





# Therapeutic options for hemarthrosis in severe hemophilic patients

## Opções terapêuticas para as hemartroses em pacientes hemofílicos graves

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### ABSTRACT

**Introduction:** Hemophilia A and B are rare congenital X-linked recessive diseases caused by lack or deficiency of the coagulation factors VIII (FVIII) or IX (FIX), respectively. The primary therapeutic approach is to replace the deficient coagulation factor, which can be achieved with factors derived from human plasma or recombinants. However, despite having a therapeutic approach, most severe cases are symptomatic and may have complications, mainly in the muscles and joints. One example of such disorder is hemarthrosis. This manifestation tends to affect mainly the knee, ankle, or elbow joints in about 80% of cases. **Objective:** to describe the primary forms of treatment for joint bleeding in patients with severe hemophilia. **Methods:** This is a qualitative research of the integrative review type meant to identify productions on topics associated with hemarthrosis and severe hemophilia. The articles were searched through the databases PubMed, Scientific Electronic Library Online (Scielo) and Virtual Health Library (BVS) with the following search descriptors: "hemarthrosis and hemophilia"; "joint diseases and Hemophilia" and corresponding terms in Portuguese. The inclusion criteria were as follows: a) scientific articles b) available in full-text c) studies available in Portuguese, English, or Spanish d) randomized clinical trials e) articles published between 2016 and 2021 f) articles containing hemarthrosis caused by severe hemophilia. As exclusion criteria, texts that had no relation to the theme, did not answer the guiding question, other types of articles that did not include randomized clinical trials and/or presented duplicates were discarded. **Results:** In total, 42 articles were found in the selected databases; eight were duplicated, and 25 were excluded for not being randomized clinical trials or because they did not contemplate the theme. After careful reading, nine articles that met the inclusion and exclusion criteria were identified. Of the eligible studies, one reported factor replacement, and eight reported physiotherapeutic treatment. **Conclusion:** Factor replacement for hemophilic patients is essential and, based on the information obtained, early replacement is beneficial for the patient to avoid joint complications. Prophylaxis is indicated in severe hemophilia and its main objective is to prevent recurrent hemarthrosis, which can cause permanent functional deformities. Some physiotherapeutic interventions are indicated to prevent joint damage in severe hemophilic patients. The findings show diversity in the physical therapy modalities employed. The complete prevention of joint damage is still a challenge. A combination of treatments and a multi-disciplinary team follow-up is necessary to ensure health and quality of life of patients.

**Keywords:** Hemophilia, Hemarthrosis, Therapeutics.

### RESUMO

**Introdução:** As hemofílias A e B são doenças congênitas raras, recessivas ligadas ao X, causadas por falta ou deficiência de fator de coagulação VIII (FVIII) ou IX (FIX), respectivamente. A terapêutica tem como conduta principal a reposição do fator de coagulação deficiente, podendo ser feita com fatores derivados de plasma humano ou recombinantes. Porém, apesar de possuir uma terapêutica, grande parte dos casos graves são sintomáticos e podem ter complicações, na sua maioria, nos músculos e nas articulações. Uma dessas desordens é a hemartrose. Essa manifestação tende a acometer principalmente articulações do joelho, tornozelo ou cotovelo em cerca de 80% dos casos. **Objetivo:** descrever as principais formas de tratamento para sangramento articular em pacientes com hemofilia grave. **Método:** Trata-se de uma pesquisa qualitativa do tipo revisão integrativa para identificação de produções sobre temas associados a hemartrose e hemofilia grave. A busca dos artigos foi através das bases de dados PubMed, Scientific Electronic Library Online (SciELO) e Biblioteca Virtual em Saúde (BVS) com os seguintes descritores de busca: "hemarthrosis and hemophilia"; "joint diseases and hemophilia" e termos correspondentes no português. Os critérios de inclusão foram os seguintes: a) artigos b) estar disponível em texto completo c) estudos disponíveis nos idiomas português, inglês ou espanhol d) ensaios clínicos randomizados e) artigos publicados entre 2016 e 2021 f) artigos que contemplem hemartrose por hemofilia grave. **Resultados:** No total, foram encontrados 42 artigos nas bases de dados selecionadas; oito estavam duplicados e 25 foram excluídos por não serem ensaios clínicos randomizados ou por não contemplarem a temática. Após leitura cuidadosa, foram identificados 9 artigos que atenderam aos critérios de inclusão e exclusão. Dos trabalhos elegíveis, um relatou sobre reposição de fator e oito artigos relataram sobre tratamento fisioterapêutico. **Conclusão:** A reposição de fatores para pacientes hemofílicos é essencial e, com base nas informações obtidas, a reposição precoce é benéfica para o paciente, evitando complicações articulares. A profilaxia está indicada na hemofilia grave e seu principal objetivo é prevenir a hemartrose recorrente, que pode causar deformidades funcionais permanentes. Algumas intervenções fisioterapêuticas são indicadas para prevenir danos articulares em pacientes hemofílicos graves. Os achados mostram diversidade nas modalidades de fisioterapia empregadas. A prevenção total dos danos articulares ainda é um desafio. É necessária uma combinação de tratamentos e acompanhamento por equipe multidisciplinar de forma a garantir a saúde e qualidade de vida dos pacientes.

