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HEMOSTASIOLOGICAL DISORDERS IN CERTAIN FORMS OF HEMORRHAGIC DIATHESIS

Matkarimova Dilfuza Saburovna[1], Davletova Shakhnoza Sardor Kizi[2], Akhmedova Zuxra Baxtiyarovna[3]

[1]Doctor of Medical Sciences, Department of Hematology, Transfusiology and Laboratory Science, Tashkent Medical Academy;

[2]Master of the Department of Faculty and Hospital Therapy of the Urgench branch of the Tashkent Medical Academy

[3]Researcher of the Republican Specialized Scientific and Practical Medical Center of Hematology, Tashkent, Uzbekistan

SUMMARY

Purpose of the study. *Based on the assessment of the role of disturbances in various links of hemostasis in the pathogenesis of IMTV and ITP and establishing their connection with the stage of diseases, optimize the hemostasiological algorithm for diagnosing the pathologies under study.*

Material and methods: *The study included 105 patients with IMTV (51 - in the stage of relapse, 54 - in the stage of remission); 135 patients with ITP (74 at the stage of relapse, 61 at the stage of remission) and 81 conditionally healthy persons without pathology of the hemostasis system (all examined were between the ages of 18 and 70). The study of the hemostasis system was carried out on a HumaClot Junior coagulometer (HC-4127, Germany) and an ALAT-2 "BIOLA" aggregation analyzer (AAS 748, Russia) using reagents "NPO RENAM, Russia".*

Results and its discussion. *Comprehensive study of the links of the hemostasis system: indicate the presence of pronounced coagulation disorders, which is one of the main mechanisms of the pathogenesis of IMTV and ITP. ITP is characterized by activation of the vascular-platelet link, moderate hypercoagulation, while ITP is characterized by a reduced activity of the vascular-platelet link of hemostasis.*

KEY WORDS: *immune microthrombovasculitis, immune thrombocytopenia, hemostatic system, vessels, platelets.*

RELEVANCE

Hemorrhagic diathesis (HD) is one of the most important problems in clinical hematology [2,5]. In connection with the increase in the number of morbidity, the aggravation of the course and the development of formidable complications among the entire large group of HD, immune microthrombovasculitis (IMTV) and immune thrombocytopenia, which are a medico-social problem of modern medicine, are of particular relevance [3,4,9,15]. Given the protracted nature, frequent relapses and chronicity of the process, as well as the likelihood of a wide variety of complications, including deaths, the ability to diagnose and treat these diseases is necessary for both a hematologist and doctors of many other specialties [5, 11, 16].

Complex disorders of the hemostatic system are one of the main mechanisms for the development of IMTV and ITP [1,2,10,12,18]. Despite the existence of many data on the vascular-platelet system, the foundations of some of the processes observed in these pathologies remain poorly understood until now [6,7,13,19]. The comparatively low information content of the previously used methods for studying hemostasis indicators significantly reduce the timely diagnosis and effectiveness of the ongoing therapy of IMTV and ITP [7,8,14,17].

Purpose. Based on the assessment of the role of disorders in various links of hemostasis in the

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pathogenesis of IMTV and ITP, and the establishment of their connection with the stage of diseases, to optimize the hemostasiological algorithm for diagnosing the pathologies under study.

MATERIAL AND METHODS

The study included 105 patients with ITP (51 in the relapse stage, 54 in the remission stage) and 135 patients with ITP (74 in the relapse stage, 61 in the remission stage), which were respectively divided into 2 large groups: 1st the group consisted of patients with ITP, the second group consisted of patients with ITP, who, according to the stage of the disease, were divided into subgroups A - stage of relapse and B - stage of remission (all subjects were aged from 18 to 70 years). All the subjects were undergoing outpatient or inpatient treatment at the NIIG clinic and the PC of the Ministry of Health of the Republic of Uzbekistan. The control group consisted of persons of the Uzbek population of comparable age without pathology of the hemostasis system (n = 81).

