ORIGINAL ARTICLE

PROSPECTIVE PILOT STUDY TO ASSESS MOTOR ACTIVITY AND THE STATE OF THE HEMOSTASIS SYSTEM IN THE ACUTE PERIOD OF ISCHEMIC STROKE DURING SYSTEMIC THROMBOLYTIC THERAPY

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Yaroslava Yu. Havlovska, Nataliya V. Lytvynenko, Oleksandr L. Havlovskiy, Anastasia D. Shkodina
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To investigate changes in motor activity and indicators of the state of the hemostasis system in the acute period of ischemic stroke during systemic thrombolytic therapy and without its use.

Materials and methods: We examined 26 male and female patients with a clinical diagnosis of ischemic stroke, who were hospitalized on the first day of the disease to the neurological departments. Patients were divided into 2 groups: group 1-patients who underwent systemic thrombolytic therapy (sTLT) (n=11), group 2-patients who did not receive sTLT (n=15). To compare the coagulogram parameters, 12 healthy patients were examined (control group). Examination of patients was performed on the 1st and 14th day of the disease (clinical examination, assessment of motor activity, coagulation test). Stroke severity was determined by the overall score of the National Institutes of Health Stroke Scale.

Results: The average age of patients in group 1 - 60.1±8.2 years old, in group 2 -61.3±5.5 years old. The number of points on the NIHSS scale in group 1 was 8.8±1.13 on 1st day and 3.7±0.79 on 14th day ($p<0.05$), in group 2 -5.7±0,94 on the 1st day and 3.1±0.93 on the 14th day($p<0.05$). The results of the study of the coagulogram indicate a significantly higher level of soluble fibrin-monomer complexes on the 1st day on the 14th day of the ischemic stroke.

Conclusions: In the acute period of ischemic stroke changes in the hemostasis system reflected the direction of the selected therapy. The use of systematic thrombolytic therapy in ischemic stroke led to a more severe decrease in stroke severity on the NIHSS scale, a significant increase in Barthel index.

KEY WORDS: Ischemic stroke, hemostasis system, systematic thrombolytic therapy, motor activity

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INTRODUCTION

Ischemic stroke (IS) is a worldwide problem that is relevant to both economically developed countries and developing countries. Every year, about 17 million cases of stroke are registered in the world (in the European Union - 1.75 million, in the United States - 700 thousand). Among them 6 million people die from stroke and its complications) [1].

According to modern international studies in the structure of cardiovascular pathology, the proportion of stroke is bigger than such a myocardial infarction by about 30% (the so-called "stroke paradox"). In Ukraine IS remains one of the main causes of disability, which significantly reduces the quality of life and working potential [2]. The incidence of IS in Ukraine is 280-290 cases per 100 thousand populations and exceeds the average incidence of IS in economically developed European countries (200 per 100 thousand population). According to official statistics, 40 to 45 thousand people die of stroke in Ukraine every year [3].

International protocols recommend systemic thrombolytic therapy (sTLT) as one of the main methods of treatment, which can significantly reduce the number of unwanted effects [4]. However, it should be noted that the effect of sTLT depends on the initial state of the hemostasis system, which directly affects the recovery process of patients in the acute period of IS [5].

Motor disorders in the post-stroke period develop among 3/4 of patients and most patients have got a persistent motor defect. By the end of the acute period of IS, among the motor disorders in patients, paresis of the extremities of moderate or mild degree is most often observed, which partially depends on the location of the stroke [6]. Deficiency of motor function due to stroke affects the mobility of patients, their limitations in everyday life, social aspects of functioning, which leads to a low probability of returning to the professional activity. All these factors contribute to the reduction of the quality of life of patients. Both modern treatments and innovative rehabilitation methods used to restore lost functions are an important aspect in the management of patients with IS.

It is known that the hemostasis system is interrelated with the dynamics of recovery of lost neurological functions, mainly in the acute period of IS [7]. Thus, the prognosis of illness depends on the initial state of the hemostasis system. The conjugation of hemostasis activation processes with the severity of the disease and the degree of reversibility of neurological symptoms allows

to assess the state of compensatory mechanisms of the blood-vascular wall among patients in the dynamics of acute and recovery periods of IS and predict their course and result. Hypercoagulation is a common hemostasiological manifestation of the acute stage of IS [8]. A better understanding of the state of the hemostasis system at IS with and without sTLT is clinically useful and can lead to increased treatment effectiveness [9].