**Palavras-chave:** Hemofilia, Hemartrose, Terapêutica.

## INTRODUCTION

In 2015, Brazil had a record of 22,932 people with hereditary coagulopathy, of those, about 50% corresponded to hemophilia, with the State of São Paulo having the highest number of people affected <sup>1</sup>. Because it is a rare hereditary disease linked to the X chromosome, this condition affects men more frequently than women, with the World Federation of Hemophilia registering approximately 1.125.000 men affected by the pathology. However, although the data are already expressive, up to 75% of cases are underdiagnosed, and only 30% receive adequate treatment <sup>2</sup>.

Furthermore, hemophilia can be divided into type A, characterized by a factor VIII deficiency and representing the most prevalent form with about 85% of cases; or type B, in which factor IX is deficient and affects approximately 15% of patients. According to the basal levels of these coagulation factors, in which the deficiency would result in bleeding tendency, this disease can be classified into three categories as to its severity. When levels are below 1%, it is defined as severe, levels between 1% and 5%, moderate, and between 6% and 40%, mild <sup>3</sup>.

Hemophilia treatment is associated with the prevention of bleeding and complications to which the patient is susceptible, especially those that affect the joints and account for 80% of episodes. It aims, therefore, to improve the patient's quality of life, prevent and treat the hemorrhages resulting from this condition, and also its consequences <sup>4</sup>.

The main therapeutic approach is to replace the deficient coagulation factor, which can be achieved with factors derived from human plasma or recombinants. It is used under two modalities, being the first associated with prophylaxis with regular use of coagulation factors, while the second is done on demand with the administration of these factors after hemorrhagic episodes. In addition, regular follow-up by a multidisciplinary team, including hematologists, physiotherapists, orthopedists, and other professionals, as well as patient and family guidance and education processes, are indicated as an important part of these patients' treatment <sup>5</sup>.

Thus, hemophilia is one of the diseases that require the most resources for its adequate and

continuous management and treatment. However, in Brazil, coagulation factors and specialized care are fully funded by the Brazilian Unified Health System <sup>6</sup>.

Despite having a therapeutic plan, most severe cases are symptomatic and can have complications, mostly in the muscles and joints. One of these disorders is hemarthrosis, intra-articular bleeding, which can result in the development of chronic arthropathy. This manifestation tends to affect mainly the knee, ankle, or elbow joints in about 80% of cases. It can be divided into acute, which includes an initial episode of bleeding in the joint; subacute, in which repeated events of hemarthrosis occur in the same joint; and, finally, chronic arthropathy, in which there is already a loss of function <sup>3,7</sup>.

The pathophysiological process regarding hemarthrosis involves the participation of inflammatory cells, interleukins, neoangiogenesis and the formation of a protein complex called inflammasome that contributes to the inflammation process. Consequently, damage to the synovial membrane of the joint is established and can result in arthropathy <sup>8,9</sup>.

