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ORIGINAL RESEARCH ARTICLE

Disease awareness in hemophilia: impact on therapeutic adherence and clinical outcomes

Conciencia de enfermedad en hemofilia: impacto en la adherencia terapéutica y los resultados clínicos

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Abstract

Introduction: *Hemophilia is an inherited bleeding disorder that requires multidisciplinary management to reduce long-term complications. Disease awareness may influence treatment adherence and clinical outcomes.* **Objective:** *To analyze the relationship between disease awareness and adherence to prophylactic therapy in patients with hemophilia.* **Material and methods:** *A review of assessment tools and strategies addressing psychosocial, educational, and economic barriers to adherence was conducted.* **Results:** *Higher disease awareness was associated with improved adherence, reduced bleeding episodes, and better preservation of joint function.* **Conclusions:** *Disease awareness is a key determinant of adherence in patients with hemophilia. Interventions that enhance patient self-management may improve long-term health outcomes.*

Keywords: *Hemophilia. Health knowledge. Treatment adherence.*

Resumen

Introducción: *La hemofilia es un trastorno hemorrágico hereditario que requiere manejo multidisciplinario para reducir las complicaciones a largo plazo. La conciencia de enfermedad podría influir en la adherencia terapéutica y en los resultados clínicos.* **Objetivo:** *Analizar la relación entre la conciencia de enfermedad y la adherencia al tratamiento de profilaxis en pacientes con hemofilia.* **Material y método:** *Se revisaron herramientas de evaluación y estrategias orientadas a superar barreras psicosociales, educativas y económicas que afectan a la adherencia.* **Resultados:** *Una mayor conciencia de enfer-medad se asoció con mejor adherencia, menor frecuencia de hemorragias y mejor preservación de la función articular.* **Conclusiones:** *La conciencia de enfermedad constituye un factor clave en la adherencia terapéutica en los pacientes con hemofilia. Las intervenciones dirigidas a fortalecer la autogestión del paciente podrían mejorar los resultados de salud a largo plazo.*

Palabras clave: *Hemofilia. Conocimiento. Adherencia al tratamiento.*

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Introduction

Hemophilia is a chronic genetic disorder characterized by a deficiency of coagulation factor VIII (hemophilia A) or factor IX (hemophilia B), which predisposes affected individuals to spontaneous or post-traumatic bleeding episodes. Clinical classification is based on the level of coagulation factor activity and is divided into mild, moderate, and severe forms.[1] With therapeutic advances over recent decades, management has shifted from on-demand treatment of bleeding episodes to prophylactic strategies aimed at preventing hemorrhage and the consequent joint deterioration.[2] However, these therapeutic advances achieve their maximum effectiveness only when adequate patient adherence is present.

In this context, disease awareness has taken on a central role in the comprehensive management of hemophilia. This concept refers to the degree to which patients understand their diagnosis, the impact of the disease on daily life, and the need for continuous treatment.[3] Multiple studies have shown that greater disease awareness is associated with better adherence to prophylactic treatment, which in turn translates into fewer bleeding episodes, slower progression of hemophilic arthropathy, and improved quality of life.[1,4] Conversely, limited or distorted perception of the disease may lead to treatment discontinuation and the development of preventable complications.[5]

Systematic assessment of disease awareness and its relationship with therapeutic adherence has become a key line of research in hemophilia. Tools such as the Haemo-Adhaesion questionnaire have made it possible to study this relationship in different populations and contexts, showing consistent results:[6] patients with a better understanding of their condition present improved clinical and functional outcomes. In addition, evidence indicates that sustained educational interventions can reinforce treatment self-management, reduce the need for hospitalization, and promote a more active patient role in health care.[5]

Therapeutic adherence, however, is influenced by multiple factors. Among them, psychological and educational aspects are particularly relevant, especially in adolescents and young adults, who often underestimate the risks associated with the disease.[7] Structured educational programs tailored to different developmental stages have proven effective in this age group. Furthermore, socioeconomic factors such as access to health care centers, treatment costs, and resource availability directly affect treatment continuity. In this regard, health systems with inclusive and equitable policies achieve better adherence outcomes.[1,2]

Another determining factor is the family and social environment. Family support, interdisciplinary health care teams, and belonging to patient communities or support groups strengthen adherence and contribute to better quality of life.[8] The incorporation of technologies such as mobile applications and reminder systems, together with active patient participation in therapeutic decision-making, has also proven to be a promising strategy for improving adherence.

