



THE EFFECT OF THERAPEUTIC CRYOAPHERESIS ON CLINICAL AND BIOCHEMICAL PARAMETERS OF HEMOPHILIA PATIENTS

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Abstract

The results of the analysis of the obtained laboratory data allow us to state that therapeutic cryoapheresis, introduced into the complex of therapy for patients with hemophilia, has practically no side effects on the patient's body. It should be noted that the use of this method in treatment helps to reduce the degree of anemia, eliminates the phenomenon of dysprotenemia while maintaining the function of liver cells.

Keywords: hemophilia, transfusion-corrective therapy

Introduction

In the treatment of patients with hemophilia, the main attention is paid to the development of special methods of plasmapheresis aimed at removing plasma components, which play a key role in the pathogenesis of immune disorders, a more reliable and effective method - cryoglobulin apheresis. To replace the volume of the obtained plasma, autologous plasma was used, taken from the patient during previous PF operations, from which cryoglobulins were removed by precipitation in the cold. Autologous plasma has a number of significant advantages over the use of other substitutes: the therapeutic efficacy of the medium itself (the absence of cryoglobulins), a relatively low cost, and a lower risk of transmission of viral hepatitis. Of the studied patients (51), relatively equal groups were composed - the main and the comparison group. The main group consisted of 25 patients who, along with transfusion-corrective therapy, received a course of therapeutic cryoapheresis. The comparison group consisted of 26 patients who received only transfusion-corrective (basic) therapy.





It should be noted that the initial clinical status and age of patients in each group were identical.

Indications for the inclusion of cryoafereza in the complex of therapeutic measures were frequent and persistent recurrences of bleeding, long periods of hematoma resorption, resistance to ongoing therapy, frequent post-transfusion reactions and profound disorders in the immune status of patients with hemophilia.

A total of 80 cryoapheresis operations were performed, on average, 4.0 ± 0.5 procedures per patient. The volume of blood extracted in each procedure was determined by the generally accepted calculation of oCP, taking into account the height, body weight of the patient and the severity of the condition. Intensive therapeutic cryoapheresis, i.e. extraction of more than $1/3$ oCP per operation was carried out in 43 procedures, which is 53.7% of the total. This regime was used mainly in the older age group (over 17 years old).

On average, 2670.0 ± 33.0 ml of plasma was subjected to cryotreatment during one course of treatment and 312.0 ± 14.0 ml of cryopreservation was removed. The interval between operations is 2-3 days. The duration of one session is from 40 minutes to 2 hours 30 minutes.

The majority - 23 (92%) patients underwent therapeutic kroiapheresis quite satisfactorily. Only during 4 procedures, at the stage of administration of the last portions of plasma, patients experienced a reaction in the form of a slight chill, which quickly stopped when the return rate slowed down (less than 50 drops per minute), in none of the cases it was necessary to end the procedure prematurely.

Difficulties in carrying out cryoapheresis procedures were in 12 cases, in 5 patients (20%). This was associated with poor access to the peripheral vein of patients and led to a decrease in the rate of blood exfusion, thrombosis of the needle, the formation of clots in the plastic container, difficult reinfusion of autoerythrocytes and ultimately required repeated venipuncture, which lengthened the procedure.

In 3 (12%) patients, hemodynamic reactions were observed, characterized by a temporary decrease in blood pressure (up to 80/50 mm Hg), tachycardia, and were caused by inadequate plasma replacement. This condition was easily stopped by intravenous injection of plasma-substituting solutions and did not interfere with the continuation of the procedure.

In the patients studied by us, no clinical manifestations of citrate intoxication were observed.

Thus, no significant deviations were found in the general condition of the observed patients during cryoapheresis procedures.



The effectiveness of the applied method of therapeutic cryoapheresis on the clinical manifestation of articular symptoms of hemophilia was evaluated in points, including pain intensity, stiffness, swelling, and the degree of limitation of joint function. The number of points proportionally reflected the severity of the clinical manifestation. When comparing these clinical symptoms in the two above compared groups of patients, significant differences were revealed (Table 1). At the same time, it should be noted that these indicators were recorded at approximately the same time interval, corresponding to the duration of the cryoapheresis course. As can be seen from the presented table, by the end of the course of cryoapheresis therapy, patients have a significant decrease in scores compared with the group of patients who did not receive this procedure for the same period of time. That is, in patients of the main group, for the same period of time, pain syndromes stopped faster, stiffness of the joints disappeared, hematomas resolved faster and swelling of the joints decreased, and the affected joint was restored earlier. In addition, against the background of the use of therapeutic cryoapheresis, the duration of transfusion-corrective therapy with antihemophilic blood products, their doses and frequency of administration decreased.

Table 1 Dynamics of the main articular symptoms of hemophilia (M±m)

Parameters	Control group (n=12)		Main group (n=12)		P	P1	P2
	Before treatment (in points)	After treatment (in points)	Before CF (in points)	After CF (in points)			
Pain	2,3±0,10	0,48±0,08	2,36±0,10	0,28±0,06	<0,001	<0,001	<0,05
stiffness	1,86±0,18	0,88±0,11	1,02±0,18	0	<0,001	<0,001	<0,01
puffiness	2,12±0,22	0,46±0,10	2,04±0,33	0,22±0,08	<0,001	<0,001	<0,05
Function dysfunction	2,62±0,38	1,68±0,11	2,55±0,42	1,05±0,20	<0,05	<0,01	<0,01

P - is the significance of the difference between the indices before and after treatment in patients of the control group, P1 - is the significance of the difference between the indices before and after cryoapheresis, P2 - is the significance of the difference between the indices of the compared groups after treatment. Along with this, the use of therapeutic cryoapheresis in complex transfusion-corrective therapy has reduced the length of stay of patients in the hospital. Thus, with the generally accepted method of treatment, patients stayed in the hospital for 25.8±2.4 k/days, and with the



inclusion of therapeutic cryoapheresis, the duration of bed-days decreased to 20.2 ± 1.3 k/days.

