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COMPARISON OF INSTRUMENTAL METHODS OF HEMOSTASIS RESEARCH

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Abstract

Urgency of the Problem. It is known that deep vein thrombosis of the lower extremities and pulmonary thromboembolism play an important role in the structure of postoperative morbidity and mortality, and these complications are characteristic of patients with different profiles. Considering the above, we consider it important to introduce into clinical practice new diagnostic methods that would be effective, reliable, and allow us to conduct research in real time. **The Objective:** to compare the methods for the instrumental study of blood coagulation properties and assess the capabilities of the method of low-frequency piezoelectric thromboelastography value in clinical practice. **Materials and methods.** Used various methods of instrumental studies of blood coagulation properties in the study of the functional state of the hemostatic system in a group of 60 healthy volunteers, as well as 74 patients with postthrombophlebitic syndrome. The ARP-01M Mednord APC indicators were correlated with data reproducible with the TEG® 5000 apparatus. To evaluate the reproducibility of the technique, a series of measurements of hemostasis parameters in healthy volunteers was performed. **Conclusion.** AIC ARP-01M Mednord is a compact, convenient and safe in operation coagulology analyzer that meets all the requirements of medical equipment. Due to these qualities, it can be successfully used not only in clinical laboratories, but also at the patient's bed, in the operating room, in an ambulance car.

Key words: hemostasis, instrumental examinations, blood coagulation.

The incidence of deep vein thrombosis (DVT) is 100 cases per 100,000 population, while thromboembolic complications taking the third place among cardiovascular diseases after coronary heart disease and stroke [1, 2]. According to various authors, in the overall mortality rate among hospitalized patients, pulmonary embolism (PE) ranges from 7,2 to 10,0%, and according to The Worcester DVT Study, which was published in 1991, 170,000 new and 90, 000 repeat episodes of thrombosis and thromboembolism note that DVT and COPD cause 250,000 hospitalizations in the United States every year [1, 3]. However, it can not be ruled out that real rates of detection and mortality from thromboembolic diseases may be even higher, because DVT often runs asymptomatic. Not more than one in every five patients who died from pulmonary embolism had clinical signs of DVT, and only 10% of nonfatal venous thrombosis could have been diagnosed during the patient's life.

Thus, in the majority of cases, when pulmonary embolism is the direct cause of death, the pre-existing thrombosis is not diagnosed either clinically or laboratoryly, or by means of instrumental research methods, but is a discovery of autopsy. The same authors rightly point out that today there is no clinical, laboratory or instrumental evidence that would almost certainly indicate the presence of pulmonary embolism and DVT and that many clinical symptoms that were traditionally considered specific are found in 1-54% of cases (depending on symptom), but no more [4, 5].

Given the foregoing, it is important to introduce into clinical practice new diagnostic methods that would be effective, credible and allow for real-time research [3]. For this purpose the methods of instrumental research of rheological properties of blood are best suited. Currently, the "gold standard" of instrumental diagnostics abroad has recently been using the TEG 5000 Thrombelastograph. However, limited research capabilities, the cost of the device and the research itself raises questions about the relevance of this method in daily practice. A brilliant alternative is the hardware-software complex for clinical and diagnostic research of the rheological properties of blood ARP-01M "Mednord", intended for continuous registration of the basic parameters of the process of formation of a blood clot and its lysis (Fig. 1).

Fig. 1. ARP-01M «Mednord»

The principle of the device is to record the viscous characteristics of blood or plasma in the process of its coagulation by measuring the energy of the extinction of the oscillation of the mechanical resonance element (probe) located in the test sample placed in the thermostat cuvette. A wavelength piezoelectric converter results in flat sound oscillations of the probe with a given amplitude. The mechanical energy of the extinction of the oscillation of the probe, which depends on the change in the characteristics of the test medium, is transformed into a receiving piezoelectric converter in the electric potential and recorded by a potentiometer. In this case, the measurement of the investigated characteristics of the sample is continuous.

