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The Home Care Delivery Program in Hemophilia: A Descriptive Italian Multicentric Study on Patients, Caregivers, and Clinicians' Points of View

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Abstract:

BACKGROUND: For patients affected by haemophilia, Patient Support Programs (PSPs) may be a support tool to assist patients and physicians in optimising treatment and improving disease management. PSP on the Pharmacokinetics (PK) service in Italy aims to support haemophilia A or B patients.

MATERIALS AND METHODS: This report analyses data of patients and physicians who benefited from the PK program from October 2018 to October 2022. Data was collected by a web-based questionnaire and by telephone calls. We provide a descriptive report on the benefits of participation in the PK program for patients with haemophilia and medical professionals involved in their care.

RESULTS: In total, 69.6% of the respondent patients stated they were very satisfied with the Program, and 97.7% said they would benefit from the service again. Among the interviewed physicians, 60% felt satisfied with the Program and thought it was helpful.

CONCLUSION: Patient satisfaction remained consistently high, with sustained improvements in all aspects of life. Medical professionals also reported positive outcomes in their patient interactions and satisfaction with the Program. PSPs have empowered patients to manage their pathology, increasing their satisfaction with treatments and quality of life.

Keywords:

Hemophilia, home care, patient support programs, quality of life

Introduction

Hemophilia is a rare disease characterized by a deficiency of coagulation factors, i.e. factor VIII (FVIII) deficiency in hemophilia A and factor IX deficiency in hemophilia B. This deficiency causes excessive blood loss or uncontrolled hemorrhaging following injuries or trauma to the joints, muscles, and soft tissue.[1] A coagulation defect on the X chromosome causes hemophilia. In women, having two X chromosomes allows compensation from the unaffected X chromosome to produce FVIII or IX if one X chromosome is affected. However, men lack coagulation factor genes on the Y chromosome; hence, they cannot compensate for the defect. Women can, however, be healthy carriers and could also be affected in some rare cases in which the only present X chromosome is bearing the defect.[1-3] The National Registry of Congenital Coagulopathies 2020 contains data from the Italian Hemophilia Centers and refers to 9784 people with congenital

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bleeding disorders: 2944 with hemophilia A, 707 with hemophilia B, 2802 with von Willebrand disease, and 3331 with defects of other coagulation factors.[4] The severity of the disease distinguishes three forms: mild, moderate, and severe, based on the residual activity of the factor present in the blood.[3] Patients with severe hemophilia suffer from hemorrhages, even minor, either spontaneously or after trauma. Frequent hemorrhages in the joints, muscles, and soft tissue are painful and incapacitating and significantly impact patients' quality of life (school, work, and private life) and can prove fatal if not properly treated.[5,6] Hemophilia treatments mainly aim to prevent life-threatening and/or muscle and joint bleeding.[7] In the last century, treatments were limited to on-demand therapies, i.e., the infusion of concentrate after the occurrence of the bleeding, also allowing home therapy a prompt and successful aid.[8] Several studies have tried to understand the disease-related issues concerning hemophilia management, treatment, disease control, and impact on the work, psychosocial, and quality of life of patients with hemophilia (PWH) and their caregivers.[9-12] In high-income countries, such as those in the United States and Europe, this information has been collected mainly through surveys involving health-care professionals, with few involving patients and caregivers. Recently, the possibility of implementing different treatment approaches has changed, shifting from a standard to personalized treatment.[9-11] Patient support programs (PSPs), which assist patients and health-care professionals in optimizing treatment and improving disease management, have increased treatment adherence and persistence across various autoimmune diseases.[13,14] PSPs address all the concerns to ensure patients are independent, secure, knowledgeable, and have better treatment adherence. PSPs are now considered a "must-have" for the sector as a result of the boost due to the COVID-19 emergency.[15] Home therapy enables optimal early treatment, resulting in less pain, dysfunction, and long-term disability, and significantly lower hospitalization rates for bleeding complications, especially for those on prophylaxis compared to episodic therapy. Home therapy also provides people with hemophilia immediate access to clotting factor concentrates (CFCs) or other coagulation therapies and hemostatic agents (e.g., emicizumab, desmopressin (DDAVP), and antifibrinolytics), and this enables immediate access to CFCs. Home therapy does provide people with hemophilia with a significantly improved quality of life, including reduced absence from school and work, increased safety when participating in a wider range of sports and physical activities, increased employment stability, and increased freedom to travel.[16,17] Congenital bleeding disorders are among the most expensive diseases requiring complex and specialized treatments and high-intensity care.[18] Italy has a strong regional and territorial unevenness in the availability of this type of service. Thus, this is probably due to the difficulty in providing services by local health authorities (ASLs), which, especially in the South of Italy, are part of a socioeconomically disadvantaged context.[19] Most of the CFC's dispensations to hemophiliac patients are centralized in a few hemophilia treatment centers (HTCs), necessitating frequent visits and long travel distances.[20] This article describes the connection between participation in the home delivery program and patient satisfaction, quality of life, and treatment adherence. In addition, the study examines how PSP affects the attitude and approach of professionals who treat hemophiliac patients.

