Perceived Levels of Pain Associated With Bone Marrow Aspirates and Biopsies

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Bone marrow aspiration and biopsy (BMAB) is an invasive procedure that is routinely performed by hematologists and medical oncologists for the diagnosis and staging of both hematologic and solid malignancies. The medical literature provides few data about the degree of pain experienced by patients who undergo this procedure, and not much is known about the factors that can modify their perception of pain.[1–6] Usually, BMAB is performed at the bedside or in the outpatient setting, and no formal guidelines exist concerning the precautions to be taken in order to minimize such pain. In most cases, an analgesic effect is obtained only with local injection of an anesthetic agent. However, some physicians and medical centers use additional measures, such as oral or intravenous analgesia and conscious sedation, either routinely or upon patient request.[7,8]

In this study, we evaluated the effectiveness of several BMAB approaches in an attempt to reduce patient pain. These strategies included doubling the dose of local anesthesia, doubling the wait time between the administration of local anesthesia and the procedure, using a topical anesthetic spray, and using an oral regimen combining analgesic drugs (acetaminophen and oxycodone) and anxiolytic compounds (lorazepam).

METHODS

After institutional review board approval, we conducted a retrospective review of collected

ABSTRACT

Background: Little is known about the degree of pain experienced by patients undergoing a bone marrow aspiration and biopsy (BMAB).

Objective: To evaluate the effectiveness of several strategies aimed at reducing the pain score.

Methods: We conducted a retrospective analysis of 258 consecutive adult patients who underwent BMAB via 6 different approaches, the first 5 of which were performed by one physician. Group A received local anesthesia with 1% lidocaine hydrochloride (5 mL) and a 5-minute wait time before the procedure; group B received local anesthesia with a double dose (10 mL) of lidocaine; group C received 5 mL of local anesthesia with a 10-minute wait; group D received 5 mL of local anesthesia plus a topical spray with ethyl chloride; group E received oral analgesia and anxiolysis 30 minutes before the procedure in addition to the group A dosage of lidocaine; and group F received the same anesthesia as did group A, but the BMAD was performed by a less experienced practitioner.

Results: On a 0 to 10 scale, the mean pain level among the 258 patients was 3.2 (standard deviation = 2.6). Rate of complications was low (<1%). Several strategies failed to improve the pain level, including the administration of a double dose of local anesthesia, waiting longer for the anesthesia effect, and the additional use of a topical anesthetic spray or oral analgesia and anxiolysis. Pain levels were not increased when the procedure was done by a less experienced practitioner. Younger age and female gender were associated with higher pain levels.

Conclusions: Given that the average level of perceived pain during BMAB is low to moderate (approximately 3 on a 0-10 scale), the routine use of conscious sedation for this procedure may not be indicated. Several strategies aimed at reducing the pain level, including doubling the dose of anesthesia and using an oral prophylactic regimen of analgesia and anxiolysis, failed to improve pain scores.

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data from 258 consecutive adult patients who underwent BMAB from 2007 to 2010 at the myeloma clinic of our institution. All patients signed the appropriate informed consent for the procedure. Preprocedure assessment included documentation of drug allergies, relevant past medical history, a review of current medications, and a clinical assessment of cardiovascular and

respiratory functions. Oxygen, resuscitation drugs, and flumazenil (a benzodiazepine-reversal agent) were available at the procedure site. Postprocedure assessment was performed within 10 minutes after the completion of BMAB; it included assessment of vital signs, cardiovascular and respiratory functions, and pain intensity. Pain level was graded by asking the patient to assign any value between 0 ("no pain at all") and 10 ("worst possible pain"), using the Wong-Baker FACES Pain Rating Scale.[9]

All BMABs were obtained from the posterior superior iliac crest, with the exception of those in 7 morbidly obese patients who required a second bone marrow aspirate from the sternum. The procedure was performed by a single physician (G.T.), who had adequate experience (>100 BMBAs).

