



# Analysis Of Pain Related To Hemophilic Arthropathy: Characteristics And Management In Patients With Hemophilia First National Experience

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## **Abstract:**

**Background:** The major morbidity experienced by patients with hemophilia (PWH) today is joint disease. Although the administration of antihemophilic factor to prevent bleeding has been demonstrated to prevent hemophilic joint disease when applied assiduously, PWH who develop severe arthropathy may experience relentless pain, loss of motion and functional disability. In Morocco, faced to the difficult access to antihemophilic factors and easy access to analgesic drogues, the management of hemophilic arthropathy and the pain that can cause it is very delicate. The aim of this first study in morocco in this field is to conduct a survey to assess the pain experienced by PWH and the therapeutic means used.

**Methods:** A self-assessment questionnaire was developed from "the Brief Pain Inventory" (BPI) that was adapted to our context and to our population in order to characterize the pain and to evaluate the nature and the effectiveness of the treatments as well as the patient's satisfaction of their care.

**Results:** One hundred three PWH participated in the survey, the median age was 28 years, eighty seven percent of pain was acute. The median number of pain episodes per year was at 3 times. Ninety-one percent of our patients presented at least one episode of painful arthropathy less in their lives. The median intensity of the most intense pain was at 9. The knee is reported in 84% of cases. The pain impacted quality of life in 43% of cases. Ninety-two percent of patients are regularly using analgesic drugs. The median efficacy rate of analgesics before any use of antihemophilic factor has been estimated at 70%.

**Conclusion:** The study showed that the development of an education program and an effective pain management in hemophilia is essential to reduce the burden that pain places on patients and improve their quality of life.

**Keywords:** hemophilia, arthropathy, pain, management

## **Introduction:**

Hemophilia is a rare X-linked congenital bleeding disorder characterized by bleeding manifestations, including spontaneous bleeding episodes into muscles and joints [1,2]. Recurrent joint bleeds are the hallmark of severe hemophilia and they commonly affect weight-bearing joints, such as knees or ankles, and they can lead to the development of hemophilic arthropathy (HA), a debilitating condition causing pain and affecting functionality, participation and as such quality of life in patients with hemophilia (PWH) [3]. Most PWH experience acute pain with bleeds and may suffer from chronic pain due to synovitis or arthropathy.

In Morocco, in 2019, according to the Moroccan association of hemophilia, the total number of PWH was estimated at 1008, distributed over 16 hemophilia treatment centers, but this number remains underestimated compared to reality. The median age is 31 years, eighty-five percent of patients had hemophilia A and 15% had hemophilia B, thirty-three percent of patients have severe hemophilia, 62% of patients have HA and only 16% of these patients are on prophylaxis.

It is known that prophylaxis have a significant role in the prevention of HA [4-9]. However, the therapeutic care of the constituted arthropathies remains problematic. Adult PWH mainly use factor VIII/factor IX to lessen chronic articular pain. In persistent pain, as second step after paracetamol, for adults, traditional or cox 2-selective NSAIDs are recommended. The third step would include strong opioids [1,10]. Whenever possible, the underlying condition should be treated (physiotherapy, anti-inflammatory treatment, radiosynoviorthesis, surgical interventions such as synovectomy, joint replacement or arthrodesis).

In Morocco, the care of PWH is faced with several problems: the long periods of rupture of factor which is estimated at 1-4 months / year, the difficulties of access to care, the unavailability of home factor for the majority of patients (just a few persons had this opportunity (18%)), difficulty in initiating and maintaining prophylactic treatment and the absence of physiotherapist dedicated to PWH in many centers. In addition to the young age of our population and easy access to 1st and 2nd level of analgesics in pharmacies, our patients are able to self-medicate in the event of pain. All these factors bring us face to face with two major problems; dependence on analgesics and the side effects that analgesia can cause.

The objective of this first study in morocco in this field is to conduct a survey to assess the pain experienced by PWH and the therapeutic means used.

