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The influence of early thrombolysis on C-reactive protein values and functional outcome after acute ischemic stroke.

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Abstract

The aim of the study was to evaluate the effectiveness of early thrombolysis of patients after acute ischemic stroke on C-reactive protein (CRP) values and functional improvement. From 62 patients with acute ischemic stroke that were evaluated, 32 received thrombolytic therapy (Group A), and 30 were without thrombolytic therapy (Group B). Degree of the neurological deficit was evaluated by the functional independence measure (FIM) test at the admission and after early rehabilitation program (14 days after admission). We found significant increase in FIM values ($p<0.01$) and significant decrease for CRP values ($p<0.01$) after early rehabilitation program. Concerning thrombolytic therapy administration, there is significant correlation between FIM values ($p<0.01$) and between CRP values ($p<0.01$) at admission and after 14 days in both group of patients. The group that received thrombolytic therapy after early rehabilitation program showed significant negative correlation between FIM and CRP values ($p<0.05$). Our study pointed out that thrombolytic therapy applied according to the protocol for the acute ischemic stroke in the stroke unit might increase better functional recovery of these patients.

Keywords: Stroke, Thrombolysis, C-Reactive Protein, Functional Outcome, Rehabilitation.

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Introduction

Thrombolytic therapy for the treatment of intracranial artery occlusion with recombinant tissue plasminogen activator (rtPA) is shown to improve circulation thus it is used for the treatment of patients with acute ischemic stroke [1]. Previous studies reported benefits of thrombolytic therapy for the patients with acute ischemic stroke [2,3]. Despite the fact that the results of the thrombolytic therapy are promising ones, it should be noticed that only a few of patients who have had acute ischemic stroke satisfy the protocol rules to get thrombolytic therapy. This is mainly to the fact of short therapeutic window. However, in the study of IST-3 collaborative group et al., it was stated that improvement of functional outcome is noticed even when thrombolysis was performed within 6 hours after acute ischemic stroke [4]. Bearing in mind that rehabilitation in patients with acute ischemic stroke was proven to influence recovery and improves functional outcome, we hypothesized that applied thrombolytic therapy might, additionally along with rehabilitation treatment, improve functional gains in these patients.

Previously it was noticed that the elevated C-reactive protein (CRP) values could be considered as a risk factor for the ischemic stroke [5,6]. It was stated as well that the CRP might be the independent predictor as a risk marker for the future stroke [6].

The aim of the study was to evaluate the effectiveness of early thrombolysis of patients after acute ischemic stroke on C-reactive protein (CRP) values and functional improvement.

Patients and Methods

Study group

In our prospective study we have evaluated 62 patients that were admitted to the special hospital for Cerebrovascular diseases hospital "St. Sava", for the treatment of acute ischemic stroke. The patients were randomly selected for the

protocol data. The study followed the principles of good clinical practice and was approved by Institutional Review Board. Prior inclusion into the study, patients were evaluated by board certified Neurologists, Internists and Physiatrists.

Study parameters

Regarding the administration of thrombolytic therapy, 32 patients with acute ischemic stroke received thrombolytic therapy, according to the protocol for application of the recombined tissue plasminogen-rTPA, at the hospital "St Sava" (Group A), while 30 patients were treated with standard procedures without implementation of thrombolytic therapy (Group B). The patients were randomly selected into above mentioned groups after informed consent from patient or legal guardian in cases where patients were not in a position to make independent decisions.

The CRP was obtained from blood samples that were collected from patients that were admitted due to the ischemic stroke. Serum concentrations of CRP were used for the findings interpretation.

Early rehabilitation of eligible participants started after stabilization of vital parameters, on average between 24-36 hours after the acute ischemic stroke. Early rehabilitation was performed according to the individual programme. Degree of the neurological deficit at the admission to the hospital and after the completed early rehabilitation was determined by the functional independence measure (FIM) test. FIM test is widely used to assess degree of functional independence in numerous conditions. It is considered to be reliable tool for estimation of functional status changes during defined periods of time, and is consisted of 18 categories graded from 1-7 each [7]. On two occasions FIM was measured: at admission and after early rehabilitation program (14 days after admission).

