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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

INTRAVENOUS THROMBOLYTIC THERAPY EXPERIENCE FOR ISCHEMIC STROKE PATIENTS IN A SECONDARY CARE HOSPITAL

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ABSTRACT

INTRODUCTION: This study, aims to show the intravenous thrombolytic therapy (IV-tPA) given to patients with ischemic stroke within the first 4.5 hours to affect prognosis according to demographic, etiological and clinical factors.
METHODS: The study was conducted retrospectively and included 26 acute ischemic stroke patients who only received intravenous thrombolytic therapy in Cankiri State Hospital between January 1, 2019, and January 1, 2020. Demographic information, risk factors, stroke etiologies, symptom to needle time were questioned. First and 24th hours NIHSS scores, pre-stroke, discharge, or first week and third month mRS scores and complications were evaluated.
RESULTS: It was determined that demographic, and etiological factors, ischemic stroke types and the time of IV-tPA administration did not affect prognosis in patients (p>0,05). It was shown that those with mild and moderate baseline and 1st-- hour NIHSS scores had a better prognosis than those with severe scores (p <0.05).
DISCUSSION AND CONCLUSION: The study showed that patients with a low NIHSS score at baseline had better 3rd-month mRS. In addition, it has been shown that thrombolytic therapy can be given,and complications can be managed in a secondary care hospital.
Keywords: Ischemic stroke, intravenous thrombolysis, secondary care hospital.

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İKİNCİ BASAMAK BİR HASTANEDE İSKEMİK İNME HASTALARINA İNTRAVENÖZ TROMBOLİTİK TEDAVİ DENEYİMİ

ÖZ

GİRİŞ ve AMAÇ: Bu çalışmada, iskemik inme geçiren hastalara ilk 4.5 saat içerisinde verilen intravenöz trombolitik tedavinin (IV-tPA), demografik, etyolojik, klinik faktörlere göre prognoza etkisinin gösterilmesi amaçlanmıştır.
YÖNTEM ve GEREÇLER: Çalışma retrospektif olarak yapılmış olup, çalışmaya 1 Ocak 2019-1 Ocak 2020 tarihleri arasında Çankırı Devlet Hastanesinde, sadece intravenöz trombolitik tedavi verilen 26 akut iskemik inme hastası dahil edilmiştir. Demografik bilgiler, risk faktörleri, inme etyolojileri, semptom başlangıcı ile trombolitik tedavi veriliş zamanı arasındaki süreleri sorgulandı. Birinci ve 24. saat NIHSS skorları, inme öncesi, taburcu ya da 1. hafta ve 3.ay mRS skorları ve komplikasyonlar değerlendirildi.
BULGULAR: Hastaların demografik, etyolojik ve iskemik inme nedenlerinin ve IV-tPA veriliş zamanının prognoza etkisinin olmadığı saptanmıştır ($p>0.05$). Başlangıç ve 1. saat NIHSS skoru hafif ve orta derecede olanların, ağır derecede skoru olanlara oranla daha iyi prognoza sahip olduğu gösterilmiştir ($p<0.05$).
TARTIŞMA ve SONUÇ: Çalışmada, başlangıçta NIHSS skoru düşük olan hastaların, 3. ay mRS'larının daha iyi olduğu gösterilmiştir. Ayrıca 2. basamak bir hastanede trombolitik tedavinin verilebileceği ve komplikasyonlarının yönetilebileceği de gösterilmiştir.

Anahtar Sözcükler: İskemik inme, intravenöz trombolizis, ikinci basamak hastane.

INTRODUCTION

Stroke is an important global health problem, and the importance of stroke will increase with the demographic changes that occur in developing countries as well as the increase in the elderly population (1). Stroke is the second most common cause of death in our country. In our country, the incidence of stroke is reported to be 177/100,000, and the prevalence is reported to be 254/100,000 (2).

