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## Research Article

# Management of the Procedural Pain Induced by Bone Marrow Biopsies: An Observational Study

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### ABSTRACT

**Introduction:** Bone marrow biopsy is an investigation procedure in hematology which might lead to procedural pain. Therefore, our study aimed to assess procedural pain intensity and to identify factors associated with pain experience.

**Methods:** We performed an observational study of consecutive patients who underwent a bone marrow biopsy in a tertiary hospital hematology ward. The pain was assessed using a visual analogue scale (0-100 mm) before, during and after the procedure. We also collected data as premedication strategy, anxiety, physician's experience and the experience of a previous biopsy.

**Results:** Forty consecutive patients were recruited. The biopsies were mostly performed for diagnostic purposes (45%). Thirty percent had local anesthesia alone and 70% had local anesthesia plus any other medication. The mean pain before the procedure was 9mm (SD=1.7), during 36mm (SD=2.7) and after 9.5mm (SD=1.0). No statistical difference has been shown between the different pain prophylaxis (p=0.622). The level of anxiety before the procedure was significantly correlated with the procedural pain experienced ( $r^2=0.323$ ,  $p=0.042$ ), while the length of the procedure and previous experience of the procedure were not.

**Conclusion:** This study suggests that bone marrow procedural pain can be improved and highlights several promising mitigation-strategies to address this issue.

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## Background

Despite improvements in pain management over the past decades, acknowledgment and management of procedural pain remain poor [1, 2]. In 2008, Coutaux *et al.* reported that 55% of hospitalized patients described a painful care-related event during their stay; 57% of these events were rated as intense or extremely intense [3]. This issue represents a major threat to the achievement of good quality care, particularly because healthcare professionals have a tendency to underestimate the pain experienced by their patients. In 2004, Kuball *et al.* study results highlighted evidence that physicians had a tendency to underestimate the severity of pain experienced by patients, compared to

the patient's auto-assessment and the nurse's assessment [4]. The tendency to underestimate might prevent physicians from prescribing effective premedication for pain prophylaxis.

One of these potentially painful procedures, bone marrow biopsy, now plays a key role in the journey of patients with hematologic diseases. Indeed, during diagnosis and the follow-up of some hematologic diseases, the bone marrow biopsy indications are numerous and might be needed several times during the course of care [5]. Even though these procedures represent an improvement in the management of hematologic diseases, patients mostly consider them as traumatizing and painful [6-8]. Moreover, evidence shows that experienced pain is worsened by the repetition of the procedure and procedure-related anxiety [4, 9]. The

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present study aims to assess procedural pain intensity and to identify the factors associated with an increase in pain intensity during the procedure.

## Material and Methods

We performed a pilot monocentric observational study of patients who had a bone marrow biopsy between April and June 2014 and April and May 2015 at the regional specialist department of hematology in the (blinded for peer-review). The protocol has been approved by the institutional ethics committee of the (blinded for peer-review).

### I Patients

Eligible patients were patients suffering a malignant hematologic disease, attending a day care center and who were able to give consent. We excluded patients who suffered from cognitive impairment, or a psychiatric disorder. Only adult patients were included as the center only cares for patients over 18 years age.

### II Procedure

Forty participants who underwent a bone marrow biopsy were consecutively recruited during two recruiting periods in the hematology department of the tertiary center. The participants' pain was assessed by a research nurse before, during (at the time of the aspiration) and after the procedure. The pain was assessed using a Visual Analogue Scale (VAS) 15 minutes before, during and after the procedure. We did not intervene in the procedure or in the pain management plan. Based on their clinical experience and the scientific literature, a scientific committee, including hematologists, palliative care physicians, clinical nurses and a research nurse defined the relevant data to collect in the Case Report Form (Appendix 1). Pain prophylaxis methods were recorded. They were defined as the medications (pain killers and anxiolytics) used to prevent procedural pain. We also recorded

sociodemographic data, data relatives to the patient's hematologic disease, to the management of the hematologic disease, and to the bone-marrow biopsy itself (such as the reason to perform the procedure, the length of it, who performed it, and the level of anxiety before the procedure assessed using a Visual Analogue Scale of 10 points from 0 "no anxiety at all" to 10 "worst anxiety imaginable").

