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Comparative evaluation of hemostasis in patients with myocardial infarction in thrombolytic therapy

Abstract:

The relationship between the changes of the hemostatic and kallikrein-kinin systems of blood from bleeding complications in patients with myocardial infarction in the thrombolytic therapy. Disturbances of the hemostatic system and abnormal activation of the kallikrein-kinin system, both in terms of the traditional conservative and the dynamics and the early and late thrombolysis. Discussed pathogenetic significance of interaction kinin system and induced thrombolysis increasing fibrinolytic activity in the development of reperfusion syndrome. Dynamics of parameters of the hemostatic function and shows the advantages of comparative clinical safety of early thrombolysis, compared with late. Is promising an early thrombolysis during treatment with inhibitors of the activation of the kallikrein-kinin system.

Keywords: Myocardial infarction, thrombolytic therapy, reperfusion syndrome, haemostasis, the kallikrein-kinin system.

Actuality:

Optimization of thrombolytic therapy in patients with acute myocardial infarction is still relevant. Reperfusion bleeding complications forced to seek safe ways to effectively restore blood supply to ischemic focus, including taking into account the state of the hemostatic system (1,2).In this connection, it should pay attention to the activation of the kallikrein-kinin system as a result of acute myocardial ischemia (3-6)The purpose of this study was to evaluate the hemostatic and the kallikrein-kinin system in patients with acute myocardial infarction in thrombolytic therapy.

Materials and Methods:

A total of 82 patients with acute macrofocal myocardial infarction macrofocal aged 34-67 years. The first group consisted of patients (n = 21, tab.1) with early thrombolysis, which streptaza or streptodekaza infusion conducted within 2-2.5 hours after the onset of acute coronary syndrome. In the second group (n = 21, tab.2) thrombolysis started at a later time (3-6 hours," late thrombolysis"). The third (control) group (n = 40, tab.3) included patients who received only traditional conservative therapy. The tables are also given for comparison the normal values of the haemostatic and kinin systems of blood in 44 healthy subjects not included in the total number of patients examined. At 6 hours after thrombolysis was performed heparinization for 5-7 days at a daily dose of 20-25 thousand units. To assess the hemostatic used: Trombin time sec.; APTTsec (activated partial thromboplastin time); PRI% (reserve index of plasminogen);FDP mg% (fibrinogen degradation products); AT % (antithrombin) Fibrinogen; XII F.L.- XII Factor Lisis; (7) . Status of kallikrein-kinin system was judged in terms of the concentration of prekallikrein and kallikrein in the blood (4)

Results and Discussions:

Group 1 patients (Table 1) with early thrombolysis pay close attention to normal baseline thrombin time, APTT, AT, fibrinogen and PRI%. A moderate increase in FDP can be seen as a consequence of a compensatory activation of fibrinolysis, which is manifested in the first 2-3 hours of acute myocardial

ischemia. 1 hour after administration of the drug were almost the maximum reduction in HI FL, with a moderate increase in the TT and APTT, a sharp increase in the FDP and the decrease of fibrinogen and PRI%, indicating a significant increase in fibrinolytic activity. Even after 3 hours there is a slight decrease in the TT and APTT, further reduction PRI% and HP-FL. A day continues positive trend indicators fibrinolytic activity and the approximation to normal coagulation parameters. On the 5th day of fibrinolytic parameters in normal with a slight shortening of the TT and APTT. AT III in the first 2-3 hours of acute myocardial ischemia remains in the normal range, the infusion of thrombolytics is somewhat reduced by the end of the day begins to return to normal.

