International Journal of Pediatrics and Genetics
Vol. 2 No. 8 (2024)
ISSN: 2995-5483

The Use of Therapeutic Cryoapheresis in the Treatment of Patients with Hemophilia

Yusupov Fazliddin Tozhievich
PhD, Assistant of the Department of Therapy 3, Samarkand Medical University, Samarkand, Uzbekistan

Rabbimova Dilfuza Toshtemirovna
DcS, Associate Professor, Head of the Department of Propaedeutics of Childhood Diseases, Samarkand Medical University, Samarkand, Uzbekistan

Abstract: The analysis of the obtained laboratory data indicates that therapeutic cryoapheresis, when incorporated into the treatment regimen for patients with haemophilia, exhibits minimal side effects on the patient's body. Notably, this method aids in reducing anaemia severity and resolves dysproteinemia while preserving liver cell function.

Key words: haemophilia, therapeutic cryoapheresis, biochemical parameters.

Methods and Study Design. Among the 51 patients studied, two relatively equivalent groups were formed: the main group and the comparison group. The main group included 25 patients who received a course of therapeutic cryoapheresis alongside transfusion-corrective therapy, while the comparison group comprised 26 patients who received only transfusion-corrective (basic) therapy. The initial clinical status and age of patients in each group were identical.

Inclusion Criteria

Cryoapheresis was indicated for patients experiencing frequent and persistent bleeding, prolonged hematoma resorption, resistance to therapy, frequent post-transfusion reactions, and significant immune status disorders. A total of 80 cryoapheresis operations were performed, averaging 4.0±0.5 procedures per patient. The volume of blood extracted in each procedure was determined by standard calculations, considering the patient's height, body weight, and condition severity.

Procedure Details

Intensive therapeutic cryoapheresis, involving the extraction of more than one-third of the calculated blood volume per operation, was conducted in 43 procedures (53.7% of the total), primarily in patients older than 17 years. On average, 2670.0±33.0 ml of plasma was processed per treatment course, with 312.0±14.0 ml of cryoprecipitate removed. The interval between operations was 2-3 days, and each session lasted between 40 minutes and 2 hours 30 minutes.

The majority of patients (23 or 92%) tolerated therapeutic cryoapheresis well. Only four procedures elicited mild reactions such as slight chills, which were quickly mitigated by slowing the return rate of plasma (less than 50 drops per minute), without necessitating premature termination of the procedure. Difficulties encountered during 12 procedures in 5 patients (20%) were primarily due to poor peripheral vein access, leading to reduced blood exfusion rates, needle thrombosis, clot formation in plastic containers, and challenges in reinfusing autoerythrocytes, ultimately requiring repeated venipuncture and extending the procedure duration.

Hemodynamic reactions, characterized by temporary drops in blood pressure (to 80/50 mmHg) and tachycardia due to inadequate plasma substitution, were observed in 3 patients (12%). These conditions were easily managed with intravenous plasma-substituting solutions, allowing the procedure to continue. No clinical manifestations of citrate intoxication were observed in the studied patients.

No significant deviations in the general condition of patients were detected during cryoapheresis procedures. The effectiveness of therapeutic cryoapheresis was evaluated based on the clinical manifestation of joint symptoms in hemophilia, including pain intensity, stiffness, swelling, and the degree of joint function limitation. The severity of clinical manifestations was assessed using a point system, revealing significant differences between the main and comparison groups (Table 14). These indicators were recorded within the same time interval corresponding to the duration of the cryoapheresis course.

The data suggest that hypersympathicotonia is prevalent in children with central nervous system damage, as evidenced by significantly higher IN values compared to healthy children. This elevated IN reflects greater strain on adaptation mechanisms, placing these children at higher risk for developing severe infectious and inflammatory diseases, including sepsis.

Table 1 Dynamics of the main joint symptoms of hemophilia (M=m)

Indicators	Control group (n=12)				P	P1	P2
	Before treatment (in points)	After treatment (in points)	Up to 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
	1,86±0,18	0,88±0,11	1,02±0,18	0	<0,001	<0,001	<0,01
Stiffness	2,12±0,22	0,46±0,10	2,04±0,33	0,22±0,08	<0,001	<0,001	<0,05
	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 reliability of the difference between the indicators before and after treatment in patients of the control group.

