



# Effect of Public Education Regarding Stroke Warning Signs on Pre-Hospital Delay and Frequency of Tissue Plasminogen Activator Therapy in Stroke Patients: A Quasi-Experimental Study

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## Abstract

**Background:** Treatment with tissue plasminogen activator (tPA) is one of the effective therapeutic strategies for treating stroke. Its effectiveness is associated with the period between the onset of symptoms and initiation of the treatment. An earlier intervention can result in better results and prognosis.

**Objectives:** The aim of this study was to determine the effect of public education regarding stroke warning signs on pre-hospital delay and frequency of tPA therapy in stroke patients referring to the emergency department.

**Methods:** In this quasi-experimental study, the research population included all stroke patients referring to an emergency department in an urban area of Iran in 2016 - 2018. Educational intervention included the distribution of educational pamphlets through the city, the installation of banners, radio training programs, etc. began in November 2017 and lasted one year. Patients' information was collected one year before and one year after the intervention. Data were analyzed with independent *t*-test and chi-square test using SPSS version 18 software.

**Results:** According to the results, in the post-intervention phase, the frequency of referrals in all three intervals (less than 3 hours, 3 - 6 hours, and more than 6 hours) were increased compared with the pre-intervention phase. There was no significant difference regarding the frequency of treatment with tPA between two intervals.

**Conclusions:** Based on the results, public education can raise awareness regarding the symptoms of stroke and prevent serious neurological defects after ischemic stroke, based on which the used intervention is highly recommended.

**Keywords:** Ischemic Stroke, Warning Signs, Thrombolytic Therapy, Tissue Plasminogen Activator (tPA), Pre-Hospital Delay, Public Education

## 1. Background

Stroke is one of the main causes of mortality and disability worldwide (1). Each year, more than 5.5 million people worldwide die due to stroke, of which two-thirds have reported in developing countries (2, 3). Although the incidence of stroke in other countries ranges from 100 to 300 per 100,000 people, in Iran, it has been reported more than other countries (4). Some recent studies have suggested that the age of acute cerebral stroke in Iran is lower than its global average age and is associated with a higher mortality than developed countries (5, 6).

Most patients suffer from serious neurological defects after the acute phase of stroke, so that about 70% of these

patients are not able to work and also about 30% need help to walk (7, 8). The complications of stroke, including medical expenses, rehabilitation, and disability annually impose a huge burden on the health system of the countries and families, as well. Therefore, interventions to reduce the costs associated with acute stroke are economically important (9, 10).

Obviously, recognizing and treating the risk factors, primary and secondary prevention, as well as treating the acute phase of stroke to reduce the complications and disabilities are one of the most important health priorities in each community (11).

One of the therapeutic strategies for stroke is throm-

bolytic therapy. Since 1996, after the approval of an intravenous thrombolytic drug by the American Drug and Food Society, the treatment of ischemic stroke has changed (12). Tissue plasminogen activator (tPA) produces plasmin and dissolves blood clots. Its administration immediately following a stroke can rapidly destroy the clots. Thus, the surrounding tissues will not be destroyed due to nutritional deficiencies and the blood flow will reach to the normal level (13).

The effectiveness of these methods is associated with the period between the onset of symptoms and initiation of the treatment. Therefore, an earlier intervention can result in better results and prognosis. This period should preferably be less than three hours (14-16). However, according to the results of a study by Raty et al., only 5.6% of the patients were referred to the clinics at the desired time (17). In Iran, according to study by Ghiasian et al., the mean delay time was 7.4 hours (18).

Familiarity with the symptoms of stroke, how to deal with these patients, and an earlier treatment are very important, which are largely dependent on the education and awareness of the community. In this regard, various global studies have been conducted with an educational approach to raise the level of awareness of the community about the warning signs of stroke and the need for early referral of patients after the onset of symptoms (19-24). In Iran, only few descriptive relevant studies have been conducted to address the causes of delay (18, 25), and also no interventional study to increase the public awareness was found. Therefore, this study was conducted due to the importance of this subject and limited relevant studies.

## 2. Objectives

This study aimed at determining the effect of public education regarding stroke warning symptoms on pre-hospital delay and frequency of tPA treatment in stroke patients referring to the emergency departments in an urban area of Iran.

## 3. Methods

### 3.1. Subjects

This semi-experimental study was conducted on all stroke patients referred to an emergency department in an urban area of Iran during 2016 - 2018. They were selected by census method based on inclusion and exclusion criteria. Inclusion criteria included patients aged 18 years or older who referred to the emergency department

with stroke-like symptoms, including weakness, numbness, and speech difficulties. Exclusion criteria were a history of hemorrhagic stroke, seizure at stroke onset, internal bleeding, intracranial hemorrhage, recent surgery, platelet count of less than  $100 \times 10^3/\mu\text{L}$ , and untreated blood pressure greater than 185/110 mmHg.

