



Clinical pain research

Anxiety and pain during bone marrow aspiration and biopsy

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ABSTRACT

Background: Previously we found that pre-procedural nervousness and tension (translated into English as “anxiety”), assessed on a non-validated five-point scale, correlated with pain intensity of the various stages of bone marrow aspiration and biopsy (BMAB). The fewer the previous BMAB procedures the stronger the pain from a repeated procedure. The primary purpose of the present observational study is to evaluate the state of anxiety just before BMAB and to find out whether it affects the pain experiences during the various stages of the BMAB procedure. We also examined whether first-timers differ from patients with previous BMAB experience in the degree of anxiety and intensity of BMAB procedural pain. **Methods:** A total of 166 adult outpatients undergoing the BMAB from the Helsinki University Hospital were enrolled, 48 of them being first-timers. The level of anxiety was measured with State-Trait Anxiety Inventory (STAI) and the pain experiences associated with the various stages of the procedure were evaluated on the NRS-scale (Numerical Rating Scale 0–10) and using the Finnish pain vocabulary. BMAB was planned to be performed under lidocaine infiltration anaesthesia but, on request, patients were allowed to receive premedication with diazepam orally or alfentanil i.m. If, in spite of supplemental local anaesthetic the patient still felt pain from the sampling needle tip, i.m. alfentanil was administered. **Results:** There was a clear association between anxiety and pain during all stages of the procedure, except during biopsy. The NRS scores varied from 0 to 10 in all the various stages of BMAB. The first-timers did not differ from the more experienced patients with regard to pain experiences; only the pain felt during the local anaesthetic infiltration was milder ($P=0.007$) in first-timers than in the others. Procedural pain in those who were given analgesic or sedative premedication was similar ($P>0.05$) to that in the non-pre-medicated patients. The words characterizing the pain of the various stages belonged to a major extent (76–90%) to the sensory class of words.

Conclusion: Pre-procedural anxiety had a major impact on the pain ratings. The first-timers and patients with previous experience of BMAB had a similar degree of pre-procedural anxiety, as well as of the intensity of procedural pain, except that infiltration of local anaesthetic was less painful in the first-timers. **Implications:** Identification of anxious (fearful) patients prior to BMAB, and premedicating them individually may improve satisfaction in both patient and caregiver.

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1. Introduction

Bone marrow aspiration and/or biopsy (BMAB) usually cause anxiety and pain [1,2] and therefore BMABs are done under local anaesthesia, with or without premedication in adults, and under deep sedation or general anaesthesia in children.

Pain intensity correlates with anxiety in different medical procedures [3–5]. In our previous study on the effect of local anaesthesia

for BMAB, we found a relationship between nervousness and/or tension just before the BMAB and pain experienced during the various phases of the BMAB-procedure [6]. Patients having had only a few (0–5) BMABs seemed to be more nervous and tense than the more experienced patients and hence the former ones reported stronger procedural pain than the more experienced patients.

The purpose of the present clinical trial was to evaluate the state of anxiety, using a validated anxiety test just before BMAB and to find out whether it correlates with the pain experience during the various stages of BMAB. In addition, we evaluated whether first-timers differ from patients with previous BMAB experience regarding the degree of pre-procedural anxiety and procedural pain.

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2. Methods

2.1. Patients

After approval of the Hospital Ethics Committee (Helsinki Uusimaa Health District, diary number 77/13/03/02/2009) and informed written consent, a total of 166 adult outpatients from the Department of Haematology, Helsinki University Hospital were enrolled into the study. The exclusion criteria were allergy to the local anaesthetics, BMI (body mass index) over 32 kg/m² and unstable angina pectoris. Each patient could be enrolled only once into the study.

2.2. Tests for anxiety

Before the first interview (performed 30–60 min before BMAB) the patients were given the S-part of the STAI (State-Trait Anxiety Inventory)-form. State-Trait Anxiety Inventory [7] is one of the most common validated tests measuring different aspects of anxiety. The test has two parts in which the S-part measures the state of anxiety (STAI-S) during acute stressful events. The test score ranges from 20 to 80 points; the higher the score the greater the intensity of anxiety.