Subjects and Methods

Involved subjects

The analysis deals with the survey data involving all patients and clinicians who benefited from PSP from 2018 to 2022. Fifty-nine patients benefited from the service in the considered time frame, and the total number of clinicians was 14. The project was conducted in accordance with the Declaration of Helsinki.

Inclusion criteria for patients

- Presence of hemophilia A or B with FVIII deficiency,
- Treatment with antihemorrhagic drugs and blood clotting factors, for which there has been a request for adhesion by the attending physician.

Inclusion criteria for physicians

- Those who have activated the PSP for their patients.

Survey design

The survey was conducted with two web-based questionnaires in Italian (one for PWH or parents/caregivers and one for clinicians). The surveys consist of multiple-choice questions and were administered to all subjects through the SurveyMonkey® (Momentive Inc.) software that meets the requirements of privacy and security of data collection (EU Regulation 2016/679); the subjects have access to the survey through the link sent by email or SMS. In the case of pediatric patients, a parent or caregiver is supposed to oversee answering the questions. The surveys were created by a multidisciplinary study group composed of experts in outcome research, HTC specialists, and data scientists, which developed the survey questionnaires based on three different phases process. For patients, the questionnaires included information about gender, age class (≤25, 25–60, and >60), and geographical origin (South, Center, and North of Italy), and then, five questions about the program evaluation and seven questions about the impact of the program on activities of daily living. Five questions are about the program evaluation, and eight are about the service's usefulness

for patient management. Clinicians are asked to profile how many hemophilia A or B patients they manage and where they come from (South, Center, and North of Italy). If patients or physicians do not respond after 1 month of sending the survey, the contact center will contact them to ask if they would like to survey by a telephone operator.

Patient support program description

Figure 1 reports the description of PSP phases. The support evaluated in this study consists of the complete pharmacokinetics (PKs) service at the patient's home concerning the activity of home blood sampling, processing, centrifuging, freezing, storage, and delivery to the hemophilia reference center of the samples taken to perform the assays necessary for PK analysis. Providing this service aims to promote a better quality of life for patients and their caregivers and reduce the number of hospital admissions. The care model is designed to offer maximum flexibility through a customized service, with resources dedicated to the needs of the individual patient and the hemophilia center. Specifically, the PSP is divided into the following sub-activities:

Statistical analysis

Statistical analysis consists of descriptive statistics. Absolute frequency (n) and percentage (%) are reported for nominal and ordinal data. Data are also described with the geophysical map visualization method. Subgroup analysis is employed considering the geographical provenience. The analysis focused on identifying possible patterns across these groups because the study was not powered to allow for formal statistical comparisons within groups or subgroups. All analyses were performed with the open-source statistical R environment (version 3.4.3, the R Foundation for Statistical Computing, Vienna, Austria).

Results

Out of the 59 patients contacted, 23 responded to the survey. 13% (n = 3) of respondents are caregivers, and 87% (n = 20) are patients. The patients' age distribution is: ≥60 years = 8.70%, ≤25 years = 34.8%, and between 26 and 60 years = 56.5%. 52.2% of patients are residents in Southern Italy, 17.4% in the center, and 30.4% in the north. Figure 2 shows the geographical distribution of patients based on the information provided by patients in question one of the surveys regarding the difficulty of reaching the hemophilia centers. There are 54 hemophilia centers in Italy, mostly concentrated in Northern Italy. Among the respondents living in the North of Italy, 71.4% declare that they have difficulties reaching the hemophilia centers, and residents in Central Italy report the same difficulties. In the South, 41.7% of respondents find many difficulties. These results, therefore, indicate the need to facilitate patient management in the treatment of hemophilia.

