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# Changes in coagulation in patients with ischemic stroke

**Khramtzov D.N., Vikarenko M.S., Kozlova G.G., Vorokhta Y.N.**

**University Clinic of Odessa National Medical University, Odessa, Ukraine**

Summary

Changes in coagulation in patients with ischemic stroke.

Khramtzov D.N., Vikarenko M.S., Kozlova G.G., Vorokhta Y.N.

University Clinic of Odessa National Medical University, Odessa, Ukraine

The aim of the study was to assess the dynamics of coagulation indices in patients with acute ischemic stroke.

The study revealed that atherothrombotic type of stroke prevailed in patients (66.8%), cerebrovascular thrombosis (20.0%) was less common, cardioembolic type was noted in 22.2% of cases. The average inpatient days were 18.1±1.1. The coagulogram patterns demonstrated hypercoagulation on the 1$^{st}$ day after stroke onset, on the 3$^{rd}$ hypercoagulation persisted,. By the seventh day, normalization of mean values of screening parameters of hemostasis was established, and by the 14th day of stroke there was a tendency to hypocoagulation. In patients with hemorrhagic transformation, the values of ICC and ICP parameters increased by day 7, in addition, there was an increase in the content of fibrinogen. A visual display of the blood coagulation activity allows for more accurate selection of anticoagulation therapy, prevention of hemorrhagic transformation.

Key words: stroke, coagulation, diagnosis

Among the vascular diseases stroke is one of the leading causes of disability and mortality [3, 9, 12]. Despite significant progress in the stroke management, the issues of diagnosis, prognosis, prevention and treatment of acute ischemic stroke are still being challenge for clinician [1, 3, 9, 11]. Acute stroke occurrence is 0,15-0,3% of the population of economically developed countries [12]. About 110 thousand cases of stroke are registered annually in Ukraine [3, 7].

Great importance in the pathogenesis of stroke are played by the dysfunction of the hemostasis system [1, 4, 5, 8, 13, 14]. However, mechanisms of hemorrhagic transformation of ischemic stroke, development of manifestations of disseminated intravascular coagulation syndrome in stroke are still unclear [5, 13]. There is reason to consider that the leading mechanism of coagulation disorders in stroke is the interaction of tissue (thromboplastin, kallikrein, plasminogen activator) and humoral factors, proteinases and their inhibitors, followed by the initiation of blood coagulation, fibrinolysis and kininogenesis [2, 4, 5, 8, 14]. The intensity of changes is influenced by the size of the focus of ischemia, its localization, the presence of concomitant pathology [11, 13].

The aim of the study was to assess the dynamics of coagulation indices in patients with acute ischemic stroke.

Materials and methods. The study was carried out in the Stroke Unit of the University Clinic of the Odessa National Medical University (Odessa, Ukraine) in 2016. 45 in-patients with acute stroke were examined. In addition to studies of regulated national clinical protocols, patients underwent piezothromboelastography using hardware-software complex ARP-01M Mednord (Russia). This complex is designed for continuous registration of the main parameters of the process of formation of a blood clot and its lysis [6].

The principle of the device work is the registration of viscous characteristics of blood or plasma in the process of its coagulation by measuring the damping energy of oscillations of a mechanical resonance element (probe) located in the test sample placed in a thermostated cell. The exciting piezoelectric transducer results in flat sound oscillations of the probe with a given amplitude. The mechanical energy of attenuation of the probe oscillations, which depends on the changing characteristics of the medium under investigation, is converted by the receiving piezoelectric transducer into an electrical potential and recorded by a potentiometer. In this case, the measurement of the test characteristics of the sample is continuous. The device provides the graphic and numeral output on PC with the the software (IKS GEMO-3) [6].

Accordingly to results of diagnostic tests patients received antiaggregant and anticoagulant treatment. For confirmation of hemorrhagic transformation CT scanning was used (Acquillon Toshiba, Japan).

Statistical processing of the obtained results was carried out using the software Statistica 10.0 (StatSoft Inc., USA).

Results of the study.

The study revealed that atherothrombotic type of stroke prevailed in patients (66.8%), cerebrovascular thrombosis (20.0%) was less common, cardioembolic type was noted in 22.2% of cases. Gender ratio (F/M) was 1.2. The average inpatient days were 18.1±1.1.

The analysis of the dynamics of the screening parameters of the coagulogram demonstrated hypercoagulation on the 1$^{st}$ day, registered in the majority of patients according to the indices of activated partial thromboplastin time (APTT), the international normalized ratio, fibrinogen level and other indices.