2.3. Interview before the bone marrow aspiration and/or biopsy

The pre-procedural interview, performed in the out-patient clinic 30–60 min before BMAB, consisted of questions about current medical condition, existing diseases, pre-existing pain before the procedure and use of medicines. The patients were also asked about their experiences from the previous bone marrow aspirations and/or biopsies and also from other minor interventional medical procedures.

2.4. The BMAB procedure

If sedative premedication was requested, diazepam 5–10 mg was administered orally 20–30 min before BMAB. If the patient requested an analgesic, alfentanil 0.5–1 mg i.m. was given just before the procedure.

Lidocaine 20 mg/ml with adrenaline 5 µg/ml was infiltrated with a 21G needle at the puncture site, either the sternal manubrium (6 ml), sternal body (8 ml) or the iliac crest (10 ml). Two minutes later the haematologist tested the adequacy of local anaesthesia with the tip of the sampling needle. If the anaesthesia was not sufficient, half of the initially used amount of lidocaine solution was added to the puncture area. If the patient felt pain from the tip of the aspiration or biopsy needle despite supplemental local anaesthetic, alfentanil 0.5 mg i.m. was given. Then the bone marrow puncture was conducted with a 14–16G aspiration needle and if an iliac crest biopsy was needed, an 8G needle (Angiotech, T-lock™, Gainesville, FL, USA) was used.

2.5. Interviews after the bone marrow aspiration and/or biopsy

The patients were interviewed within 30 min after the procedure. The pain experiences during the procedure and immediately after it were asked and recorded during this interview.

The patients were interviewed by telephone 24 h after the procedure. The pain medication consumed and the grade of pain intensity were asked and recorded. The occurrence of any adverse effects such as haematomas or active bleeding was recorded.

2.6. Tests for pain

During the post-intervention interview performed within 30 min after the BMAB the pain experiences recalled from the various stages of the procedure were scored on the NRS 0–10 (0 = no pain, 10 = worst imaginable pain). During the interview the Finnish pain vocabulary [8] was also applied to differentiate between the qualities of pain. The Finnish pain vocabulary is modified from the McGill Pain Questionnaire [9]. It contains Finnish pain related words classified to the classes mentioned in the McGill Pain Questionnaire, i.e., sensory, affective and evaluative words.

2.7. Statistics

Before any specific statistical analysis we conducted the basic tests for normality, i.e. the Kolmogorov–Smirnov and Shapiro–Wilk-tests. The demographic data, the anxiety scores (STAI-S) and pain scores on NRS were not normally distributed. The association between the NRS pain scores (0 = no pain, 10 = worst imaginable pain) and other variables (STAI-score, demographics, pain or sedative medication) were analyzed using ordinal regression stratified by phase of the procedure. Also the Mann–Whitney *U*-test and Kruskal Wallis-test were used when appropriate. The proportions in different groups were compared using the χ^2 -test. SPSS version 17.0 (Chicago, IL, USA) was used in the statistical analyses.

3. Results

The patient characteristics stratified by first and non-first-timers are presented in Table 1. The study included 166 patients, 48 of whom were first-timers. All of those enrolled completed the study.

3.1. Medicines

3.1.1. Pain medication

The regular use of medication for pain, sedation and anxiety were recorded during the first interview before the BMAB. As presented in Table 1, sixteen patients (9.6%) were using regular pain medication, 4 of these patients used two different pain medications. Fifteen patients (9.0%) had taken temporary pain medication within 24 h before the procedure due to different reasons (headache, pain in the lower extremities or joints, pain in various parts of the body). In total, 25 patients (15.1%), 8 of whom were first-timers, had taken some kind of pain medication, regular or temporary, at home within 24 h before the procedure. As expected, these patients felt more pain before the procedure (median NRS 2.0) compared to the other patients (median NRS 0) ($P < 0.001$) but the procedural pain experience of the various parts was similar ($P > 0.05$) in these two patient categories.