Therefore, as hemarthrosis is one of the main complications presented in severe hemophilic patients, this study proposed to carry out an integrative review in the literature to analyze the main forms of treatment for joint bleeding in patients with severe hemophilia. This study was based on the following guiding question: what are the therapeutic options for the management of severe hemophilic patients with hemarthrosis?

## METHODS

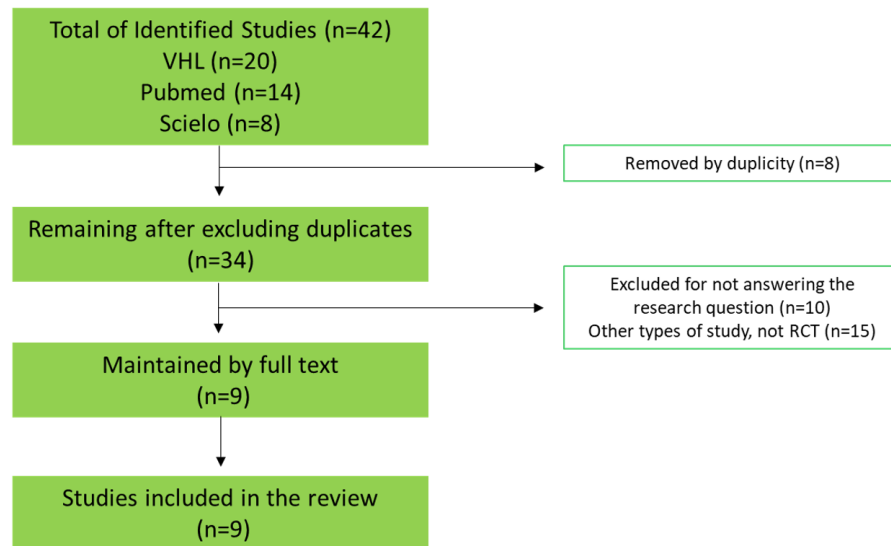
This is a qualitative research of the integrative review type<sup>10,11</sup> to identify productions about themes associated with hemarthrosis and severe hemophilia. The articles were searched through the databases *PubMed*, *Scientific Electronic Library Online (Scielo)*, and *Virtual Health Library (VHL)* with the following search descriptors: "hemarthrosis and hemophilia"; "joint diseases and hemophilia" and corresponding terms in Portuguese. The inclusion criteria were as follows: a) scientific articles b) available in full-text c) studies available

in Portuguese, English, or Spanish d) randomized clinical trials e) articles published between 2016 and 2021 f) articles containing hemarthrosis caused by severe hemophilia. As the exclusion criteria, texts that had no relation to the theme, did not answer the guiding question, other types of articles that did not include randomized clinical trials and/or presented duplicates were discarded. The selected articles were analyzed by four researchers according to the information contained in the abstracts and, subsequently, each one was read in full. Guided by these criteria, the main data containing information for analysis were extracted. Data were compiled in Excel software and analyzed by four reviewers in a document shared between everyone.

## RESULTS

In total, 42 articles were found in the selected databases; eight were duplicated and 25 were excluded for not being randomized clinical trials or because they did not contemplate the theme. After careful reading, nine articles that met the inclusion and exclusion criteria were identified. Although the Scientific Electronic Library Online (SciELO) database was searched, no articles from this database were selected for final analysis. Figure 1 shows the selection flowchart of studies included in the integrative review, according to the methodology.

One of the eligible studies reported factor replacement and eight reported physiotherapeutic treatment. The selected articles were included in Table 1.