In the treatment of patients with ischemic stroke, alteplase, a recombinant tissue plasminogen activator, is used for intravenous thrombolysis within 4.5 hours from the onset of symptoms (3). In the United States of America, the use of alteplase for intravenous thrombolytic therapy in ischemic stroke patients was approved in 1996 (4). Considering the losses of DALY (Disability Adjusted Life Year) due to death and disability associated with ischemic stroke, the importance of intravenous thrombolytic therapy and interventional therapies becomes more prominent.

In our study, we aimed to share our experiences with intravenous thrombolytic therapy in Çankırı.

METHODS

The study was conducted retrospectively through the files of IV-tPA patients administered by a single physician; and only the patients with acute ischemic stroke patients, who were administered intravenous thrombolytic therapy at Çankırı State Hospital between January 1, 2019 and January 1, 2020, were included in the study.

This study was conducted in accordance with the ethical standards specified in Helsinki Declaration, and was approved by the Karabük University Faculty of Medicine Non-Interventional Research Ethics Committee (No: 2020/307, Date: 27.08.2020).

Demographic information, risk factors, the etiology of stroke, time between onset of symptoms and the time of administration of thrombolytic therapy were inquired. NIHSS (National Institute of Health Stroke Scale) scores at baseline, first hour and 24 hours were evaluated along with the mRS (modified Rankin Scale) scores before the stroke, at discharge, or at the 1st week and 3rd month and the complications. In our study, the NIHSS score was classified into two groups as 15 and below, and over 15. In mRS scoring, scores between 0-2 were defined as independent and the scores between 3-5 were defined as dependent.

In the classification of the cause of ischemic stroke, the classification described in the Org 10172 Study in Acute Stroke Treatment was used (5). The suitability of the patients for IV-tPA was determined according to existing stroke guidelines (6, 7). IV-tPA was administered to all

patients within 4.5 hours (270 minutes) from the onset of symptoms, at a dose of 0.9 mg/kg. Brain computed tomography imaging of all patients was performed in the emergency department. Patients, who did not receive interventional treatment after IV-tPA, were included in the study. IV-tPA was administered to the patients in the general intensive care unit. Control brain computed tomography imaging was performed in all patients 24 hours after the administration of IV-tPA. Hemogram, coagulation and biochemical tests, lipid profile, electrocardiography, echocardiography and carotid vertebral ultrasonography tests were performed for all patients included in the study. Magnetic resonance imaging, MR-angiography and 24-hour rhythm Holter recording were performed for the patients, where necessary.

Patients, who were administered IV-tPA, were followed up in the Neurology outpatient clinic, and their information was also filed. The 3rd month mRS scores were obtained from the information on these files. The mRS scores ≤2 were considered as good prognosis, and the mRS scores ≥3 were considered as poor prognosis.

IBM SPSS Statistics Version 20.0 software was used for the statistical analysis of the data. The categorical variables were presented as numbers and percentages. The numerical measurements were presented as mean and standard deviation (with the median and minimum/maximum values when necessary). The inter-group comparisons of the categorical variables were performed with the Chi-square test. The level of statistical significance was accepted as 0.05 in all tests.

RESULTS

The mean age of the 26 patients included in the study was 71 (71.42 ± 14.58). Table 1 presents the details regarding demographic data, risk factors and distribution of ischemic stroke etiologies of the patients included in the study.

The mean period of initiation of IV-tPA to the patients was determined as 177.57 ± 49.3 minutes. Before the administration of IV-tPA, the mean NIHSS was 13.76 ± 4.84; and the mean of NIHSS at the 1st hour after the administration of IV-tPA was 10.84 ± 5.89. The mean of the 24th hour NIHSS was evaluated as 9.11 ± 6.41. In the follow-up after the administration of IV-tPA, 11.5% (n= 3) of the patients developed intracerebral hemorrhage and

Table 1. Demographic data of patients.

