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The comparative study between treatment with Cryoprecipitate and recombinant Factor VIII in Hemophilia in children

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Abstract

Introduction: Hemophilia A is a genetic disorder caused by a deficiency or absence of coagulation Factor VIII, leading to impaired blood clotting and prolonged bleeding, especially into joints and muscles. Without appropriate treatment, recurrent bleeding can result in chronic joint damage and disability. Traditionally, Cryoprecipitate, a blood product containing concentrated clotting factors, has been used to manage bleeding episodes in patients with Hemophilia A. However, with advancements in biotechnology, recombinant Factor VIII, a synthetic product, has become an alternative. Recombinant Factor VIII eliminates the risks associated with blood-derived products, such as viral transmission, and offers more consistent dosing and availability. Despite these advantages, recombinant therapies are significantly more expensive. This study seeks to compare the clinical efficacy, safety of Cryoprecipitate versus recombinant Factor VIII in pediatric patients with Hemophilia A, providing critical insights for optimal management strategies.

Purpose: The purpose of this study is to compare the clinical outcomes, safety of Cryoprecipitate versus recombinant Factor VIII in the management of children diagnosed with Hemophilia A.

Materials and methods: This retrospective study included 32 pediatric patients diagnosed with Hemophilia A, treated either with Cryoprecipitate or recombinant Factor VIII. Clinical data were collected on bleeding frequency, Factor VIII recovery. Statistical analyses were conducted to determine significant differences between the two groups.

Results: The study demonstrated that treatment with recombinant Factor VIII resulted in significantly improved clinical outcomes compared to Cryoprecipitate. In the group treated with recombinant Factor VIII, patients required scheduled hospitalizations for routine follow-up and management, with no reports of acute bleeding episodes during these admissions. This contrasts sharply with the Cryoprecipitate group, where all hospitalizations were precipitated by acute bleeding events, necessitating urgent intervention.

Conclusions: Recombinant Factor VIII demonstrates superior efficacy in managing Hemophilia A in children compared to Cryoprecipitate. Recombinant therapy provides better clinical outcomes, justifying its use in modern treatment protocols.

Keywords: Crioprecipitat; Hemophilia; Factor VIII; Factor VIII recombinat

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1. Introduction

Hemophilia is a rare hereditary disorder characterized by impaired blood clotting due to the lack or reduced activity of clotting factors. The two main forms are Hemophilia A, caused by a deficiency of Factor VIII, and Hemophilia B, caused by a deficiency of Factor IX. In the absence of appropriate treatment, hemophilia can lead to severe bleeding, joint dysfunction, and disability. Over the years, hemophilia treatment has evolved significantly, from classic therapies based on blood-derived products to innovative treatments, including recombinant agents and biological therapies like Emicizumab.

Initial period – Therapy with blood-derived products. At the beginning of the 20th century, treatment for hemophilia was limited and rudimentary, relying on whole blood transfusions. This treatment was not an effective solution, as whole blood contained only small amounts of active clotting factors. The evolution toward the use of plasma and fresh frozen plasma (FFP) concentrates improved treatment, but significant risks remained, including adverse reactions and the possibility of transmitting infectious diseases [1].

Introduction of Cryoprecipitate. An important step in hemophilia treatment was achieved in the 1960s with the development of cryoprecipitate, a plasma-derived product rich in Factors VIII and XIII. Cryoprecipitate was an improvement over the use of whole plasma and was used for several decades as the standard treatment for Hemophilia A. Although cryoprecipitate significantly reduced mortality associated with major bleeding, the risks of viral infections, such as HIV and hepatitis, remained a serious issue [2].

Recombinant coagulation factor therapy. In the 1980s, the HIV epidemic and bloodborne hepatitis highlighted the urgency of developing safer therapies. With advances in biotechnology, recombinant coagulation factors were produced, which no longer carried the infection risks associated with plasma products. The first recombinant Factor VIII was approved for use in the 1990s, revolutionizing the treatment of Hemophilia A. These recombinant agents have provided patients with increased safety and a constant supply, thus reducing the risks of hemorrhagic complications and infection transmission [3].