**Fig. 1:** Flowchart of selection of studies included in the integrative review.

**Table 1**

Characterization of articles

Title	Year	Authors	Category	Objective	Conclusion
Comparison of the efficacy and safety of 12-month low-dose factor VIII tertiary prophylaxis vs on-demand treatment in severe haemophilia A children.	2019	Chozie et al.	Factor VIII replacement	Determine the efficacy and safety of prophylaxis low dose tertiary factor VIII (FVIII) compared to treatment on demand in children with severe hemophilia A in Indonesia.	Prophylaxis with low doses of FVIII was associated with a significant reduction in bleeding frequency and better joint function.
Effect of manual therapy in patients with hemophilia and ankle arthropathy: a randomized clinical trial.	2020	Donoso-Úbeda et al.	Physiotherapeutic treatment	Evaluate the effects of manual therapy with fascial therapy on joint bleeding, joint pain and joint function in patients with hemophilic arthropathy of the ankle.	Fascial therapy is favorable for patients with hemophilic ankle arthropathy.

(continues..)

**Table 1***(continuation)*

Title	Year	Authors	Category	Objective	Conclusion
Effectiveness of an Educational Physiotherapy and Therapeutic Exercise Program in Adult Patients with Hemophilia: A Randomized Controlled Trial.	2017	Cuesta-Barriuso et al.	Physiotherapeutic treatment	Evaluate the effectiveness of an educational intervention physical therapy with exercises at home in physical improvement, pain perception, quality of life and disease behavior in patients with hemophilic arthropathy.	Physical therapy based on educational sessions and home exercises can improve pain perception in patients with hemophilic ankle arthropathy.
Effects of myofascial release on frequency of joint bleedings, joint status, and joint pain in patients with hemophilic elbow arthropathy: A randomized, single-blind clinical trial.	2021	Cuesta-Barriuso et al.	Physiotherapeutic treatment	Evaluate the efficacy of myofascial release in patients with hemophilic arthropathy of the elbow.	Myofascial release decreases frequency of elbow bleedings, and improved joint status and perception of elbow pain in patients with hemophilic elbow arthropathy.
Efficacy of pulsed high-intensity laser therapy on pain, functional capacity, and gait in children with haemophilic arthropathy.	2018	El-Shamy et al.	Physiotherapeutic treatment	Evaluate the effects of high intensity pulsed laser therapy (HILT) on pain, functional capacity and gait in children with hemophilia.	HILT is an effective modality in reducing pain, increasing functional capacity, and improving gait performance in children with haemophilic arthropathy.
Functionality and range of motion in patients with hemophilic ankle arthropathy treated with fascial therapy. A randomized clinical trial.	2020	Cuesta-Barriuso et al.	Physiotherapeutic treatment	Evaluate the safety and efficacy of a physical therapy protocol with fascial therapy in order to improve the functionality and range of movement of patients with hemophilic arthropathy of the ankle.	Fascial therapy achieves improvements in terms of frequency of hemarthrosis in patients with hemophilic ankle arthropathy. Ankle functionality improved in patients treated with manual therapy. This technique can improve ankle range of motion.
Manual and educational therapy in the treatment of hemophilic arthropathy of the elbow: a randomized pilot study.	2018	Cuesta-Barriuso et al.	Physiotherapeutic treatment	Evaluate the safety of two programs of physiotherapy of manual therapy, and home exercises applied to educational sessions in patients with hemophilic arthropathy of the elbow.	The treatment with manual therapy improved the range of movement and circumference of arm, and lessened pain in hemophilic patients with chronic elbow arthropathy.
Pulsed Nd:YAG laser: effects on pain, postural stability, and weight-bearing pattern in children with hemophilic ankle arthropathy.	2020	Elnaggar	Physiotherapeutic treatment	Verify the effects of pulsed laser Nd: YAG on pain, postural stability and plantar weight support pattern in children with hemophilic arthropathy of the ankle. One group with laser and physical activity and the other with only physical activity.	Pulsed Nd:YAG laser is a potentially effective therapy for pain relief, postural control enhancement, and weight-bearing pattern adjustment in children with hemophilic ankle arthropathy.
The effectiveness of manual therapy in addition to passive stretching exercises in the treatment of patients with haemophilic knee arthropathy: A randomized, single-blind clinical trial.	2021	Cuesta-Barriuso et al.	Physiotherapeutic treatment	Evaluate the effectiveness of manual therapy and passive muscle stretching exercises to reduce the frequency of hemarthrosis and pain and improve joint health and range of motion in patients with hemophilic knee arthropathy.	Manual therapy using joint traction and gliding manoeuvres, in addition to passive muscle stretching, reduces the frequency of hemarthrosis in patients with haemophilia.

