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ADVANCES IN PEDIATRIC RESEARCH

Evaluation of lidocaine infiltration efficiency for pain relief during bone marrow aspiration in children with cancer

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Abstract

Background: Bone marrow aspiration (BMA) is a painful procedure often requested in paediatric haematology and oncology. The role of local anaesthesia during BMA is matter of debate. This study assessed pain induced by BMA in children who received standard analgesic premedication with or without additional subcutaneous administration of local anaesthesia.

Methods: This non-randomised prospective study included 100 patients (age range 5-21 years) who underwent BMA for the diagnosis or treatment of malignancy in a paediatric oncology unit between March 2009 and October 2010. Patients received standard premedication with topical anaesthesia, inhaled nitrous oxide, anxiolytics and analgesics, which was combined or not with administration of local anaesthesia (lidocaine). The children, nurses and doctors all graded procedural pain using a visual analogue scale (VAS). Data were statistically analysed, with each procedure serving as a statistical unit.

Results: For 100 BMA procedures performed during the study period, the mean pain rating by children was 2.2, with 38 subjects reporting no pain. Use of lidocaine (19%) induced a mean pain score of 1.6, with 11 patients (57.9%) reporting no pain. Without lidocaine, the mean score was 2.3, and only 27 children (33.3%) reported no pain. Patients undergoing BMA for the first time more frequently graded pain as "0" (p=0.008). Ratings by patients and caregivers correlated poorly; 29.6% of nurses and 34.7% of doctors underestimated procedural pain.

Conclusions: Our findings do not clearly demonstrate that addition of local anaesthetic to standard premedication reduces BMA-induced pain. Nevertheless, we provide valuable information on VAS scoring during BMA with standard premedication.

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Introduction

Paediatric care procedures are the most frequent source of pain for hospitalised children with chronic or acute diseases [1]. In the setting of paediatric haematology and oncology, efforts to prevent pain induced by lumbar puncture (LP), bone marrow aspiration (BMA), vascular access implantation, or port-a-cath puncture are often inadequate. Despite the vast amount of literature available on procedural pain in children [2], few epidemiological or medical studies address pain induced by BMA, which is

frequently performed during the treatment of haematological and solid malignancies. It is difficult to evaluate the average pain intensity related to BMA using a visual analogue scale (VAS). Few reports describe an effective scoring system, and scores vary by study and premedication protocol [3-6]. Even in the recent publication from Kato et al., it is not possible to find any data on pain scores induced by this procedure [7].

Although French medical societies published clinical practice recommendations for the management of procedure-related pain in children in 2005 [8] and 2009 [9], there is no nationally accepted standard for the management of BMA-related pain in paediatric oncology. Premedication protocols vary from simple topical application, such as lidocaine and prilocaine cream (a eutectic mixture of local anaesthetics; EMLA®) to general anaesthesia. Alternatively, patients may receive different combinations of anxiolytics, analgesics, EMLA cream, and/or nitric oxide [10-12]. Recommendations to use lidocaine for local anaesthesia have been published [9], but no study has been conducted to demonstrate its efficacy.

We undertook this prospective study to improve knowledge on the intensity of pain induced by BMA in children, to assess the efficacy of a standard analgesia protocol, and to determine whether additional administration of a local anaesthetic (lidocaine) helped to prevent pain.

Methods

Study participants

Participants included patients aged 5 to 21 years treated at the Paediatric Haematology and Oncology Institute (IHOP) in Lyon and due to undergo BMA between March 2009 and March 2010. After acquiring parental or patient consent, we collected information about demographics, type of disease, number of previous BMA procedures, and operator experience. Following the procedure, children were asked to use a VAS to score the level of their perception of pain during the procedure from 0 (no pain) to 10 (worst pain). Nurses and doctors present during the procedure were asked to use the same scale to grade their perception of patients' level of pain at the end of the procedure.

Premedication protocol

Analgesia administration was the same for all patients: EMLA cream was applied to the site of BMA at least one hour before the procedure. Anxiolytics (hydroxyzine) were administered between 30 min and one hour before the procedure, and narcotic pain relievers (nalbuphine or morphine at a maximum dose of 10 mg) were administered between 45 min and one hour before the procedure. Inhalation of nitrous oxide was begun at least 5 min before the procedure and continued throughout. Depending on the operator's practice, some patients received an injection of lidocaine 2% (0.5 to 2.0 mL) through the skin, into subcutaneous tissues and periosteum, all around the site of BMA and after 5 min of nitrous oxide inhalation. Parents were invited to be present to support their children during the procedure.