A total of 32 patients received analgesic supplementation with i.m. alfentanil, 7.9 µg/kg, on average, in a median time of 5.0 min (range 1–15 min) before BMAB. The proportion of the first-timers receiving alfentanil premedication (15 patients, 31.3%) was greater ($P = 0.013$) than that in those patients who had experienced BMAB before (17 patients, 14.4%). However, alfentanil premedication did not have any statistically significant effect on pain from lidocaine infiltration ($P = 0.917$), bone marrow aspiration ($P = 0.660$) or biopsy ($P = 0.375$).

3.1.2. Medication for sedation and anxiety

Fourteen patients, two of whom were first-timers, were using medication for sedation or anxiety on a regular basis. Eight

Table 1
Patients. Demographic data of the participants.

	First-timers	≥1 previous BMABs
Gender (male/female)	26/22	74/44
Age (years) (mean, range)	54 (21–87)	53 (17–84)
Height (cm) (mean, SD)	172 (9)	173 (10)
Weight (kg) (mean, SD)	77 (17)	76 (15)
Site of aspiration, <i>n</i>		
Sternal manubrium	5	31
Corpus sterni	9	18
Crista iliaca	32	68
Type of procedure		
Bone marrow aspiration	15	79
Bone marrow aspiration and biopsy	33	37
Bone marrow biopsy	0	2
Diagnoses, <i>n</i>		
Non-Hodgkin lymphoma	3	29
Myeloma	2	7
Leukemia (acute/chronic)	0/2	41/16
Other malignancy	3	2
Myelodysplastic syndrome	0	5
Anaemia	4	2
Healthy donor	9	0
Other	25	16
Performed by		
Doctors in training, <i>n</i>	16	20
Specialists, <i>n</i>	32	98
Regular pain medication, <i>n</i>	3	13
NSAIDs	2	1
Paracetamol	2	1
Paracetamol–codeine–combination	1	2
Tramadol	0	2
Strong opioids	0	4
Pregabalin	0	3
Amitriptylin	0	2
Temporary pain medication, <i>n</i>	6	9
NSAIDs	4	2
Paracetamol	1	2
Paracetamol–codeine–combination	0	2
Tramadol	1	2
Strong opioids	0	1
Regular sedative medication, <i>n</i>	2	12
Temporary sedative medication, <i>n</i>	0	8

patients had taken temporary sedative medication (benzodiazepines, zopiclone or other sedative medicines) within 24 h before the procedure. These patients were generally more anxious (median STAI-S score 43.5) than others (median STAI-S score 37.0) ($P=0.019$). Patients using sedative medication experienced pain of similar intensity during all stages in comparison with the others ($P>0.05$).

Ten patients were given oral diazepam (5–10 mg) in the outpatient clinic prior to the procedure on request. Their median STAI-S score was 53.5. No statistically significant pain relieving effect was found in comparison between this group and the others ($P>0.05$).

Table 2
Distribution of the pain experiences (NRS 0–10) stratified by the first-timers and the more experienced patients during different phases.

Phase	First time or not	Range	NRS–median	Statistical significance (Mann–Whitney <i>U</i> -test)	Statistical significance (ordinal regression)
Local anaesthetic infiltration	1st timers, %	0–10	2.0	$P=0.004$	$P=0.007$
	≥1 previous BMABs, %	1–9	3.0		
Bone puncture	1st timers, %	0–10	2.0	$P=0.503$	$P=0.161$
	≥1 previous BMABs, %	0–10	2.0		
Aspiration	1st timers, %	0–10	3.0	$P=0.134$	$P=0.541$
	≥1 previous BMABs, %	0–10	3.5		
Biopsy	1st timers, %	0–10	4.0	$P=0.030$	$P=0.051$
	≥1 previous BMABs, %	0–10	2.0		
30 min after BMAB	1st timers, %	0–8	0	$P=0.559$	$P=0.365$
	≥1 previous BMABs, %	0–9	0		