### III Outcomes

The primary outcome was to assess the intensity of bone marrow related procedural pain. Our secondary outcome was to explore the influence of several potential worsening factors, such as anxiety before and during the biopsy (using a VAS), the experience of a previous biopsy, the length of the procedure and the physician's experience.

### IV Analysis

The difference in pain rating between the different premedication strategies was compared using a Student T-test. To do so, we compared ratings before and during the procedure in the different groups. Mann-Whitney tests were used to analyze the association with anxiety, the experience of a previous procedure, the length of the procedure and the physician's experience of it. Results were considered statistically significant for a threshold  $\alpha=0.05$ ; the analysis was performed using SPSS 20.0 (Chicago, Inc).

### Results

We included 40 patients of whom 19 (48) were women and 21 (53%) were men. The mean age of the sample was 58. Biopsies were mostly performed for diagnostic purposes (45%) or as part of the treatment plan of malignant lymphoma (28%). No biopsy was performed for chronic lymphoid leukemia, myeloma or myelodysplastic syndromes (Table 1).

**Table 1:** Characteristics of the population.

Characteristic	Number (%)
Mean age (in years)	58
Gender:	
Female	19 (48)
Male	21 (53)
<i>Reason for the bone marrow biopsy:</i>	
Acute leukaemia	1 (3)
Chronic lymphoid leukaemia	0 (0)
Myeloproliferative disorders	4 (10)
Malignant lymphoma	11 (28)
Myeloma	0 (0)
Myelodysplastic syndromes	0 (0)
Diagnostic purpose	18 (45)
Other reason	6 (15)
<i>Ongoing treatment at the time of the biopsy:</i>	
Therapeutic abstention	12 (30)
Curative care plan	10 (25)
Active treatments without the purpose of curing the disease	5 (13)
Palliative care plan	0 (0)
Missing data	13 (33)

## I Pain Assessment

Before the procedure, VAS for pain was 9 mm and VAS for anxiety was 40 on average. During the procedure, the mean VAS for pain was 36 mm and it dropped to 9.5 mm one minute after the procedure. There was a statistical difference in VAS-rating for pain between before and during biopsy ( $p < 0.0001$ ) but not between pain during and after the biopsy ( $p >$

0.05) (Table 2). Seventy-three percent of the sample felt anxious about the procedure. This was mostly because of a previous painful procedure ( $N=9$ , 31%), a lack of information about the procedure ( $N=7$ , 24%), the fear of experiencing pain ( $N=5$ , 17%) and information given by a next-of-kin or found on the Internet ( $N=4$ , 14%). Three patients were anxious because they feared the results (11%) and one was anxious but for no identified reason (3%) (Table 2).

**Table 2:** Pain assessment and associated variables.

Variable	Number (%)
Mean pain on a VAS before the procedure (in mm)	9
Mean pain on a VAS during the procedure (in mm)	36
Mean pain on a VAS after the procedure (in mm)	9.5
Mean anxiety on a VAS before the procedure (in mm)	40
Mean length of the procedure (in minutes)	11.4
Felt anxious about the procedure	29 (73)
<i>Painkillers before the procedure:</i>	
Ladder 1	9 (22.5)
Ladder 2	5 (12.5)
Ladder 3	1 (2.5)
Anxiolytics before the procedure	5 (13)
<i>Pain prophylaxis:</i>	
Local anaesthesia	40 (100)
No prophylaxis other than local anaesthesia	12 (30)
Painkillers alone	7 (17.5)
Paracetamol	2 (5)
Strong opioids	3 (7.5)
Paracetamol plus strong opioids	2 (5)
Anxiolytics alone	6 (15)
Nitrogen Monoxide-oxygen mixture (NMM) alone	11 (27.5)
Painkillers and anxiolytics	2 (5)
Anxiolytics and NMM	1 (2.5)
Painkillers and NMM	1 (2.5)
Painkillers, anxiolytics and NMM	0 (0)
<i>Professional who performed the procedure:</i>	
Senior physician	6 (15)
Junior physician	27 (68)
Medical student	7 (18)

NRS: Numeric rating scale.

NMM: Nitrogen Monoxide-oxygen mixture.