Prophylactic therapy and its impact on quality of life. In recent decades, hemophilia treatment has shifted from on-demand therapy (administered only in the event of bleeding) to prophylaxis, where Factor VIII or IX is administered regularly to prevent bleeding. This paradigm shift has significantly reduced the number of hemorrhagic episodes, improving patients' quality of life, especially for children. Studies have shown that early prophylaxis can prevent joint damage and reduce the rate of emergency hospitalizations [4].

Biological treatments – The introduction of Emicizumab. A major breakthrough in hemophilia treatment came with the development of Emicizumab, a bispecific monoclonal antibody approved for the treatment of Hemophilia A. Emicizumab mimics the activity of Factor VIII without being an actual clotting factor. This medication was initially approved for patients with Factor VIII inhibitors but has also proven effective in patients without inhibitors. One of Emicizumab's main advantages is its subcutaneous administration, which significantly reduces the frequency of intravenous injections required for recombinant Factor VIII treatments. Additionally, Emicizumab provides more stable control of bleeding, and recent studies suggest it can reduce the need for hospitalizations and emergency interventions [5].

The impact of innovative therapies on patients' lives. With the introduction of biological treatments such as Emicizumab, patients with Hemophilia A enjoy a significantly improved quality of life. In addition to its efficacy, Emicizumab therapy offers the convenience of subcutaneous administration and reduces the frequency of hospitalizations. These advancements are essential in preventing long-term complications and offer new hope to young patients who can avoid the severe complications associated with recurrent bleeding [6].

1.1. Prophylactic Therapy and Its Impact on the Quality of Life in Hemophilia Patients

Prophylactic treatment is an essential component in the management of hemophilia, aiming to prevent recurrent bleeding episodes and reduce the risk of joint damage and other long-term complications. Unlike on-demand therapy, which is administered only in the event of a bleeding episode, prophylaxis involves the regular administration of clotting factors to maintain their levels within a range that prevents spontaneous bleeding.

1.1.1. Prophylactic Administration Schemes

Prophylactic administration schemes can vary depending on the severity of hemophilia, the patient's age, and their individual response to treatment. In general, prophylaxis can be continuous or intervention-based, with doses adjusted to maintain clotting factor levels above a minimum threshold considered safe (usually above 1% of normal levels).

Continuous Prophylaxis (Regular Prophylaxis):

- Frequency of Administration: specific 2-3 times a week.
- Doses Used: A variety of doses depending on the product used and the individual needs of the patient. For example, recombinant Factor VIII can be administered in doses of 25-50 IU/kg, depending on the factor's activity and the frequency of bleeding episodes.
- Goal: To maintain a constant level of clotting factor to prevent spontaneous bleeding and reduce joint damage.
- Intermittent Prophylaxis (Intervention-Based Prophylaxis):
- Frequency of Administration: Additional administrations during periods of intense physical activity or in high-risk situations.
- Doses Used: Similar to continuous prophylaxis but adjusted based on specific needs.
- Goal: To prevent bleeding in high-risk contexts without maintaining a constant factor level.

Impact of Prophylaxis on Quality of Life

The implementation of prophylactic therapy has demonstrated a significant improvement in the quality of life for hemophilia patients, especially in children. Studies have highlighted the following benefits:

1.1.2. Reduction in Bleeding Episodes

Prophylaxis reduces the frequency and severity of bleeding episodes, diminishing the need for emergency interventions and hospitalizations [10].

1.1.3. Prevention of Joint Damage

Regular administration of clotting factors prevents joint bleeds, which can lead to hemophilic arthropathy and decreased mobility [9].

1.1.4. Improvement in Physical Activity and Social Participation

Patients on prophylaxis can participate more actively in physical and social activities, leading a more normal life with fewer restrictions due to the fear of bleeding [7].

1.1.5. Reduction in Psychological Impact

The stability provided by prophylaxis reduces the anxiety associated with bleeding risks, contributing to better mental health for both patients and their families [8].