In group A, all patients received local anesthesia with the subcutaneous and periosteal infiltration of 5 mL of lidocaine hydrochloride 1% aqueous solution (total dose, 50 mg). A skin wheal was raised with lidocaine hydrochloride via a 25-gauge × 5/8-inch (1.6 cm) needle; then, a 21-gauge × 1.5-inch (3.8 cm) needle was used for deeper infiltration. In patients with excessive soft tissues ("deep bones"), local anesthesia was given through a "spinal" needle (22-gauge × 3.50-inch [0.7 × 90 mm] BD Quincke spinal needle; BD, Franklin Lakes, New Jersey). The BMAB was started 5 minutes after completion of the local anesthesia. The needle used for BM aspiration was a Jamshidi needle (15-gauge × 3-inch [7.6 cm]; Cardinal Health, McGaw Park, Illinois). For the biopsy, a Jamshidi needle (11-gauge × 4 [10 cm]; Cardinal Health) was used.

The same technique was used in group B, with the exception of the lidocaine dose, which was doubled to 100 mg (10 mL of 1% solution). Patients in group C received 5 mL of 1% lidocaine, the same dose as in group A, but the wait time between completion of the local anesthesia and the start of the BMAB procedure was extended to 10 minutes.

In group D, a topical cutaneous spray of ethyl chloride was used a few seconds before the lidocaine needle was introduced. The target area was sprayed for 5 to 7 seconds from a distance of 10 to 20 cm.

Patients in group E received analgesia with acetaminophen 650 mg and oxycodone 10 mg (Percocet® 10/650) orally in a single dose, along with the anxiolytic lorazepam (Ativan®) 2 mg orally.[10] Both drugs were taken 30 minutes before the procedure; then, the standard dose of 5 mL lidocaine was administered 5 minutes before the procedure. Patients who received analgesics and benzodiazepines were instructed not to operate machinery or vehicles and to have a responsible adult present for 6 hours after discharge. Each group consisted of consecutively treated patients.

Assignment to groups A through E did not follow preestablished criteria but was retrospective and based on the sequential change over time of the procedural approach by G.T. Previously, G.T. performed the procedure with only 5 mL of 1% lidocaine hydrochloride for local anesthesia, the simplest approach (as in group A). He noticed that several patients complained of pain and, in the absence of published

Table 1
Basic Patient Characteristics

	MALES	FEMALES
Number (%)	139 (54%)	119 (46%)
Age, mean (SD), y	61.1 (±12.9)	60.5 (±11.4)
Race/ethnicity, no. (%)		
Caucasian	118 (85%)	103 (86%)
African American	10 (7%)	8 (7%)
Hispanic	8 (6%)	7 (6%)
Asian	3 (2%)	1 (1%)
Height, mean (SD), cm	175 (±7)	161 (±7)
Weight, mean (SD), kg	90 (±18)	76 (±18)
BMI, mean (SD)	29.1 (±5.1)	29.3 (±6.6)
Use of spinal needle, no. (%)	26 (19%)	35 (29%)

formal guidelines for anesthesia with BMAB, decided to double the dose of lidocaine for future procedures (group B). He still noticed several patients complaining of pain with the new approach, and he again decided to change strategy (group C), etc. There was no initial intent of conducting a prospective study.

The BMABs in group F were not performed by G.T. but by a less experienced (<20 BMABs) health-care provider, either a physician assistant or a first-year hematology-oncology fellow in training and under supervision. Like patients in group A, those in group F received only 5 mL of 1% lidocaine hydrochloride as a local.

Statistical analysis was performed using SAS® software, version 9.1 (SAS Institute, Cary, North Carolina). Ordinal logistic regression (proportional odds model) was used to study the dependence of pain level on predictor variables such as age, sex, race, height, weight, body mass index (BMI), length of specimen, use of spinal needle, topical spray, and oral analgesia/anxiolysis. Statistical power was set at 80%. $P < .05$ was considered to be statistically significant.