Table 1 reports the answers to patient's satisfaction with the home support program. In total, 69.6% of the respondents stated they were very satisfied with the program, and 97.7% stated they would benefit from the service again. Table 2 shows the answers to questions investigating how the program contributed to the patient's activities of daily living: 91.3% of the respondents from Southern Italy declared that the program has helped improve daily life activities, 100% of the respondents declared an improvement in daily life activities, thanks to the program. For patients who already underwent the PK curve at hemophilia centers, it is more effective to do it at home: 88.2% of patients who had already undergone PK at a hemophilia center said they preferred home support. 91.3% of the patients indirectly report an increase in their well-being related to activities of daily living, stating that without the

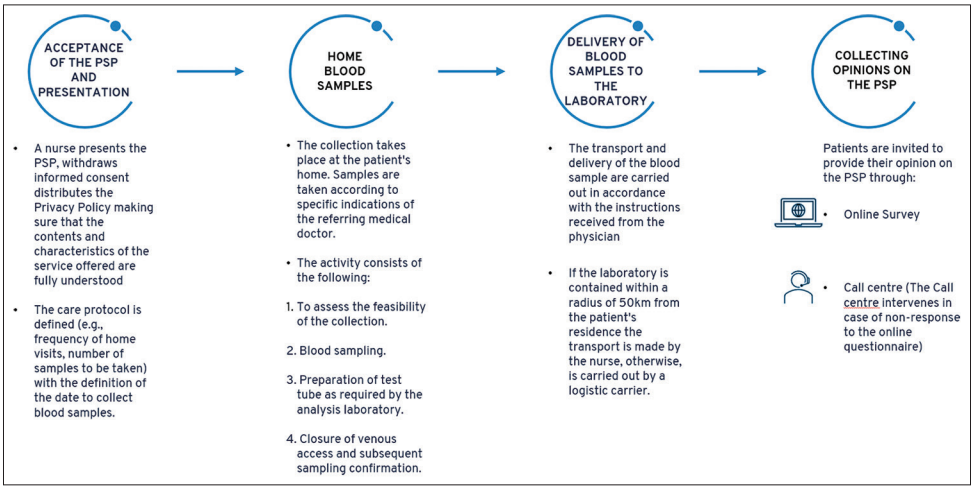

Figure 1: Flowchart of the steps of the description of the PSP phases. PSP = Patient support program

program, they would certainly have lost more working or study-related hours. Of the clinicians, out of the 14 doctors contacted, 10 responded to the survey. Among the responding physicians, 10.0% declared to routinely manage <20 PWH A, 50% more than 100 PWH A, 20% between 20 and 50 PWH A, and 20% between 50 and 100 PWH A.

Regarding managing the patients affected by hemophilia B, 50% of respondent physicians declared to manage <20 patients and 50% between 20 and 50 patients. The doctors stated that most patients they care for are (60.0%) either patients residing in a region other than that of the HTC, while 40% are regional patients. Table 3 shows the clinicians' opinions about the program and, thus, their confidence level in letting the patient be managed at home. Among the clinicians interviewed, 60% felt that they were satisfied with the program and thought it was helpful to the patient. Although 70% of the clinicians stated that they found it difficult to manage the program, 100% of the clinicians interviewed stated that they would use it again for their patients.