Thus, the question of studying changes in motor functions and the hemostasis system in the acute period of ischemic stroke under sTLT and without its use remains relevant. The obtained results will allow to consider the possibility of optimizing the restoration of motor functions taking into account the state of the hemostasis system.

THE AIM

To Investigate changes in motor activity and indicators of the state of the hemostasis system in the acute period of IS during sTLT and without its use.

MATERIALS AND METHODS

A prospective cohort design was chosen for the pilot study. We examined 26 male and female patients with a clinical diagnosis of IS, who were hospitalized on the first day of the disease to the neurological departments of Poltava Regional Clinical Hospital and Poltava City Clinical Hospital №1. Inclusion criteria defined: acute period of ischemic non-lacunar stroke (mild and moderate stroke according to the National Institutes of Health Stroke Scale - NIHSS <15), ischemic stroke in the carotid pool, clear consciousness or a state of mild stupor (13 - 15), age from 50 to 80 years, no history of stroke. Exclusion criteria: severe condition of the patient (constipation or coma at the time of hospitalization), concomitant pathology that impairs motor function, history of stroke. Depending on the results of the clinical examination, patients were divided into 2 groups: group 1 - patients who underwent systemic thrombolytic therapy (sTLT) (n = 11), group 2 - patients who did not receive sTLT (n = 15). To compare the coagulogram parameters, 12 healthy patients were examined (control group). Patients of groups 1 and 2 underwent infusion, antihypertensive, antiplatelet therapy II in accordance with international and domestic protocols. Examination of patients was performed on the 1st and 14th day of the disease (clinical examination, assessment of motor activity, coagulation test). All patients were informed about the possible benefits and outcomes of participating in the study and gave informed consent to participate in the study. The study was conducted in accordance with the requirements of the Declaration of Helsinki.

Stroke severity was determined by the overall score of the NIHSS scale. Assessment of activity in everyday life according to the Barthel index (BI). The state of the hemostasis system was studied by analysis of an extended coagulogram, which included: prothrombin index, prothrombin time, international normalized ratio, thrombin time, activated partial thromboplastin time, concentration of fibrinogen and soluble fibrin-monomer complexes.

Quantitative data are presented in the form of arithmetic mean (M) and standard error (**σ**). The difference between the indicators on the 1st and 14th day of the disease was determined by a paired T-test for normally distributed. Differences between the three groups for coagulogram parameters were detected by one-way analysis of variance ANOVA with Bonferroni correction, and to compare BI in the two groups used a T-test for independent samples. The results were considered statistically significant at $p < 0.05$ [10].

RESULTS AND DISCUSSION

The average age of patients in group 1 - 60.1 ± 8.2 years old, in group 2 - 61.3 ± 5.5 years old. No significant difference in age and sex between groups was found. The number of points on the NIHSS scale in group 1 was 8.8 ± 1.13 on 1st day and 3.7 ± 0.79 on 14th day ($p < 0.05$), in group 2 - 5.7 ± 0, 94 on the 1st day and 3.1 ± 0.93 on the 14th day ($p < 0.05$). We did not find significant differences between the quantitative indicators of the scale of stroke severity in groups of patients on both the 1st and 14th day. At the same time, it was found that in group 1 (using sTLT) on the 14th day the NIHSS scale decreased by 58.0% compared to 45.6% in group 2 (without sTLT).

Physical activity was assessed by the index of activity in everyday life (BI), as shown in Figure 1.

BI in group 1 was 49.1 ± 7.03 points on the 1st day and 82.3 ± 4.88 points on the 14th, which corresponded to a pronounced and mild dependence. It should be noted that BI among patients of this group on the 14th day increased by 33.2 points (40.3%).

In group 2 the average value of BI on the 1st day was 76.7 ± 4.54 points, which corresponded to a moderate dependence in everyday life and was significantly higher than the same indicator in the group 1 ($p < 0.05$). On the 14th day of the disease among patients of group 2 BI had no significant dynamics compared with the onset of the disease and amounted to 83.0 ± 7.06 points ($p > 0.05$), which corresponded to a slight dependence in everyday life. There were no statistically significant differences between groups by BI on the 14th day. The increase in activity in everyday life was 6.3 points (7.6%), which was significantly lower compared to group 1.