RESULTS

Of the 258 patients who underwent BMAB, 54% were men and the mean age was 61 years (range, 19−87). The summary of patient characteristics is shown in Table 1. On a 0 to 10 scale, the mean pain level among the 258 patients was 3.2 (standard deviation = 2.6). A score of 0 (complete absence of pain) was reported by 36 patients (14%); scores of 8 to 10 (severe pain) were reported by 20 patients (8%) (Figures 1 and 2). Group analysis of BMABs that were performed by the same physician showed that mean pain levels were 3.6 (±2.8 SD) in the 61 patients of group A (5 mL lidocaine with a 5-minute wait), 3.0 (±2.6 SD) in the 82 patients of group B (10 mL lidocaine with a 5-minute wait), 3.4 (±3.0 SD) in the 23 patients of group C (5 mL lidocaine with a 10-minute wait), 2.5 (±2.3 SD) in the 18 patients of group D (ethyl chloride topical spray, immediately followed by 5 mL lidocaine with a 5 minute wait), and 2.8 (±2.3 SD) in the 34 patients of group E (acetaminophen, oxycodone, and loraz

Distribution of pain levels in 258 adult patients

Wong-Baker FACES Pain Rating Scale		PAIN LEVEL	% of patients
HURTS WORST		9-10	4%
HURTS WHOLE LOT		7-8	9%
HURTS EVEN MORE		5-6	14%
HURTS LITTLE MORE		3-4	23%
HURTS LITTLE BIT		1-2	36%
NO HURT		0	14%

Figure 1   Wong-Baker FACES Pain Rating Scale.

The Wong-Baker FACES Pain Rating Scale is adapted from Hockenberry MJ, Wilson D. *Wong's Nursing Care of Infants.* 9th ed. St Louis, MO: Mosby/Elsevier; 2011:1259. Used with permission. Copyright, Mosby.

epam with a 30-minute preprocedure wait, followed by 5 mL lidocaine with a 5-minute preprocedure wait). When the procedure was performed by the less experienced health-care provider in the 36 patients of group F, the mean level of perceived pain was 3.4 ($\pm$2.4 SD) (same regimen as group A). Statistical analysis found no significant differences in pain scores among groups A through F. In all, 40% of the patients

underwent BMAB for the first time; 60% of the patients had previously experienced the procedure. Univariate logistic analysis found that this factor was not associated with different pain levels (data not shown).

Univariate ordinal logistic regression of the dependence of pain levels on various predictors found that older patients were more likely to report lower pain levels (odds ratio [OR] = 1.30 for 10-year increase of age, 95% confidence interval [CI] 1.05−1.57, P = .013), taller patients were more likely to report lower pain levels (OR = 1.025 for 1-cm increase, 95% CI 1.001−1.050, P = .040), and men were more likely to have lower pain levels than women (OR = 1.66, 95% CI 1.02−2.70, P = .048). Outcomes were not influenced by race (P = .17), patient weight (P = .90), BMI (P = .26), or first-time BMAB (P = .12).

Several patients required the use of a longer (spinal) needle to reach and anesthetize the periosteum, and at univariate analysis, those patients were more likely to report a higher pain level (OR = 1.82, 95% CI 1.10−3.03). However, in multivariate logistic regression, the effect of spinal needles on pain perception disappeared after adjustment for sex. In fact, women were 1.970 times more likely to require spinal needles than men. In 7 patients who were severely obese (BMI >40), spinal needles could not reach the periosteum, and a marrow aspirate was obtained from the sternum. The needle's depth of penetration into the bone, estimated by the length of bone fragment extracted at the biopsy site (mean = 8 mm; range, 0–22 mm), did not influence the pain scores (P = .15 after univariate analysis).