In accordance with the purpose of the study, all subjects underwent a comprehensive study of the indicators of the hemostasis system. The study of hemostasis included: 1.vascular-platelet link of the hemostasis system (counting the number of platelets according to hemogram parameters in peripheral blood using phase contrast microscopy, determination of platelet aggregation induced by ADP (1.0 and 0.5 mmol), von Willebrand factor (WF), retraction of a blood clot in a test tube according to Baluda V.P. et al. (1980); 2.coagulation link of the hemostasis system (determination of activated partial thromboplastin time of plasma (APTT), prothrombin index (PTI), thrombin time (TT), quantitative orthophenanthroline test detecting soluble fibrin-monomeric complexes (SFMC) in plasma, the amount of fibrinogen; 3. activity of antithrombin III (AT III); 4. Anticoagulant and fibrinolytic system (XII – a dependent fibrinolysis according to Eremin GF and Arkhipov A.G. , 1982). The study of the hemostasis system was carried out on a HumaClot Junior coagulometer (HC-4127, Germany) and an ALAT-2 "BIOLA" aggregation analyzer (AAS 748, Russia) with a Using reagents from NPO RENAM, Russia.

Statistical processing of the obtained data was carried out by the method of variation statistics, using the Microsoft Office Excel-2003 program with the calculation of the mean square deviation and the arithmetic mean error by the method of moments (M ± m), the criterion of reliability of the Student's differences (t) and the degree of reliability (p).

RESULTS AND CONCLUSIONS

Analysis of the results of the complex studies of the hemostasis system using standardized highly informative methods in patients with IMTV and ITP at different stages showed the presence of multidirectional shifts in all the studied links of hemostasis. Comparative analysis in the 1st group made it possible to establish the features of the pathology of hemostasis in patients with IMTV that differ in the stages of relapse and remission: in the A subgroup, in relation to the control, an increase in platelet aggregation induced by ADP (1 mmol) to 78.9 ± 1.7% ($p > 0.05$) and (0.5 mmol) up to 34.5 ± 1.28% ($p < 0.001$) and significantly significant levels of fibrinogen up to 4.61 ± 0.08 g / L ($p < 0.001$) (Fig. 1.), the level of EF was significantly higher by 1.33 times in relation to the control and 1.38 times in relation to the B subgroup (Fig. 2.). All these indicators in the B subgroup significantly decreased in relation to the control ($p < 0.001$).

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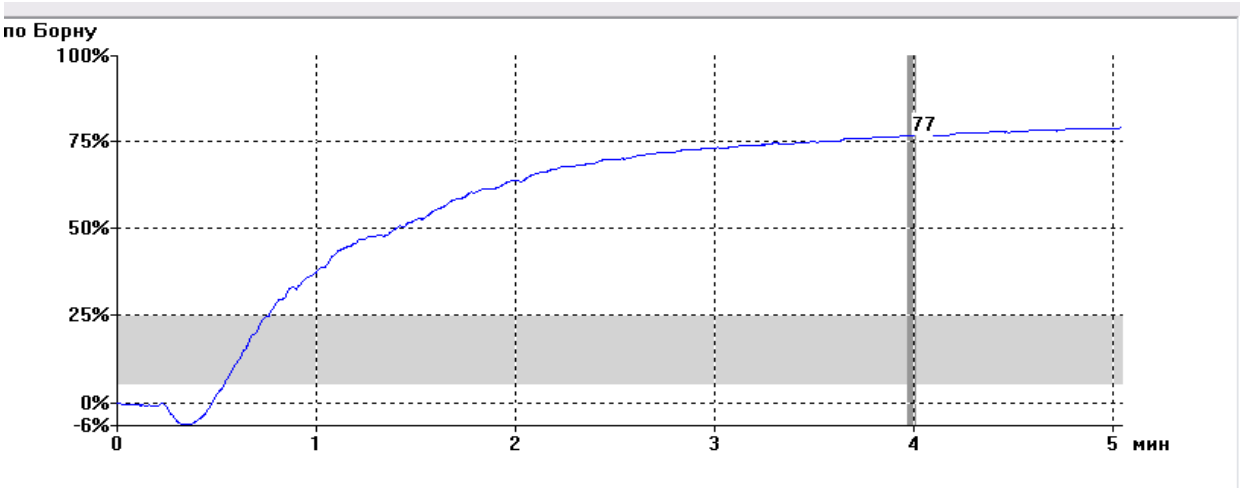