Statistical analysis

All completed surveys were collected, charted, entered into a computer, and then analysed using SAS software (version 9.1). Each BMA was considered a statistical unit. Qualitative variables were described using numbers and percentages, whereas quantitative variables were presented as medians (minimum and maximum) and mean ± standard deviations (SD). We used the Wilcoxon non-parametric test or the Kruskal-Wallis test to evaluate the association between pain score and other variables, and the χ^2 test to assess the association between pain scores higher than 0 (and scores of 4 and higher) and other variables.

Results

Table 1 details the demographics of the 100 study patients (aged 5 to 21 years, mean ± SD, 11.1±4.4; median, 11.0; 72 males, 28 females). Ninety-four patients had malignancies (leukaemia, lymphoma or solid tumours), and six had haematological disorders (idiopathic thrombocytopaenic purpura, neutropaenia).

Table 1. Patient characteristics

	N=100
Age (years)	
Mean	11.1 (4.4)
Median (min-max)	11.0 (4.0–20.0)
Gender	
Female	28 (28.0%)
Male	72 (72.0%)
Lidocaine infiltration	
No	81 (81.0%)
Yes	19 (19.0%)
Type of disease	
Malignancy	94 (94.0%)
Hematologic disorder	6 (6.0%)

Table 2 shows pain scores reported by children, nurses and doctors. Medical staff gave the lowest scores (mean ± SD, 1.8±2.2; median, 1.0). Only 50% of pain scores correlated between patients and their nurses and doctors, with caregivers tending to underestimate procedural pain (29.6% for nurses, 34.7% for doctors). The mean pain estimate was the same for doctors and nurses (1.8) and slightly higher for patients (2.2).

Table 3 shows that for 34 patients, this was the first BMA procedure they had undertaken, and that 66 had undergone the procedure before. Mean pain ratings did not differ substantially between the two groups (2.0 versus 2.3), but significantly more of those undergoing BMA for the first time rated pain as 0 (without pain) (19 in 34 [55.9%] versus 19 in 66 [28.8%]; p=0.008).

Demographic characteristics of patients who received lidocaine infiltration (n=19) compared to those who didn't (n=81) does not differ by age, gender or diagnosis. The mean pain score for 19 patients who did receive lidocaine infiltration was 1.6. Scoring of pain as 0 by 11 of these patients (57.9%) demonstrated significantly less pain among those who received lidocaine (p=0.047). The mean pain score of the other 81 patients was 2.3; only 27 of these 81 (33.3%) scored their pain as 0 (Table 4).

Table 2. Pain ratings in children undergoing bone marrow aspiration (BMA), and correlation between pain scores reported by patients, nurses and doctors

Pain scores	N=100
Patients	
Missing	0
Mean	2.2 (2.3)
Median (min–max)	2.0 (0.0–8.0)
Nurses	
Missing	2
Mean	1.8 (2.2)
Median (min–max)	1.0 (0.0–9.0)
Doctors	
Missing	2
Mean (SD)	1.8 (2.2)
Median (min–max)	1.0 (0.0–9.0)
Difference in pain assessment between patients and nurses	
Missing	2
Overestimation by nurses	19 (19.4%)
Same estimation	50 (51.0%)
Underestimation by nurses	29 (29.6%)
Difference in pain assessment between patients and doctors	
Missing	2
Overestimation by doctors	15 (15.3%)
Same estimation	49 (50.0%)
Underestimation by doctors	34 (34.7%)

Table 3. Pain score at first bone marrow aspiration

	First BMA		Test
	No	Yes	
	n=66	n=34	
Pain score			
Missing	0	0	Wilcoxon
Mean	2.3 (2.1)	2.0 (2.6)	p=0.218
Median (min–max)	2.0 (0.0–8.0)	0.0 (0.0–8.0)	
Pain score >0			
No	19 (28.8%)	19 (55.9%)	$\chi 2$
Yes	47 (71.2%)	15 (44.1%)	p=0.008
Pain score ≥4			
No	48 (72.7%)	25 (73.5%)	$\chi 2$
Yes	18 (27.3%)	9 (26.5%)	p=0.932

Table 4. Pain score and lidocaine infiltration

	Lidocaine administered		Test
	No	Yes	
	n=81	n=19	
Pain score			
Missing	0	0	Wilcoxon
Mean	2.3 (2.3)	1.6 (2.1)	*p*=0.212
Median (min–max)	2.0 (0.0–8.0)	0.0 (0.0–6.0)	
Pain score >0			
No	27 (33.3%)	11 (57.9%)	χ2
Yes	54 (66.7%)	8 (42.1%)	*p*=0.047
Pain score ≥4			
No	58(71.6%)	15 (78.9%)	χ2
Yes	23 (28.4%)	4 (21.1%)	*p*=0.516

Scoring of pain did not differ significantly according to operator experience, but we did observe elevated scores (>4) when a junior clinician performed the procedure (29.8% versus 12.5%), even though the difference was not significant (p=0.223) (Table 5).