The device provides output to the personal computer a graph of change of the resistivity of the investigated medium by oscillation of the probe attached to the vibroelectric sensor, and the software (ICS hemo-3) provides the calculation of the corresponding amplitude and chronometric parameters:

Ai — current indicator of aggregate state of blood;

TI — current time, min.;

A0 — initial rate of aggregate state of blood, t0;

A1 — the amplitude of contacts of the phase of coagulation of the blood, RH;

t1 — time of contact phase of coagulation, min;

ICC — the intensity of the contact phase of coagulation;

CTA — constant of thrombin activity;

TBC — time of blood coagulation;

ICD — the intensity of the coagulation drive;

TPC — time of polymerization of the clot (t4);

CPA — clot polymerization amplitude (A4);

ICP — the intensity of clot polymerization;

Ma — maximum clot density (fibrin-thrombocytarial blood structure);

T — time of formation of fibrin-platelet structure (total blood coagulation time), min;

TTI — total blood coagulation intensity;

IRLC — the intensity of retraction and lysis of the clot.

In turn, the TEG 5000 Thrombelastograph has a slightly different operating principle, and therefore other measurement parameters. The TEG® analyzer measures the physical properties of a blood clot using a special cylindrical cup for which a blood sample is placed. The cup performs rotational movements relative to its axis at an angle of 4-45°. Each rotational cycle lasts 10 seconds. A pin immersed in a blood sample suspended on a torsion wire. The rotational moment of the cup rotation is transmitted to a dipped-like rod only after the bundle formed by the fibrin-platelet connection begins to connect the cup and rod together. The strength of these bonds determines the angle of rotation of the rod: if the blood does not curtail - does not transmit the rotation, the loose clot only partly transmits the rotation, and a solid clot causes the rod to move synchronously with the cup. Thus, the angle of rotation of the rod directly depends on the strength of the formed clot.

As soon as the blister begins to crumble or collapse (lysis), the ligaments are torn, the interaction between the cup and the rod weakens, and the movement of the cup on the rod decreases. The rotation of the rod will be transformed from a mechanical to an electrical signal, which is fixed using a computer. As a result, we can measure the time when the beginning of the formation of the first strands of fibrin, the kinetics of clot formation, the clot strength (elasticity in din/cm^2), and the process of dissolving the clot, whether fibrinolysis occurs or not (Figure 2). To interpret the graphical information displayed by the TEG® analyzer, five basic parameters of clot formation and its lysis are measured.

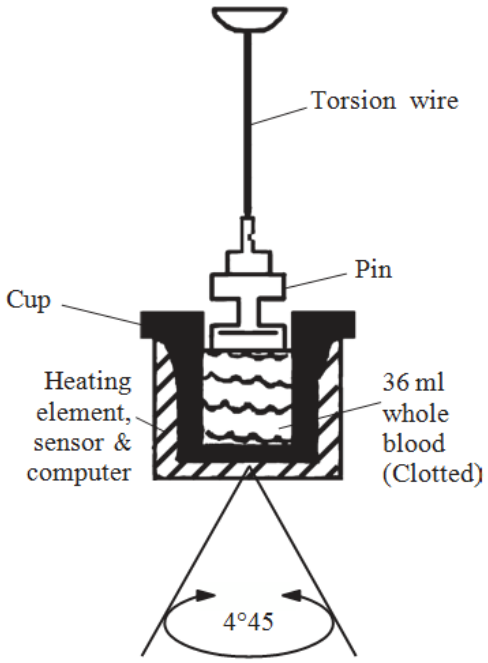

Fig. 2. The principle of operation of the device TEG 5000

R — time from the moment when the sample was placed in the analyzer until the first fibrin threads were formed. It is a characteristic of the enzymatic part of the coagulation cascade.

K — The time from the beginning of the clot formation to achieve a fixed level of its strength reflects the kinetics of increasing the strength of the clot.

