stroke, 25 were transported to the hospital by ambulance and 25 patients were transported by personal vehicles. The mean stroke onset to hospital entrance time in those transported by ambulance and personal vehicles were 75.4 and 98.3 minutes, respectively (range 10-140 minutes).

Of the remaining 575 stroke patients who arrived at the hospital after 3 hours, delay in decision to call the paramedics team or delay in decision to transfer the patients by personal vehicle, constituted 45% of prolonged stroke onset to hospital entrance time followed by long distance to the hospital in 40%.

The mean hospital entrance to completed investigations times in the early arrived stroke patients who were transported by ambulance or personal vehicles, were 116.2 and 116.6 minutes, respectively (range 20-360 minutes). Only 44% of the early arrived stroke patients remained within the 3-hour time window to complete CT and laboratory tests.

The mean hospital entrance to completed investigations time in 575 stroke patients who arrived at hospital after 3 hours was 124.1 minutes (range 32-352 minutes).

Table 1 represents the frequency of contraindications of intravenous thrombolysis in 50

Table 1: Frequency of contraindications of intravenous thrombolysis in 50 early arrived and 575 late arrived stroke patients

Type of contraindication	Number (%) in early arrived patients (total 50)	Number (%) in late arrived patients (total 575)
Uncontrolled hypertension	15 (30%)	161 (28.3%)
Sever stroke-NIHSS>25*	13 (26%)	147 (25.6%)
Evidence of extensive infarction in CT	6 (12%)	115 (20%)
Age above 80 years	4 (8%)	40 (6.9%)
Acute myocardial infarction	1 (2%)	4 (0.7%)
Prior stroke in recent 3 months	1 (2%)	8 (1.4%)
Prior stroke in diabetics	2 (4%)	20 (3.5%)
Oral anticoagulant therapy	1 (2%)	10 (1.7%)
Heparin therapy and elevated PTT	2 (4%)	29 (5%)
Recent major surgery	1 (2%)	11 (1.9%)
Hemodialysis	1 (2%)	2 (0.3%)
Multiple contraindications	15 (30%)	205 (35.6%)
Minor stroke	3 (6%)	23 (4%)

*NIHSS=National Institute of Health Stroke Scale, PTT: partial thromboplastin time

early arrived stroke patients. Of the 50 early arrived stroke patients, 42% had no contraindication to thrombolysis therapy and the remaining were excluded because of the contraindication. Meanwhile, 86% of our early arrived stroke patients missed thrombolysis therapy because of a delay in diagnostic procedures and presence of the contraindications even without financial problems for tPA therapy.

Among the 625 stroke patients, seven patients including five men and two women received intravenous thrombolysis. Among the early arrived stroke patients, 15 patients (12 men, 3 women) could afford the tPA costs by themselves. However, 60% of these candidates of thrombolysis had a contraindication for treatment and 46.6% remained within the 3-hour time window to complete CT and other diagnostic procedures. Only 20% of these candidates of thrombolysis had no contraindication and remained within the 3-hour window to complete the diagnostic procedures.

Of the 575 stroke patients who arrived at the hospital after 3 hours, 63.5% had a contraindication for intravenous tPA therapy. Detailed frequency of contraindications in this late arrived group of patients is shown in table 1.

Discussion

Eligible patients for intravenous thrombolysis constituted 14% of our stroke patients who arrived at the hospital in the 3-hour window (1.1% of the whole stroke patients). In a university hospital in Thailand, 2.1% of patients with acute stroke were eligible and received intravenous thrombolysis.⁵ More than half of our stroke patients who arrived at the hospital in the 3-hour window had a contraindication for intravenous tPA and were excluded from the therapeutic plan. This is similar to other reported data.⁶

Delay in performance of CT and laboratory tests excluded 56% of our 50 early arrived stroke patients and therefore, delayed arrival to the hospital is a main problem of this treatment in Iran. If we were able to avoid delayed transfer of patients to hospital by education programs on TV or other media, we might have an additional 259 stroke patients in the 3-hour time window in the hospital. In this ideal situation, 95 other stroke patients would have had no contraindication for thrombolysis therapy; however, half of these patients would have missed tPA therapy because of prolonged diagnostic procedures time. This delay is caused by the lack of priority for candidates of thrombolysis in performance of triage, CT imaging, and laboratory tests. Executive avoidance of this delay doubles the number of eligible Iranian

stroke patients for intravenous tPA therapy.

The mean hospital entrance to completed diagnostic procedures time was reported to be 73 minutes in Thailand.⁵ This time period has been minimized to 21.7 minutes in Taiwan due to implementation of an intrahospital stroke code.⁷ Organization of stroke team and executive priority for triage and investigation of stroke patients may have a similar influence in Iran. A 30-minute interval for performance of the CT scan and report of coagulation study results offer an excellent time frame for conduction of thrombolysis therapy.⁸ Fifty four stroke patients were evaluated in New Delhi. The mean stroke onset to hospital entrance time and mean hospital entrance to completed investigations time in this group was 140 minutes and 24 minutes, respectively.⁹ Most stroke patients in an Indian hospital were not aware of the importance of the time window in stroke management.¹⁰ Production and broadcasting of stroke education programs by TV and other media have reduced the stroke onset to hospital entrance time in other countries and may have a similar effect in Iran.¹¹

Only 30% of our early arrived stroke patients were able to pay the cost of tPA by their own savings. The most important barrier of thrombolysis with tPA in our hospital is non-coverage of this drug by Iranian health insurance systems.¹² About 400 stroke patients have received intravenous tPA in different centers across India and most of these centers were in the private sector.¹ Centers with resources to give intravenous and intra-arterial tPA are limited to some urban areas in the developing world.¹ Although about 14 hospitals have this resource and infrastructure in Iran, these medical centers admit less than one third of Iranian stroke patients.¹²

Conclusion

The barriers of tPA therapy in Iran include the lack of covering the costs of tPA therapy in stroke patients by Iranian health insurance systems, absence of stroke education programs by TV or other media, and absence of priority for triage and investigations of stroke patients in emergency departments.

Conflict of Interest: None declared

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