## **Materials and method:**

A self-assessment questionnaire was developed from "the Brief Pain Inventory" (BPI), it is a pain assessment tool that measures both the intensity of pain and interference of pain in the patient's life. It also queries the patient about pain relief, pain quality, and patient perception of the cause of pain [11]. This questionnaire was adapted to our context and to our population in order to characterize the pain, its origin, its intensity and its frequency and to evaluate the nature and the effectiveness of the treatments as well as the patient satisfaction of their care (Annex 1). The survey was conducted on 2017, patient's responses were collected on files written in French then translated into Arabic, the questionnaire was previously tested on 10 patients, analyzed by Excel 2019 and they were statistically analyzed by IBM SPSS Statistics 14.0 software. The intensity of the pain and the effectiveness of the treatments were measured using the visual analog scale (VAS) typically ask a patient to mark a place on a scale that aligns with their level of pain where "0" stands for "No Pain", "10" stands for "Extreme Pain", (from 1 to 3) stands for mild pain, (from 4 to 6) stands for moderate pain and (from 7 to 10) stands for severe pain [12]. Chronic pain is pain that is ongoing and usually lasts longer than 3 months and the acute pain that lasts less than 3 months.

## **Results:**

Of 113 respondents, ten PWH who never experienced pain was excluded from the study, they represented 9% of cases. One hundred and three (91%) PWH participated in the survey, eighty-four were hemophiliacs A (82%) and 19 hemophiliacs B (18%), the median age was 28 years [7-68 years].

Among of these 103 patients, seventy-six patients (74%) have a major hemophilia, nine patients (9%) have a moderate hemophilia and 18 patients (17%) have minor hemophilia. Thirty percent of patients received scheduled injections of prophylactic factor in combination with physiotherapy and the rest were all treated on demand.

Eighty seven percent of pain was acute, three percent of pain was chronic and 10% of patients had both types of pain. Fifty-eight patients (56%) reported more than 10 episodes of pain per year.

The median number of pain episodes per year was at 3 times. The median intensity of the most intense pain was at 9 (severe pain) of the VAS and the median intensity of the least intense pain was at 3 (mild pain) of the VAS.

The most reported location was the knee in 84% of cases, followed by the ankles reported in 57% of cases and the elbows 55% of cases; twenty-eight patients (27%) reported pain that affects all the joints.

The pains impacted activities of daily living in 60% of patients, walking in 65% of patients, sleeping in 70% of patients, mood in 70% of patients but also social relationships in 45% of patients and impacted quality of life in 43% of patients.

Ninety-two percent of patients are regularly using analgesic drugs. The consumption is even daily for some of them. The 3 levels of analgesic drugs are represented with paracetamol in 74% of the cases, Corticosteroids in 60% of cases and Nefopam 52% of cases, Tramadol in 47% of cases. Morphine in 16% of cases. NSAIDs in 12% of cases and oxycodone-paracetamol in 11% of cases. the majority combine at least two pain killers.

Beside these drug therapies, pain management included non-drug techniques such as the use of ice bladder revealed in 84% of cases, physiotherapy in 30% of cases.

The median efficacy rate of analgesics before any use of factor concentrates has been estimated at 70%.

## **Discussion:**

Our study was conducted on 2017 with the aim of locally evaluating the management of pain related to HA in PWH in our care center. Another more in-depth study is underway by using questionnaires more targeted and more predictable.

Both acute and chronic pain are common in PWH. Adequate assessment of the pain origin is essential to advise a good management. While the clotting factor should be given as quickly as possible to stop the bleeding, other drugs are often needed to control the pain. Chronic HA develops in patients who have not been treated properly with clotting factor concentrates to stop the bleeding from the joints.

The mechanisms involved in the development of the hemophilic arthropathy are still not well known and probably multifactorial. Diagnostic imaging offers an objective assessment of joint structural outcome with earlier changes of HA best assessed with either ultrasound (US) or MR imaging [13,14].