1.1.6. Long-term Cost Savings

Although prophylaxis involves higher initial costs, long-term savings can be achieved by reducing the number of complications, hospitalizations, and costly surgical interventions [9].

Examples of Prophylaxis Regimens in Practice

An example of a continuous prophylaxis regimen might involve administering 25 IU/kg of recombinant Factor VIII three times a week. This regimen has been associated with a significant reduction in spontaneous bleeds and maintaining clotting factor levels above 1%, thus preventing joint damage [10].

For more active patients or those who experience frequent bleeds, the regimen may be adjusted to four or more weekly administrations, with doses tailored to maintain clotting factor levels within ranges considered optimal for preventing bleeding [11].

Considerations for Adherence to Treatment

Adherence to the prophylactic regimen is crucial for the success of therapy. Factors such as administration frequency, regimen complexity, and impact on lifestyle can influence patient adherence. The introduction of therapies requiring

less frequent administration, such as Emicizumab, has significantly improved adherence by offering better control of bleeding and reducing the need for frequent infusions [12].

2. Materials and Methods

In this research, we used both medical records for a descriptive retrospective study and data collected directly from patients hospitalized in the pediatric hematology department. The retrospective study included a detailed analysis of the records of patients with hemophilia, highlighting the type of treatment administered (Cryoprecipitate or recombinant Factor VIII). Additionally, clinical and paraclinical evaluations were conducted based on current observations of hospitalized patients, contributing to a comprehensive perspective on the effectiveness of the compared treatments.

3. Results

In our study, we rigorously selected 32 patients from an initial group of 90, all of whom were diagnosed with hemophilia, which was subsequently confirmed. We divided these patients into two distinct groups: 16 were treated with cryoprecipitate, while the other 16 received recombinant FVIII. The medical details of these patients were meticulously examined, starting from their first hospitalization when the diagnosis was established, and we carefully analyzed their clinical evolution over a three-year period. We accurately recorded the number of hospitalizations per year and documented in detail the clinical manifestations of the hemorrhagic syndrome. This comprehensive analysis allowed us to thoroughly assess the effectiveness and impact of the administered treatment on the progression of the disease and the health status of our patients [Table 1].

Tabel 1 General characteristics of groups

		Substitution therapy					
		Cryoprecipitate		**FVIII**		**Total**	
		Nr. pac.	**%**	**Nr.pac.**	**%**	**Nr.pac.**	**%**
Type	HA	15	93.75	15	93.75	30	93.75
	HB	1	6.25	1	6.25	2	6.25
	Total	16	100.00	16	100.00	32	100.00

Hemophilia, a genetic condition with a significant impact on quality of life, is characterized by the early onset of symptoms, necessitating prompt and effective diagnosis. In our study, we observed that the children included were identified with this condition within the first two years of life. We found that 68.75% of cases (22 patients) received a confirmed diagnosis within the first year of life, while 31.25% of cases (10 patients) were diagnosed in the second year of life. These data clearly illustrate the early impact of hemophilia and emphasize the need for a practical approach in detecting and managing this condition, providing essential insights for improving the quality of life of patients [Table 2].

Table 2 Determining the age of primary diagnosis

		Substitution therapy					
		Cryoprecipitate		**Factor VIII**		**Total**	
		Nr.	**%**	**Nr.**	**%**	**Nr.**	**%**
Age of primary diagnosis	1-12 months	11	68.75	11	68.75	22	68.75
	12-48 months	5	31.25	5	31.25	10	31.25
	Total	16	100.00	16	100.00	32	100.00

In the first year of clinical monitoring, it was found that patients required at least one hospitalization for replacement therapy. During this time frame, 56.25% of cases (9 children) treated with cryoprecipitate and 31.25% of cases (5 children) treated with recombinant Factor VIII required hospitalizations. Repeated hospitalizations were also observed in both treatment groups: two hospitalizations were necessary in 18.75% of cases (3 children) for cryoprecipitate and in 25.00% of cases (4 children) for Factor VIII; three hospitalizations were recorded in 18.75% of cases (3 children) for cryoprecipitate and in 12.50% of cases (2 children) for Factor VIII; four hospitalizations were necessary in 6.25% of cases (1 child) for cryoprecipitate and in 18.75% of cases (3 children) for Factor VIII. Notably, only in the group treated with Factor VIII were repeated hospitalizations of up to seven times in one year recorded, affecting 12.50% of cases (2 children), thus suggesting an increased degree of complexity in managing and controlling this condition in this specific therapeutic context [Table 3].