	N= 26 (%)
Gender	Male 12 (46.2)
	Female 14 (53.8)
Hypertension	21 (80.8)
Diabetes Mellitus	7 (26.9)
Coronary Artery Disease	10 (38.5)
Hyperlipidemia	11 (42.3)
Smoking	11 (42.3)
Atrial Fibrillation	14 (53.8)
Stroke type	
Cardioembolic	19 (73.1)
Small Artery Disease	4 (15.4)
Large Artery Disease	2 (7.7)
Unknown	1 (3.8)

7.7% (n= 2) of the patients developed infections, while no complications occurred in 80.8% (n= 21). Of the patients, 15.3% (n= 4) died. Two of these 4 patients died due to septic shock secondary to pneumonia, and the other 2 died due to cardiac reasons.

The proportion of patients under 80 years of age was 65.4% (n= 17), and 34.6% (n= 9) of the patients were 80 and older. The pre-ischemic stroke mRS score was 1 in three patients, while the other 23 patients had a mRS score of 0. The mean mRS at the 1st week/discharge was 3.65 ± 2.01, and the mean mRS at the 3rd month was 2.84 ± 2.23. Of the patients, 34.6% (n= 9) had the first week/discharge mRS scores between 0 and 2, 65.4% (n= 17) had the first week/discharge mRS scores between 3 and 6. The percentage of the patients with the 3rd month mRS scores between 0 and 2 was determined as 42.3% (n= 11), and the percentage of the patients with the 3rd month mRS scores between 3 and 6 was determined as 57.7% (n= 15). The pre-treatment NIHSS score was found to be 15 and below in 61.5% (n= 16) of the patients, and 38.5% (n= 10) had pre-treatment NIHSS scores above 15. The percentage of the patients with 1st hour NIHSS score of 15 and below was 76.9% (n= 20), and the percentage of the patients with 1st hour NIHSS score above 15 was 23.1% (n= 6). It was found that 84.6% (n= 22) of the patients had 24th hour NIHSS score of 15 or below, and 15.4% (n= 4) of the patients had 24th hour NIHSS scores above 15. Intravenous thrombolytic treatment was administered to 53.8% (n= 14) of the patients in the first 180 minutes, while 46.2% (n= 12) were administered between 181-270 minutes.

When the age, gender, duration of IV-tPA

administration, risk factors (hypertension, diabetes mellitus, coronary artery disease, hyperlipidemia, smoking, atrial fibrillation), stroke types of the patients included in the study were compared with the 3rd month mRS scores, no statistically significant difference was found (p>0.05). When the NIHSS scores calculated before the administration of IV-tPA and the 1st hour NIHSS scores were compared with the 3rd month mRS scores, a statistically significant difference was found (p<0.05). When the 24th hour NIHSS scores were compared with the 3rd month mRS scores, no significant difference was found (p>0.05) (Table 2).

Table 2. Comparison of demographic data, etiological reasons, stroke types and NIHSS scores with 3rd month mRS scores.

Variables		Independent-Good Prognosis mRS (0-2) (n)	Dependent-Poor Prognosis mRS (3-6) (n)	p
Age	<80	8	9	0.683
	≥80	3	6	
Gender	Male	8	4	0.054
	Female	3	11	
Time of ITT administration	0-180 min	8	6	0.209
	181-270 min	3	9	
Hour 0 NIHSS score	≤15	10	6	**0.014**
	>15	1	9	
1st hour NIHSS score	≤15	11	9	**0.024**
	>15	0	6	
24th hour NIHSS score	≤15	11	11	0.113
	>15	0	4	
Ischemic Stroke Type	Cardioembolic	8	11	0.267
	Small artery disease	1	3	
	Large artery disease	2	0	
	Unknown	0	1	
Hypertension	Yes	9	12	1.000
	No	2	3	
Diabetes Mellitus	Yes	3	4	1.000
	No	8	11	
Coronary Artery Disease	Yes	5	5	0.689
	No	6	10	
Hyperlipidemia	Yes	5	6	1.000
	No	6	9	
Smoking	Yes	7	4	0.109
	No	4	11	
Atrial Fibrillation	Yes	5	9	0.736
	No	6	6	

DISCUSSION AND CONCLUSION

Patients who underwent IV-tPA in a secondary hospital, were retrospectively analyzed, and the mean duration of IV-tPA administration was found to be 177.57 ± 49.3 minutes. In the AHA/ASA 2018 guidelines, the first goal was determined to be at least 50% of patients to be administered IV-tPA in the first 60 minutes (8). In fact, recent studies suggest that IV-tPA should be administered within the first 20-30 minutes after the patient presents to the emergency department (4). In our study, it was observed that the time of IV-tPA administration was later than the recommended durations. This was believed to be due to reasons such as not being familiar with this treatment and the steps during patient referral and the procedure, insufficient understanding regarding the importance of the treatment, and the lack of certain technical infrastructures.

