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DISORDER OF HOMEOSTASIS AND BLOOD AGGREGATION IN PATIENTS WITH OBSTRUCTIVE JAUNDICE OF NON-NEOPLASTIC ETHIOLOGY

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Indicators of homeostasis have been studied in 457 patients with obstructive jaundice. 232 of them had cholestasis for 10 days and 225 — for 3-6 week. Indicators have been studied before and after the membrane, antioxidant and antiplatelet therapy in 140 patients. Increase in viscosity, erythrocyte aggregation, decrease of their deformability, blood coagulation potential and increase of fibrinolytic activity of blood have been observed in patients with obstructive jaundice on the background of disorder of lipid metabolism and endogenous intoxication. All these changes are more manifested in patients from the second group with prolonged obstructive jaundice when cytolytic processes progress along with cholestatic ones. All this requires prompt diagnosis and active preoperative correction.

Keywords: blood rheology, jaundice, membrane, antioxidant, antiplatelet therapy

У 457 больных механической желтухой изучены показатели гомеостаза. У 232 из них с 10-дневным холестазом и у 225 — с 3–6 недельным. У 140 больных изучены показатели до и после мембранотропной, антиоксидантной и дезагрегантной терапии. У больных с механической желтухой на фоне нарушений липидного обмена и эндогенной интоксикации наблюдается повышение вязкости, агрегационной способности эритроцитов, снижение их деформируемости, свертывающего потенциала и повышение фибринолитической активности крови. Более выражены все эти изменения у больных второй группы с длительной механической желтухой, когда наряду с холестатическими развиваются и прогрессируют цитолитические процессы. Все это требует своевременной диагностики и активной предоперационной коррекции.

Ключевые слова: реология крови, механическая желтуха, мембранотропная, антиоксидантная, дезагрегантная терапия

Introduction

Steady increase of incidence of gallstone disease and number of patients with obstructive jaundice is observed world over. Mortality from it remains high — from 8 to 44% [1,3]. It is considered that one of the main causes of deaths in obstructive jaundice progressive liver failure [2]. It is associated with severe morphological and functional disorders, appearing as result of intoxication and combined with hemodynamic, rheological and hematological disorders [4]. Changes in rheology and hemocoagulation usually precede appearance of clinical signs of complications [4].

Table 1

Physical and chemical properties of blood depending on duration of cholestasis and preoperative preparation (M ± m, R)

Parameters		Duration of cholestasis				Norm
		Up to 10 days (n = 232)		Up to 3–6 weeks (n = 225)		
		before	after	before	after	
Blood cells	Er (10^{12}/l)	4,12 0,05 3,02-4,98	4,17 0,08 3,20-5,08	3,48** 0,07 3,10-4,50	3,68 0,06 3,22-4,48	4,0-5,0
	Hb (r/l)	119,2 0,9 113,0-132,0	120,1 0,9 110-129	104,3* 1,8 86-122	112,3 1,2 98-122	120-160
	Tr (10^9/l)	220,4 3,7 70,0-292,0	236,2 8,2 118-298	188,0** 6,5 108-280	202,2 6,1 162-282	180-320
Rheology	Ht (%)	36,8 0,2 33,0-38,0	37,7 0,4 30,0-40,0	32,2** 0,5 26-36	33,5 0,4 27-36	36-50
	Coefficient of dynamic viscosity (mPa*sec)	6,99 0,14 4,80-7,98	6,65 0,06 5,5-6,95	8,08** 0,10 6,79-8,78	7,39 0,12 6,00-8,43	4,73-6,90
	Yield value (n/m^2x10^{-3})	0,98 0,05 0,35-1,45	0,40* 0,02 0,24-0,68	0,99 0,08 0,28-1,45	0,78 0,05 0,60-1,25	0,11-0,89
	Coefficient of erythrocyte aggregation (N/m^2x10^{-5})	1,59 0,05 1,15-2,28	1,45 0,03 1,20-1,79	2,73** 0,06 2,17-3,45	2,09* 0,06 1,20-2,69	0,50-2,29
	Coefficient of erythrocyte deformability (units)	0,300 0,004 0,246-0,340	0,309* 0,004 0,250-0,328	0,281** 0,004 0,232-0,304	0,297* 0,004 0,262-0,340	0,360-0,380
ORE (%)	min	0,410 0,004 0,38-0,46	0,400 0,002 0,38-0,42	0,370** 0,004 0,32-0,40	0,408* 0,001 0,34-0,46	0,40-0,45
	max	0,270 0,006 0,2-0,34	0,250* 0,004 0,20-0,30	0,196** 0,003 0,16-0,23	0,216* 0,004 0,17-0,26	0,27-0,35
SCE (%)		46,5 0,7 36-52	45,0 0,4 40-52	53,7** 0,7 48-62	47,9* 0,9 40-58	30-40
Coagulation	Prothrombin index (%)	89,0 0,9 80-100	84,2* 0,4 75-90	80,0** 2,7 54-108	87,0 2,1 68-100	80-100
	Plasma glucose tolerance (min)	8,8 0,3 6-12	9,4 0,2 7,0-12,0	11,2** 0,8 3-18	10,4 0,5 6-16	7-11
	Fibrinogen (g/l)	3,81 0,05 3,08-4,42	2,64* 0,18 1,75-5,60	1,94** 0,18 1,08-4,68	2,16 0,09 1,20-2,88	2,20-4,00
	Fibrinase (sec)	69,5 0,9 58-80	52,5* 2,9 20-85	68,7 2,8 38-100	65,7 2,5 42-98	55-85
	Fibrinolytic activity (min)	213,3 3,5 172-250	230,9* 5,0 170-280	171,0** 7,7 108-280	187,3 7,1 120-260	180-240