Table 3 Assessment of the number of hospitalizations in the first year after the primary diagnosis

		Substitution therapy					
		Cryoprecipitate		**Factor VIII**		**Total**	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Number of hospitalizations in the first year of monitoring	1	9	56.25	5	31.25	14	43.75
	2	3	18.75	4	25.00	7	21.88
	3	3	18.75	2	12.50	5	15.63
	4	1	6.25	3	18.75	4	12.50
	7	0	0.00	2	12.50	2	6.25
	Total	16	100.00	16	100.00	32	100.00

In the second year of clinical monitoring, it was observed that 6.25% of patients (1 child) did not require hospitalization for treatment. However, at least one hospitalization for replacement therapy was necessary in 25.00% of cases (4 children), with an equal frequency for both types of treatment. Repeated hospitalizations were also recorded in the second year, for both cryoprecipitate and Factor VIII: two hospitalizations were necessary in 6.25% of cases (1 child) for cryoprecipitate and in 12.50% of cases (2 children) for Factor VIII; three hospitalizations were necessary in 18.75% of cases (3 children) for cryoprecipitate and in 25.00% of cases (4 children) for Factor VIII; four hospitalizations were necessary in 25.00% of cases (4 children) for cryoprecipitate and in 18.75% of cases (3 children) for Factor VIII; five hospitalizations were necessary in 6.25% of cases (1 child) only for Factor VIII; seven hospitalizations were necessary in 6.25% of cases (1 child) only for cryoprecipitate; nine hospitalizations were necessary in 6.25% of cases (1 child) only for Factor VIII; ten hospitalizations were necessary in 6.25% of cases (1 child), with an equal frequency for both groups. Notably, in the group treated with cryoprecipitate, repeated hospitalizations of up to 11 times in one year were recorded, affecting 6.25% of cases (1 child), illustrating the complexity and diversity of care and management needs for this condition in a clinical context [Table 4].

Table 4 Assessment of the number of hospitalizations in the second year after the primary diagnosis

		Substitution therapy					
		Cryoprecipitate		**Factor VIII**		**Total**	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Number of hospitalizations in the second year of monitoring	0	1	6.25	0	0.00	1	3.13
	1	4	25.00	4	25.00	8	25.00
	2	1	6.25	2	12.50	3	9.38
	3	3	18.75	4	25.00	7	21.88
	4	4	25.00	3	18.75	7	21.88
	5	0	0.00	1	6.25	1	3.13

	7	1	6.25	0	0.00	1	3.13
	9	0	0.00	1	6.25	1	3.13
	10	1	6.25	1	6.25	2	6.25
	11	1	6.25	0	0.00	1	3.13
	Total	16	100.00	16	100.00	32	100.00

In the third year of clinical monitoring, as in the second year, 6.25% of patients (1 child) did not require hospitalization for treatment. At least one hospitalization for replacement therapy was necessary in 21.88% of cases (7 children), with a frequency of 25.00% (4 children) for replacement therapy with FVIII and 18.75% (3 children) for treatment with Cryoprecipitate. Repeated hospitalizations were also recorded in the third year, for both cryoprecipitate and Factor VIII:

- Two hospitalizations were necessary in 12.50% of cases (2 children) for cryoprecipitate and in 25.00% of cases (4 children) for Factor VIII;
- Three hospitalizations were necessary in 18.75% of cases (3 children) for cryoprecipitate and in 6.25% of cases (1 child) for Factor VIII;
- Four hospitalizations were necessary in 12.25% of cases (2 children) for cryoprecipitate and in 18.75% of cases (3 children) for Factor VIII;
- Five hospitalizations were necessary only for patients with cryoprecipitate replacement in 12.50% of cases (2 children);
- Seven hospitalizations were necessary only for patients with cryoprecipitate replacement therapy in 6.25% of cases (1 child);
- Eight or ten hospitalizations were necessary in 6.25% of cases (1 child) only for Factor VIII;
- Ten hospitalizations were necessary in 6.25% of cases (1 child), with an equal frequency for both groups.

Notably, in the group treated with cryoprecipitate, repeated hospitalizations of up to 11 times were recorded in the third year, affecting 6.25% of cases (1 child), thus illustrating the complexity and diversity of care and management needs for this condition in a clinical context [Table 5].

Table 5 Assessment of the number of hospitalizations in the third year after the primary diagnosis

		Substitution therapy					
		Cryoprecipitate		**F VIII**		**Total**	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Number of hospitalizations in the third year of monitoring	0	1	6.25	2	12.50	3	9.38
	1	3	18.75	4	25.00	7	21.88
	2	2	12.50	4	25.00	6	18.75
	3	3	18.75	1	6.25	4	12.50
	4	2	12.50	3	18.75	5	15.63
	5	2	12.50	0	0.00	2	6.25
	6	1	6.25	0	0.00	1	3.13
	7	1	6.25	0	0.00	1	3.13
	8	0	0.00	1	6.25	1	3.13
	10	0	0.00	1	6.25	1	3.13
	11	1	6.25	0	0.00	1	3.13
	Total	16	100.00	16	100.00	32	100.00

3.1. The comparative study results between Cryoprecipitate and Recombinant Factor treatment regarding the control of bleeding syndrome recurrences

The analysis of the data from the provided table shows the distribution of substitution treatment with cryoprecipitate and factor VIII (F VIII) for managing hematomas—this being the admission diagnosis. The data are presented as the number of admissions and corresponding percentages for different degrees of hematoma severity during treatment. Additionally, the figures suggest that, despite balanced therapeutic preferences, there are variations in treatment efficacy depending on the severity of the hematoma. The results indicate that for higher-grade hematomas (grades 2 and 3), treatment with F VIII was predominant, possibly reflecting a higher efficacy of this treatment in severe cases. This aspect is crucial as it suggests that F VIII may be more effective in the management of severe hematomas, while cryoprecipitate may suffice for milder cases. These findings are fundamental for improving treatment protocols and for personalizing therapy based on the individual needs of patients, with the ultimate goal of optimizing clinical outcomes and reducing the risks associated with treatments. [Table 6

Table 6 Comparative characteristics of the number of admissions with the diagnosis of hematoma in various locations depending on the type of treatment administered (Cryoprecipitate or Recombinant Factor)

		Substitution therapy					
		Cryoprecipitate		**F VIII**		**Total**	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Hematoma	0	3	18.75	0	0.00	3	9.38
	1	4	25.00	0	0.00	4	12.50
	2	1	6.25	5	31.25	6	18.75
	3	2	12.50	5	31.25	7	21.88
	4	1	6.25	1	6.25	2	6.25
	5	1	6.25	1	6.25	2	6.25
	6	1	6.25	1	6.25	2	6.25
	7	1	6.25	0	0.00	1	3.13
	8	0	0.00	1	6.25	1	3.13
	10	1	6.25	0	0.00	1	3.13
	12	1	6.25	0	0.00	1	3.13
	15	0	0.00	1	6.25	1	3.13
	18	0	0.00	1	6.25	1	3.13
	Total	16	100.00	16	100.00	32	100.00