α — angle, built on the tangential to thromboelastogram from the point of formation of a bunch. Displays the growth rate of fibrin nets and their structure formation (increasing the buccal strength). Characterizes the level of fibrinogen.

MA — maximum amplitude, characterizes the maximum dynamic properties of fibrin and platelet binding with GPIIb / IIIa and reflects the maximum strength of clot. At 80% of the MA is due to the number and properties (the ability to aggregate) platelets, by 20% - the amount of fibrin formed.

LY30 —change in the area under the curve of the thromboleastogram during subsequent MA 30 mins in relation to the area under the curve of the thromboelastogram without signs of lysis (rectangle with altitude MA), expressed as a percentage. It is a characteristic of the dissolution process of the clot - lysis.

Materials and methods of research. The functional state of the hemostasis system in the group of 65 healthy volunteers, as well as 68 patients with post-thrombophlebitis syndrome (PTFS) was investigated. In the group of patients with PTFS, background studies of haemocoagulation status and daily dynamic monitoring of changes in the functional state of hemostasis after heparin administration, a comparative assessment of ARP-01M Mednord and TEG® data for 8 days before and after a single administration of Cardiomagnol (150 mg) were conducted. To evaluate the reproducibility of the technique, a series of measurements of hemostasis parameters were performed in each healthy volunteer.

Material for research (whole unstable blood) was collected in the surveyed according to the generally accepted method, siliconized needles with a wide lumen from the cubital vein. Subsequently, a correlation analysis was performed with the results obtained using control hemostatic techniques.

Results of the research and their discussion. The presented tables (Table 1, 2, 3) give the data of the analysis of the circulatory system of blood (in the averaged form) obtained by us during the study. After studying all the indicators obtained on the basis of these methods of studying the aggregate state of blood, it is possible to infer their correlation analysis of the intensity of the coagulation drive.

Table 1

Indicators ARP-01M "Mednord"

Index	M±σ
A0 — initial viscosity, relative units	222,25±15,33
R (t_1) — time of contact coagulation beginning, min.	2,36±0,34
ICC — the intensity of the contact phase of coagulation	84,30±10,91
CTA — constant of thrombin activity	15,22±3,46
TBC — time of blood coagulation	8,42±1,68
ICD — the intensity of the coagulation drive	21,15±3,30
ICP — the intensity of clot polymerization	14,45±1,40
MA — maximum activity, relative units	525,45±71,50
T — the time of formation of the fibrin-platelet structure (total blood coagulation time), min	48,50±4,25
IRLC — the intensity of retraction and lysis of the bunch	16,45±1,60

Table 2

Indices of thromboelastogram TEG 500

Index	M±σ
R — time of reaction, min	10,42±2,67
K — tine of clot formation, min	6,88±2,43
MA — maximum amplitude, mm	45,37±6,12
FA — fibrinolytic activity, %	12,41±3,58

Table 3

Correlation analysis of blood coagulation tests

ARP-01M «Mednord»TEG 5000	TEG 500	Correlation
CTA	K	0,95
TBC	R	0,66
ICD	R	0,75
MA	MA	0,96
IRLC	FA	0,86

Conclusions

1. APK-ARP-01M "Mednord" is compact, convenient and safe in operation by a coagulogical analyzer, which meets all the requirements for medicine to devices of this class. Due

to these qualities, it can be successfully used not only in the conditions of clinical laboratories, but also at the patient's bed, in the operating room, in the conditions of the ambulance.

2. APK APP-01M "Mednord" allows to determine the total assessment of all parts of the hemocoagulation and lysis, as well as their interaction. Its indicators are characterized by objectivity and informativity, which is confirmed by close correlations with the indicators of traditional coagulogical techniques.

3. The parameters ICD, CTA, ICC can be successfully used to control heparin therapy in patients, and indicators of TBC, t1 and A0 - to control disaggregation therapy.

4. The ability to display the process on paper using the printer and transfer research data to various computer databases allows to use the device not only for clinical needs, but also for statistical and scientific analysis.

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