No significant adverse reactions are reported in our study.

Table 5. Pain ratings by operator experience

	Operator experience		Test
	Intern	Senior	
	n=84	n=16	
VAS patient			
Missing	0	0	Wilcoxon
Mean	2.2 (2.4)	1.8 (1.8)	*p*= 0.691
Median (min–max)	2.0 (0.0–8.0)	2.0 (0.0–5.0)	
Score of patient pain ≥ 0			
No	32 (38.1%)	6 (37.5%)	χ2
Yes	52 (61.9%)	10 (62.5%)	*p*=0.964
Score of patient pain ≥4			
No	59 (70.2%)	14 (87.5%)	χ2
Yes	25 (29.8%)	2 (12.5%)	*p*=0.223

Discussion

Although this type of pain management is widely used in the USA, in Europe, there is still some reluctance to offer paediatric oncology and haematology patients deep sedatives or general anaesthesia for painful procedures because of the inherent risks.

Protocols including the use of propofol, morphine and ketamine, either alone or in combination, have been widely described for procedural sedation and have proven to be effective. However, the use of these drugs is associated with side effects; a substantial percentage of interventions result in a significant decrease in cardiovascular parameters and increased recovery time. This limits their use, especially for non-anaesthesiologists [13]. Sedation with midazolam is commonly used in the United States but is associated with high pain scores. This is not surprising because we know that this drug is not an analgesic but has an anxiolytic effect associated with amnesia. In a study of 102 painful procedures such as BMA and LP in 96 children, Crock and colleagues reported a median pain score of 6 for procedures with midazolam sedation and 0 for procedures under general anaesthesia [4].

In France, resource constraints limit the use of general anaesthesia for painful procedures. Until 2005, when standard option recommendations were published [8], no clinical practice recommendation had been given for these procedures. In 2009, the French Agency for the Safety of Health Products (AFSSAPS) published good clinical practice recommendations concerning procedural pain in children, but did not clearly specify guidelines for BMA [9].

The first objective of our prospective study was to evaluate the efficacy of a standardised analgesic premedication for preventing pain induced by BMA in children with cancer. A VAS score of 4 or greater is commonly understood to be unsatisfactory; in our study, the mean VAS score for the 100 procedures was 2. This is lower than values reported in an unpublished national survey by the SFCE group (Société Française du Cancer de l'Enfant), carried out before the beginning of our study in 32 French oncology units, where the mean VAS score was 4. In our study, 73 patients (73%) reported a VAS score below 4, and 38 (38%) had a score of 0. These results allow us to conclude that this standardised premedication provides satisfactory analgesia and is

more effective than most protocols used in other institutions.

However, BMA remained painful - 27 patients (27%) scored their pain as 4 or higher, so greater effort needs to be made to improve the care of children undergoing this procedure. Study of predictive factors to identify children at risk of high pain levels would allow the proposal of stronger procedural protocols for systematic pain, such as sedation with drugs like ketamine or general anaesthesia.

In this study, age was not found to influence VAS scores. However, a significantly greater number of patients undergoing BMA for the first time scored their procedural pain as 0 ($p=0.008$). We analysed this factor because of the a priori hypothesis that memory of a previous procedure could affect the evaluation of pain [14]. This information is important for adaptation of premedication and care in subsequent procedures.

The second objective of our study was to evaluate the benefit of local lidocaine infiltration during BMA. No clear evidence of such benefit has been published. Ideally, only a well-designed randomised study could assess the superiority of lidocaine. Nevertheless, our prospective study with two patient groups can provide some basic information. Only 19 (19%) BMA procedures were performed with lidocaine infiltration, and significantly more VAS scores of 0 were reported in this group ($p=0.047$). This information tends to confirm the benefit of lidocaine for reducing pain levels, but our conclusion is limited by the small group size and the absence of randomisation.

