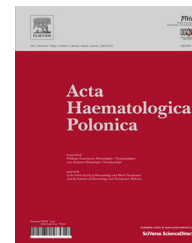




Contents lists available at ScienceDirect

Acta Haematologica Polonica

journal homepage: www.elsevier.com/locate/achaem



Original research article/Praca oryginalna

Effective pain reduction during bone marrow biopsy and aspiration – Technique over experience



Emil Jaddini¹, Nikolaj Hjortholm², Emilian Snarski^{3,*}

¹Department of General Surgery and Orthopaedics, Kungälv Hospital, Sweden

²Department of Orthopaedic Surgery, Hillerød Hospital, Denmark

³Department of Hematology, Oncology and Internal Medicine, Medical University of Warsaw, Poland

ARTICLE INFO

Article history:

Received: 12.02.2016

Accepted: 12.04.2016

Available online: 20.04.2016

Keywords:

- Bone marrow
- Biopsy
- Aspiration
- Pain
- Hematology

ABSTRACT

Background: Bone marrow biopsy and aspiration (BMBA) is a diagnostic procedure within the field of internal medicine. The intensity of the pain felt by the patients often goes unrecognized by the medical staff. No extant studies have addressed pain intensity experienced during each particular step of a BMBA. **Objectives:** The aim was to analyze the pain intensity and explore the extent to which the technique applied by the doctor performing the biopsy influences the pain level. **Methods:** A survey comprising 17 questions was created and it addressed characteristics of the patients, previous experience and pain intensity on each step of the procedure. **Results:** 125 patients were enrolled into the study. Age ($p = 0.009$), gender ($p = 0.02$), pain during previous biopsies ($p < 0.0001$) and adequate information ($p = 0.04$) were shown to have significant impact on the pain intensity levels. There was a significant difference in the pain levels on different steps of the procedure perceived by the patients, when comparing the doctors with similar experience performing BMBA ($p = 0.01$ to $p < 0.0001$ depending on the step of the procedure). **Conclusions:** The differences in the pain scores between the doctors are most likely caused by differences in technique of BMBA. The analysis of the individual technique of the doctors performing the least painful biopsies may give answers needed for educational intervention aimed at pain reduction during BMBA.

© 2016 Polskie Towarzystwo Hematologów i Transfuzjologów, Instytut Hematologii i Transfuzjologii. Published by Elsevier Sp. z o.o. All rights reserved.

Introduction

Bone marrow biopsy and aspiration (BMBA) is an essential diagnostic procedure within the field of internal medicine, enabling bone marrow specimens to be collected for

histopathological and cytopathological examination and immunophenotyping [1–3]. A BMBA can also be a painful procedure and a significant ordeal for many patients. The significance and importance of the patient's experience with BMBA remains unrecognized by many physicians [4]. There are no clear guidelines on how to reduce this pain,

* Corresponding author at: WUM - Katedra i Klinika Hematologii, Onkologii i Chorób Wewnętrznych, SPCSK, ul. Banacha 1a, 02-097 Warsaw, Poland. Tel.: +48 662 700 772.

E-mail address: emiliansnarski@gmail.com (E. Snarski).

<http://dx.doi.org/10.1016/j.achaem.2016.04.003>

0001-5814/© 2016 Polskie Towarzystwo Hematologów i Transfuzjologów, Instytut Hematologii i Transfuzjologii. Published by Elsevier Sp. z o.o. All rights reserved.

and the field remains under-researched. Furthermore, physicians underestimate the severity of the pain [5–7].

Research thus far has focused on the pharmacological reduction of pain using local anesthesia, usually Lidocaine or a similar agent [8]. Various trials have addressed other means of analgesia for the pain associated with this procedure, including pharmacological trials administering combinations of analgesics, sublingual fentanyl, intravenous sedation with benzodiazepines or, most recently, nitrous oxide/oxygen or nitrous oxide alone [9]. Alternative methods of reducing pain have also been investigated, including hypnosis as an adjunct to local anesthesia, cognitive behavioral therapy (shown to be ineffective), art/music therapy and contralateral ice massage during the procedure [9–12]. Recently, powered bone marrow-acquiring devices were tested and compared with the classical manual approach [9].