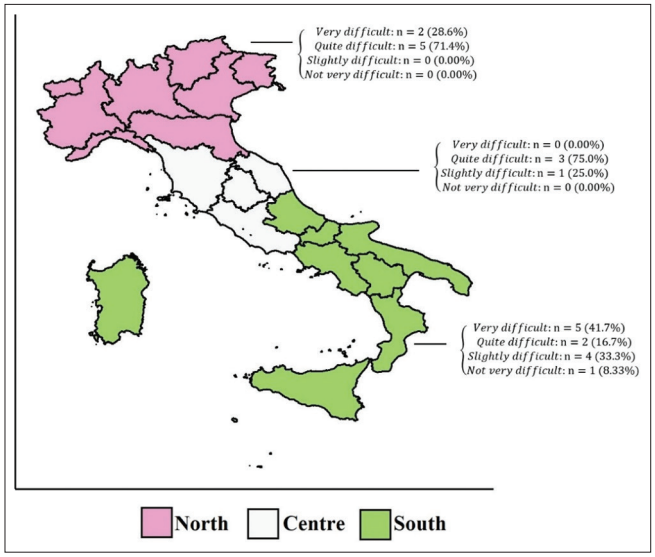

Figure 2: The geographical distribution of patients with hemophilia difficulty in reaching the hemophilia center for treatment is expressed as absolute frequencies and column percentages (regarding the information provided in Q1: Question 1 of the patient's survey)

Discussion

The Italian Association of Hemophilia Centers has long started a process of developing a Professional Accreditation System for centers that treat hemophilic syndromes and rare hereditary and acquired bleeding diseases. The project is aimed at achieving high professional standards by the centers, as well as the adoption of continuous improvement policies and best practices, "certified" following a rigorous and independent evaluation process that aims to ensure maximum transparency on the guaranteed quality levels of care.[21] Despite the effort to have spatial homogeneity in the Italian hemophilia centers' distribution, the health-care system's capacities and patient conditions make it difficult for many to be treated at such centers.[18] This research reports informative results for policy by providing information regarding hemophilia patients' difficulties in the management of their conditions in terms of the difficulties in reaching hemophilia centers and how the home-based support program could benefit in terms of quality of life and perception of this vulnerable small part of the population affected by a rare condition. Policy implication arising from this research is the consideration that health and social services could be brought closer together. Recognizing that access to health care is linked to the need for social support is a particularly important consideration for PSPs serving vulnerable populations. This aspect is very important because many patients rely on family members or community members for assistance in managing their condition, and this support network can be crucial to their health.[22] Recognition that caregivers are an essential component of patient care should highlight the need to allocate resources to support caregivers who care for family members or friends with chronic illnesses in their homes. An implication for health services research and health program evaluation is the importance of

Table 1: Respondents of patients with hemophilia satisfaction with the program by geographical area and overall expressed as absolute frequency and column percentage

Questions	Overall (*n*=23)	North (*n*=7)	Center (*n*=4)	South (*n*=12)
Q2: How satisfied are you overall with the program?				
Not at all	0	0	0	0
Slightly	0	0	0	0
Enough	7 (30.4)	0	2 (50.0)	5 (41.7)
Very much	16 (69.6)	7 (100.0)	2 (50.0)	7 (58.3)
Q3: Did the program meet your expectations?				
No	0	0	0	0
Yes	23 (100.0)	7 (100)	4 (100.0)	12 (100)
Q4: Would you benefit from the program again?				
No	1 (4.35)	0	0	1 (8.33)
Yes	22 (95.7)	7 (100)	4 (100.0)	11 (91.7)

considering patients' experiences when developing or improving program services; therefore, a needs assessment must always be conducted to make programs more suitable for patients. Incorporating patient surveys as part of research or program evaluation for improvement could help make PSPs more patient-centered.[23] Increasing awareness of PSPs' availability to patients within the medical and patient communities can enable patients to access value-added services that can help improve health outcomes. As we can see from the results, these PSPs improved patients' convenience and satisfaction. This study provides information from both perspectives of patients or their caregivers and of specialist physicians in the hemophilia context.

Medical professionals were also surveyed on their satisfaction with the program and asked to evaluate the impact of the program on their approach to patients. Medication adherence is a key component of the success of the program. The program may have empowered patients to better manage their condition by supporting patient adherence.

Limits

Our surveys present some limitations associated with this type of study and web-based data collection. Telephone calls were considered for nonresponse to the online survey. However, the selection bias due to web-based administration, which could disadvantage the digitally uneducated, even if reduced, is not eliminated. Furthermore, the surveys are not validated instruments but appear for the first time in this study and were constructed specifically for this case. Indeed, some information could be biased by caregivers that could underestimate or overestimate the requested information. Finally, part of the survey participants enrolled in the early phase of the COVID-19 pandemic possibly impacting answers regarding the quality-of-life aspects. Finally, this study was performed in a small cohort, and further research is needed to demonstrate the impact of PSPs on adherence.