## DISCUSSION

The therapeutic options of hemarthrosis include factor replacement for hemophilia A and B and physiotherapeutic treatment.

### Replacement of the Deficient Factor

A study by Chozie et al. (2019) evaluated the use of Factor VIII in 50 children with severe Hemophilia A between the ages of 4 and 18, with the primary outcomes being the number of bleeding in the joints and the episodes of total bleeding during the research. As for the participants, there were no dropouts or losses during the study. The control group was composed of 25 children and was characterized by the use of the factor by free demand and the test group, with the same number of participants, used 10 IU per kg of body weight twice a week for 12 months, as prophylaxis. The research showed that both joint bleeding and total bleeding were significantly lower ( $p < 0.001$ ) in the prophylaxis group compared to the on-demand group. The comparison between the participants was also executed using the Hemophilia Joint Health Score (HJHS) to evaluate the musculoskeletal function, which showed progressive and statistically significant improvement (95% CI) in the experimental group and not in control, and Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) for early detection of arthropathy which, however, showed no statistically significant difference<sup>12</sup>.

### Physiotherapeutic Treatment

Therapeutic planning for patients with hemophilia considers techniques to improve joint dysfunctions and chronic pain. One of these techniques is manual therapy. In a study by Cuesta-Barriuso et al. (2021) evaluating the effectiveness of manual therapy and passive muscle stretching exercises to reduce the frequency of hemarthrosis and pain and improve joint health and range of movement in patients with hemophilic knee arthropathy, twenty-eight patients with age over 18 years were randomized. Manual therapy sessions included joint traction and gliding maneuvers, as well as passive muscle stretching. The intervention included a 60-minute

session, twice a week for 12 weeks. The frequency of knee hemarthrosis (self-reported), joint health (Hemophilia Joint Health Score), range of motion (goniometry), and perceived knee pain (visual analog scale) were evaluated. An initial evaluation was performed at the end of the intervention and after a 12-week follow-up period. The frequency of hemarthrosis decreased significantly in the experimental group compared to the control group ( $F = 11.43$ ;  $p < 0.001$ ). Compared to the control group, the experimental group had consistently better results in joint health variables ( $F = 13.80$ ;  $p < 0.001$ ), the amplitude of movement in knee flexion ( $F = 24.29$ ;  $p < 0.001$ ), and loss of extension ( $F = 8.90$ ;  $p < 0.001$ ) and perceived pain ( $F = 49.73$ ;  $p < 0.001$ ). Thus, manual therapy using joint traction and gliding maneuvers, in addition to passive muscle stretching, reduced the frequency of hemarthrosis in patients with hemophilia. In addition, manual therapy with passive muscle stretching exercises improved joint health, range of motion, and joint pain perception<sup>13</sup>.

Joint dysfunctions, in particular arthrofibrosis, are very relevant consequences in patients with hemophilic arthropathy, and result from recurrent hemarthrosis. These dysfunctions occur because the fibrotic processes can, in the long term, lead to a progressive loss of movement of the affected joint, in addition to the fascial system involvement, which contributes to the loss of elasticity and flexibility of the joint's collagen fibers. In this context, Cuesta-Barriuso et al. (2020) evaluated the safety and efficacy of a fascial physiotherapy protocol for hemophilic patients aged between 18 and 65 with hemophilic arthropathy in the ankle. The selected individuals were randomized into a control group ( $n=32$ ) and an experimental group ( $n=33$ ). The control group was not the object of any intervention, while the experimental group was submitted to a fascial therapy protocol aiming to improve the functionality and range of ankle movement. The fascial therapy aims to remove the restriction of fascial tissue through mechanical stimuli that promote a piezoelectric effect in the crystalline matrix of the fascia; It was performed through a protocol with fascial techniques applied manually by the physiotherapist in both lower limbs, in sessions lasting 45 minutes once a week for 3 weeks. The patients were evaluated at the beginning,