In our study, when the dependency levels of the age groups below 80 and over 80 years old were compared, no significant difference was found (p= 0.683). This indicates that there is no relationship between age and prognosis in patients, who were administered IV-tPA. Thus, when the age group of 80 and above and the age group of below 80 and below were compared within the combined analysis of "Virtual International Stroke Trials Archive" (VISTA) and

"Safe Implementation of Treatments in Stroke" (SITS), it was demonstrated that there was no difference in the effectiveness of IV-tPA (9). In addition, it was found that the gender of the patients, who were administered IV-tPA, had no effect on prognosis (p= 0.054).

When the risk factors of patients, who were administered IV-tPA, were examined, atrial fibrillation was noted with a rate of 53.8%. Hypertension was observed at a rate of 80.8%. In addition, when the etiologies of ischemic stroke were examined, cardioembolic causes were found as 73.1%. When the ECASS III, WAKE-UP, SITS-MOST studies were examined, it was noteworthy that the rates of atrial fibrillation, hypertension and cardioembolic stroke were significantly higher in our study (3,10,11).

Looking at the data in the literature, it was observed that the administration of IV-tPA in the first 4.5 hours would be beneficial. In addition, it was found that thrombolysis performed for 180-270 minutes did not yield as good results as the administration in the first 180 minutes (12-14). In our study, the mRS scores of the patients, who were administered IV-tPA between the first 180 minutes and 180-270 minutes, were compared, and no statistical significance was determined (p= 0.209). This was believed to be related with the low number of patients.

It was determined that patients with NIHSS score of 15 and below at the time of the symptom onset had better results with IV-tPA compared to patients with a NIHSS score of above 15 (p= 0.014). It was also found statistically significant that patients with a 1-hour NIHSS score of 15 and below had a better prognosis compared to patients with a NIHSS score of 15 or above (p= 0.024).

In our study, it was found that types of ischemic stroke (large artery disease, small artery disease, cardioembolic, unknown) did not differ in terms of prognosis after the administration of IV-tPA (p= 0.267). In addition, risk factors of ischemic stroke (hypertension, diabetes mellitus, coronary artery disease, hyperlipidemia, smoking, atrial fibrillation) were found to have no effect on prognosis (p>0.05).

Non-fatal intracerebral hemorrhage developed in 11.5% (n= 3) of the patients, who were administered intravenous thrombolytic therapy. Septic shock developed in 2 (7.7%) patients. 15.4% of the patients (n= 4) died. In the ECASS III study, the rate of any intracerebral hemorrhage was 27%, and the rate of fatal intracerebral hemorrhage was found to be 0.7% in the group of patients administered IV-tPA between 3 and 4.5 hours. Mortality rate was determined as 7.7%. The infection rate was found to be 3.8% (10). In the light of this information, the rate of intracerebral hemorrhage was found to be lower in our study, and no fatal intracerebral hemorrhage was observed. Mortality rate was notably high in our study. The reason for this was predicted as the small number of patients.

As a result, we believe that IV-tPA treatment can be administered in a secondary hospital, and its complications can be managed. We believe that similar studies would further encourage and motivate neurologists working under similar conditions in terms of administering IV-tPA to the suitable patients.

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Ethics

Ethics Committee Approval: The study was approved by the Karabuk University Faculty of Medicine Noninterventional Clinical Studies Ethics Committee (Number: 2020/307, Date: 27.08.2020).

Informed Consent: This study is an retrospective analysis, there is no need an informed consent.

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