Conclusions

PSPs are an important resource for patients affected by hemophilia and needing treatment or medication that they can usually only obtain at specialized centers. PSPs are provided by governments, nongovernmental organizations, and private companies and can allow patients to manage their disease faster and/or even independently. PSPs, which, unlike national health services, are more flexible and easier to change, need to be constantly updated based on feedback from patients, thus enabling the service to be increasingly improved by making it of quality and, thus, offering patients the possibility of noting an improvement in their quality of life. The results of this study provide updated evidence on patients', caregivers', and clinicians' perceptions of disease control, treatment satisfaction, and access to care in Italy. In conclusion, the positive experience of the home delivery project reported directly by the patients and their caregivers, and the benefits of physicians justify the implementation of these services. We recommend exploring enhanced collaboration between social services and health-care sectors/organizations as a mechanism to optimize health-care outcomes.

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Table 2: The impact of the program on patients with hemophilia daily living activities by geographical area and on overall respondent patients expressed as absolute frequency and column percentage

Questions	Overall (*n*=23)	Nord (*n*=7)	Centre (*n*=4)	Sud (*n*=12)
Q5: Has the program helped improve your daily life activities?				
No	2 (8.70)	1 (14.3)	1 (25.0)	0
Yes	21 (91.3)	6 (85.7)	3 (75.0)	12 (100)
Q6: Have you ever undergone PK curves by visiting the hemophilia center?				
No	6 (26.1)	1 (14.3)	1 (25.0)	4 (33.3)
Yes	17 (73.9)	6 (85.7)	3 (75.0)	8 (66.7)
Q7: If yes, compared to the period when you were undergoing this activity at the hemophilia center, do you feel that the program has improved your living conditions?				
No	2 (11.8)	0	0	2 (25.0)
Yes	15 (88.2)	6 (100)	3 (100)	6 (75.0)
Q8: Without the program, would you have missed additional work or school hours?				
No	2 (8.70)	0	1 (25.0)	1 (8.33)
Yes	21 (91.3)	7 (100)	3 (75.0)	11 (91.7)

PK=Pharmacokinetic

Table 3: Physician's opinions and satisfaction with the program are expressed as absolute frequency and column percentage

Questions	Overall (*n*=10)
Q1: Are you generally satisfied with the program?	
Not at all	0
Slightly	0
Enough	4 (40.0)
Very much	6 (60.0)
Q2: Are you satisfied with the quality of the blood samples you receive?	
Not at all	0
Slightly	0
Enough	4 (40.0)
Very much	6 (60.0)
Q3: Do you think it was a difficult program to manage?	
Not at all	0
Slightly	7 (70.0)
Enough	3 (30.0)
Very much	0
Q4: Was there already a similar service at your clinical center?	
No	6 (60.0)
Yes	4 (40.0)
Q5: Has the use of the program decreased the workload of your clinical center?	
Not at all	0
Slightly	0
Enough	5 (50.0)
Very much	5 (50.0)
Q6: Do you think the program positively influences the management of the disease for the patient?	
Not at all	0
Slightly	0
Enough	6 (60.0)
Very much	4 (40.0)
Q7: Would you benefit from the program again?	
No	0
Yes	10 (100)

Conflicts of interest

Orazio De Gregorio and Francesca Brambillasca as HNP employees declare the following conflicts of interest: AbbVie Srl, Alnylam Italy Srl, Bayer Italia SpA, BioMarin Pharmaceutical Italia Srl, Chiesi Farmaceutici Spa, CSL Behring Italy Spa, Gilead Sciences Italy Srl, GSK Italy Spa, Insmed Italy Srl, Kyowa Kirin Italy, Novartis Farma Spa, Novo-Nordisk Italy SpA, Roche Italy Spa, Sanofi Italy, Sobi Italy, Pfizer Italy Srl, Takeda Manufacturing Italia Spa, Wellspect Srl; all outside of the submitted work.

Annamaria Porreca and Angelo Claudio Molinari declare any conflicts of interest.

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