during, and after 5 months of the intervention, being monitored regarding the frequency of hemarthrosis episodes in the ankle (self-reported), the amplitude of ankle movement (goniometry) and functionality of the lower limbs (Six Minute Walk Test - 6MWT). The experimental group presented significant improvements in relation to the intervention group ( $p < 0.001$ ), and between the first and last evaluation of this group, there was an evolution in all variables evaluated ( $p < 0.05$ ). Comparing the second and third evaluations, the maintenance of the progress obtained since the beginning of the intervention ( $p > 0.05$ ) regarding the occurrence of bleeding and degree of dorsiflexion was demonstrated. The control group presented alterations between the first and second evaluations, with worse values for plantar flexion and dorsiflexion ( $p < 0.01$ ) in both members. Previous studies had already pointed out the safety of fascial therapy for patients with hemophilic arthropathy of the ankle, which was confirmed by the present study, contributing to an improvement related to hemarthrosis, ankle mobility, and gait<sup>14</sup>.

The study guided by Cuesta-Barriuso et al. (2021) presents another physiotherapy method for arthropathy in hemophilic patients: myofascial release techniques. It consisted of the randomization of 67 patients under treatment demand, without prophylaxis or hemostatic coverage with factor VIII/IX, 34 belonging to the control group and 35 to the experimental group. The technique consisted of carrying out light biomechanical loads in the soft tissue of the elbow, stimulating mechanoreceptors in the muscular fascia and, thereby, releasing fascial restrictions and restoring healthy tissue. Thus, it aimed to reduce the restrictions of the fascial system by promoting the reorientation of collagen fibers, improving pain terms and functionality, and re-establishing the perception of disability in patients with hemophilic arthropathy. As a result of the study, there were significant changes ( $p < 0.001$ ) in the frequency of elbow hemarthrosis ( $F = 20.64$ ), in the state of the joints ( $F = 31.45$ ), and the level of pain in the perceived joints ( $F = 30.08$ ). Although the positive results were only achieved after three treatment sessions, their benefits were maintained for a period of 3 months. Therefore, as it is a short-term intervention, requiring few resources

to carry it out and offering improvements even after the sessions, manual therapy by myofascial release may be one of the treatments of choice in cases of hemophilic arthropathy with high levels of deterioration and joint elbow pain<sup>15</sup>.

In this same context, this technique was associated with home exercise and educational sessions to treat elbow arthropathy. The study conducted by Cuesta-Barriuso et al. (2018) evaluated the safety of two physiotherapeutic programs in patients with elbow arthropathy. The 27 patients selected with a mean age of 34.48 years were randomized and allocated into three groups, one control group and two intervention groups, the first with manual therapy protocol and the second with the protocol of educational physiotherapy sessions. The interventions in the manual therapy group were performed twice a week with a duration of 60 minutes each; they consisted of a physiotherapeutic program with thermotherapy and cryotherapy techniques, accompanied by articular traction techniques, specific muscle stretching and proprioceptive neuromuscular facilitation techniques. On the other hand, the education group underwent six 90-minute educational interventions that took place every two weeks, accompanied by daily sessions of 20-30 minutes of stretching exercises, isometric exercises for the biceps and triceps, and proprioceptive exercises at home. The educational interventions addressed topics such as clinical aspects of hemophilia, types of injuries and treatments, as well as orientation on the exercises that should be performed at home. The total duration of the interventions in both groups was 12 weeks. The interventions safety was evaluated based on bleeding, signs and symptoms (self-reported), the amplitude of movement of the elbow (goniometry), Perimetry of the arm, the strength of the brachial biceps muscle (the rupture test), and perception of joint pain (visual analog scale). The patients were evaluated at the beginning of the study, at the end of 12 weeks and after a 6-month follow-up period. After the end of the treatment, only the patients submitted to manual therapy presented changes, with improvement of pain perception ( $p = 0.006$ ), elbow flexion ( $p = 0.022$ ) and arm perimeter ( $p = 0.050$ ). After the follow-up period, the improvements in the range of motion and

pain were maintained ( $p = 1.00$  and  $p = 0.069$ ). No changes were observed in the parameters of the group of educational interventions as well as in the control group, which remained after the follow-up period. Finally, both physical therapy programs, manual therapy and physical therapy activities at home were considered safe because they did not cause elbow hemarthrosis during the study period. However, manual therapy can improve flexion and pain perception in patients with hemophilic elbow arthropathy and these results can be maintained for a 6-month period<sup>16</sup>.