The multivariate logistic model was built by first including age, sex, and other predictors that were found to be significant in univariate analysis. Stepwise regression was then used to further select predictors. In the multivariate logistic regression, only age and sex retained their impact; older patients were more likely to have lower pain levels (OR = 1.029 for 1-year increase, 95% CI 1.008−1.050, P = .0057) and men
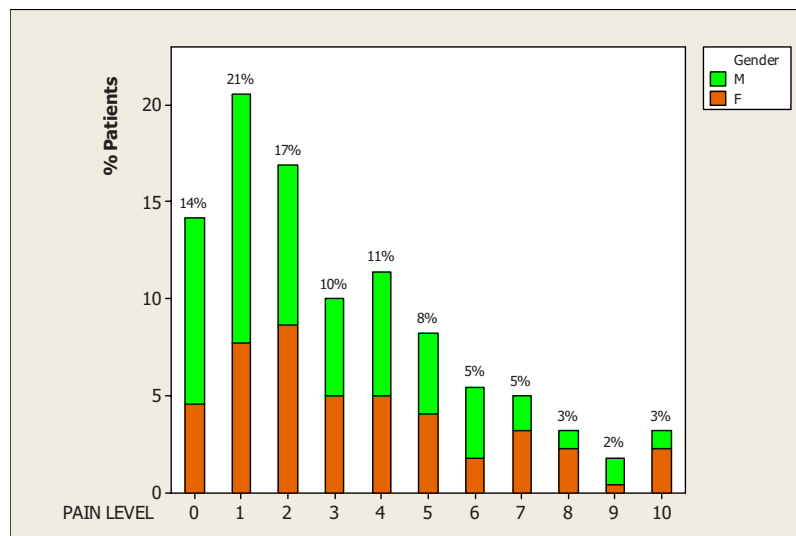

Figure 2   Distribution of Pain Levels in 258 Adult Patients.

were more likely to have lower pain levels than women (OR = 1.79, 95% CI 1.09–2.93, *P* = .0208).

There were no life-threatening complications observed after the procedures. Respiratory and cardiovascular functions were unaffected in all patients. Adverse events observed during or after the procedure included prolonged bleeding (defined as bleeding lasting longer than 5 minutes) from the site of puncture (2 patients), panic attack (1 patient), and needlestick injury to the physician during the administration of local anesthesia (1 patient). No episodes of bleeding with hemodynamic instability were observed, even when the procedure was done during therapeutic anticoagulation with either low–molecular weight heparin (2 patients) or warfarin (1 patient). The 2 patients who experienced prolonged external bleeding at the site of puncture were using nonsteroidal anti-inflammatory drugs. Bleeding was stopped with local measures only. In 19 patients, the specimen of the core biopsy was lost within the bone or the soft tissues while the biopsy needle was extracted. In 14 patients, the tip of the aspirate needle kinked due to very hard bones (of note, all these patients had received bisphosphonates, either pamidronate or zoledronic acid, as a monthly intravenous infusion for more than 1 year).

DISCUSSION

In hematology-oncology clinics BMAB is a commonly performed procedure. Although it evokes feelings of intense fear among patients, we found that the level of pain experienced during a BMAB is generally modest. Pain levels were similar regardless of the anesthetic strategy adopted during the procedure. The strengths of our study are the multiple interventions evaluated and the relatively large number of patients. The main weaknesses of the study are the retrospective nature of the analysis and the lack of randomization. However, with the exception of group F, all procedures were performed by a single physician, with the intent of minimizing potential confounding factors. This eliminates the variability expected among different health-care providers regarding different technical approaches to BMAB or different levels of training. Interestingly, in a study of 100 consecutive BMABs performed by many physicians at various levels of training (eg, internal medicine house staff, physician fellows, and hematology-oncology attending physicians), the average pain score was 1.7 on a 0 to 5 scale,[11] a result very similar to ours.

To reduce pain levels, we utilized several strategies; but they did not seem to provide a meaningful benefit, according to our retrospective analysis. Doubling the dose of local anesthetic or waiting longer for it to take effect did not decrease the pain scores. We doubt that further increases of lidocaine doses would lead to a clinical benefit. In this study, we used a total dose of 50 to 100 mg lidocaine for local anesthesia, but doses >100 mg may not be entirely safe, especially in patients who weigh <100 lb (45 kg).[12] Some patients commented that their pain was more intense during the first part of the procedure (when we used the small needle for injecting local anesthesia into the skin and subcutaneous tissues) than during the second part of the procedure (when we used a needle

to penetrate the bone); patients described no pain but only a sensation of "pressure" for this second part of the procedure. For this reason, at a certain point we decided to use ethyl chloride spray to anesthetize the skin before the puncture for anesthesia. However, even this method did not seem to be effective at reducing the pain level.