We observed significantly more elevated scores (>4) when a junior clinician performed the procedure (29.8% versus 12.5%). Though our small sample size limits the significance of this finding, the result points to the ethical need for training young doctors to avoid unnecessary pain. General anaesthesia, or the use of a training manikin, should be recommended for junior doctors' vocational training in paediatric haemato-oncology, especially for the first use.

VAS scores given by patients and by nurses and doctors were correlated in only 50% of the procedures, and we noted that caregivers tended to underestimate patient pain in 29% to 35% of cases. These findings are confirmed by several other studies [15,16].

Finally, the absence of adverse effects with the described protocol demonstrated that sedation analgesia is reliable and safe when well standardised and carried out in safe conditions.

Conclusions

The administration of a standardised multimodal analgesic medication before BMA in children yields low, acceptable procedure-induced pain scores. This non-randomised prospective open study performed in a small number of patients cannot clearly demonstrate that the addition of local anaesthetic administration to standard analgesic treatment reduces the pain caused by BMA, even if it seems to lower pain scores. Nevertheless, it provides an interesting advance on the current literature by defining VAS pain scores associated with BMA performed with a standard premedication. These data should serve for statistical calculations in future randomised studies.

References

1. Cramton RE, Gruchala NE. Managing procedural pain in pediatric patients. Curr Opin Pediatr. 2012;24:530-8.
2. Lee GY, Yamada J, Kyololo O, Shorkey A, Stevens B. Pediatric clinical practice guidelines for acute procedural pain: a systematic review. Pediatrics/ 2014;133:500-15.
3. Park SH, Bang SM, Nam E, Cho EK, Shin DB, Lee JH, et al. A randomized double-blind placebo-controlled study of low-dose intravenous lorazepam to reduce procedural pain during bone marrow aspiration and biopsy. Pain Med. 2008;9:249-52.
4. Crock C, Olsson C, Phillips R, Chalkiadis G, Sawyer S, Ashley D, et al. General anaesthesia or conscious sedation for painful procedures in childhood cancer: the family's perspective. Arch Dis Child. 2003;88:253-7.
5. Vanhelleputte P, Nijs K, Delforge M, Evers G, Vanderschueren S. Pain during bone marrow aspiration: prevalence and prevention. J Pain Symptom Manage. 2003;26:860-6.
6. Holdsworth MT, Raisch DW, Winter SS, Frost JD, Moro MA, Doran NH, et al. Pain and distress from bone marrow aspirations and lumbar punctures. Ann Pharmacother. 2003;37:17-22.

7. Kato Y, Maeda M, Aoki Y, Ishii E, Ishida Y, Kiyotani C, et al. Pain management during bone marrow aspiration and biopsy in pediatric cancer patients. Pediatr Int. 2014;56:354-9.
8. Schmitt C, Theobald S, Fabre N, Kasparian C, Séblain C, Boutard P, et al. Standards, options and recommendations for the management of procedure-related pain (lumbar puncture, bone marrow aspiration or biopsy, blood sampling) in children patients with cancer (summary report). Bull Cancer. 2006;93:805-11.
9. AFSSAPS.fr. Prise en charge médicamenteuse de la douleur aiguë et chronique chez l'enfant. Recommandations [Internet]. Agence Française de Securité Sanitaire des Produits de Santé; 2009. Available from: http://pediadol.org/Afssaps-Prise-en-charge.html
10. Krauss B, Green SM. Procedural sedation and analgesia in children. Lancet.2006;367:766-80.
11. Weisman SJ, Bernstein B, Schechter NL. Consequences of inadequate analgesia during painful procedures in children. Arch Pediatr Adolesc Med. 1998;152:147-9.
12. Krauss B, Green SM. Sedation and analgesia for procedures in children. N Engl J Med. 2000;342:938-45.
13. Gottschling S, Meyer S, Krenn T, Reinhard H, Lothshuetz D Nunold H, et al. Propofol versus midazolam/ketamine for procedural sedation in pediatric oncology. J Pediatr Hematol Oncol. 2005;27:471-6.
14. Rocha EM, Marche TA, von Baeyer CL. Anxiety influences children's memory for procedural pain. Pain Res Manag. 2009;14:233-7.
15. Manne SL, Jacobsen PB, Redd WH. Assessment of acute pediatric pain: do child self-report, parent ratings, and nurse ratings measure the same phenomenon? Pain. 1992;48:45-52.
16. Hamers JP, Abu-Saad HH, van den Hout MA, Halfens RJ, Kester AD. The influence of children's vocal expressions, age, medical diagnosis and information obtained from parents on nurses' pain assessments and decisions regarding interventions. Pain. 1996;65:53-61.