Cuesta-Barriuso et al. (2017) conducted a randomized study with 20 patients over 18 years of age (mean age of the patients was  $30.95 \pm 1.9$  years), from which half was allocated to the educational intervention group and the other half to the control group. The strategy of this study was based on 60-minute educational sessions every 2 weeks on the physiopathology of hemophilia, clinical manifestations, postural counseling and prevention counseling to prevent recurrent bleeding. In addition, doubts about the clinical evolution of hemophilic arthropathy, functional limitations and joint pain management were resolved. Associated with educational sessions, patients followed a 15-week exercise period, once a day, 6 days a week. The program included upper and lower limb muscle stretching exercises, isometric exercises, proprioceptive exercises with visual support, and 20-minute walks. The patients in the intervention group kept a record of the exercises performed at home and monitored their evolution; the patients in the control group did not receive any educational session and did not do any exercise at home. After the intervention, repeated measures variance analysis showed significant changes in the intervention group for the 3 evaluations performed. Quality of life assessment improved in 6 domains: physical health (PZ.003), daily activities (PZ.006), joint need (PZ.004), joint pain (PZ.005), emotional functioning (PZ.045) and overall quality of life (PZ.003). Regarding the behavior of the disease, differences were observed in terms of general hypochondria (PZ.038) and psychological versus somatic perception of the disease (PZ.007). However, the improvement of joint pain perception by the visual analog scale was significant only for the ankle joints (PZ.007).

Regarding the physical scales, no significant improvement was observed in terms of examination in the treatment group by the Gilbert scale. As for the patients in the control group, no differences were noticed after the study, neither in the physical scales nor in the quality of life and behavior of the disease. Therefore, it was concluded that the educational intervention was satisfactory with regard to the patient's perception of quality of life, although no significant improvement was observed in terms of joint involvement, except for the ankle joint<sup>17</sup>.

A research was carried out by Donoso-Úbeda et al. (2019) involving 65 participants aged 18 years or older who had hemophilic ankle arthropathy. Three sessions of manual fascial therapy lasting 45 minutes were used in the experimental group consisting of 33 individuals. After 5 months of intervention, the primary outcome, in this case, the frequency of joint bleeding was measured through self-report. As a result, a statistically significant lower number of bleeding episodes ( $p < 0.001$ ) was observed in the members who received the therapy and a greater deterioration of the joint in the control group<sup>18</sup>.

In addition to the physiotherapy-only protocols, methods that associate physiotherapy with other techniques to treat hemarthrosis are cited in the literature. Elnaggar's study (2020) addresses the association between physiotherapy treatment and the use of pulsed laser Nd:YAG to treat children with hemophilic knee arthropathy. The 40 children selected for the study were from 8 to 16 years old, and were randomized into two groups, the treatment group received intervention with pulsed laser Nd:YAG and physical exercises, and the placebo group received laser placebo and physical exercises. Participants underwent physical activity sessions with a maximum duration of 30 minutes, 3 times a week, for 4 consecutive weeks, with exercises aimed at pain relief, improvement of flexibility, muscle strength and proprioception. Therapies with pulsed laser Nd:YAG and with visible light were performed 3 times a week for 4 weeks in the intervention and placebo groups, respectively. The patients were evaluated according to the intensity of the pain (self-reported), postural stability (Neurocom Balance system), and weight support pattern (Tekscan HR Mat™

Barefoot Pressure Mapping System) pre- and post-treatment. For the treatment group, the intensity of pain, postural control and weight support pattern improved significantly when comparing the pre- and post-treatment variables ( $p < 0.05$ ), with a relevant effect on all variables ( $d > 0.8$ ). The placebo group also presented a significant improvement in all parameters in the post-intervention evaluation ( $p < 0.05$ ), however, the effects on the variables were mostly evaluated as small to medium. Thus, the study shows that the intervention using the pulsed laser Nd: Pulsed YAG in association with physical exercises for four consecutive weeks is generally more effective than isolated exercises for the parameters evaluated in children with hemophilic arthropathy of the ankle<sup>19</sup>.