The table below presents comparative data on substitution treatment with Cryoprecipitate and substitution treatment with F VIII for the management of hemarthroses. According to the table data, 28.13% of cases (9 children) were admitted due to hemarthrosis in 3 joints, with a frequency of 25% of cases (4 children) managed with F VIII, and 31.25% (5 cases) treated with Cryoprecipitate. Hemarthrosis in 24 joints was recorded only in the group of patients receiving substitution treatment with Cryoprecipitate. The data suggest that both Cryoprecipitate and F VIII are used with a uniform distribution in the treatment of hemarthrosis; however, F VIII demonstrated better efficacy, with a relatively small number of maximally affected joints—5 joints recorded with a frequency of 18.75% (3 cases) in the F VIII treatment group, compared to substitution treatment with Cryoprecipitate, where joint involvement in the form of hemarthrosis was recorded in 24 joints in 6.25% of cases (1 child) [Table 7].

Table 7 Comparative characteristics of the number of admissions with the diagnosis of hemarthrosis in various locations depending on the type of treatment administered (Cryoprecipitate or Recombinant Factor)

		Substitution therapy					
		Cryoprecipitate		**F VIII**		**Total**	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Hemarthrosis	0	3	18.75	1	6.25	4	12.50
	1	2	12.50	2	12.50	4	12.50
	2	1	6.25	6	37.50	7	21.88
	3	5	31.25	4	25.00	9	28.13
	4	1	6.25	0	0.00	1	3.13
	5	0	0.00	3	18.75	3	9.38
	6	1	6.25	0	0.00	1	3.13
	8	1	6.25	0	0.00	1	3.13
	11	1	6.25	0	0.00	1	3.13
	24	1	6.25	0	0.00	1	3.13
	Total	16	100.00	16	100.00	32	100.00

The data regarding the distribution of substitution treatment with Cryoprecipitate and Factor VIII (F VIII) for the management of massive hemorrhages have been analyzed, with 2 massive hemorrhages recorded in 1 patient managed with Cryoprecipitate. This observation is significant and could suggest that the efficacy of Cryoprecipitate treatment in preventing or controlling massive hemorrhages may be lower than that of treatment with Factor VIII. Overall, the data suggest that, in cases of massive hemorrhage, treatment with Factor VIII may be more effective than Cryoprecipitate. However, it is important to consider each individual case and evaluate the benefits and risks according to specific needs and conditions [Table 8].

Table 8 Comparative characteristics of the number of admissions with the diagnosis of massive hemorrhage in various locations depending on the type of treatment administered (Cryoprecipitate or Recombinant Factor)

		Substitution therapy						
		Cryoprecipitate		**F VIII**		**Total**		
		Nr	**%**	**Nr**	**%**	**Nr**	**%**	95% IÎ
Massive hemorrhge	0	15	93.75	16	100.00	31	96.88	
	2	1	6.25	0	0.00	1	3.13	-3,0 + 9,26
	Total	16	100.00	16	100.00	32	100.00	

The table below provides data on minor hemorrhages in patient groups treated with Cryoprecipitate and F VIII. It is observed that in the group treated with F VIII, a higher percentage of patients, specifically 43.75% (7 children), had no minor hemorrhages. In comparison, in the group treated with Cryoprecipitate, only 12.5% (2 children) did not experience minor hemorrhages. This suggests a higher efficacy in preventing minor hemorrhages among patients treated with F VIII. In cases where minor hemorrhages occurred, a higher percentage of patients treated with Cryoprecipitate (25%, or 4 children) experienced more than 3 minor hemorrhages, compared to those treated with F VIII, where only 12.5% (2 children) had more than 3 minor hemorrhages. This observation suggests a relatively lower efficacy of Cryoprecipitate in controlling minor hemorrhages compared to F VIII. The data indicate that treatment with F VIII offers better control of minor hemorrhages compared to Cryoprecipitate. Patients treated with F VIII had a higher

percentage of absence of minor hemorrhages and a lower percentage of patients with a high number of minor hemorrhages compared to those treated with Cryoprecipitate. These findings may suggest superior efficacy of F VIII treatment in the prevention and control of minor hemorrhages in this patient population [Table 9].