Table 1. The dynamics of indicators of hemostasis with early thrombolysis

Parameter	norm (n=44)	Used thrombolytic	input	1 hour after thrombolysis	4 hour after thrombolysis	24 hour after thrombolysis	5th day	14th day
T t.sec	15,34+0,11	streptaza (n=12) Streptodekaza (n=9)	14,69+0,37 14,0+0,49	23,30+0,95*** 21,5+0,57***	21,38+0,67*** 19,25+0,44**	16,30+0,36* 16,62+0,4**	14,92+1,18 14,62+0,19	15,30+0,21 14,87+0,24
APTT, sec	43,97+0,48	streptaza (n=12) Streptodekaza (n=9)	41,53+1,14 42,25+1,52	59,38+1,08*** 60,87+1,71***	54,76+0,89*** 54,75+1,75***	41,84+1,01 45,5+1,77	41,0+0,99 44,37+1,41	47,69+1,65* 47,75+1,06*
FDP Mg%	1,64+0,61	streptaza (n=12) Streptodekaza (n=9)	10,46+1,10 11,00+3,20	46,76+4,79*** 30,0+5,59*	51,69+4,67*** 19,0+3,20	21,53+2,56*** 12,0+1,61	2,15+1,01** 1,5+0,78*	0,15+0,16*** 0,12+0,13*
AT-III%	98,86+0,54	streptaza (n=12) Streptodekaza (n=9)	87,38+1,34 87,62+1,21	79,92+1,17** 84,25+1,45	76,15+1,19*** 82,5+1,37	83,76+1,49 87,12+1,31	83,84+1,56 85,25+1,32	88,92+1,79 87,87+1,09
FG g/l	3,19+0,09	streptaza (n=12) Streptodekaza (n=9)	7,23+0,20 7,7+0,41	3,74+0,11*** 5,93+0,27*	3,26+1,59 4,93+0,12**	3,26+0,25*** 2,83+0,08***	3,03+0,24*** 2,5+0,20***	3,03+0,12*** 2,65+0,25***
PRI%	99,89+0,2	streptaza (n=12) Streptodekaza (n=9)	88,53+1,41 87,62+2,13	80,84+1,71** 82,87+2,06	76,53+1,45*** 80,12+2,05*	81,76+1,61* 87,75+1,15	86,46+1,55 90,25+0,94	90,07+1,22 92,62+1,24
XII-F.L. min)	6,2+0,38	streptaza (n=12) Streptodekaza (n=9)	41,30+1,69 41,37+3,03	9,61+0,64*** 30,37+3,14*	8,38+0,36*** 23,37+1,82**	6,846+0,61*** 9,12+0,31***	6,76+0,45 7,62+1,28	5,23+0,75*** 5,87+0,31***

* p < 0,05; ** p < 0,01; *** p < 0,001

The patients in Group II with late thrombolysis was a slight shortening of the TT and APTT, a decrease of AT% and PRI% and a significant increase in digital values XII FL indicate that the initial state of hypercoagulability (Table 2). 1 hour after the infusions showed a slight statistically significant improvement in the coagulation system. In contrast to early thrombolysis is no significant increase in fibrinolytic activity, resulting in the preservation of high numbers XII FL and reducing the PRI%. After 1 and 5 days after the start of thrombolysis coagulation and fibrinolytic systems remain almost unchanged and if the TT and APTT are slightly higher than the normal value, the fibrinolytic activity in the blood is low. For late thrombolysis, due to a significant decrease in blood reserves plasminogen (PRI%), there is no advantage streptazy have higher fibrinolytic activity over Streptodekaza.

Table 2. The dynamics of indicators of hemostasis with late thrombolysis

Parameter	norm (n=44)	used thrombolytic	input	1 hour after thrombolysis	4 hour after thrombolysis	24 hour after thrombolysis	5th day	14th day
T t.sec	15,34+0,11	Streptaza n=14	13,14+0,23	14,35+0,23***	15,0+0,24***	18,07+0,25***	17,5+0,18***	14,92+0,25***
		Streptodekaza n=7	13,57+0,39	14,42+0,21	14,71+0,19*	17,42+0,39***	16,57+0,32***	14,85+0,15*
APTT, sec	43,97+0,48	Streptaza n=14	40,5+0,64	45,21+1,12**	46,21+1,09**	47,0+0,58***	47,0+0,34***	48,0+0,72***
		Streptodekaza n=7	40,57+0,66	43,71+0,96***	45,28+0,65**	47,0+0,66***	47,85+0,28	47,71+0,56***
FDP Mg%	1,64+0,61	Streptaza n=14	7,71+0,29	9,14+0,80	12,57+1,13**	22,85+3,12***	6,57+0,55	3,0+0,28***
		Streptodekaza n=7	7,42+0,61	742+0,61	9,14+1,23	19,42+4,93	4,57+0,61*	2,28+0,30***
AT-III%	98,86+0,54	Streptaza n=14	70,85+0,76	75,07+1,23	76,71+1,12	80,78+1,25***	82,5+1,24***	80,85+0,79
		Streptodekaza n=7	71,28+1,04	73,71+1,01	75,71+1,09*	78,42+1,17**	80,57+1,19**	79,28+0,56**
FG g/l	3,19+0,09	Streptaza n=14	7,14+0,41	4,50+0,29***	3,07+0,28***	2,96+0,30***	2,42+0,28***	2,82+0,2***
		Streptodekaza n=7	7,44+0,45	5,04+0,33***	4,47+0,32***	2,85+0,34***	3,27+0,22***	3,26+0,12***
PRI%	99,89+0,2	Streptaza n=14	68,14+1,54	65,71+1,62	63,92+1,69**	61,71+2,16*	62,21+1,97	64,64+1,87
		Streptodekaza n=7	71,0+1,0	68,57+1,10	65,42+0,90*	62,14+0,72**	62,85+0,64	66,71+1,1*4
XII-F.L. (min)	6,2+0,38	Streptaza n=14	84,92+0,95	83,28+1,05	81,57+1,06*	74,5+1,98**	70,57+1,84***	49,64+1,4***
		Streptodekaza n=7	85,57+1,57	83,85+1,57	83,71+1,59	90,0+1,59*	73,85+1,93**	64,0+1,64***

* $p < 0,05$; ** $p < 0,01$; *** $p < 0,001$.