Statistical analysis

The findings were presented as mean values with standard deviation (MV ± SD). Mann Whitney U test for two independent samples was used for statistical evaluation of FIM and CRP changes, between patients who received thrombolytic therapy and those who did not receive it (Group A/Group B) at admission and after early rehabilitation program. Wilcoxon signed rank test for comparisons of two related samples was used to assess statistical difference of FIM and CRP changes, in Group A and Group B respectively, between admission and after early rehabilitation program. To evaluate degree of FIM correlations between admission and after early rehabilitation program we used Spearman's rank correlation. Pearson correlation was used for comparisons of FIM and CRP values between patients who received thrombolytic therapy and those who did not receive it (Group A/Group B), both at admission and after early rehabilitation program. Statistical significance was set at $p<0.05$.

Results

There is no significant difference in CRP and FIM values between Group A and Group B at admission ($p>0.05$), while such difference exists 14 days after admission for both parameters, where we have noticed significant increase for FIM values in Group A ($p<0.01$) and significant decrease for CPR values in Group A ($p<0.01$) (Table 1). The CRP values in study group ranged from 17 to 83 mg/L. There is significant decrease in CRP values and significant increase in FIM values after 14 days post admission in both study groups ($p<0.01$) (Table 1).

Table 1. *CRP and FIM values in different study groups (Group A and Group B).*

	Group A		Group B		p value Group A /Group B
	(MV ± SD)	p value	(MV ± SD)	p value	
FIM at admission	47.82 ± 18.76	<0.01*	48.33 ± 19.29	<0.01*	>0.05**
FIM 14 days after admission	90.57 ± 33.81		62.71 ± 22.86		<0.01**
CRP at admission	37.61 ± 16.52	<0.01*	43.84 ± 18.27	<0.01*	>0.05**
CRP 14 days after admission	25.87 ± 14.66		31.49 ± 17.81		<0.01**

*Wilcoxon Signed Rank test; *Mann Whitney U test

In the group of patients who received thrombolytic therapy, there is significant correlation between FIM values at admission and 14 days after admission (Spearman's correlation=0.73; $p<0.01$) and between CRP values at admission and 14 days after admission (Spearman's correlation=-0.68; $p<0.01$) (Table 2). In same group of patients, there is non-significant negative correlation between FIM values and CRP values at admission (Pearson correlation=-0.21; $p>0.05$) while 14 days after admission there

was significant negative correlation (Pearson correlation=-0.43; p<0.05) (Table 2).

Table 2. Correlations between CRP and FIM values in different study groups (Group A and Group B).

	Group A		Group B	
	Correlation	p value	Correlation	p value
FIM (at admission/14 days after admission	0.73*	<0.01	0.77*	<0.01
CRP (at admission/14 days after admission	-0.68*	<0.01	-0.64*	<0.01
CRP/FIM values at admission	-0.21**	>0.05	-0.27**	>0.05
CRP/FIM values 14 days after admission	-0.43**	<0.05	-0.31**	>0.05

*Spearman's correlation; **Pearson correlation

For the patients who did not received thrombolytic therapy, there is as well significant correlation between FIM values at admission and 14 days after admission (Spearman's correlation=0.77; p<0.01) and between CRP values at admission and 14 days after admission (Spearman's correlation=-0.64; p<0.01) (Table 2). In same group of patients, there is non-significant negative correlation (Pearson correlation=-0.27; p>0.05) between FIM values and CRP values at admission, and 14 days after admission (Pearson correlation=-0.31; p>0.05) (Table 2).

In Figure 1 we presented the presence of focal changes in patient after acute ischemic stroke, and in Figure 2, resolution of focal changes 14 days after thrombolytic treatment in same patient.

