



Attitude and Knowledge of Emergency Medicine Professionals Regarding the Use of Tissue Plasminogen Activator in the Treatment of Acute Ischemic Stroke: A Cross-Sectional Study

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Abstract

Background: One of the main parts of the early treatment of Acute Ischemic Stroke (AIS) is the attitude and knowledge of Emergency Medicine (EM) specialists. This study aimed to investigate the knowledge and attitude of emergency physicians working in Iran about the prescription of tissue Plasminogen Activator (tPA) in AIS.

Methods: This was a cross-sectional questionnaire-based study including EM physicians working in different cities of Iran in 2020. A previously used English questionnaire was translated into Persian. After face validity and reliability assessment, the final questionnaire was designed as a Google form and sent to 400 EM professionals.

Results: 128 physicians filled in the forms. 64.8% of participants had sufficient attitude and 68% had sufficient knowledge about tPA treatment in AIS. The knowledge regarding tPA treatment was higher in the age >40 years, male gender and physicians with up-to-date information ($P < 0.05$), but no significant association was found for the attitude. Logistic regression analysis showed that the amount of information about tPA administration in AIS (OR=3.475, 95% CI = 1.242-9.723, $p = 0.018$) and age (OR=0.336, 95% CI = 0.130-0.865, $p = 0.024$) had the greatest impact on the level of knowledge for tPA treatment.

Conclusion: About two-thirds of EM professionals in Iran had sufficient knowledge and attitude about tPA administration in AIS. Having up-to-date information and age >40 years were the major predictors of higher knowledge of AIS treatment. Holding some training workshops together with strengthening infrastructures such as establishing intensive stroke units would help to increase the use of tPA in AIS in Iran.

Keywords: Acute ischemic stroke, Attitude, Emergency medicine, Knowledge, Physicians, Tissue plasminogen activator

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Introduction

According to the Center Disease Control (CDC) latest update, approximately 795,000 strokes occur in the United States each year, 77% of which occur for the first time and the majority (87%) are ischemic (1-4). The incidence of stroke in Iran is almost higher than in many European countries and is about 43 per 100,000 general population (5,6).

There has been a significant difference between the cost of treatment and complications of stroke with or without using tissue Plasminogen Activator (tPA) (7). In the treatment of Acute Ischemic Stroke (AIS), tPA is the only medicine approved by the US Food and Drug Administration (FDA). It can be used only in the first 4.5 hours after the onset of symptoms (8). tPA administration has been shown to reduce mortality and morbidity after AIS (9). The most important complication following the use of this drug is cerebral hemorrhage (10-12).

There are some evidence (13), for increasing life expectancy in Iranian populations, therefore it is estimated that the prevalence of AIS will be increased. Furthermore, specialists and residents of Emergency Medicine (EM) are among the first healthcare providers to visit the patients. On the other hand, in some centers, a neurologist is not available and management of stroke is performed by EM specialists. Therefore, a prompt diagnosis and early treatment of AIS need sufficient attitude and knowledge for using tPA in EM professionals. For instance, Paul *et al* evaluated the perspective of emergency ward staff at 19 Australian hospitals regarding the implementation of thrombolysis care for acute stroke. They reported that approximately 90% agreed that thrombolysis would enhance overall survival. Despite this fact, about a half claimed some obstacles and deficiencies such as late bed availability (14).

To our knowledge, there was no study in Iran to assess the knowledge and attitude of emergency medicine professionals about the use of tPA in AIS. Therefore, this study aimed to evaluate the knowledge and attitude of EM physicians working in Iran regarding the administration of tPA in AIS.

Materials and Methods

This was a cross-sectional questionnaire-based study conducted from February 2020 to March 2021 including

specialists and residents of EM in educational and non-educational hospitals of Iran. Specialists having a degree in EM from the Ministry of Health or those undergoing their residency course in EM were entered the study. The questionnaire utilized in this study was obtained from the Al-Khatami study after obtaining permission from the authors. The questionnaire was first translated into Persian and then its validity was checked by 10 academic neurology attendings and EM specialists and necessary corrections were made. The final questionnaire includes 18 questions with 5 attitude and knowledge questions. Then, to check reliability, the questionnaire was administered to 10 EM professionals with an interval of 2 weeks and correlation of 2 answers of these 10 EM specialists was 0.9 (p-value <0.001). All of the 5 knowledge and attitude questions had a positive meaningful correlation from 0.38 to 0.7 with the sum of all questions and from 0.43 to 0.99 with the sum of each category questions (p-value <0.001). The final questionnaire was designed using Google Form and sent to EM specialists and residents through e-mail and virtual communication apps. The participants' information was used without disclosing their identities. The questionnaire was filled voluntarily. The sample size of this study was determined based on the Al-Khatami study (15). Thus, taking into account the knowledge of 41% and a first type error of 5% and accuracy of 5%, the sample size was calculated to be 372, which was increased to 400.