Most PWH adults experience limitations in daily living activities and a chronic articular pain, which affects their mental health. Pharmacologic treatment of pain in PWH adult has been often proven to be inadequate. [10,15-18]. When the pain is disabling, orthopedic surgery may be indicated [19]. Patients with persistent pain should be referred to the specialized pain management team.

In our study, ninety-one percent of our patients presented at least one episode of painful arthropathy in their lives. A survey of 90 caregivers and individuals with hemophilia and inhibitors evaluated the relationship between health-related quality of life (HRQoL) and productivity, as measured by absenteeism [20], showed that 89% (n = 598) of patients with hemophilia reported that pain had interfered with their daily life in the past 4 weeks, and 301 PWH (50%) reported constant pain [21].

In 50 patients suffering from severe coagulopathy, followed at the “hopitaux Universitaires de Strasbourg (HUS)” resources and skills center, studying the pain management related to chronic HA [22], forty percent of patients have recourse to NSAIDs despite their adverse events, celecoxib being however the most frequently used. Thirty percent of patients benefit regularly from physiotherapy sessions, including massages, cryotherapy. Transcutaneous electrical nerve stimulation (TENS) are used in 11% of patients. Fourteen percent are trying alternative medicine such as acupuncture, moxibustion, relaxation, hypnosis or music therapy.

A similar survey was carried out in Paris by Pénélope Randuineau [23], out of 22 patients, fourteen patients (64%) received regular and scheduled injections of factor concentrates and 8 patients (36%) were treated with Requirement. All patients (100%) experienced pain during the previous year, presenting 65% of cases acute pain, thirty percent a chronic pain and 5% of cases both types of pain. Four patients (19%) reported pain less than 2 or 3 times a year, the average intensities of hemarthrosis pain and secondary joint damage were 5.4 and 3.9 respectively. Paracetamol and celocoxib were used by 18 patients (82%) and 9 patients (41%), respectively. Seventeen patients (77%) are satisfied with their pain management.

Our results remain different from the literature in terms of characteristics of bread, and also in terms of management; our patients do not have easy access to prophylaxis which partly explains the large number of annual episodes and the importance of the pain intensity on the VAS. the use of NSAIDs is neglected compared to other analgesic treatments as well as the use of non-medicated techniques explained by the difficult access to them.

The pain management must be multidisciplinary, and taken in charge by a specialized team including hematologists, rheumatologists, surgeons, radiologists, functional rehabilitation physicians, physiotherapists and pain physician. However, for some years, non-medicated analgesic techniques made their way: hypnosis, music therapy, relaxation and Transcutaneous electrical nerve stimulation (TENS). These techniques represent an effective complement or even an alternative to medicines. Each patient suffering from arthropathy can manage his pain in a personal way through all these therapeutic alternatives.

## **Conclusion:**

Despite increasing treatment modalities to prevent and stop joint bleeding, its consequences still have major impact on the life of PWH. Blood-induced inflammation in combination with erythrocyte-derived iron has devastating effects on the joint. This may result in acute and chronic pain.

Our data suggests that pain is widely prevalent but the severity and interference seem to be minimal in around half the patients. Further understanding of the severity and pain management requires correlation with joint damage and bleed prevention.

Treatment involves a multimodal approach, focusing on physical and psychological aspects and involving a combination of pharmacotherapy, education and exercise.

This is comforting our idea to develop medical consultations with a pain treatment specialist.