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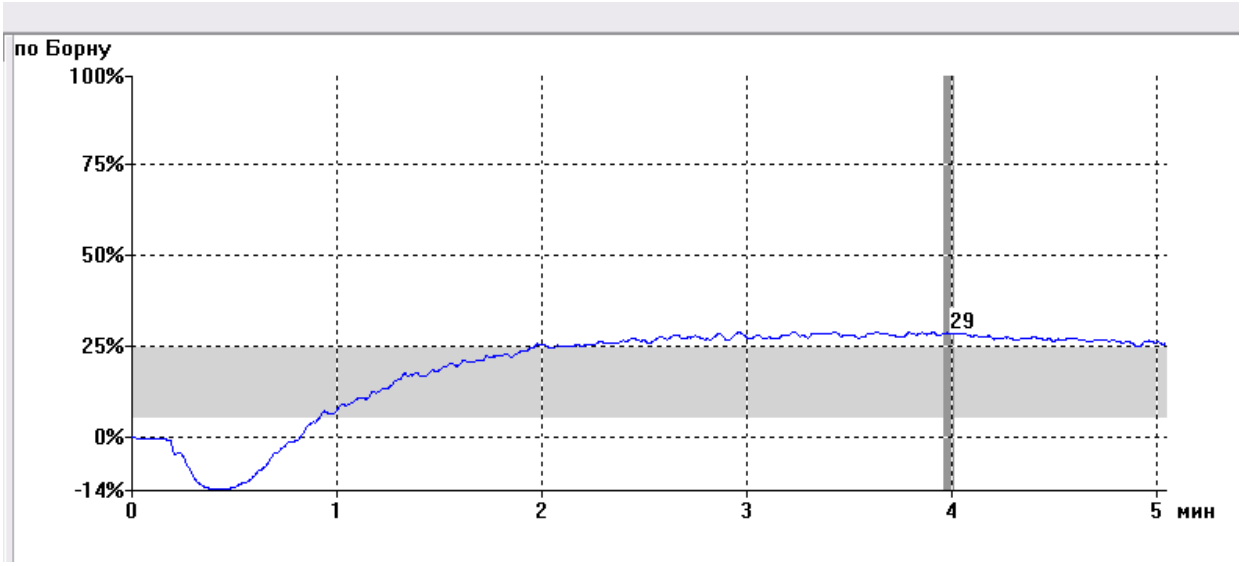

Fig. 1. Registration of platelet aggregation induced by ADP at a concentration of 1.0 mmol (A) and 0.5 mmol (B) in a patient with an IMTV in the relapse stage.