Table I shows the data of the study of coagulogram parameters in groups of patients on the 1st day of IS.

The results of the study of the coagulogram shown in Table I indicate a significantly higher level of soluble fibrin-monomer complexes on the 1st day on the 14th day of the IS compared with the control group. At the same time, the indicator was significantly higher in group 1, which is quite natural when conducting sTLT. No statistically significant differences between groups on other indicators were found.

The dynamics of coagulogram parameters in group 1 of patients are shown in table II.

There was a significant decrease in the level of soluble

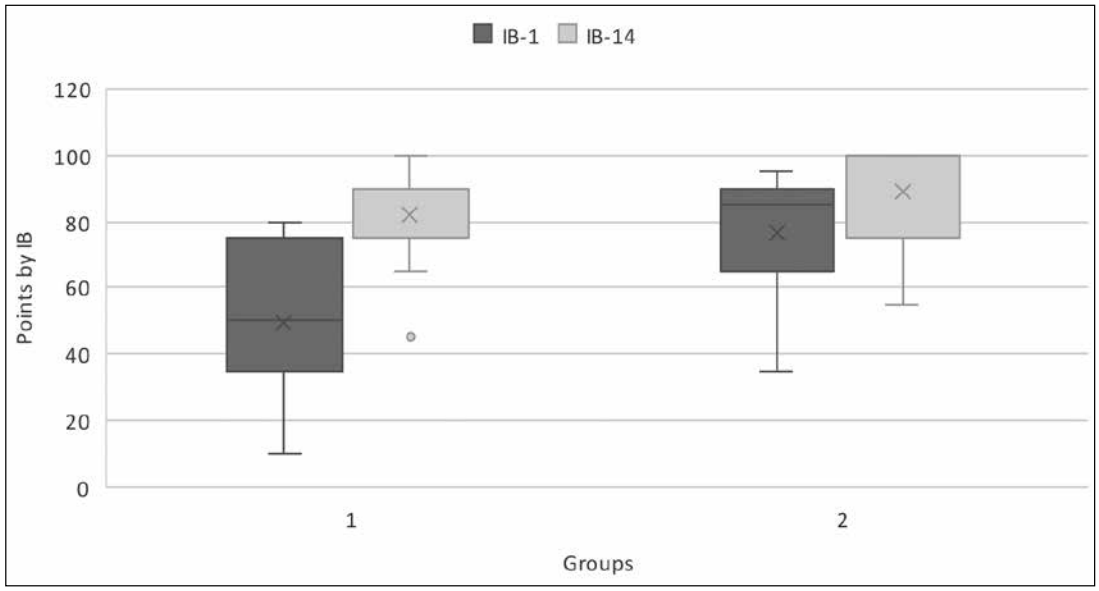

Fig. 1. Assessment of activity in daily life for BI in groups 1 and 2 on the 1st and 14th day of the disease.

Table I. Indicators of coagulogram in the control, 1 and 2 groups of patients on the 1st day of IS

Indicator	Groups		
	Control group (n=10)	Group 1 (n=11)	Group 2 (n=15)
Prothrombin index, %	92,83±4,57	101,1±3,93	94,17±4,5
Prothrombin time, s	11,89±0,33	11,61±0,28	12,21±1,08
International normalized ratio	0,95±0,03	0,9±0,3	0,99±0,05
Thrombin time, s	9,88±0,12	9,95±0,19	9,68±0,38
Activated partial thromboplastin time, s	29,5±1,12	27,11±1,1	27,46±1,26
Fibrinogen, g/l	3,58±0,26	3,11±0,36	4,24±0,33
Soluble fibrin-monomer complexes, ng/ml	2,7±0,28	17,6±1,23*	12,89±1,46* **

Note: * - p <0.05 relative to the Bonferroni correction control group
** - p <0.05 between groups 1 and 2

fibrin-monomer complexes in group 1 on the 14th day compared with the 1st day (p <0.05), while soluble fibrin-monomer complexes on the 14th day of the disease was significantly higher than the values in the control group (11.7 ± 1.83 ng/ml in group 1 compared with 2.7 ± 0.25 ng/ml in the control group, p <0,05). From other indicators of the coagulogram significant changes were not revealed.