In light of these findings, the overall objective of the present study was to analyze the relationship between disease awareness and treatment adherence in patients with hemophilia, and its impact on clinical outcomes.

Methods

Study design

We conducted a longitudinal, prospective study with unstructured educational interventions over a 6-month period. The aim was to analyze the evolution of disease awareness and its relationship with therapeutic adherence and clinical outcomes in patients with hemophilia. The study was carried out within the framework of routine clinical practice; no additional visits were scheduled and no therapeutic changes were made. Educational interventions were limited to routine medical consultations and focused on communication and patient engagement. In adolescents and young adults, when lack of attention during the consultation was observed (e.g., mobile phone use), patients were directly addressed to encourage their involvement in understanding the disease and the therapeutic regimen. The study was approved by the institutional ethics committee, and all participants provided written informed consent.

Population and sample

The sample consisted of 2 groups:

- Patients older than 16 years with a diagnosis of hemophilia A who regularly attended clinical follow-up visits at the Hemophilia Foundation of Santa Fe (Rosario branch).
- Primary caregivers of patients younger than 16 years with hemophilia, also followed at the same institution.

Only patients or caregivers who provided informed consent and had complete clinical records at study entry were included.

Assessment instrument: disease awareness survey

A survey designed by the interdisciplinary team of the Hemophilia Foundation of Santa Fe was used to assess disease awareness. This instrument was developed based on prior evidence and validated at the institution, as no previously validated tool specifically assessing disease awareness in people with hemophilia was available. The survey consists of 15 items distributed across three main sections, exploring different dimensions of disease awareness:

- Section 1: knowledge of the disease. Includes questions on the genetic origin of hemophilia, the role of coagulation factors, differences between hemophilia A and B, and basic interpretation of common clinical tests.
- Section 2: self-care and treatment adherence. Assesses understanding of the prophylactic treatment regimen, frequency and regularity of administration, recognition of warning signs, and actions taken in bleeding situations.
- Section 3: perception of disease impact. Explores patient or caregiver perceptions regarding the physical, emotional, and social impact of hemophilia, including limitations in daily activities, adherence in school or work settings, and family coping.

Responses were recorded using 3- or 5-point Likert scales depending on the item. Partial scores and a total disease awareness score were calculated. The questionnaire was administered in paper format by trained personnel in a controlled clinical environment.

Procedure

Included patients and caregivers were evaluated at 2 time periods:

- Time 0: at study entry.
- 6 months: during a follow-up visit of the same participants assessed at time 0.

Notably, at the initial assessment, participants were not informed that they would be reassessed at 6 months, in order to minimize response bias and ensure spontaneity at the second evaluation.

At both visits, the following data were collected:

- Disease awareness survey.
- Annualized bleeding rate: number of bleeding episodes occurring over 6 months, extrapolated to an annual period.
- Progression of joint damage: assessed using the HEAD-US (Haemophilia Early Arthropathy Detection with Ultrasound) protocol.[9]
- Adherence to prophylactic treatment: determined according to the method proposed by Duncan et al.,[4] which includes actual treatment administration frequency relative to the prescribed regimen, as well as the occurrence of preventable events.

Statistical analysis

Categorical variables were compared between time points using McNemar's test, and continuous variables using paired Student's t test. The relationship between disease awareness and clinical variables was evaluated using Pearson's or Spearman's correlation coefficient, as appropriate. A p value < 0.05 was considered statistically significant. Statistical analysis was performed using R software.

Results

A total of 48 participants were included: 30 male patients with hemophilia A (mean age, 19.3 years [range, 8-28]) and 18 caregivers (mean age, 42.1 years [range, 31-59]), of whom 72% were women and 28% men. All caregivers had a direct parental relationship (father, mother, or partner) and were affiliated with the Hemophilia Foundation of Santa Fe. Each patient was paired with their primary caregiver; therefore, no cases were duplicated.