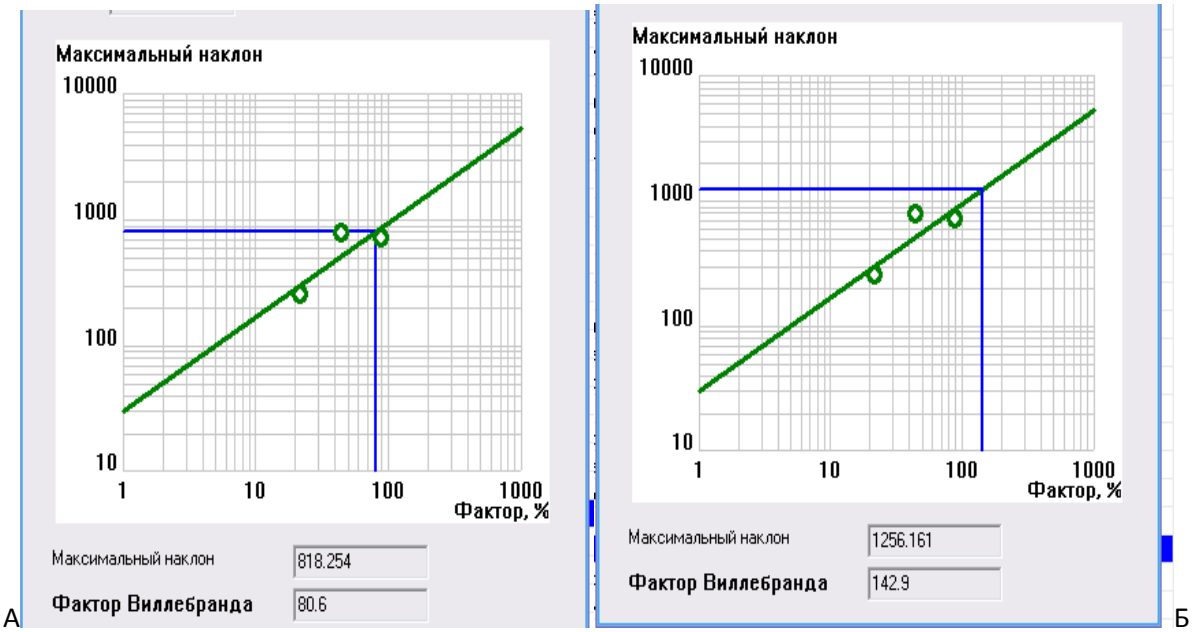

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Fig. 2 Registration of von Willebrand factor in a patient with IMTV in the stage of relapse (A) and remission (B).

The indicators of the coagulation link of hemostasis also differed from those in the control, as the APTT in subgroup A was significantly shorter by 1.06 times ($p < 0.001$); PTI and TT were 104 ± 1.33% ($p < 0.001$) and 12.3 ± 0.16 sec ($p < 0.001$), 95.6 ± 0.81% ($p < 0.001$) and 13.3 ± 0, 17 sec ($p < 0.001$), respectively (in control 91.0 ± 1.01% and 8.86 ± 0.10 sec). Along with this, the AT III indices decreased in both subgroups by 1.12 and 1.09 times, and the SFMC, on the contrary, increased by 2.16 and 1.4 times ($p < 0.001$) in relation to those in the control.

In addition, the study of the fibrinolysis system revealed a significant decrease in XIIa-dependent fibrinolysis in the studied subgroups (Table 1).

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Table 1.
Indicators of the hemostasis system in patients with IMTV and in the control group (M ± m)

Indicators of the hemostasis system	Unit of measurement	Control (n = 81)	IMTV (n=105)	
			High (n=51)	Remission (n=54)
Aggregation of platelets with ADP (1.0 mmol)	%	56,8±0,90	78,9±1,7	43,5±1,17***
Aggregation of platelets with ADP (0.5 mmol)	%	28,9±0,44	34,5±1,24***	23,9±0,74***
APTT	sec	30,7±0,24	28,8±0,47***	33,5±0,44***
PTI	%	91,0±1,01	104±1,33***	95,6±0,81***
Thrombin time	sec	8,86±0,10	12,3±0,16***	13,3±0,17***
Fibrinogen	g / l	3,20±0,05	4,61±0,08***	3,5±0,07***
XII a - dependent fibrinolysis	min	6,42±0,13	11,0±0,30***	7,0±0,12***
AT III	%	106±0,97	94,2±0,99***	97,1±1,0***
SFMC	mkg / ml	3,85±0,05	8,32±0,32***	5,34±0,22***
FV	%	100,4±1,4	134±4,37***	97,3±0,85

Note: *** - p <0.001. Reliable compared to control group

The revealed features of disorders in the hemostasis system at the stage of recurrent IMTV are due to the influence of the immunocomplex process leading to persistent hypercoagulation and microthrombotic formation, a decrease in the activity of AT III, and an increase in SFMC.

In the 2nd A subgroup of patients, a decrease in the number of platelets to 25.4 ± 1.34 X 109 / L and platelet aggregation induced by ADP (1 mmol) to 4.8 ± 0.52% (p> 0.05) and (0.5 mmol) to 1.97 ± 0.26% (p <0.001) (Fig. 3.), retractions up to 0.06 ± 0.01 (Table 2.).