Note: * — the difference before and after treatment; ** — difference in duration of biliary occlusion.

In biliary occlusion up to 3-6 weeks content of blood cells decreased (from $p < 0.05$ to $p < 0.01$). Dynamic viscosity was in 1.2 times higher than upper limit of normal and indicators of viscosity of 10-days cholestasis. At the same time maximum shear stress corresponded to the beginning levels of the first group. Aggregation of red blood cells increased and their deformability reduced in comparison with the previous group. According to sorption capacity of red blood cells endogenous intoxication increased in 1.2 times. In the coagulation system prothrombin index, fibrinogen decreased, increased tolerance of plasma to heparin and blood fibrinolytic activity were registered, 60% of patients had hypocoagulation and 30% — hypercoagulation, which indicated deep disorders of rheology and hemostasis. Significant increase of gamma globulin on the backgroung of average dysproteinemia was registered among liver function tests. Bilirubin shortly increased in 2.7 times, alanine transaminase — in 3.7 times, aspartate transaminase — in 1.9 times, alkaline phosphatase increased in 1.9 times. Thus cytolytic processes significantly increased along with cholesta-

Table 2

Dynamics of homeostasis parameters before and after preoperative preparation of 1-6 days (M ÷ m, M ÷ M)

Parameters		Duration of cholestasis				Norm
		Up to 10 days		Up to 3–6 weeks		
		before	after	before	after	
Plasma proteins	Total (g/l)	66,0 0,3 63,5-75,8	71,4* 0,6 60-85	64,3 0,9 55-74	65,9 0,6 62-76	60-88
	Albumin (A) (%)	43,1 0,4 38,6-54,6	51,4* 0,5 43,3-54,6	42,6 0,8 33,0-53,0	43,6 0,9 34,0-58,0	55-62
	Gamma globulin (γ-gl) (%)	24,0 0,3 23,2-30,8	19,5* 0,09 18,0-20,2	28,2** 0,8 22,2-40,6	24,9* 0,7 20,0-38,0	15,1-21,0
	Coefficient of alb/glob.	0,76 0,02 0,62-0,91	1,06* 0,02 0,83-1,20	0,76 0,03 0,49-1,13	0,84 0,04 0,51-1,38	1,2-2,0
Residual nitrogen		23,9 0,2 19-26	18,4* 0,2 5,2-22,0	25,0 0,9 16,4-36,2	22,2 0,5 16-27,8	14,0-20,0
Bilirubin	Total (umol/L)	82,5 6,6 33,2-180	66,8 5,0 26,2-144,0	225,3** 15,4 68,8-430,0	165,5 4,6 120,9-221,7	8,55-20,5
	Direct (umol/L)	65,4 5,3 26,2-144	24,2* 0,7 17,8-32,5	108,5** 13,8 27,2-282,5	107,9 3,5 58,6-128,2	25%
Enzymes	Alanine transaminase (mmol/l)	0,71 0,09 0,22-2,00	0,407 0,04 0,16-1,10	2,62** 0,02 0,74-3,66	1,79* 0,02 0,70-3,00	0,1-0,68
	Aspartate transaminase (mmol/l)	0,40 0,01 0,14-0,50	0,26* 0,009 0,12-0,38	0,75** 0,03 0,18-0,94	1,12* 0,05 0,48-1,70	0,1-0,45
	Coefficient of De Rittis	0,56 0,02 0,37-0,83	0,65* 0,02 0,55-0,93	0,300 0,009 0,22-43	0,67* 0,02 0,55-0,93	1
	Alkaline phosphatase (units/l)	136,0 4,5 85-190	106* 5,2 71-190	262,2 12,4 101,370	217,5* 13,4 82-410	10-60
Lipids	Cholesterin (mmol/l)	4,20 0,06 3,2-5,2	4,03 0,08 3,00-5,10	6,04** 0,19 4,80-9,10	5,19* 0,20 3,80-8,28	3,1-6,0
	Lecithin (mmol/l)	1,71 0,04 1,2-2,26	1,45* 0,04 1,00-2,00	3,77** 0,12 2,32-4,89	3,25* 0,09 2,18-4,22	1,1-2,0
	ß-lipoproteins (g/l)	12,1 0,2 8,2-15,0	10,2* 0,4 7,1-19,0	61,7** 1,8 40,2-79,8	54,0* 1,4 38,0-71,0	1,3-7,3