Of the patients, 80% (n = 24) had severe hemophilia A and 20% (n = 6) had moderate hemophilia A with a severe bleeding phenotype (≥ 3-4 spontaneous hemarthroses per year, presence of ≥ 1 target joint, or repeated need for treatment for clinically relevant spontaneous bleeding). The same participants completed the survey at both time points: at study entry and at 6 months.

Section 1: Knowledge of the disease (Fig. 1)

At baseline, only 43.3% of patients (n = 13) correctly identified the type of hemophilia they had. This proportion increased significantly at 6 months, reaching 76.7% (n = 23) (p = 0.008). Similarly, 36.7% (n = 11) were aware of the severity of their diagnosis at baseline vs 73.3% (n = 22) at the 2nd assessment (p = 0.012).

A critical issue was lack of knowledge regarding treatment: 56.7% of patients (n = 17) were unable to

name either the type or the commercial name of their coagulation factor at baseline. This proportion decreased to 26.7% (n = 8) at 6 months (p = 0.015).

Among caregivers, overall knowledge of the disease also improved. At baseline, 77.8% (n = 14) correctly identified the basic mechanisms of coagulation, increasing to 94.4% (n = 17) at 6 months (p = 0.021).

Notably, in the group of adolescents and young adults (16-24 years), only 25% correctly identified the mode of inheritance of hemophilia at baseline; this percentage increased to 56% at 6 months (p < 0.05).

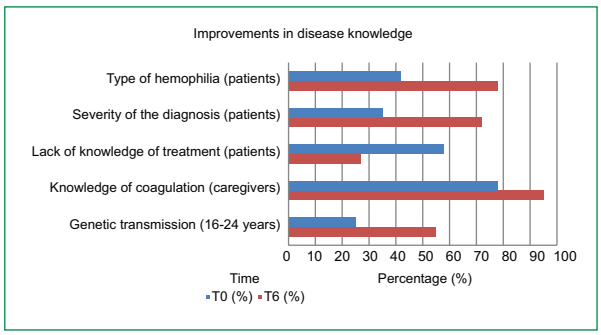

Figure 1. Changes in disease knowledge between the baseline visit and the 6-month follow-up.

Section 2: Self-care and treatment adherence

At baseline, only 40% of patients (n = 12) reported strict adherence to the prescribed prophylactic regimen. At 6 months, this proportion increased significantly to 73.3% (n = 22) (p = 0.004). Improved adherence was associated with a significant reduction in the annualized bleeding rate: median of 5.2 events per year at baseline vs 1.9 events per year at 6 months (p = 0.003).

Among caregivers, 83.3% (n = 15) reported feeling confident administering treatment in the absence of health care personnel at baseline; this proportion increased to 94.4% (n = 17) at 6 months (p = 0.031).

Of note, in the 16-24-year age group, low initial engagement in self-care was observed, reflected by limited attention during consultations (eg, mobile phone use when receiving instructions). However, this pattern showed slight improvement following the educational intervention.

Section 3: Perception of disease impact

Perception of the disease improved in both groups. At baseline, 46.7% of patients (n = 14) perceived hemophilia as a major limitation in daily life, whereas at 6 months this proportion dropped down to 20% (n = 6) (p = 0.009). In parallel, the proportion of patients who stated that they "can lead a normal life if they take proper care" increased from 50% (n = 15) to 83.3% (n = 25) (p = 0.002).

Among caregivers (n = 18), initial perception of hemophilia as a major limitation was higher, at 61.1% (n = 11), but decreased to 27.8% (n = 5) at 6 months (p = 0.01). Likewise, the proportion of caregivers who believed that "a normal life is possible with appropriate care" increased from 44.4% (n = 8) to 77.8% (n = 14) (p = 0.005).

Concern regarding the possibility of spontaneous bleeding decreased significantly in both groups. Among patients, 66.7% (n = 20) reported high concern at baseline, decreasing to 36.7% (n = 11) at 6 months (p = 0.01). Among caregivers, concern was initially higher, with 83.3% (n = 15) reporting high concern, decreasing to 50% (n = 9) at follow-up (p = 0.02).