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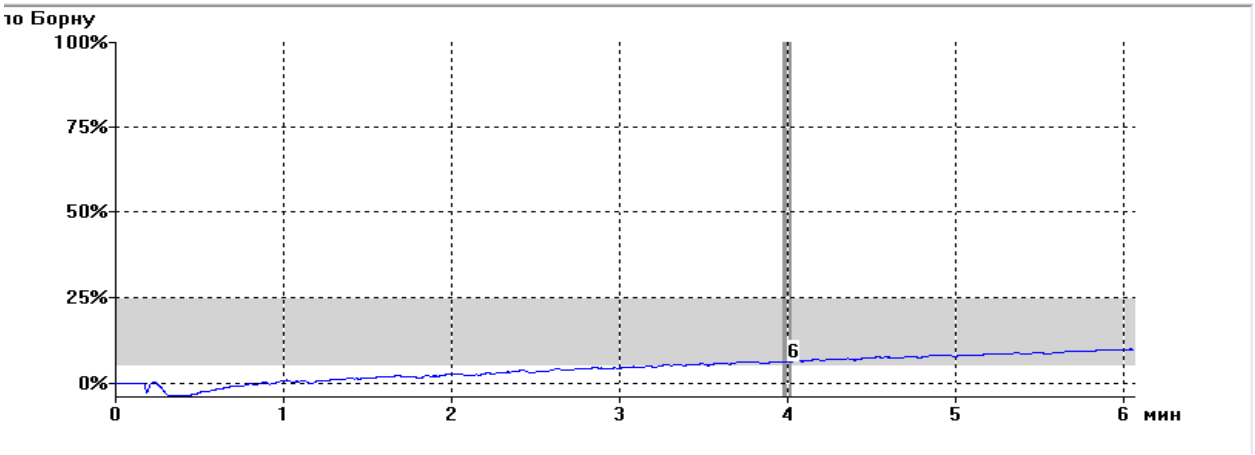

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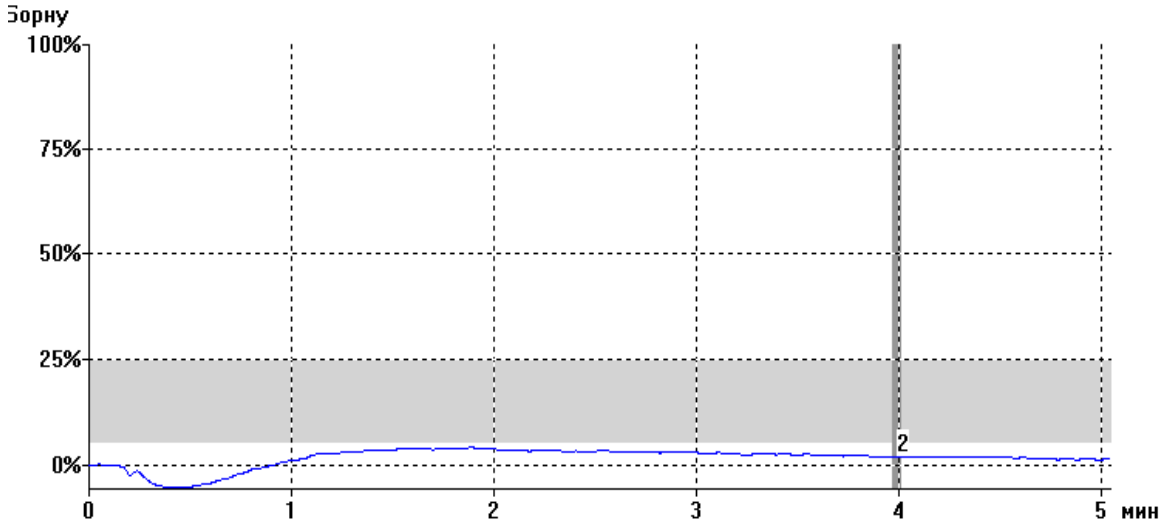

Fig. 3. Registration of platelet aggregation induced by ADP at a concentration of 1.0 mmol (A) and 0.5 mmol (B) in a relapsed ITP patient.

The indicators of TT and APTT in relation to the control group in ITP patients differed little from those in the control group (Table 2).