Note: * — the difference before and after treatment; ** — difference in duration of biliary occlusion

sis. Significant disorders are registered in lipid metabolism: increased cholesterol, phospholipids and sharply increased (in 5.1 times) beta-lipoprotein, which causes alteration of structure and properties of cell membranes and severe blood rheological disorders (Table 1.2). Revealed disorders require integrated multi-component therapy taking into account severity of patient condition.

In the first group of patients with duration of biliary occlusion up to 10 days pre-operative preparation aimed to correction of disorders has been carried out from 1 to 7 days (average 1-3 days). Patients of the second group — from 1 to 7 days (average 4 days). In patients with acute liver failure this therapy was not more than 8 hours, then external drainage of the thoracic duct has often been performed, and day later biliary decompression with continuing complex therapy has been conducted.

Complex therapy included: mebrane, antiplatelet, hemotransfusional, detoxicational, protein-replacement therapy, intravenous infusions of polyelectrolyte solutions, polarizing glucose-insulin-potassium mixtures and hepatotropic, hemotransfusion, vitamin therapy. Membrane therapy consisted of α-tocopherol acetate (200-300 mg intramuscularly), essentiale (10.0 ml per 200 ml of 0.5% glucose solution intravenously), fresh frozen plasma (200-300 ml in a day or two). Ascorbic acid (by 10.0 ml of 5% solution 2-3 times intravenously) was administered. For correction of cytopenias we applied hemotransfusional therapy including the use of thawed cryopreserved washed fresh erythrocytes (TCWFE) or washed fresh erythrocytes (WFE), erythrocyte mass (EM). The average dose of administered solutions was 150-300 ml/day. To fill leukocytes we used leukocyte mass (LM), leukocyte suspension (Ls) in similar doses. Deficiency of platelet was corrected with intravenous infusion of platelets. Hepatotropic therapy included: essentiale (6 capsules/day), gepalif (3 capsules/day), sirepar (2.0 ml/day). Detoxication therapy comprised use of albumin, plasma, saline solutions with following forced diuresis. As antiplatelet therapy we used curantyl (0.15 g/d), trental (0.5 g/d), intravenous infusion of rheopolyglucin (400 ml/day) in courses of 3-4 days. Correction of immunological disorders included using of blood plasma, leukocyte suspension, intravenous infusion of hyperimmune plasma, gamma globulin. Vitamin therapy was carried out with vitamin A, group B, vikasol was administered intramuscularly according to indications (hypoproteinemia).

As result of treatment in patients with the first group cell content and rheology of blood slightly improved; the most significant improvement was in coefficient of erythrocyte deformability and maximum shear stress, which was primarily due to improved lipid metabolism particularly with reduction of beta-lipoprotein. Also hemostasis improved (Table 1,2). Dysproteinemia and gamma-globulinemia decreased. Concentration of residual nitrogen almost returned to normal, fibrinogen decreased moderately but not significantly, transaminases almost returned to normal. Cell content of blood in second group also remained virtually unchanged, high blood viscosity decreased but still remained, maximum shear stress improved, but lesser than aggregation and deformability of red blood cells in first group, their osmotic resistance improved and endointoxication moderately reduced . Indicators of blood coagulation system slightly improved without significant credibility.

Conclusion

Thus, in patients with obstructive jaundice on the background of disorder of lipid metabolism and endogenous intoxication we observed increase of viscosity, erythrocyte aggregation, reduction of their deformability, blood coagulation potential and increase fibrinolytic activity of blood. Hemorrhagic complications in obstructive jaundice promote activation of anticoagulation system of blood, especially fibrinolysis. Increased fibrinolytic activity indicates risk of occurrence of postoperative bleeding and decline — of thrombotic complications. All these changes are more significant in patients from the second group with prolonged obstructive jaundice, when cytolytic processes progressed along with cholestatic ones. All this requires prompt diagnosis and active preoperative correction. If we are basing only on clinical symptoms, this will lead to delay in identifying severe morphological and functional changes in liver and multiorgan failure. In these cases surgical correction is often too late and gives high mortality rate because complex multi-component active preoperative preparation for at least 3-5 days is required. It should be noted that changes in parameters of blood rheology usually precede the appearance of clinical signs of complications. Therefore, in terms of its prevention and early treatment it is important to identify through laboratory studies the mechanisms underlying the development of complications. Preoperative complex, conservative therapy should be directed to correction of disorders of blood aggregation and liver functions.

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