### 3.2. Intervention Protocol

Educational pamphlets and posters were prepared based on the latest guidelines of the Neurology Association and were made available to the general public. Accordingly, 3000 pamphlets were distributed in high schools, religious places and ceremonies, medical places, offices and organizations. Posters were distributed through the county (crossroads, shopping centers, etc.) and also urban and rural centers providing health services. In addition, neuroscientists lectured on radio and Friday prayer rites. This training emphasized the warning signs of stroke (speech impairment, paralysis of the hand, and facial paralysis), and early referral of the patient to the treatment center (supplementary file Appendix 1). These symptoms were presented as the banners and installed in the considered centers. The definition of stroke and its causes, symptoms, and complications were highlighted in the educational pamphlets. They also emphasized on the attention to the warning signs and making a calling "Emergency 115".

### 3.3. Data Collection

Data collection tool was a checklist for demographic and outcome variables (age, sex, the mean time of referral to the emergency department since the onset of symptoms, type of transferring, the frequency of treatment with tPA, and the reasons for not receiving the drug). The checklist was prepared based on a review of the literature and the validity of its content was approved by the neurologists.

The training program was fully implemented in October 2017 and continued for one year. Then, the patients' information was collected for one year before the study, from October 1, 2016 to the end of September 2017, as the pre-intervention data and also their information from October 2017 to the end of September 2018 was collected as the post-intervention information. The checklist was completed by the patients' recorded data in the Hospital Information System (HIS) and the application "724".

### 3.4. Ethics and Statistical Analysis

The research was approved by the Ethics Committee of Rafsanjan University of Medical Sciences (approval code: IR.RUMS.REC.1396.107). The subjects were assured of the

confidentiality of information and also the observance of trust in the use of texts. Finally, the data were analyzed using descriptive and analytical statistics (Independent *t*-test and chi-square) using SPSS software version 18.

#### 4. Results

According to the data obtained by the HIS, the number of cases referred to the emergency department with complaints of stroke symptoms was 236 subjects during the pre-intervention period, of whom 51 cases (21.6%) received tPA. This number reached 275 subjects one year after the intervention, of whom 58 cases (21.1%) received tPA. According to this data, data on ischemic stroke was recorded in the application “724”, which is a national system.

Based on the results of the demographic variables, most of the patients aged over 60 years and had high blood pressure and diabetes. There was no significant difference between the two groups in terms of these variables (Table 1).

**Table 1.** Demographic Characteristic of the Patients Before and After the Intervention<sup>a</sup>

Variables	Pre Intervention	Pre Intervention	P Value
Age	71.54 ± 12.88	68.09 ± 14.63	0.12
Weight	69.43 ± 9.57	70.53 ± 8.71	0.45
Blood sugar	149.50 ± 88.63	145.52 ± 65.49	0.74
Systolic blood pressure	146.74 ± 24.96	144.07 ± 27.58	0.53
Diastolic blood pressure	84.06 ± 18.57	84.93 ± 15.97	0.75

<sup>a</sup>Values are expressed as mean ± SD.

The time of symptom onset and the time of emergency department arrival were recorded for patients and the difference between these two times was calculated as the delay time. Based on the results of Independent *t*-test, the average delay during both times was more than 3 hours and there was no significant difference between them (*P* = 0.06). The difference between two times was divided into the intervals of less than 3 hours, 3-6 hours, and more than 6 hours. The results of chi-square test showed an increase in the frequency of patients in each interval in the post-intervention period compared with the pre-intervention period (*P* = 0.01). Regarding the mode of transmission, in both times, based on the results of the chi-square test, most of the subjects were transferred to the Emergency Department by “Emergency 115” and there was no significant difference between two times (*P* = 0.42).

In addition to the delay in referral, no need to tPA was also one of the reasons for not receiving tPA drug at two times (Table 2). In patients who received the tPA, only one

case had a systemic hemorrhagic and referred for angioplasty due to arterial thrombolysis and in other cases, no adverse events were reported.

**Table 2.** The Frequency of Variables Before and After the Intervention<sup>a</sup>

Variables	Pre Intervention	Pre Intervention	P Value
<b>Gender</b>			0.58
Female	33 (50)	42 (45.7)	
Male	33 (50)	50 (54.3)	
<b>Pre hospital delay (h)</b>			0.01
< 3	54 (81.8)	59 (64.1)	
3 - 6	7 (10.6)	9 (9.8)	
> 6	5 (7.6)	24 (26.1)	
<b>Method of transmission</b>			0.42
Emergency 115	45 (68.2)	57 (68)	
Private car	21 (31.8)	35 (32)	

<sup>a</sup>Values are expressed as No. (%).