Table 2.
Indicators of the hemostasis system in ITP patients and in the control group (M ± m)

Indicators of the hemostasis system	Unit of measurement	Control (n = 81)	ITP (n = 135)	
			High(n=74)	Remission (n = 61)
Platelet count	thousand /mcl	220,3±2,84	25,4±1,34***	190,6±3,7***
Aggregation with ADP (1.0 mmol)	%	57,1±0,97	4,8±0,52***	53,1±0,86***
Aggregation with ADP (0.5 mmol)	%	29,1±0,52	1,97±0,26***	26,3±0,47***
APTT	Sec	30,5±0,28	30,7±0,41	30,5±0,35
PTI	%	90,8±1,10	94,5±1,05***	91,5±1,26
Thrombin time	Sec	8,9±0,12	10,2±0,20***	9,9±0,23***
Fibrinogen	g/l	4,1±0,53	3,34±0,057	4,3±0,70
XIIa dependent fibrinolysis	min	6,4±0,15	9,4±0,028***	6,5±0,20
Retraction		0,30±0,009	0,06±0,01***	0,29±0,0024

Note: *** - p <0.001. Reliable compared to the height of the disease

A comprehensive study of the indicators of the hemostasis system in ITP patients determined their significance in accordance with the stage of the disease. Thus, a statistically significant decrease in the number of platelets, platelet aggregation induced by ADP and retraction of a blood clot are statistically significant in the stage of ITP recurrence, while in the stage of remission, only a decrease in the indicator of platelet aggregation induced by ADP remains significant (Fig. 4). This, in turn, indicates that in

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patients in remission, the study of other hemostasis indicators is not informative.

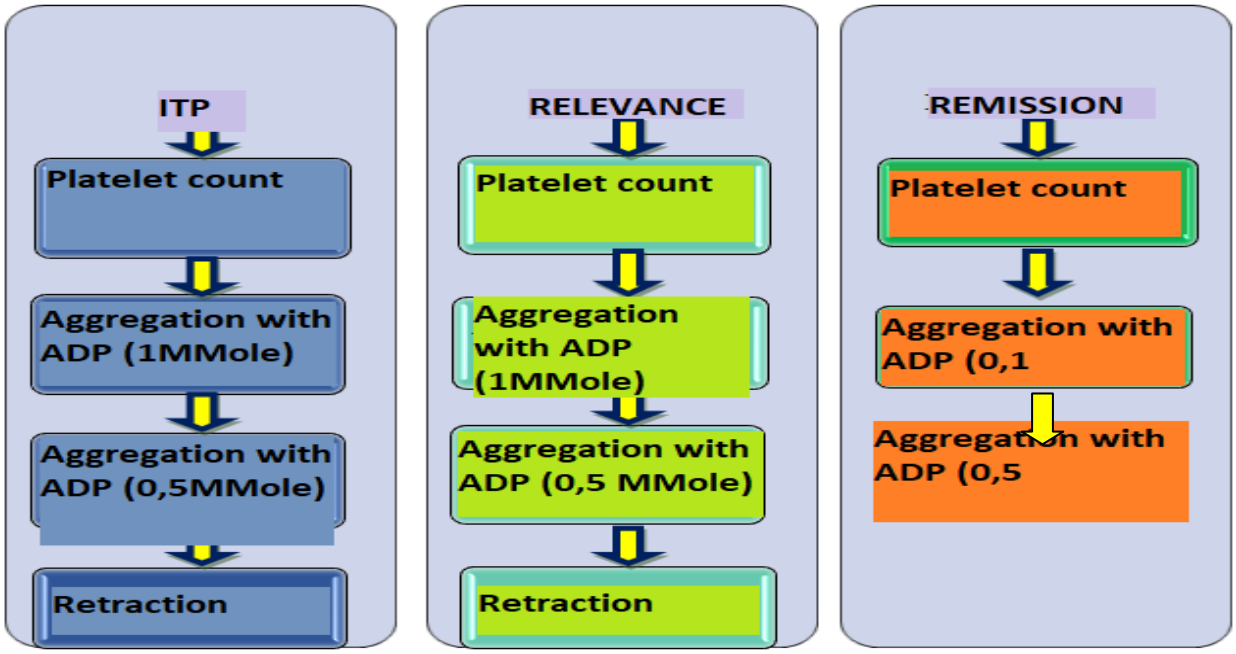
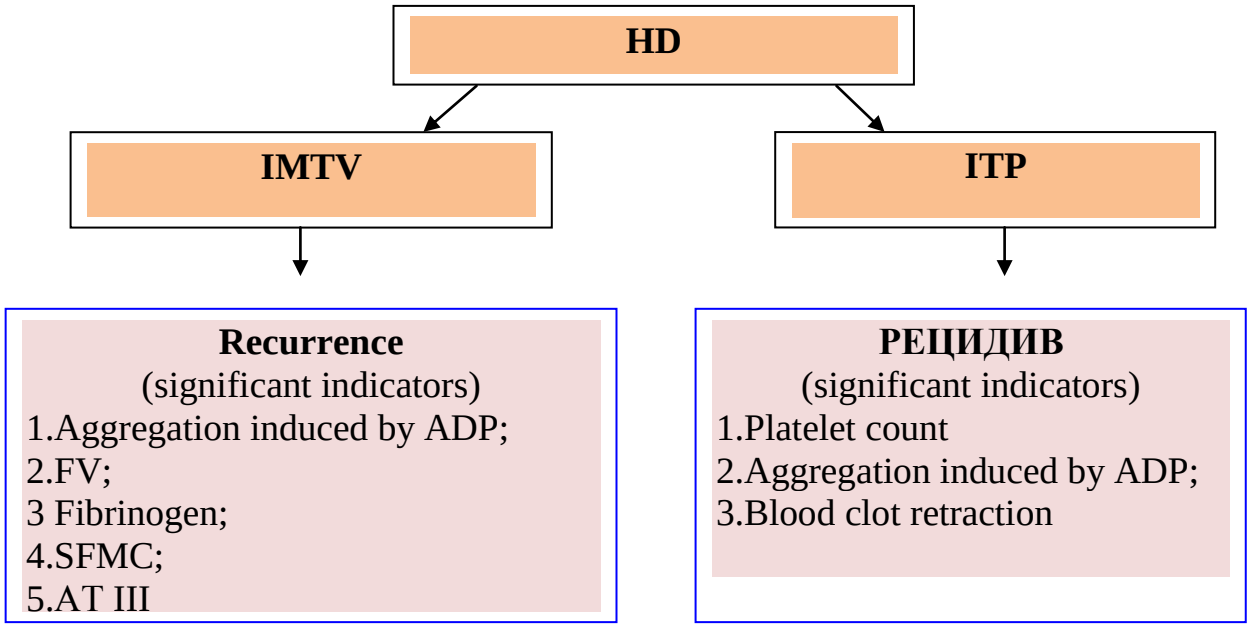