## II Pain Prophylaxis

There was no statistical difference in VAS-ratings for pain during the procedure ( $p=0.622$ ) between patients who had local anesthesia alone ( $N=19$ , mean VAS= 35.7mm, SD=23.8) and patients who benefited from local anesthesia plus any other prophylaxis ( $N=21$ , mean VAS = 37.6, SD= 25.3) (Table 2).

## III Associated Factors

There was a significant positive correlation between VAS-ratings for pain ratings during the procedure and VAS for anxiety rated before the procedure ( $r^2=0.323$ ,  $p=0.042$ , CI 95% [0.008; 0.429]). Patients who had a VAS for pain over 30 mm ( $N=28$ , 70%) experienced a non-significantly longer procedure (mean length = 12 min, SD=7.8) when compared to patients who had a VAS for pain under 30 ( $N=12$ , 30%,

mean length=10, SD=5.7) ( $p=0.508$ ). Patients who had a previous bone marrow biopsy ( $N=11$ , 27.5%) had a non-significantly higher pain rating on a VAS (mean=42.7, SD=2.6) when compared to patients who had never experienced the procedure ( $N=29$ , 72.5%, mean=34.5, SD=2.3) ( $p=0.685$ ). The pain was similar, regardless of who carried out the procedure or their professional experience ( $p>0.05$ ) (Table 2).

## Discussion

Our study aimed to assess pain intensity during bone marrow biopsies and to identify factors associated with pain. In addition, our results highlighted the fact that anxiety before the procedure was correlated with the pain experienced during the procedure. More than half of our sample declared having experienced moderate pain (VAS comprised between 30 and 59mm) and about one in seven a severe pain (VAS over 59mm). These results are consistent with the current literature and support the

importance of implementing pain mitigation-strategies as this is a preventable outcome [4, 10].

To properly implement successful strategies, premedication protocols must consider the pharmacokinetics of pain-prophylaxis medications. Indeed, pain is experienced only during the procedure; for this reason, long-lasting medications should probably be avoided, and preference should be given to short-lasting painkillers [4]. In 2008, Steedman *et al.* showed that, in addition to the local anesthesia, nitrogen monoxide-oxygen mixture decreased the rate of severe pain from 33% to 14% in patients undergoing bone marrow biopsies [11]. On the other hand, the sublingual fentanyl showed disappointing results [12]. Further research is needed to develop premedication protocols that could effectively and safely be implemented [10].

We found that procedural pain was correlated with anxiety before the procedure, a result consistent with the literature about procedural pain, especially in cancer patients [3, 7, 13, 14]. Interestingly, the majority of our sample had bone marrow biopsy for diagnostic purpose, and it is, therefore, possible that they may experience anxiety due to the uncertainty of the results [7, 15]. Our results also suggest that anxiety is increased by the lack of information before the procedure, suggesting that interventions to alleviate the procedure-related anxiety could be a relevant tool to mitigate procedural pain. Uncertainty can increase anxiety, and we, therefore, suggest that physicians should carefully address this issue by taking the time to inform the patient about the procedure.

Additionally, patients who had previous negative experience of a painful bone marrow biopsy might be more likely to be anxious and to experience an increase in pain. Consistent with the literature, in our sample, patients who had had a previous bone marrow biopsy had a greater level of pain [16-18]. In their study, Coureau *et al.* showed that patients who experienced a previous painful procedure were more likely to experience a painful procedure again [3]. We suggest that careful attention be paid to patients likely to experience multiple bone marrow biopsies; particularly those patients who suffer from a long-lasting hematologic illness or those included in therapeutic protocols with multiple iterative biopsies [14]. Finally, studies suggest that procedural pain could lead to hyperalgesia and long-lasting pain [1, 19]. As chronic pain adversely impacts the quality of life, its prevention must be a priority in those populations that often suffer several other burdensome symptoms [20-22].

## Conclusion

Overall, physicians should do their utmost to mitigate procedural pain during the bone marrow biopsy. An important way forward would be to recognize situations that lead to anxiety or uncertainty, such as patients that are likely to experience multiple biopsies. Robustly designed studies are needed to define the best premedication strategy to prevent bone marrow biopsy related pain.

## Funding

None.

## Conflicts of Interest

None.

## Data Availability

Data are available upon request to the corresponding author.

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