Perceived self-efficacy in disease management increased significantly. Among patients, the proportion who felt capable of managing their condition increased from 40% (n = 12) to 76.7% (n = 23) (p = 0.004). This change was particularly marked in adolescents (n = 12), in whom perceived self-efficacy increased from 25% (n = 3) to 66.7% (n = 8) (p = 0.03). Among caregivers, self-efficacy increased from 55.6% (n = 10) to 88.9% (n = 16) (p = 0.008).

Notably, 100% of participants (patients and caregivers) expressed interest in receiving additional information and education about hemophilia at the end of the study, underscoring the importance of systematic educational interventions (Table 1).

In the subgroup of patients on emicizumab, a specific pattern of therapeutic adherence was identified. During episodes of joint pain or other hemophilia-related symptoms, adherence increased significantly. However, this improvement was transient: once acute symptoms resolved and perceived threat diminished, adherence tended to progressively decline. This pattern was observed even in patients with adequate plasma drug concentrations and no inhibitors.

Discussion

Disease awareness in individuals with hemophilia A represents a critical and dynamic dimension that directly influences treatment adherence and, consequently,

Table 1. Changes in knowledge, self-care, and disease perception between baseline and 6-month visits

Variable	Baseline	6 months	p
Patients, n (%)			
Knowledge of type of hemophilia	13 (43.3%)	23 (76.7%)	0.004
Knowledge of disease severity	11 (36.7%)	22 (73.3%)	0.006
Does not know medication (name or factor type)	17 (56.7%)	8 (26.7%)	0.018
Strict adherence to prophylaxis regimen	12 (40.0%)	22 (73.3%)	0.011
Perceives hemophilia as a major limitation	14 (46.7%)	6 (20.0%)	0.022
Believes a normal life is possible with proper care	15 (50.0%)	25 (83.3%)	0.003
Adolescents recognizing mode of transmission (16-24 years)	4/16 (25.0%)	9/16 (56.0%)	0.049
Caregivers, n (%)			
Knowledge of basic coagulation mechanisms	14 (77.8%)	17 (94.4%)	0.157
Feels confident administering treatment without health care staff	15 (83.3%)	17 (94.4%)	0.317
Both groups, n (%)			
Desire further education on hemophilia at study completion	48 (100%)	48 (100%)	-

clinical outcomes. Our findings confirm what has been previously reported in the literature: greater understanding of the disease is associated with improved adherence, a lower frequency of bleeding events, and a more positive perception of quality of life.[10]

The behavior observed in patients receiving emicizumab highlights an emerging clinical paradox. Despite the high efficacy and convenience of treatment, adherence tends to decline as symptoms are mitigated and the disease becomes less perceptible. This underscores that, even in scenarios of optimal clinical control, disease awareness remains an essential component of management. The absence of symptoms should not be equated with the absence of disease, and commitment to treatment must be sustained beyond overt physical discomfort.

The improvement observed in knowledge regarding hemophilia severity, type of treatment, and perceived self-efficacy following simple, systematic educational interventions indicates that these strategies have a tangible clinical impact. In particular, the adolescent subgroup, which started from a lower baseline level of knowledge, showed significant gains, although it continues to represent a challenge because of lower initial engagement in self-care. The transition from adolescence to adulthood remains a critical period that requires personalized, sustained, and patient-centered interventions.

At our center, educational strategies have been implemented to empower both patients and caregivers. In adolescents, active participation in clinical consultations is strongly encouraged, aiming to shift the exclusive focus from the responsible adult toward direct dialogue with the young patient. Practices such as extended consultation time, clear and age-appropriate therapeutic explanations, and encouragement to listen and actively participate during medical visits have been incorporated. These low-cost actions seek to build autonomous and sustained disease awareness.

In this context, the concept of a "hemophilia-free mind," proposed by Krumb and Hermans,[11] is appealing as an intervention goal, although it should be interpreted with caution. Far from implying disengagement, this concept refers to a healthy integration of the diagnosis, in which the disease does not define the patient's identity or limit aspirations. Achieving this state requires not only therapeutic efficacy but also continuous education and strengthening of the patient-health care team relationship.[11]

Nevertheless, structural barriers persist. Inequalities in access to prophylaxis and diagnostic technologies, such as musculoskeletal ultrasound, hinder early detection of joint complications and limit the impact of educational interventions, particularly in resource-limited settings.[2] In this regard, it is essential to develop educational materials and strategies tailored to the sociocultural realities of each community, integrating biomedical information with psychosocial and family aspects.