3.2. Pain and anxiety

3.2.1. Procedural pain

Median NRS for local anaesthetic infiltration was 3 (range 0–10), for bone puncture 2 (range 0–10), for aspiration 3 (range 0–10) and for biopsy 3 (range 0–10). The median pain felt immediately after the procedure on NRS was 0 (range 0–9). The clinical experience of the physician performing the procedure (trainee vs. specialists) did not have any notable effect on the pain ratings. Pain experiences during local anaesthetic infiltration ($P=0.001$), aspiration ($P<0.001$) and biopsy ($P=0.013$) were inversely correlated with age. There were no statistically significant differences in anxiety scores or pain experiences between males and females when gender was evaluated in the ordinal regression as a confounding factor.

3.2.2. First-timers and the more experienced patients

The differences between first-timers and patients with previous experience from BMAB are shown in Table 2. There were no significant differences in anxiety scores between the groups (median STAI 36.5 for first-timers and 38.5 for others). However, first-timers sensed less pain (NRS median 2.0) during local anaesthetic infiltration compared to the other patients (NRS median 3.0) ($P=0.007$). There were no significant differences between the groups during other stages of the procedure after adjusting for confounding factors.

Eighteen patients had inadequate local anaesthesia and therefore they received a second local anaesthetic infiltration. Four of these patients were first-timers. One first-timer needed three lidocaine infiltrations at the discretion of the haematologist and redirection of the sampling needle. Four patients, three of whom were first-timers, experienced so intense procedural pain that they were given alfentanil intramuscularly during the procedure. Their doses varied from 5.9 µg/kg to 16.6 µg/kg.

The first-timers needed more post-procedural pain medication at home (17 patients, 35.4%) than the rest of the patients (18 patients, 15.2%) ($P=0.004$). In spite of this, there were no significant differences in pain intensity reported in the 24-h interview between the first-timers and the other patients. Thirty-five patients took post-procedural pain medication; some of them took more than one type of pain medication. The post-procedural pain medication at home consisted of ibuprofen (16 patients), paracetamol (18 patients), paracetamol–codeine–combination (4 patients), tramadol (3 patients), oxycodone (1 patient) and pregabalin (1 patient).

3.2.3. Association between pain and anxiety

Table 3 shows that the degree of anxiety correlated with the intensity of the procedural pain, except for pain during biopsy.

During local anaesthetic infiltration, over 90% of words used to describe the pain were sensory with no significant differences between patients having low, intermediate or high STAI scores.

Table 3

Anxiety scores measured as STAI-S (State-Trait Anxiety, S-part) in patients feeling mild pain (NRS < 4) or clinically significant pain (NRS ≥ 4) (NRS 0–10; Numeral rating scale, 0 = no pain; 10 = worst pain imaginable).

Pain experience		STAI, median (range)	Statistical significance (ordinal regression)
Before the procedure	NRS < 4 (n 148, 89.2%)	37.0 (20.0–71.0)	$P = 0.731$
	NRS ≥ 4 (n 18, 10.8%)	40.5 (25.0–59.0)	
Local anaesthetic infiltration	NRS < 4 (n 98, 59.0%)	35.0 (20.0–71.0)	$P = 0.008$
	NRS ≥ 4 (n 68, 41.0%)	42.5 (24.0–71.0)	
Puncture	NRS < 4 (n 117, 71.3%)	37.0 (20.0–71.0)	$P = 0.049$
	NRS ≥ 4 (n 47, 28.7%)	41.0 (25.0–61.0)	
Aspiration	NRS < 4 (n 92, 56.1%)	35.0 (20.0–64.0)	$P = 0.003$
	NRS ≥ 4 (n 72, 43.9%)	40.5 (24.0–71.0)	
Biopsy	NRS < 4 (n 42, 58.3%)	36.0 (20.0–71.0)	$P = 0.824$
	NRS ≥ 4 (n 30, 41.7%)	40.0 (25.0–64.0)	
Immediately after the BMAB	NRS < 4 (n 154, 93.3%)	37.0 (20.0–71.0)	$P = 0.010$
	NRS ≥ 4 (n 11, 6.7%)	48.0 (32.0–55.0)	