P1 - the reliability of the difference between the indicators before and after cryoaferesis.

P2 - the reliability of the difference between the indicators of the compared groups after treatment.

As can be seen from the table below, by the end of the course of cryoaferesis therapy, patients showed a significant decrease in scores compared to the group of patients who did not receive this procedure in the same period. That is, in patients of the main group, pain syndromes were stopped faster over the same period, joint stiffness disappeared, hematomas resolved faster and joint swelling decreased, and the affected joint was restored earlier. In addition, against the background of the use of therapeutic cryoaferesis, the duration of transfusion-correcting therapy with antihemophilic blood drugs, their doses and the frequency of administration decreased.

Along with this, the use of therapeutic cryoaferesis 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 were hospitalized at 25.8 ±2.4 k/day, and when therapeutic cryoaferesis was turned on, the duration of bed days was reduced to 20.2 ± 1.3 k/day.

Thus, when comparing the clinical results in the main and compared groups, it was found that the inclusion of therapeutic cryoaferesis 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, shortening the recovery period.

To identify the nature of the effect of cryoaferesis on hemogram parameters and the functional state of the liver, a study of these indicators was conducted in a group of patients receiving cryoaferesis in a treatment package.

Table 2 Laboratory data indicators in dynamics (n=22) (M=m).

Indicators	healthy (n=20)	Before cryopheresis	After cryopheresis	P	P1
Hemoglobin	138,6±2,2	111,3±3,6	123,3±1,8	P<0,001	P<0,05
g/l	4,8±0,1	4,0±0,1	4,3±0,1	P<0,001	P<0,05
Red blood cells,	285,0±4,2	212,8±9,8	254,9±8,2	P<0,001	P<0,05
x10/l	3,6±0,4	4,9±0,5	4,0±0,5	P>0,05	P>0,05
Platelets,	77,1±1,1	72,6±0,9	68,7±0,7	P<0,05	P<0,05
x10/l	46,6±0,7	36,7±0,4	40,8±0,5	P<0,001	P<0,001
OOZ	3,1±0,4	3,1±0,1	3,0±0,1	P>0,05	P>0,05
mm/h	6,0±0,1	8,1±0,4	5,6±0,4	P<0,001	P<0,001
Blood protein,	8,2±0,2	7,0±1,2	8,4±0,6	P>0,05	P>0,05
g/l	13,2±0,6	17,7±1,2	12,9±1,0	P<0,001	P<0,05

Results and Discussion

Significant Differences Indicators

- P: Significant differences with indicators in healthy individuals.
- P1: Significant differences between the indicators before and after treatment.

As illustrated in Table 15, there were statistically significant differences in hemoglobin levels in patients with hemophilia before and after cryoapheresis (111.3±3.6 g/L and 123.3±1.8 g/L, respectively, P<0.05). Similar changes were observed in erythrocyte and platelet counts: before cryoapheresis, their levels were 4.0±0.1 x 10^12/L and 212.8±9.8 x 10^9/L, respectively, and after the treatment, they increased to 4.3±0.1 x 10^12/L and 254.9±8.2 x 10^9/L (P<0.05 in both cases).

When examining the total protein content in blood serum, it was observed that its level slightly decreased after cryoapheresis, amounting to 68.7±0.7 g/L compared to the initial value of 72.6±0.9 g/L (P<0.05). However, a positive effect of cryoapheresis on the qualitative composition of plasma proteins was noted. Elevated levels of α2-globulin and γ-globulin before cryoapheresis (8.1±0.4 g/L and 17.7±1.2 g/L, respectively) significantly decreased after the treatment (5.6±0.4 g/L and 12.9±1.0 g/L, P<0.001 and P<0.05, respectively), reaching levels comparable to those in healthy individuals.

To assess liver enzymatic function, the content of transferases (ALT and AST) and bilirubin levels were measured before and after cryoapheresis, with no significant differences found (P>0.05 for all studied values).

Thus, the analysis of the obtained laboratory data indicates that therapeutic cryoapheresis, when included in the treatment regimen for patients with hemophilia, has minimal side effects. The use of this method in treatment helps to reduce anaemia severity, resolves dysproteinemia, and preserves liver cell function.