On the third day of the stroke, hypercoagulation persisted, but was less pronounced. By the seventh day, normalization of mean values of screening parameters of hemostasis was established, and by the 14th day of stroke there was a tendency to hypocoagulation. Despite the persisting dynamics from hypercoagulation to hypocoagulation, the mean prothrombin time and prothrombin index (PTI) values were within normal values throughout all the follow-up period.

The dynamics of changes in the thromboelastogram as a whole corresponded to the above. In the first day of acute cerebral ischemia, hypercoagulability is revealed on the background of normal or depressed activity of the fibrinolytic system.

*Table 1.* **Indices of functional hemostasis in the stroke patients**

| Index | Reference values [6] | **1st day** | **3rd day** | **7th day** |
|---|---|---|---|---|
| A0 (initial viscocity), CU. | 222.3±15.3 | 229.3±18.7 | 231.4±16.4 | 223.6±16.5 |
| R ($t_1$, time of contact coagulation), minutes | 2.4±0.3 | 2.2±0.3 | 2.3±0.3 | 2.3±0.3 |
| ICC* (Intensity of contact phase of coagulation) | 84.3±10.9 | 89.9±11.1 | 88.6±9.6 | 85.2±11.4 |
| CTA* (constant of thrombin activity) | 15.2±3.4 | 16.1±3.6 | 15.9±3.4 | 15.9±3.8 |
| BCT ($t_3$,blood clotting time), minutes | 8.4±1.7 | 4.5±1.9 | 5.5±1.6 | 7.7±1.7 |
| ICD* (Intensity of Coagulation drive) | 21.2±3.7 | 26.5±4.2 | 25.1±3.6 | 22.2±3.8 |
| ICP* (Intensity of Clot Polymerization) | 14.5±1.4 | 15.1±1.5 | 14.8±1.2 | 14.9±1.3 |
| MA (maximum density of the clot), CU | 525.5±70.5 | 544.4±66.7 | 531.2±45.8 | 530.3±.7 |
| T (time of clot fibrin-platelets structure formation), minutes | 48.5±4.3 | 36.7±4.6 | 41.8±3.8 | 44.7±4.6 |
| IRLC (Intensity of retracation and lysis of the clot),% | 16.5±1.4 | 9.9±1.1 | 13.2±1.3 | 14.5±1.1 |
| PT (prothrombin time), sec | 21.6± 3.3 | 10.3± 1.3 | 13.0±1.2 | 14.1± 1.1 |
| IRN* (international normalized ratio) | 1.2±0.04 | 0.9±0.06 | 1.0±0.06 | 1.0±0.06 |
| TT (thrombine time), sec | 15.6±.2 | 13.2± 2.7 | 13.9± 2.4 | 14.1±2.5 |
| APTT (activated partial thromboplastin time), sec | 32.5±4.2 | 24.7±3.3 | 25.5±3.1 | 29.9±3.6 |
| Fibrinogen, g/l | 3.2±0.8 | 5.1±0.6 | 4.6±0.5 | 4.0±0.5 |

Further, there is a distinct increase in hypercoagulation or, conversely, a decrease in the concentration of clotting factors by consumption type and the activity of the anticoagulant unit of the system of regulation of the aggregate state of the blood.

With hemorrhagic transformation (8 cases or 17.8%), a combination of moderate hypercoagulation with abrupt fluctuations in the inhibited fibrinolytic activity of blood was detected in different periods of an acute period. In particular, during the first 24 hours, on average, the intensity of spontaneous platelet aggregation and their retractility increase by 20%%. The time of onset of clot formation decreased by 30%, and the maximum clot density increased by 15%. By the third day, fibrinolytic activity continued to decrease (Table 1).

In patients with hemorrhagic transformation, the values of ICC and ICP parameters increased by day 7, in addition, there was an increase in the content of fibrinogen. The fibrinolytic activity remained low, with a tendency to increase the dispersion of the index.

Conclusion. Thus, a low-frequency piezotromboelastogram makes it possible to evaluate the initial stage of coagulation, ie, the vascular-platelet component of the hemostatic system (initiation/amplification, the intensity of contact coagulation), the coagulation component (the thrombin activity constant, the coagulation drive intensity, intensity of fibrin polymerization), the time of formation of cross-linked fibrin, the maximum density of the fibrin clot, the intensity of retraction and lysis of the clot. A visual display of the blood coagulation activity allows for more accurate selection of anticoagulation therapy, prevention of hemorrhagic transformation.

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