Table 9 Comparative characteristics of the number of admissions with the diagnosis of minor hemorrhages in various locations depending on the type of treatment administered (Cryoprecipitate or Recombinant Factor)

		Substitution therapy					
		Cryoprecipitate		**F VIII**		**Total**	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Minor hemorrhages	0	2	12.50	7	43.75	9	28.13
	1	3	18.75	2	12.50	5	15.63
	2	4	25.00	5	31.25	9	28.13
	3	3	18.75	0	0.00	3	9.38
	4	4	25.00	1	6.25	5	15.63
	6	0	0.00	1	6.25	1	3.13
	Total	16	100.00	16	100.00	32	100.00

The data in the following table suggest that elective admissions were exclusively for patients receiving Factor VIII treatment, while none of those treated with Cryoprecipitate had such admissions. This observation indicates that elective treatment is currently specific to patients receiving Factor VIII. The interpretation and understanding of the statistics in the table are essential to draw relevant conclusions in the context of the provided data. The calculated Chi-square (χ^2) value (16.762) is compared to a predefined significance level (0.005) to determine whether there is a statistically significant difference between the analyzed groups. This finding suggests a significant association between the type of treatment and the type of admission, as there is a statistically significant difference between the two groups [Table 10].

Table 10 Comparative characteristics of the number of elective admissions depending on the type of treatment administered (Cryoprecipitate or Recombinant Factor)

		Substitution therapy					
		Cryoprecipitate		**F VIII***		**Total**	
		Nr	**%**	**Nr**	**%**	**Nr**	**%**
Elective	0	16	100.00	5	31.25	21	65.63
	1	0	0.00	3	18.75	3	9.38
	2	0	0.00	3	18.75	3	9.38
	3	0	0.00	1	6.25	1	3.13
	6	0	0.00	3	18.75	3	9.38
	8	0	0.00	1	6.25	1	3.13
	Total	16	100.00	16	100.00	32	100.00

*Statistically significant difference at a $p<0.05$ level

4. Discussion

Our study highlighted significant differences between cryoprecipitate and recombinant factor VIII treatment in children with hemophilia. These results align with the existing literature, where older treatments such as cryoprecipitate are

considered less effective and carry greater risks compared to recombinant factors. Traditional use of cryoprecipitate has been associated with poorer control of bleeding episodes. This is supported by other studies that emphasize the limitations of cryoprecipitate, particularly the risks of transmitting infectious diseases (Mannucci, 2003). Additionally, in our study, patients treated with cryoprecipitate exhibited a higher frequency of bleeding episodes, similar to the findings reported by the World Federation of Hemophilia (2020). These patients required more frequent medical interventions to correct factor VIII deficiencies. In contrast, patients treated with recombinant factor VIII had significantly better control of bleeding episodes, a finding confirmed by both our clinical observations and the literature. Franchini and Mannucci (2012) emphasize that recombinant factors provide better protection against spontaneous bleeding, and our study supports this conclusion, observing a significant reduction in bleeding episodes among patients who received this type of treatment. Another major advantage of recombinant factor VIII therapy, as confirmed, is the increased safety regarding infectious risks. The literature, including the study by Peyvandi et al. (2016), highlights that recombinant factors reduce the risk of developing inhibitors and improve the quality of life for patients. Similarly, patients in our cohort treated with recombinant factor showed a low incidence of complications, reinforcing these conclusions.

However, in the context of the Republic of Moldova, where financial resources for advanced treatments are limited, broad access to recombinant factors remains a challenge, as also noted by the World Federation of Hemophilia (2020). Although the high costs of recombinant factors have been a barrier to their widespread use, their efficacy and safety justify efforts to expand access to this treatment.

5. Conclusion

The results of our study confirm the superiority of recombinant factor VIII treatment compared to cryoprecipitate, both in terms of controlling bleeding episodes and safety. These findings are supported by the literature, indicating that although cryoprecipitate remains a viable option in some regions with limited resources, recombinant factor therapy offers far superior outcomes for patients. Therefore, for optimal management of hemophilia, the use of recombinant factors should be prioritized where possible.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

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