References:

1. Абдукадирова 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.
2. Раббимова Д. Т. и др. Особенности распределения HLA-антигенов у младенцев с сепсисом //Вопросы науки и образования. – 2019. – №. 27 (76). – С. 32-39.

3. Раббимова Д. Т., Юсупов Ф. Т. Роль анаэробной инфекции в этиологической структуре гнойно-септических заболеваний у детей раннего возраста //ЖУРНАЛ ГЕПАТО-ГАСТРОЭНТЕРОЛОГИЧЕСКИХ ИССЛЕДОВАНИЙ. – 2022. – Т. 3. – №. 3.
4. Раббимова Д. Т., Юсупов Ф. Т. СОСТОЯНИЕ ИММУННОЙ СИСТЕМЫ И РАЗВИТИЕ ПОСТТРАНСФУЗИОННЫХ ОСЛОЖНЕНИЙ У БОЛЬНЫХ ГЕМОФИЛИЕЙ //Journal of cardiorespiratory research. – 2022. – Т. 3. – №. 2. – С. 77-80
5. Раббимова Д. Т., Юсупов Ф. Т. ЭФФЕКТИВНОСТЬ СОЧЕТАННОЙ ДЕКОНТАМИНАЦИИ И НЕЙРОПРОТЕКЦИИ В ЛЕЧЕНИИ СЕПСИСА У ДЕТЕЙ ПЕРВОГО ГОДА ЖИЗНИ //ЖУРНАЛ ГЕПАТО-ГАСТРОЭНТЕРОЛОГИЧЕСКИХ ИССЛЕДОВАНИЙ. – 2022. – Т. 3. – №. 3.
6. Абдукадирова Н. Б., Раббимова Д. Т., Хаятова З. Б. The role of connective tissue dysplasias in pathology of various body systems //Journal of Siberian Medical Sciences. – 2020. – №. 3. – С. 126-135.
7. Toshtemirovna R. D., Tozhievich Y. F. The effect of therapeutic cryoapheresis on clinical and biochemical parameters of hemophilia patients. – 2022.
8. Раббимова Д. Т. Состояние регуляции вегетативной нервной системы у младенцев с сепсисом //Science and Education. – 2023. – Т. 4. – №. 2. – С. 229-238.
9. Раббимова Д. Т., Юсупов Ф. Т. ВЛИЯНИЕ ЛЕЧЕБНОГО КРИОАФЕРЕЗА НА КЛИНИЧЕСКИЕ И БИОХИМИЧЕСКИЕ ПОКАЗАТЕЛИ У БОЛЬНЫХ ГЕМОФИЛИЕЙ //Miasto Przyszłości. – 2024. – Т. 47. – С. 410-417.
10. Раббимова Д. Т., Юсупов Ф. Т. УЛУЧШЕНИЕ ЛЕЧЕНИЯ СЕПСИСА У ДЕТЕЙ МЛАДШЕГО ВОЗРАСТА //Miasto Przyszłości. – 2024. – Т. 47. – С. 404-409.
11. Раббимова Д. Т. Характер распределения HLA-антигенов у младенцев с сепсисом //Science and Education. – 2023. – Т. 4. – №. 2. – С. 87-92.
12. Toshtemirovna R. D., Mansurovna S. G. THE ROLE OF CLOSTRIDIUM DIFFICILE IN THE DEVELOPMENT OF ANTIBIOTIC-ASSOCIATED DIARRHEA IN EARLY-AGED CHILDREN //International Journal of Medical Sciences and Clinical Research. – 2024. – Т. 4. – №. 06. – С. 12-17.
13. Mukhitdinovich S. A., Tashtemirovna R. D. Comprehensive approach to the problem of rehabilitation of infants submitted sepsis //Вопросы науки и образования. – 2017. – №. 10 (11). – С. 152-156.
14. Rabbimova D. Bacteriological investigation and method of antigen connected lymphocytes (ACL) in defining etiological structure of sepsis in children in the early age //Medical and Health Science Journal. – 2010. – Т. 4. – С. 51-54.
15. Toshtemirovna R. D., Tozhievich Y. F. The effect of therapeutic cryoapheresis on clinical and biochemical parameters of hemophilia patients //Web of Scientist: International Scientific Research Journal. – 2022. – Т. 3. – №. 5. – С. 1003-1007.