However, these studies have not addressed in detail one of the most important factors contributing to pain during the procedure, physician technique. To date, the findings have been contradictory as to whether the experience of the physician influences the pain experienced by the patients during biopsies. The results of some studies demonstrate lower perceived pain when experienced doctors perform BMBA, and other studies fail to show a difference [9]. No international guidelines have been proposed for techniques to minimize pain during BMBA, and this knowledge has typically been passed from older to younger doctors. Moreover, the pain analyses in extant studies are relatively inaccurate; patients are typically asked for their general pain sensation during the procedure. The BMBA includes several stages: anesthesia, entering the bone with the needle, bone marrow aspiration and bone extraction; each stage can be characterized by a distinct intensity of pain [4]. Because each of the steps depends on the technique applied by the operator performing the biopsy, the question arises: Will experienced operators differ from each other in the way that they perform a biopsy? The aim of this study was to analyze for the first time the pain felt by patients during various stages of the BMBA. Moreover, we wanted to identify which factors influence pain during the various stages and, most notably, the extent to which the technique applied by the doctor performing the biopsy influences the pain level.

Material and methods

The study was conducted at the Department of Hematology, Oncology and Internal Medicine at the Medical University of Warsaw. All patients over 18 years of age who were scheduled for a BMBA were offered enrollment into this study between 2011 and 2013. Only the patients who signed informed consent were asked to fill the questionnaires. Otherwise there were no other inclusion or exclusion criteria. The study design was approved by the Bioethics Committee of the Medical University of Warsaw. The doctors performing the biopsies in this study were typically hematologists or hematologists-in-training, and they all had a high level of experience performing BMBAs (per doctor the number performed ranged from a few hundred to a few thousand).

The various parts of the procedure and the pain intensity experienced by the patients were assessed by creating a 17-question survey. The questions included patient general characteristics (age, weight, height and occupation), the history of previous BMBA (number and pain intensity of previous procedures) and whether any premedication was taken. One crucial question included 7 sub-questions that addressed the pain intensity during each step of the BMBA. We asked for the level of pain intensity before the procedure and during local anesthesia administration, biopsy needle insertion through soft tissues, biopsy needle insertion through the bone, bone marrow aspiration and, if applicable, bone extraction. We asked the patient to report the pain intensity experienced after the procedure. Other questions solicited information regarding whether the pain experienced during each step was significant (intolerable) and what point on the Visual Analogue Scale (VAS) signified pain intensity that was considered intolerable. General satisfaction, environmental factors, the doctor's approach and whether enough information was provided about the procedure were also assessed. Finally, patients were given the opportunity to express their own thoughts on factors influencing pain and possible ways of reducing it.

As the questionnaire addresses the pain on different stages of procedure which can be forgotten or not understood by patients we run a pretrial quality check of questionnaire. Questionnaires were consulted with patients and their opinion was asked on possible problems with assessment of the pain on different stages of biopsy. The patients did not report any difficulties in filling the questionnaire which was later approved for the study.

All assessments of pain intensity were made using the Visual Analogue Scale (VAS), a 100 mm horizontal baseline anchored with 2 descriptions, "no pain" on the left-hand side and "worst imaginable pain in my life" on the right-hand side [13, 14]. The questionnaire was administered to the patient immediately after the procedure, and the patients were asked to return it as soon as possible before leaving the clinic. The surveys were reviewed, edited and approved by all authors. All data obtained were analyzed using Akademistatistik, Sahlgrenska Academy, Gothenburg University, Sweden.

The BMBA procedure was conducted with the patient in a supine position for sternal biopsies or prone for biopsies of the iliac crest. Aseptic technique was employed, and the area was scrubbed and draped with the sampling site exposed. The choice of biopsy site, the sternum or spina iliaca, was made by the physician performing the procedure according to the clinical indications for each patient. If only a marrow aspiration was required, the sternal site was preferred.

A local anesthetic, 2% Lidocaine, was injected subcutaneously at the sample site: up to 2 ml for the sternum and up to 10 ml for the spina iliaca, depending on the effect of the anesthetic. A few minutes after injecting the Lidocaine, the doctor gently tapped the bone with the tip of the needle while asking the patient to report any painful sensations to assess the efficacy of the local anesthesia. The sternal biopsies were made with 15 G × 5–30 mm bone marrow aspiration needles, and the trephine biopsies were made with 11 G × 100 mm Jamshidi-type needles.

A small incision was made with a surgical blade and used to insert the biopsy needle into the soft tissue until it reached the bone. Manual pressure was applied by rotating the stylet clockwise and anti-clockwise until the bone marrow cavity was reached, confirmed by a reduction in resistance.