Thus, when comparing the clinical results in the main and compared groups, it was found that the inclusion of therapeutic cryoapheresis in the complex of therapeutic measures had a positive effect on the dynamics of the disease and contributed to a faster improvement in the patient's condition and a reduction in the recovery period. To identify the nature of the effect of cryoapheresis on hemogram parameters and the functional state of the liver, these parameters were studied in a group of patients who received cryoapheresis in the complex of treatment.

As can be seen from the data presented in Table 2, hemoglobin levels in patients with hemophilia before and after cryoapheresis had statistically significant differences (111.3 ± 3.6 g/l and 123.3 ± 1.8 g/l, respectively, $p < 0,05$). Similar changes were observed in the analysis of the number of erythrocytes and platelets in the compared groups: their content before the course

Table 2 Indicators of laboratory data in dynamics (n=22, M \pm m)

Parameters	Healthy (n=20)	Before cryoapheresis	After cryoapheresis	P	P1
Hemoglobin g/l	138,6 \pm 2,2	111,3 \pm 3,6	123,3 \pm 1,8	P<0,001	P<0,05
Erythrocytes, x10/l	4,8 \pm 0,1	4,0 \pm 0,1	4,3 \pm 0,1	P<0,001	P<0,05
Platelets, x10/L	285,0 \pm 4,2	212,8 \pm 9,8	254,9 \pm 8,2	P<0,001	P<0,05
ООЗММ/ч	3,6 \pm 0,4	4,9 \pm 0,5	4,0 \pm 0,5	P>0,05	P>0,05
Blood protein, г/л	77,1 \pm 1,1	72,6 \pm 0,9	68,7 \pm 0,7	P<0,05	P<0,05
Albumen g/l	46,6 \pm 0,7	36,7 \pm 0,4	40,8 \pm 0,5	P<0,001	P<0,001
α 1-Globulin, g/l	3,1 \pm 0,4	3,1 \pm 0,1	3,0 \pm 0,1	P>0,05	P>0,05
α 2-Globulin, g/l	6,0 \pm 0,1	8,1 \pm 0,4	5,6 \pm 0,4	P<0,001	P<0,001
β Globulin g/l	8,2 \pm 0,2	7,0 \pm 1,2	8,4 \pm 0,6	P>0,05	P>0,05
ϕ -Globulin g/l	13,2 \pm 0,6	17,7 \pm 1,2	12,9 \pm 1,0	P<0,001	P<0,05

P - significant differences with indicators in healthy people

P1 - significant differences between the indicators before and after treatment.

cryoapherese was $4.0 \pm 0.1 \times 10^9$ /l and $212.8 \pm 9.8 \times 10^9$ /l, and after - $4.3 \pm 0.1 \times 10^9$ /l and $254.9 \pm 8.2 \times 10^9$ /l, respectively ($p < 0.05$ in both cases),



When studying the content of total protein in the blood serum, it was found that its level slightly decreases after a course of cryoapheresis, amounting to 68.7 ± 0.7 g/l, compared with the initial data of 72.6 ± 0.9 g/l ($p < 0.05$), but at the same time, a positive effect of cryoapheresis on the qualitative composition of plasma proteins was found. Thus, the elevated values of α_2 -globulin and γ -globulin before the cryoapheresis procedure (8.1 ± 0.4 g/l and 17.7 ± 1.2 g/l, respectively) decreased statistically significantly after the course of cryoapheresis (5.6 ± 0.4 g/l and 12.9 ± 1.0 g/l ($P < 0.001$ in the first case and $P < 0.05$ in the second case) and reached the level of these indicators in healthy people.

To assess the enzymatic function of the liver, the content of transferases - ALT and AST, as well as the level of bilirubin before and after cryoapheresis were studied, while no significant differences were found ($P > 0.05$ for all studied values).

Thus, the results of the analysis of the obtained laboratory data allow us to state that therapeutic cryoapheresis, introduced into the complex of therapy for patients with hemophilia, has practically no side effects on the patient's body. It should be noted that the use of this method in treatment helps to reduce the degree of anemia, eliminates the phenomenon of dysprotenemia while maintaining the function of liver cells.

References

1. Rose E. Nasal spray desmopressin (DDAVP) for mild hemophilia A and von Willebrand disease // An Intern. Med.- 1991.- Vol.1:114. № 7. - P. 563-568
2. Purity of factor VW concentratos and immune function in hemophiliacs // Blood. - 1992. Vol. 73, № 10, P. 2800
3. Абдукадилова Н. Б., Раббимова Д. Т., Хаятова З. Б. Роль дисплазий соединительной ткани в развитии патологии различных систем организма // Journal of Siberian Medical Sciences. – 2020. – №. 3. – С. 126-135
4. Rabbimova D. Bacteriological investigation and method of antigen connected lymphocytes (acl) in defining etiological structure of sepsis in children in the early AGE // Medical Health and Science Journal. - 2010. - Т. 4. - No. 4. - S. 51-53.
5. Раббимова Д., Юсупов Ф. Регуляторная функция внс при сепсисе у детей первого года жизни по данным кардиоинтервалографии // Журнал гепатогастроэнтерологических исследований. – 2021. – Т. 2. – №. 3.1. – С. 97-100.