Questionnaire

The final questionnaire contained 18 questions, including 5 demographic questions, 8 practical questions, 3 attitude questions, and 2 knowledge questions. The first part of the questionnaire included demographic characteristics. Data included age, sex, resident or specialist, total years of work experience, working in educational or non-educational hospitals, the total number of stroke patients visited weekly and availability of stroke team and stroke protocol in the center.

The second part was the knowledge and attitude towards the administration and effectiveness of tPA within 4.5 hours from the onset of AIS. The questions regarding the evaluation of knowledge were "do you think tPA is a part of the treatment in AIS? With

answers “yes, no, and I don’t know” and “how do you rate the level of evidence for using tPA in AIS”? With answers “high level, low level, or conflicting evidence and I don’t know”. Three questions were considered about the attitude of AIS treatment including “do you think tPA is effective in AIS during the first 4.5 hours after onset of symptoms? With answers “yes, no, and I don’t know”, “do you recommend tPA in AIS if indicated”? With answers “yes and no” and “do you recommend tPA with neurology consultation if Telestroke becomes established”? With answers “yes, no and I have no idea”. The other questions were about the most important side effect and obstacles of prescribing tPA and their willingness to participate in training courses. Participants who answered “yes” and “high level of evidence” to two knowledge questions were considered to have sufficient knowledge regarding tPA treatment in AIS. As the same was, participants who answered “yes” to all three questions of attitude were considered as those with sufficient attitude.

Statistical analysis

Data were entered into IBM SPSS STATISTICS 25 (IBM Inc., New York, USA) and analyzed. Mean, standard deviation and frequency were used. The Kolmogorov-Smirnov test was utilized to evaluate the normality of data. Chi-square test was used for comparing two groups including sufficient *vs.* insufficient knowledge and sufficient *vs.* insufficient attitude. Besides, logistic regression analyses were applied to calculate the odds ratio (OR) of all variables. A p-value below 0.05 was considered statistically significant.

Ethical consideration

Participants’ information was used without disclosing their identities. The questionnaire was filled out voluntarily. The study was approved by the ethics committee of Iran University of Medical Sciences, Tehran, Iran (ethical code: IR.IUMS.FMD.REC.1398.330).

Results

The questionnaire was sent to 400 EM residents and specialists and finally 128 questionnaires were filled in (response rate: 32%). Among them, 67 (52.3%)

were male and 61 (47.7%) were female. Most physicians (71 individuals, 55.5%), were in the age group of 30-40 years. Ninety-six (75%) participants were EM specialists and 32 (25%) were EM residents. The majority of participants had less than 5 years of work experience (50.8%) and 71.1% worked in educational hospitals. The highest number of stroke patients visited weekly was 1 to 5 patients (60.9%). In addition, 50% of the hospitals had a stroke team and 66.4% had an acute stroke protocol. Only 35.9% (46) of the participants had up-to-date information based on recent articles and guidelines regarding the tPA treatment. Baseline demographic characteristics of the study participants are depicted in table 1.

Overall, 95.3% of the participants considered tPA as a part of the treatment of AIS and 94.5% considered tPA as an effective treatment. Besides, 68% believed that there is high level of evidence for using tPA in ischemic stroke within 4.5 hours of the onset of symptoms. However, 80.5% recommended the use of tPA in AIS within 4.5 hours of the onset of symptoms, if indicated. The most important reasons for not recommending tPA included the risk of bleeding (32%) and the uselessness of the drug (28%). The participants believed that the most common complications after tPA injection are cerebral hemorrhage (79.7%) and gastrointestinal bleeding (14.1%).