After multivariate analysis, the statistically significant predictors associated with higher pain levels were younger age and female sex. We do not have a biologically plausible explanation for these findings. We expected obesity to be relevant and to predict for higher pain levels, due to the abundance of soft tissues to be penetrated by the needles; but this was not the case. However, the use of spinal needles was associated with a higher pain level, and women required spinal needles more often than did men. It is likely that the distribution of fat tissue is more relevant than its amount, and we advise that future studies incorporate measures of body fat other than BMI (eg, waist circumference). Interestingly, patients who had the BMAB for the first time did not seem to experience different pain levels from those of patients who had already had the procedure.

Our experience confirms that BMAB is a safe procedure. No episodes of bleeding with hemodynamic instability were observed. Many of the observed complications did not directly harm patient health but resulted in an inadequate biopsy specimen or potential harm (eg, needlestick injury) to the clinician performing the BMAB. An interesting finding was that the tip of the aspirate needle—but not the more robust biopsy needle—kinked in some patients who had very hard iliac bones. All these patients had multiple myeloma and received intravenous bisphosphonates monthly for more than 1 year. These drugs increase bone density, and our personal experience teaches that their prolonged use can be associated with very hard bones that cannot be easily penetrated by the needles used for bone marrow aspirates. To our knowledge, needle kinking during BMAB has not previously been reported in the medical literature.

The use of analgesia and anxiolytics before BMAB is controversial. Besides guidance on the administration of local anesthetics, no formal guidelines exist in the medical literature for analgesia and anxiolytics before this procedure. Some physicians administer sedative medications to minimize both patient awareness and discomfort during the procedure, but clinical approaches vary among clinics and individual physicians. Some doctors believe that local anesthetic infiltration alone is inadequate and offer preemptive analgesia and anxiolysis in order to provide physical and psychological relief for patients who consider the procedure frightening, uncomfortable, or painful. Results of previous studies with anxiolysis and analgesia have provided inconclusive results. Milligan et al[4] recommended lorazepam as a premedication agent before BMAB because of its amnesic effect the day following the procedure, but they found no differences in the pain scores recalled by patients immediately after the procedure. Dunlop et al[3] reported that BMAB was well tolerated after oral lorazepam plus the narcotic hydromorphone; in 66% of patients,

the pain score was 3 or less on a 1 to 10 scale. However, their study did not employ a control group. We have previously reported[10] that the addition of oral analgesia (650 mg acetaminophen and 10 mg oxycodone) plus anxiolysis (2 mg lorazepam) did not have a clinically meaningful impact on pain level. A reasonable strategy would be to consider analgesia and anxiolysis only in patients who already experienced significant pain from the procedure or are psychologically frightened by it.

We do not know whether more intense prophylactic regimens, such as those administered under conscious sedation, provide a better clinical advantage. Conscious sedation is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, spontaneous ventilation is adequate, and no interventions are needed to maintain a patent airway. The widespread acceptance of conscious sedation in BMAB is limited by several factors: (1) the prolonged recovery after sedation may be cumbersome and time-consuming for physicians and nurses; (2) no conclusive data are available to establish its effectiveness at inducing a significant reduction of pain level; (3) it increases the cost of the procedure; and (4) although generally safe,[2] it can potentially lead to clinical complications because patients may enter a state of deep sedation that requires a rescue response. It is not always possible to predict how an individual patient will react to conscious sedation, and physicians are expected to be prepared to rescue subjects who enter a state of deep sedation.

Because the mean pain score in the group of patients who were treated with only local anesthesia was about 3 on a 1 to 10 scale, we believe that BMAB does not require conscious sedation and that local anesthesia alone is an acceptable approach for most patients. We suggest that conscious sedation should not be offered preemptively or on a routine basis but should be given only in certain situations and upon patient request (eg, when the fear of the procedure or the pain associated with previous procedures is unacceptable to the patient).

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