Baseline characteristics of patients with a third (control) group are characterized by activation of the coagulation system and harsh suppression of fibrinolytic activity (Table 3).

Table 3. The dynamics of indicators of hemostasis in the conventional therapy

parameter	norm (n=44)	Input (n=40)	3 hour	6 hour	24 hour	5th day	14th day
T t.sec	15,34+0,113	13,642+ 0,144	13,833+ 0,171	14,127+ 0,164	14,166+ 0,171	13,722+ 0,124	14,388+ 0,121
APTT, sec	43,97+0,48	31,364+ 0,952	39,166+ 0,912***	39,4476+ 0,938***	38,944+ 0,878***	39,166+ 0,896*	40,055+ 0,961**
FDP mg%	1,64+0,61	8,748+ 0,156	9,5+ 0,238***	10,276+ 0,232***	10,726+ 0,257***	9,055+ 0,242	4,638+ 0,203***
AT-III%	98,86+0,2	72,611+ 1,331	74,0+ 1,341	73,652+ 1,299	73,944+ 1,292	76,055+ 1,268*	77,564+ 1,308
FG g/l	3,19+0,51	7,361+ 0,079	7,683+ 0,079***	7,744+ 0,1079***	7,784+ 0,068***	7,728+ 0,059***	4,261+ 0,052***
PRI%	99,89+0,38	57,166+ 0,988	58,942+ 0,931	59,682+ 0,933	60,5+ 0,919**	60,0+ 0,872**	57,582+ 0,828
XII-F.L. (min)	6,02+0,38	100,362+ 1,364	102,362 +1,364	109,722+ 1,33	104,388+ 1,372***	102,833+ 1,377	88,676+ 5,487**

* $p < 0,05$; ** $p < 0,01$; *** $p < 0,001$.

Low baseline AT III in 2 and 3 groups, reflect the process of blood coagulation and DIC syndrome, increased after the treatment with the use of products that will improve hemodynamic function and blood rheology (8).

Choice of an alternative method of thrombolysis may contribute to quantification of major parameters of coagulation (TT and APTT) and fibrinolytic (CP FL) systems of blood in patients of group 1. Infusion streptazy TT and APTT tended to further increase relative to baseline by 3 times, and Streptodekaza - 2.8 times, respectively.However, HP F.L. shortened by thrombolysis streptazoy almost 3 times and Streptodekaza of 24.6%. With early streptazoy T TT and APTT increased by only 58 and 43%, and Streptodekaza - by 53.6 and 43%, respectively. HP F.L. streptazy decreased after the introduction a little over 4 times and Streptodekaza by 26%. Thus, the advantage of early thrombolysis is the oppression of the main parameters of the coagulation system, which prevents the rapid organization of thrombus and facilitate the efficient lysis, while maintaining a sufficiently high fibrinolytic activity, which is in accordance with the best clinical course of the disease in patients in group I.

The need for early thrombolysis is dictated by the fact that recovery efficiency is reduced blood supply to the myocardium due to increase over time the size of the thrombus, fibrin polymerization of a blood

clot retraction and decrease its content in the plasminogen (9). So, along with up-initiated thrombolytic therapy, it is useful as an early use of suppressing the activity of blood coagulation. This prevents the rapid organization of thrombus, accelerating lysis and, thus, contribute to the successful dissolution of thrombus, even at moderate fibrinolytic activity of the thrombolytic agent, as Streptodekaza.

Our data allow us to think about the prospects of the TLB against the prior administration of inhibitors of the kallikrein-kinin system (KKS). We should look at that in terms of excess kininoobrazovaniya (authors) in the acute phase of MI is coupled activation of coagulation and kinin systems of blood, followed by a flagrant violation in the hemostatic system. Kallikrein is responsible for the formation of the activated Hageman factor that triggers the mechanism of blood clotting. Consequently, the use of inhibitors of the CCR in acute myocardial ischemia is pathogenetically substantiated.

Conclusions:

1. Dynamics of indicators svidetelstuet hemostatic function of the body and the comparative advantage of the clinical safety of early thrombolysis, compared with late.

2. Induced early thrombolysis high fibrinolytic activity of the blood increases the abnormal activation of the kallikrein-kininnovoy system, adding to the risk of complications of reperfusion of acute myocardial infarction. For late thrombolysis plasminogen depletion allowance makes lowering blood fibrinolytic activity and worsening trombolitichsekogo effect.

3. Is promising an early thrombolysis during treatment with inhibitors of the activation of the kallikrein-kinin system.

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