The stylet was removed to enable aspiration of the bone marrow. If a bone biopsy was required, a new sampling site was created by repositioning the same needle to prevent the formation of an artifact in the bone at the aspiration site. The acquired specimen was placed in a formalin solution and sent for histopathological examination. The aspiration needle was discarded.

Once the BMBA was completed, the biopsy needle was removed; pressure was applied with gauze to prevent bleeding; an adhesive patch was affixed; and a bag of ice was placed over the procedure site. Physicians who chose the sternum as the sampling site followed the same technique as described with the exception that only aspirations and no bone biopsies were performed. After the procedure was completed, patients were routinely asked to remain in the clinic for 1 h (to check for possible bleeding at the insertion site), during which time the survey data were collected.

Results

Out of 125 patients interviewed, 66 (53%) were males and 59 (47%) were females. The basic demographic data are shown in Table I. None of the patients in the study received premedication. None of the patients reported problems in understanding of filling the questionnaire. Nearly all of the patients (124 patients, 99.2%) experienced painful sensations, whereas only one (0.8%) patient reported no pain. The patients were asked first what was the significant level of pain for them – to self-assess the borderline intensity of significant pain. The patients regarded the VAS pain score of ≥ 3.67 as significant. This score level was used later to compare with actual pain felt during the biopsy and 12 patients (9.6%) presented a mean pain score of ≥ 3.67 after the procedure. Using the VAS, 48 patients (38.4%) reported a score of ≥ 3.67 during one or more of the BMBA procedure steps. Regardless of the VAS pain score, 21 patients reported experiencing intolerable pain during the procedure, and 13 out of those underwent aspirations and bone biopsies from the spina iliaca. All 13 patients (100%) stated that their experience of pain during the bone extraction was significant.

Females were more sensitive to pain than were males ($p = 0.0201$). Age had a positive impact on the average pain sensitivity, with older the patients reporting a higher pain sensitivity comparing to their younger peers ($p = 0.0086$).

BMI did not have a significant effect on pain ($p = 0.3327$). The occupation of the patient, specifically whether it was manual or intellectual, did not have a significant effect on the pain intensity ($p = 0.7109$). The 15 patients diagnosed with lymphoma reported the highest VAS pain scores (VAS 1.99).

There was not a significant difference between patients who had not undergone any previous biopsies and patients

Table I – Demographic data

Variable	Characteristics	Number of patients (%)	Mean VAS	
Gender	Male	66 (53%)	1.26	
	Female	59 (47%)	1.87	
Age	<20	0	0	
	20–29	6 (5%)	1.84	
	30–39	7 (6%)	1.60	
	40–49	12 (9%)	1.61	
	50–59	26 (21%)	1.12	
	60–69	47 (38%)	1.54	
	70–79	20 (16%)	1.93	
	>80	4 (3%)	2.16	
BMI	N/A	3 (2%)	1.21	
	<18.5	2 (1.5%)	2.07	
	18.5–24.9	45 (36%)	1.55	
	25–29.9	51 (41%)	1.58	
	>30	22 (17.5%)	1.50	
Occupation	N/A	5 (4%)	1.51	
	Manual work	39 (31%)	1.59	
	Intellectual work	53 (42%)	1.41	
Disease	N/A	33 (27%)	1.76	
	Leukemia	27 (21%)	1.56	
	Lymphoma	15 (12%)	1.99	
	Multiple myeloma	16 (13%)	1.44	
	Myeloprolif. disorders	15 (12%)	1.71	
Procedure	Others	52 (42%)	1.42	
	Sternum aspiration	29 (23%)	1.83	
	Spina iliaca aspiration	36 (29%)	1.29	
	Spina iliaca aspiration	60 (48%)	1.58	
+ Biopsy	Prior	0	42 (34%)	1.38
	Procedure	1	17 (14%)	1.87
		2	23 (18%)	1.74
		3	8 (6%)	1.64
		4	6 (5%)	1.79
		>5	29 (23%)	1.33

who had undergone one previously, despite a trend suggesting that the more procedures a patient has experienced, the less their pain intensity. A previous pain score of ≥ 3.67 ($p < 0.001$) and adequate information given by medical personnel ($p = 0.020703$) had significant impacts on the intensity of patient pain. Adequate communication with the doctor particularly prior BMBA ($p = 0.0333$), during bone extraction ($p = 0.0253$) and post BMBA ($p = 0.0267$), also had significant impacts on the intensity of patient pain. Summary of factors influencing the pain felt by the patient during the biopsy is shown in Table II.