Fig. 4. Statistically significant decrease in the level of indicators of the hemostasis system in patients with ITP at various stages of the disease (Student's t-test).

Thus, a comprehensive study of the indicators of the hemostasis system in patients with IMTV and ITP indicates the presence of multidirectional disorders. Pronounced changes in the hemostatic system during IMTV were characterized by hypercoagulation, thrombinemia, vascular-platelet disorders, which were aggravated by a decrease in the activity of antithrombin III and a high level of SFMC. Comparative analysis of the results of studying the hemostatic system in ITP patients revealed significant violations of the hemostatic potential of the blood with a decrease in the activity of platelet hemostasis, determined by a decrease in the level of platelets, their aggregation, and blood clot retraction.

Scheme 1.
Algorithm for hemostasiological examination of patients IMTV and ITP.



The studies carried out made it possible to establish not only the role of disorders of various links of the hemostasis system in the pathogenesis of IMTV and ITP, but also on their basis to optimize the algorithm for hemostasiological examination of patients (Scheme 1.).

CONCLUSIONS

1. Comprehensive study of the links of the hemostasis system: indicate the presence of pronounced disorders of coagulation, which is one of the main mechanisms of the pathogenesis of IMTV and ITP;

2. Hemostasiological disorders in IMTV and ITP determine the characteristic profile of diseases, which determines their specific feature: IMTV is characterized by activation of the vascular-platelet link, moderate hypercoagulation; with ITP, a reduced activity of the vascular-platelet link of hematase is characteristic.

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