Moreover, the study by El-Shamy and Abdelal (2018) selected 30 children with type A hemophilia, aged between 9 and 13 years, who suffered from bilateral knee hemarthrosis. They were randomly assigned to two equal treatment groups. The first group received the traditional physiotherapy program (which includes warm compresses, muscle stretching, strengthening exercises, proprioceptive training, balancing and gait training for three consecutive months 1h a day and three times a week, in addition to the prophylactic replacement of factor VII) associated with active laser, while the second group received the same physiotherapy program, however, associated with laser placebo for three consecutive months. Baseline and post-treatment evaluations used the visual analog scale (VAS) to assess pain, a 6-minute walk test (TC6) to assess functional capacity, and the system and GAITRite® to assess gait parameters. As a result, children in the laser group presented significant improvement in pain parameters, functional capacity and gait compared to those in the placebo group ( $p < 0.05$ ). The functional capacity after the treatment for laser and placebo groups was  $316.6 \pm 35.27$  and  $288 \pm 43.3m$ , respectively. Thereby, High-Intensity Laser Therapy has been shown to be an effective modality in reducing pain, increasing functional capacity and improving gait performance in children with hemophilic arthropathy. Finally, it was also concluded that this therapy had more effect than a placebo laser, as it was more effective and economical than conventional treatment methods<sup>20</sup>.

Prophylaxis, when initiated early, can potentially prevent arthropathy, deficiencies and disabilities, and is considered the “gold standard treatment” for children with severe hemophilia. However, when arthropathy already exists, prophylaxis cannot reverse it, but it seems to decrease its progression and reduce pain, inflammation and the number of episodes of bleeding, being able to maintain patient mobility and improve the quality of life<sup>6,21,22</sup>. It is important to highlight the role of physiotherapy in the treatment and prevention of hemophilic hemarthrosis in various therapy modalities. The physiotherapist should support and encourage physical activity in hemophilic patients<sup>23,24</sup>.

Given the therapeutic options presented, the primary treatment to avoid recurrent bleeding with hemarthrosis is the replacement of the coagulation factor. However, none of the currently available pharmacological treatments specifically targets synovitis, which is a known source of recurrent bleeding and the driver of hemophilic arthropathy. Finally, all patients should be collaboratively cared for by multidisciplinary teams of hematologists, rheumatologists, orthopedic surgeons, and physiotherapists at comprehensive hemophilia treatment centers<sup>25</sup>.

## FINAL CONSIDERATIONS

Factor replacement for hemophilic patients is essential and based on the information obtained, early replacement is beneficial for the patient to avoid joint complications. Prophylaxis is indicated in severe hemophilia and its main objective is to prevent recurrent hemarthrosis, which can cause permanent functional deformities.

Some physiotherapeutic interventions are indicated to prevent joint damage in severe hemophilic patients. The findings show diversity in the physical therapy modalities employed as manual therapy, myofascial release techniques, educational physiotherapy, among others, aiming at the prevention and treatment of hemophilic hemarthrosis. Further studies are needed to create physiotherapeutic protocols to treat and prevent this condition, generating scientific evidence.



A drug that has been approved for use in Brazil called Emicizumab is effective in controlling bleeding. It was not reported in this study due to the lack of studies on the control of hemarthrosis. Future studies are expected to relate the use of the drug to control this type of bleeding.

Total damage prevention is still a challenge. Therefore, a combination of treatments and a multidisciplinary team follow-up is necessary to ensure the health and quality of life of patients.

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