A few evaluative words were also used. During bone puncture, the sensory words were again the most common. The distribution of the pain words during aspiration, 76% of which belong to the sensory class, is shown in Table 4. There were no statistically significant differences in the distribution of the words to the different classes between patients having low, intermediate or high STAI-scores ($P = 0.421$).

3.2.4. Previous procedures

Those patients who expressed memorable pain from the previous procedures were more anxious (STAI median 45.0 vs. 35.0, $P < 0.001$) and had more pain during local anaesthetic infiltration (NRS median 5.0 vs. 3.0, $P = 0.003$) and aspiration (NRS median 6.0 vs. 3.0, $P < 0.001$) than the other patients.

Patients who had been anxious about the previous bone marrow punctures were more anxious also before the present procedure (STAI median 50.0 vs. 37.0, $P < 0.001$) and felt more pain during local anaesthetic infiltration (NRS median 5.5 vs. 3.0, $P = 0.015$), bone puncture (NRS median 3.0 vs. 2.0, $P = 0.010$) and aspiration (NRS median 5.0 vs. 3.5, $P = 0.004$). Also patients having been nauseous during the previous procedure were more anxious (STAI median 45.0 vs. 38.0, $P = 0.041$) and felt more pain during aspiration (NRS median 6.0 vs. 3.0, $P = 0.016$) than the others.

Patients who had previously undergone other painful medical procedures (24 patients having had moderate or strong pain) were

more anxious (STAI median 47.0 vs. 36.5, $P < 0.001$) and felt more pain during local anaesthetic infiltration (NRS 5.0 vs. 3.0, $P = 0.016$), bone puncture (NRS median 3.0 vs. 2.0, $P = 0.018$) and aspiration (NRS median 7.0 vs. 3.0, $P < 0.001$) than patients not having previous painful medical procedures. Also anxiety before previous medical procedures predicted anxiety before the present bone marrow procedure (NRS median 46.0 in the anxious patients and 37.0 in the others, $P < 0.001$) and pain during local anaesthetic infiltration (NRS median 4.0 in the anxious patients and 3.0 in the others, $P = 0.017$).

3.3. Interview on the following day

Sixty-nine patients (41.6%) did not have any pain in the puncture area during the interview. The median NRS-score was 1.0 (range 0–8). Thirty-five patients (21.1%) had taken post-procedural pain medication. Some reported local adverse effects related to the procedure such as a minor haematoma (24 patients) or haemorrhage (15 patients), redness (22 patients), edema (17 patients), or the procedure area feeling warmer than other skin areas (3 patients).

4. Discussion

A notable proportion of the patients sense clinically significant pain at the various stages of BMAB (NRS ≥ 4) (Table 3). As BMAB is usually done repeatedly in haematological patients, adequate pain relief is an important part of good care. Anxiety was strongly associated with procedural pain, except with the pain during biopsy. When patients were asked to describe the pain during different phases of the procedure the words the patients selected from the Finnish pain vocabulary were mostly from the sensory class. However, for aspiration, also affective words were used. Those patients who received pain or sedative medication before the procedure did not have any lower pain scores than the others during the procedure. Considering the pharmacokinetics of intramuscular alfentanil with peak plasma levels not until 20–30 min after administration [10], it is unlikely that alfentanil given to a few patients during BMAB had more than a placebo effect on the pain.

Pain and anxiety associated with previous procedures predicted pain and anxiety during the present bone marrow aspiration and/or biopsy but there was no clear association between the number of previous BMABs and pain levels during the procedure. The first-timers were no more anxious than the other patients.