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## Annex 1

## Questionnaire استطلاع

Identité : هوية المريض

Nom et prénom

الإسم العائلي و الشخصي:

NE :

Age :

العمر:

Type de l'hémophilie :

 الهيموفيليا المتوسطة A الهيموفيليا المعتدلة B الهيموفيليا الشديدة

نوع الهيموفيليا :

شدة المرض :

Sévérité :

 majeur modéré mineur

## Les caractéristiques de la douleur : خصائص الألم

✓ Type de la douleur :

نوع الألم :

Douleur aiguë ≤ 3 mois 

الم حاد (أقل من 3 أشهر)

Douleur chronique ≥ 3 mois 

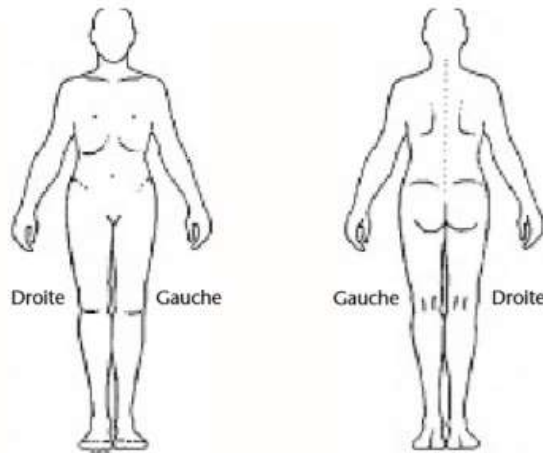
الم مزمن (أكثر من 3 أشهر)

✓ Localisation de la douleur :

مكان الألم:

Mettez sur le dessin un X à l'endroit où vous ressentez la douleur

ضع علامة X مكان الألم



Entourez d'un cercle le chiffre qui indique combien de fois vous avez eu mal par ans

ضع دائرة على الرقم الذي يرمز لعدد المرات التي تشعر فيها بالألم في السنة

0 1 2 3 4 5 6 7 8 9 10

Entourez d'un cercle le chiffre qui décrit le mieux la douleur la plus intense que vous avez ressentie durant l'année précédente

ضع دائرة على الرقم الذي يصف الألم الأكثر حدة الذي شعرت به في السنة الماضية

0 1 2 3 4 5 6 7 8 9 10

Entourez d'un cercle le chiffre qui décrit le mieux votre douleur en générale

ضع دائرة على الرقم الذي يصف المك بصفة عامة

0 1 2 3 4 5 6 7 8 9 10

Est-ce que la douleur gêne votre ?

هل يؤثر الألم على

Activité générale :	non/ لا	oui/ نعم	النشاط العام
Humeur :	non/ لا	oui/ نعم	المزاج
Capacité à marcher :	non/ لا	oui/ نعم	القدرة على المشي
Relation avec les autres :	non/ لا	oui/ نعم	العلاقة بالآخر
Sommeil :	non/ لا	oui/ نعم	النوم
Gout de vivre	non/ لا	oui/ نعم	طعم الحياة

Quels médicaments prenez-vous contre la douleur :

ما هو نوع العلاج الذي تستعمله ضد الألم

Traitement antalgique :	non/ لا	oui/ نعم	مضادات الألم
Paracétamol	non/ لا	oui/ نعم	الباراسيتامول
AINS	non/ لا	oui/ نعم	مضادات الالتهاب غير الستيرويدية
Corticoïde	non/ لا	oui/ نعم	مضادات الالتهاب الستيرويدية
Codéine	non/ لا	oui/ نعم	
Néfopan (Acupan*)	non/ لا	oui/ نعم	
Tramadol	non/ لا	oui/ نعم	ترامادول
Morphine	non/ لا	oui/ نعم	المورفين
Glace	non/ لا	oui/ نعم	ثلج
Rééducation- kinésithérapie	non/ لا	oui/ نعم	إعادة التأهيل - العلاج الطبيعي
Techniques non médicamenteuses	non/ لا	oui/ نعم	تقنيات غير طبية

Quel soulagement les traitements ou les médicaments que vous prenez vous ont-ils apporté : pouvez-vous indiquer le % d'amélioration obtenue

ما هي النسبة المئوية للتحسن التي تلقيتها من العلاجات أو الأدوية التي تتناولها

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