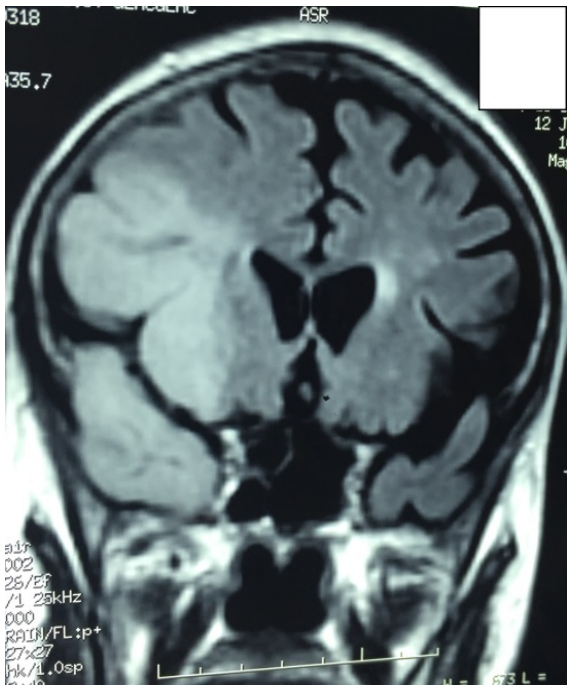

Figure 1. *MRI of focal area at admission.*

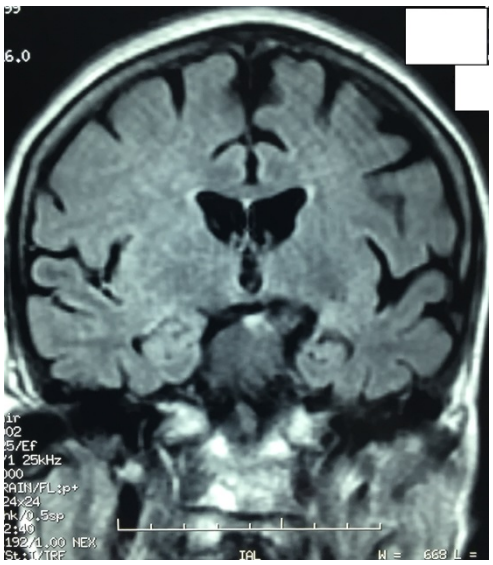

Figure 2. *MRI after 14 days from admission.*

Discussion

Previous studies underlined the importance of rehabilitation treatment in patients who suffered acute ischemic stroke [8-11]. The main role of rehabilitation for these patients is to prevent possible complications that might appear due to the inactivity; prevent functional, cognitive and social impairments, as well to improve patients' quality of life [12]. On-time and early implementation of rehabilitation treatment in patients with acute ischemic stroke reduces the complications frequency, mortality and duration of hospitalization [13]. The importance of early beginning of rehabilitation treatment in these patients relies on the fact that rehabilitation efficacy correlates to the certain degree with: period between stroke onset and the beginning of rehabilitation treatment, and treatments duration and intensity [13]. To achieve optimal rehabilitation program for the treatment of patients who suffered acute ischemic stroke, the one should be individually planed and specialized multidisciplinary neuro-rehabilitation team should be involved.

Positive effects of short-term functional improvement were described in elderly who suffered acute ischemic stroke. It was also stressed out that FIM at admission might be to the certain degree of importance as predictive factor for recovery [8-10]. Our findings are consisted with previous reports, where we have achieved significant increases in functional levels measured by FIM over the period of early rehabilitation program. The significant correlation of FIM values between different times of observation in our study for both study groups suggests that patients with higher FIM values at admission are expected to have increased potential of obtaining higher FIM values after 14 days of early rehabilitation.

The importance of rehabilitation program in functional improvement of patients who suffered recurrent ischemic stroke was demonstrated previously as well, underlying that even patients with recurrent ischemic stroke have benefit of rehabilitation in terms of FIM changes between admission and discharge periods [14].

From the results of our study it is demonstrated that patients with thrombolytic treatment have higher FIM scores, 14 days after admission, versus those who were not included into the thrombolytic treatment. These findings are in correlation with previous reports which stated that acute stroke patients which undergo thrombolytic treatment and rehabilitation program, gain improvement faster and to a larger extent [15]. Therefore, it could be assumed that other factors, aside rehabilitation treatment, might play certain role in functional improvements of patients who suffered acute ischemic stroke.

As for the FIM scores over the defined times of observation in our study, we have also pointed out the presence of significant negative correlation between CRP for both study groups. Thus, it could be assumed to the certain degree, that early thrombolytic therapy has not significant influence on CRP values changes over the first 14 days after discharge.

Our findings stressed out to the possible influence of early thrombolytic therapy on better functional outcome in ischemic stroke patients 14 days after admission with lower CRP values, since we have noticed the presence of significant negative correlation between CRP and FIM during this period of study observation. The possible mechanism that could explain such claims is in the fact of faster and better reperfusion as a consequence of early thrombolytic therapy with lesser tissue damage as well.

The limitation of the study is a small number of patients, and thus further studies are needed on larger samples to evaluate the role of thrombolytic therapy in functional recovery improvement after acute ischemic stroke.

Given the facts above, from our study findings, it should be pointed out that thrombolytic therapy applied according to the protocol for the acute ischemic stroke in the stroke unit might increase better functional recovery of these patients.

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