Our findings of common occurrence of moderate to severe pain during bone marrow aspiration and/or biopsy are in accordance with the results of other studies. For instance, Vanhelleputte et al. [1] showed that 86% of patients experienced pain during the procedure, 36% of whom rated the pain as moderate to severe. Lidén et al. [11] found that 70% of patients report pain during the

Table 4

Distributions of the pain words derived from the Finnish pain vocabulary in the patients during the aspiration. Four patients gave two words. Six patients in the non-anxious group, 7 patients in the intermediate group and 2 patients in the anxious group felt no pain at all. Two patients did not have aspiration performed at all. In total, 153 words were given.

Pain class	Low anxious score (STAI ≤ 25th percentile or 31.0 points)	Intermediate anxious score (25th < STAI < 75th percentile)	High anxious score (STAI ≥ 75th percentile or 46.3 points)
Sensory (n of words)	30	56	31
Temporal	3	4	3
Spatial	4	9	3
Punctate pressure	2	6	3
Incisive pressure	10	26	11
Constrictive pressure	3	6	4
Traction pressure	3	3	5
Thermal	2	0	2
Brightness	1	1	0
Dullness	2	1	0
Affective	0	4	3
Tension	0	4	2
Fear	0	0	1
Evaluative	6	17	6
Total	36	77	40

procedure and of these patients 56% graded the pain as moderate, 32% as severe and 3% as worst possible.

In the present study pain during local anaesthetic infiltration was found to be moderate or severe ($\text{NRS} \geq 4$) in 41% of patients. Interestingly, the first-timers sensed the pain during local anaesthetic infiltration milder than the others, which could be due to the fact that about 30% of the first-timers received alfentanil i.m. just before the procedure. Surprisingly strong pain (NRS 8–10) was experienced by some patients from the local anaesthetic infiltration, possibly due to the low pH (3.7–4.0) of the lidocaine–adrenaline solution.

When considering the different methods of pain relief during the procedure it seems important to take into account also the impact which the anxiety may have on pain experiences. Lidén and co-workers [11] found that high scores in the STAI-S, anxiety about the needle insertion and the diagnostic outcome of BMA were significantly related to the procedural pain during bone marrow aspiration and/or biopsy. Anxiety intensifies also pain during oral surgery procedure of dental implant insertion [12]. In that study, anxiety measured on VAS-scale 0–100 was found to correlate with pain at several measuring points. In addition, it also predicted postoperative recollection of pain several weeks after the operation. Anxiety levels were also found to be higher in women than in men, which did not seem to be the case in the present study.

STAI-S measures overall state anxiety. BMAB may involve different aspects possibly related to either the outcome of the BMAB procedure, the diagnosis of a malignant disease, or to the procedural pain itself, which were not specifically analyzed in our study. In a study conducted with healthy volunteers using the cold pressor test [13] the results showed that pain-related fear was, indeed, a strong predictor of pain.

Because anxiety seems to have such a notable effect on the pain ratings, special attention should be paid at reducing it. A method that reduces both the level of anxiety and pain would be nitrous oxide inhalation [14], although its routine use in BMABs requires extra investment in equipment and personnel.

To conclude, in this study anxiety was shown to have a significant effect on the pain ratings during BMAB. Pain experienced previously in other types of minor procedures seemed to predict anxiety and pain in BMAB. Although there were no differences in the STAI scores between the first-timers and the others, a clear connection between experiences from the previous BMAB procedures and the present anxiety level was seen. The pain ratings were similar in the first-timers and the other patients; only pain scores during local anaesthetic infiltration were different in these groups (lower in the first-timers).

Disclosure of conflict of interest

All authors confirm that there were no conflict of interest including any financial, personal or other relationships with other people or organizations within three years of beginning the submitted manuscript that could inappropriately influence, or be perceived to influence, their work.

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