Furthermore, they believed that the most important barriers to tPA administration were the lack of timely arrival of patients to the hospital (67.2%) and lack of intensive care unit for patients with acute stroke to be hospitalized (12.5%). Moreover, 73.4% of EM physicians were willing to participate in training courses and 80.5% were willing to prescribe tPA with remote neurological consultation in case of establishing a “Telestroke” consultation. Also, 87 participants (68%) had sufficient knowledge (answered “yes” and “high level of evidence” to two knowledge questions), and 83 participants (64.8%) with sufficient attitude (answered yes to all 3 attitude questions).

Nonetheless, the Chi-square test showed a significant association between the level of knowledge about tPA treatment and gender ($p=0.038$), age group ($p=0.010$), and up-to-date information from recent guidelines and articles ($p=0.002$). There was no meaningful association between other variables and the level

of knowledge. On the other hand, there was no significant association between the level of attitude about tPA treatment with these variables [gender ($p=0.837$), age group ($p=0.786$), and up-to-date information ($p=0.221$)] and also other variables.

Finally, logistic regression analysis showed that having up-to-date information from recent guidelines and articles on tPA administration and the age >40 years had the greatest impact on the level of knowledge about tPA administration in stroke patients (Table 2).

Discussion

Stroke is one of the leading causes of death and permanent disability worldwide (16). There is a difference in the reported incidence of regional stroke, which varies from 22 to 140 stroke patients per 100,000 population compared to some developed countries. Ischemic stroke occurs almost a decade earlier among Iranians and leads to higher mortality (5,17). Although several treatment options are emerging, the US FDA has currently approved only one drug (intravenous tPA) for the treatment of AIS.

Despite the approved efficacy of tPA as a treatment of AIS, different national registries worldwide showed that 1 to 10.2% of AIS patients received this treatment (18-21). Meanwhile, some studies evaluated the effect of intravenous tPA from 0 to 6 hours after the onset of symptoms, and a meta-analysis of these trials showed the advantage of tPA in the first 4.5 hours (22). Later, the European regulators confirmed the advantage of tPA prescribed 3 to 4.5 hours after the onset of stroke (23). Furthermore, the IST3 trial clearly showed that even in patients at maximum risk, tPA reduced the disability in case it was prescribed within 3 hours of the onset of the stroke (24).

Emergency physicians, meanwhile, are the key suppliers in the medical care chain provided for optimal treatment of patients with AIS. The 4.5-hour short window and eligibility for treatment with intravenous tPA requires a fully organized and integrated effort by emergency physicians and neurologists. Therefore, a review of the knowledge and attitudes of emergency physicians toward the use of intravenous tPA in patients with AIS is of great importance. In this study, we found that the level of knowledge and attitude of emergency physicians in Iran about the effectiveness of intravenous tPA

in AIS is relatively high and about two-third of EM professionals had sufficient knowledge and attitude for IV thrombolysis. However, about 20 percent of the participants recommended no tPA for the treatment of AIS. The EM professionals believed that the main barrier to tPA administration was the lack of timely arrival of patients to the hospital. According to the results of a review on barriers and solutions for acute stroke management in Iran, almost every hospital emergency department suffered from delayed assessment of stroke patients and long door to needle time for intravenous tPA. Data from some centers in Iran in 2017 showed that it took 116 to 160 minutes for a final decision for stroke patients (25). Limited public knowledge of stroke warning signs (26) and false attitudes toward the availability and cost-effectiveness of stroke management had been also reported as possible reasons. Excluding some large cities, other cities such as small cities may fail to have the appropriate infrastructure or facilities to manage stroke patients. In Iran, the rapid patient transfer is also challenging (27). Improper triage is another time-wasting factor in stroke management (28). Other reasons include delayed imaging or laboratory evaluations, emergency department crowding, and a high limited capacity of diagnostic modalities.

Another important reason is probably the lack of up-to-date physicians' information in this field. The results of our study showed that only one-third of emergency physicians had up-to-date information based on recent articles and guidelines on tPA treatment in acute stroke, and most physicians had little or moderate knowledge in this area. Since the guidelines for intravenous tPA use have undergone substantial changes in recent years, continuous education and learning are of great importance. Thus, holding training courses and encouraging emergency physicians and other staff involved in stroke management to participate in these courses can play an important role in improving the use of tPA therapy in the management of acute stroke in Iran.