#### 5. Discussion

According to the results of this study, in terms of demographic variables, the majority of patients at each time had high blood pressure and diabetes. The mean age in both periods was more than 65 years and the incidence of stroke was higher in men than women. In this regard, according to the results of a study by Mazaheri et al. (26), who studied the epidemiological risk factors for stroke, in line with the present study, the average age of patients was 65.93 years and the prevalence of stroke in men was more than women. Regarding the considered risk factors for ischemic stroke, hypertension had the highest prevalence (51.74%) followed by diabetes (18.83%). Other internal and external studies (4, 27, 28) have confirmed these two risk factors as the main causes of stroke that should be controlled and regarded by health care providers.

No study on stroke warning symptoms conducted in Iran was found, however some international relevant studies were found reporting different results. For example, various studies in Australia (29) and England (30, 31) have been carried out to increase the public awareness regarding these two risk factors.

Based on the results of this study, after the implementation of educational intervention, the number of people who contacted the emergency department with a complaint about stroke symptoms or referred to the emergency department was increased. In this regard, Fogle et al. conducted a 20-week educational program through a media to increase public awareness about the stroke symptoms and the need for emergency call. Based on the re-

sults, 50% to 56% of the respondents stated that if they experience the symptoms, such as numbness or paralysis, they will call the emergency department (32). In this study, only the subjects' knowledge was studied, whereas the present study examined the effect of knowledge on behavior, which is one of the strengths of this research. According to the number of referrals after the implementation of educational intervention, it can be stated that the intervention has increased the public awareness.

Based on the results of the present study, the number of people who referred to the emergency department was increased in three intervals (less than 3 hours, between 3 and 6 hours, and more than 6 hours). Hodgson et al. also divided this time to two intervals: less than 2.5 hours and less than 5 hours. Their results are consistent with the present study indicating an increase in the frequency of patients in both intervals (33). According to the findings, it can be stated that although some of the subjects did not have the symptoms of stroke, however following raising awareness at the community level, they decided to refer to the hospital. According to the results of this study, a delay in referral to the hospital in both periods was one of the main causes of no injection of tPA. Based on the results of the study by Hatamabadi et al. (25), consistent with the present study, delayed referral was one of the main causes of no receiving tPA, but the prevalence of delayed referral was 70.3%, which is far higher than the current study.

Based on the results, the average delay in both periods was more than 3 hours and there was no significant difference between the two periods. According to the results of a study by Ghiasian et al. (18), the mean delay time was 7.4 hours, which was more than that of this study. Wojner-Alexandrov et al. also in their study, using pre- and post-intervention method (similar to the present study) found no significant difference in delay time after the intervention (34). In contrast, based on the results of the study by Nishijima et al. (35) at the Aomori Hospital in Japan, who used television advertisement for raising the awareness of community, after the intervention, the mean pre-hospital delay was shorter (12 versus 13.5 hours), the percentage of referrals before 3 hours was higher (55.7% vs. 46.5%), and the percentage of referrals after 6 hours was lower (32.7% versus 39.5%). However, there was no significant difference in the percentage of patients treated with rTPA before and after the intervention, which is in agreement with our results. However, regarding pre-hospital delay, unlike the present study, the training has reduced the delay. The difference between the results of the mentioned studies and the present study was the type of used media. Therefore, the used educational intervention is suggested.

Based on the results of this study, patients were transferred to the emergency department at all intervals using

ambulance. In the study by Sun et al. on the effect of public and professional education on urgent therapy for acute ischemic stroke in Changsha, the percentage of referrals in less than 3 hours (48% versus 21.5%), the rate of using ambulance (59% versus 41.3%) and thrombolytic therapy (9.3% vs. 4.4%) in the intervention group was higher than the control group (36). In the study by Chen et al., in the intervention group, the pre-hospital delay was decreased from 180 min to 79 minutes, whereas the percentage of referral before 3 hours after the onset of stroke symptoms increased from 55.8% to 80.4% compared with the control group (37). Using the intervention and control groups is one of the differences between these studies and the present study. Therefore, using two groups, such as using two districts of major cities or two nearby cities as the intervention and control groups is also suggested.

Finally, although the results of the present study did not show a decrease in the mean delay time, there was an increase in the number of patients. This study was conducted only on one group and compared the results before and after intervention. Accordingly, the lack of using television advertisement was one of the limitations of the study. Also, similar studies in larger centers, that let the researcher to select two communities from different regions of the city, as well as using multimedia education, such as sending SMS and use of TV is also recommended.

### 5.1. Conclusions

Based on the results of this study, the implementation of educational intervention increased the awareness and referral of patients to the emergency department. This study was the first interventional study to raise the public awareness regarding these variables conducted in Iran. Therefore, further studies are needed in this area. The results can be helpful for the health care providers and the stroke-related committees.

### Supplementary Material

Supplementary material(s) is available [here](#) [To read supplementary materials, please refer to the journal website and open PDF/HTML].

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# Footnotes

**Authors' Contribution:** Study design, analysis of data and manuscript preparation: Alireza Vakilian and Tabandeh Sadeghi; data collection and revising the article: Seyed Hamid Seyedbagheri, Amir Moghadam Ahmadi, Hossein Azin, and Nazanin Jalali.

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