Similarly, the role of caregivers as active agents in treatment is particularly relevant. Their involvement and training emerge as pillars for sustaining long-term adherence, especially in environments where access to the health care system is intermittent or insufficient. Shared construction of knowledge, trust, and therapeutic commitment helps to partially overcome these structural limitations.

Finally, the systematic incorporation of tools to assess disease awareness into routine clinical practice could facilitate early identification of patients at risk for poor

adherence. This would allow more efficient allocation of resources and the development of more personalized educational programs, including longitudinal follow-up, accessible digital supports, and approaches centered on the individual and their environment.

Conclusions

The findings of this study reinforce the clinical value of promoting disease awareness in hemophilia A as an effective strategy to improve treatment adherence and reduce complications. Simple educational interventions, implemented systematically, were shown to generate sustained improvements in patient knowledge, perceived self-efficacy, and ownership of care.

Disease awareness should not be considered solely an educational objective but also an essential component of comprehensive clinical management. Future studies should aim to expand the sample size and further analyze specific subgroups to optimize educational interventions according to age, baseline level of knowledge, and sociocultural context.

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Conflicts of interest

None declared.

Ethical considerations

Protection of persons and animals. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and with the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The recommendations of the SAGER guidelines were followed, according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Mahlangu J, Oldenburg J, Callaghan MU, Shima M, Mancuso ME, Trask P, et al. Health-related quality of life and health status in persons with haemophilia A with inhibitors: a prospective, multicentre, non-interventional study (NIS). Haemophilia. 2019;25:382-91. doi: 10.1111/hae.13731.
2. Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020;26(Suppl 6):1-158. doi: 10.1111/hae.14046. Erratum in: Haemophilia. 2021;27:699. doi: 10.1111/hae.14308.
3. Schrijvers LH, Uitslager N, Schuurmans MJ, Fischer K. Barriers and motivators of adherence to prophylactic treatment in haemophilia: a systematic review. Haemophilia. 2013;19:355-61. doi: 10.1111/hae.12079.
4. Duncan N, Kronenberger W, Roberson C, Shapiro A. VERITAS-Pro: a new measure of adherence to prophylactic regimens in haemophilia. Haemophilia. 2010;16:247-55. doi: 10.1111/j.1365-2516.2009.02129.x.
5. Delgado PL. Approaches to the enhancement of patient adherence to antidepressant medication treatment. J Clin Psychiatry. 2000;61(Suppl 2):6-9.
6. Torres-Ortuño A, Cuesta-Barriuso R, Nieto-Munuera J, Castiello-Munuera A, Moreno-Moreno M, López-Pina JA. Haemo-Adhaesione: a new measure of adherence for adolescent and adult patients with haemophilia. Patient Prefer Adherence. 2020;14:455-65. doi: 10.2147/PPA.S233601.
7. Lee Mortensen G, Strand AM, Almén L. Adherence to prophylactic haemophilic treatment in young patients transitioning to adult care: a qualitative review. Haemophilia. 2018;24:862-72. doi: 10.1111/hae.13621.
8. Doré I, Caron J. [Mental Health: Concepts, Measures, Determinants]. Sante Ment Que. 2017;42:125-45.
9. Martinoli C, Della Casa Alberighi O, Di Minno G, Graziano E, Molinari AC, Pasta G, et al. Development and definition of a simplified scanning procedure and scoring method for Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US). Thromb Haemost. 2013;109:1170-9. doi: 10.1160/TH12-11-0874.
10. van Os S, Ryder N, Hart DP, Troop N. Adherence to prophylaxis in adolescents and young adults with severe haemophilia: a qualitative study with healthcare professionals. Health Psychol Behav Med. 2020;8:55-72. doi: 10.1080/21642850.2020.1718501.
11. Krumb E, Hermans C. Living with a "hemophilia-free mind" — the new ambition of hemophilia care? Res Pract Thromb Haemost. 2021;5:e12567. doi: 10.1002/rth2.12567.