Despite the fact, according to the results of our study, only 50% of hospitals had a stroke team and about one-third of hospitals had no acute stroke protocol. Moreover, emergency physicians recommended no tPA for acute stroke in our study since there were no intensive care units for stroke in many centers to

Table 1. Demographic characteristics of participants in this study

Variable	Frequency		Percentage
		N	%
Age, year	Below 30 years	5	3.9
	30-40 years	71	55.5
	Above 40 years	52	40.6
Gender	Male	67	52.3
	Female	61	47.7
Occupation	EM Specialist	96	75
	EM resident	32	25
Work Experience	Below 5 years	65	50.8
	5-10 years	41	32
	Above 10 years	22	17.2
Type of hospital	Educational	91	71.1
	Non-educational	37	28.9
The number of stroke visit per week	0	9	7
	1-5	78	60.9
	more than 5	41	32
Stroke team available at hospital, yes		64	50
Availability of a stroke protocol at hospital, yes		85	66.4
General information regarding the use of tPA in stroke	Low information	11	8.6
	Moderate information	71	55.5
	Up-to-date according to recent articles and guidelines	46	35.9

Table 2. Logistic regression analysis for effective factors in EM physicians' knowledge and attitude to use tPA during AIS

Variable	OR ¹	95% CI ¹	p-value ¹	OR ²	95% CI ²	p-value ²
Age group (below 40 vs. above 40 years)*	0.336	0.130 – 0.865	0.024	1.266	0.546 – 2.937	0.582
Gender (male versus female)	1.519	0.660 – 3.495	0.325	0.989	0.443 – 2.208	0.978
Amount of information about tPA use in acute stroke (up-to-date information vs. low and general information)	3.475	1.242 – 9.723	0.018	1.1332	0.544 – 3.257	0.530
Degree of education, (specialist vs. resident)	1.018	0.354 – 2.930	0.973	2.424	0.929 – 6.327	0.070
Experience, years (1-5 yrs. vs. above 5 yrs.)	1.123	0.474 – 2.657	0.792	1.109	0.491 – 2.504	0.804
Type of working hospital, (educational vs. non-educational)	0.794	0.273 – 2.310	0.672	2.668	0.922 – 7.717	0.070
Number of stroke patients visited, (1-5 pts vs. above 5)	0.583	0.308 – 1.965	0.203	1.121	0.482 – 2.605	0.791
Availability of a stroke team at hospital, (yes vs. no)	1.274	0.419 – 3.870	0.670	0.866	0.287 – 2.617	0.799
Availability of stroke protocol at hospital, (yes vs. no)	1.389	0.454 – 4.244	0.565	0.797	0.264 – 2.401	0.686

A vs. B; A was compared with B in all logistic regression analyses. 1 for knowledge and 2 for attitude.

continue treatment and the fear of cerebral hemorrhage after prescribing tPA. Therefore, strengthening hospital infrastructure through the establishing stroke intensive care units and Telestroke consultation with neurologists together with the development of acute stroke management protocols in all hospitals, especially in small towns would promote the use of tPA. Furthermore, a 2010 cohort study in Michigan found that 95% of emergency medicine professionals were willing to prescribe tPA if an indication existed. Moreover, in the absence of a neurologist for counseling, 65% were willing to administer tPA and 67% would prescribe it after telephone counseling (29). Also, in an online survey in Saudi Arabia in 2018 on 122 physicians, about 50% of the participants agreed with the prescription of tPA and 41% opposed it. The main reasons for not recommending tPA included lack of proven effectiveness in their idea, risk of hemorrhagic complications, insufficient experience in stroke, and legal issues (15).

We had some limitations. First of all, due to the COVID-19 pandemic and hospital overload, only 128 of 400 invited physicians filled in the forms. Also, we failed to hold interventions to improve the outcome, therefore, it is suggested to perform similar studies to assess the effect of training courses in the management of AIS.

Conclusion

The knowledge and attitude of emergency physicians about intravenous tPA administration in the treatment of AIS were relatively high. Having up-to-date information and age >40 years were the major predictors of higher knowledge in AIS treatment. Lack of timely arrival of patients to the hospital, lack of intensive care units for stroke to continue treatment, and fear of bleeding and other tPA side effects were the most important barriers to drug administration in the treatment of AIS.

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Conflict of Interest

There was no conflict of interest.

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