The dynamics of coagulogram parameters in group 2 patients are shown in table III.

The results of the study of the indicators of the hemostasis system in group 2 on the 1st and 14th day of IS indicated the absence of significant changes in the state of the hemostasis system. It should be emphasized that the level of soluble fibrin-monomer complexes in the control group was significantly higher than the value in groups 1 and 2 on both the 1st and 14th day of the disease, while in group 2 on the 14th day had a tendency to increase (14.33 ± 1.81 ng/ml on the 14th day against 12.89 ± 1.46 ng/ml on the 1st day, p <0.1).

In the acute period of IS changes in hemostasis naturally reflected the direction of the selected therapy. All patients with acute IS had elevated levels of soluble fibrin-monomer complexes, a marker of thrombinemia. In group 2 (without sTLT) there was a tendency to further increase the level of soluble fibrin-monomer complexes on the 14th day, which reflected the activity of thrombosis [11].

Restoration of motor functions among patients of group 1 in the acute period was more severe. Mild dependence persisted in the daily activities of patients who underwent sTLT. The best results of recovery of activity in everyday life in patients with IS in the acute period, who underwent sTLT, may be due to the rapid recanalization of occluded vessels and systemic effects on microcirculation [10].

CONCLUSIONS

In the acute period of IS, changes in the hemostasis system reflected the direction of the selected therapy. The use of sTLT in IS led to a more severe decrease in stroke severity on the NIHSS scale, a significant increase in BI on the 14th day of the disease compared with group 2 (without the use of sTLT). On the 1st day of IS there was a significant increase in the concentration of soluble

Table II. Coagulogram parameters in patients of group 1 on the 1st and 14th day of IS.

Indicator	Period	
	1-st day (n=11)	14-th day (n=11)
Prothrombin index, %	101,1±3,93	105,6±3,45
Prothrombin time, s	11,61±0,28	11,85±0,3
International normalized ratio	0,9±0,3	0,91±0,02
Thrombin time, s	9,95±0,19	10,06±0,21
Activated partial thromboplastin time, s	27,11±1,1	29,75±1,07
Fibrinogen, g/l	3,11±0,36	3,59±0,21
Soluble fibrin-monomer complexes, ng/ml	17,6±1,23	11,7±1,83 *

Note: * - p <0.05 - reliability index in group 1 on the 1st and on the 14th day of the IS

Table III. Coagulogram parameters in patients of group 2 on the 1st and 14th day of IS.

Indicator	Period	
	1-st day (n=15)	14-th day (n=15)
Prothrombin index, %	94,17±4,5	96,33±3,5
Prothrombin time, s	12,21±1,08	11,09±0,93
International normalized ratio	0,99±0,05	0,97±0,03
Thrombin time, s	9,68±0,38	10,1±0,32
Activated partial thromboplastin time, s	27,46±1,26	27,35±1,01
Fibrinogen, g/l	4,24±0,33	3,76±0,36
Soluble fibrin-monomer complexes, ng/ml	12,89±1,46	14,33±1,81

Note: * - p <0.05 - reliability index on the 1st and 14th day of the IS

fibrin-monomer complexes in both groups of patients with significantly higher levels in group 1. On the 14th day of IS in both groups of patients there was a high level of soluble fibrin-monomer complexes compared with the control group with a significant decrease in soluble fibrin-monomer complexes in group 1 and growth in group 2. The above changes may require further study of the possibility of optimizing the treatment of this cohort of patients taking into account changes in the hemostasiological properties of blood.

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ORCID and contributionship:
Yaroslava Yu. Havlovska: 0000-0002-7199-4183 [A, B, D, E]
Nataliya V. Lytvynenko: 0000-0002-4889-3608 [A, F, E]
Anastasia D. Shkodina: 0000-0002-7198-5498 [C, D]
Oleksandr L. Havlovskiy: 0000–0002–7799–9938 [B, E]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Yaroslava Yu. Havlovska
Poltava State Medical University
23 Shevchenko St., 36000 Poltava, Ukraine
tel: +380961180685
e-mail: yarapl94@gmail.com

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