Comparing aspirations from the sternum and spina iliaca indicated that aspirations from the sternum were more painful than were aspirations from the iliac crest at each procedural step. Patients undergoing aspiration from the sternum reported VAS scores of 2.32 vs. 2.16 for aspirations from the spina iliaca ($p = 0.7809$). When comparing aspirations at these 2 sites, the stage involving the application of local anesthesia together with the biopsy needle insertion showed a significant difference in pain (Table III).

Twelve doctors participated in the study. Two doctors enrolled more than 20 patients, whereas the other doctors enrolled only a few patients each. For the statistical analysis, the 2 doctors who had enrolled the most patients were analyzed and compared to the combined results from other

Table II – Main factors connected with lower pain during the bone marrow aspiration and biopsy

Variable	p	Corrected p-value
Younger age of patient	0.0086	0.0172
Male gender of patient	0.0201	0.0201
Skills of the doctor performing the biopsy	0.0004	0.0012
Pain scores <3.67 during previous BMBA	<0.0001	<0.001
Adequate information prior to procedure	0.0365	<0.001

This table summarizes significant pain influencing factors. p-Values have been corrected for mass significance using Bonferroni-Holms method.

doctors at the clinic. The analysis revealed a significant difference between the doctors. Doctor B was less likely to cause pain during each step of the procedure when compared to doctor A ($p < 0.001$) and to the combined results from the other doctors ($p < 0.001$) (Table IV). To exclude a possible patient selection bias, the self-reported pain sensitivity levels of patients treated by doctor A and doctor B were compared and showed no significant difference in self-reported pain sensitivity, mean VAS score of 2.97 vs. 4.83 ($p = 0.07599$). Therefore, the doctor performing the biopsy has a significant impact on the average pain felt during the procedure ($p = 0.0004$).

According to the patients, the 3 most frequently mentioned factors influencing pain were proper anesthesia (mentioned 44 times), bone marrow biopsy technique (mentioned 18 times) and the attitude or stress level of the patient (mentioned 15 times).

Discussion

A bone marrow biopsy and aspiration remains a procedure that is dreaded by patients worldwide. For many patients, the pain experienced during this procedure is significant. Because the procedure is being performed more often and is expanding in use from hematologists to doctors of regenerative medicine who require bone marrow as a source of stem cells, it is likely that the need for marrow biopsies will increase. To date, research in this field is limited, and the procedure itself has not changed much over the years. We hypothesized in our previous work [9] that the technique applied by the physician (rather than his/her experience in performing the biopsy) might play a significant role in reducing pain. To test this hypothesis, we developed a new approach in which we asked patients to report their pain intensity levels at each step of the procedure, analyzing for the first time the pain intensity at each step of the procedure. The data indicated significant

Table III – Role of procedural site as pain influencing factor

Variable	Sternum	Spina iliaca	S. iliaca asp.	+ Bone biopsy
Pre-procedural pain	0.69	0.25	0.09705	0.31
Local anesthesia application	2.38	0.85	0.00167	1.28
Biopsy needle insertion into soft tissue	2.38	1.41	0.04843	1.40
Bone penetration	2.18	2.00	0.76146	1.96
Bone marrow aspiration	2.32	2.16	0.78099	2.42
Bone extraction	–	–	–	2.74
Post procedural pain	1.07	0.83	0.56318	0.76

This table comparing pain intensity levels obtained during bone marrow aspirations from sternum vs. aspirations from spina iliaca and mean pain intensity levels during BMBA.

Table IV – Differences in pain scores between doctors performing BMBA

Variable	Prior BMBA	L. anesthesia ¹	B. needle sft. ²	B. needle pntr. ³	Bone asp. ⁴	Bone extr. ⁵	Post BMBA
Dr. A vs. Dr. B							
VAS scores	0.73/0.21	2.04/1.11	1.97/0.79	2.36/0.80	2.38/0.76	1.61/1.14	0.23/0.26
p values	0.2541	0.0053	0.0188	0.0067	0.0121	0.2912	0.3278
Dr. A vs. Dr. C-L							
VAS scores	0.73/0.27	2.04/1.18	1.97/1.72	2.36/2.22	2.38/2.86	1.61/3.06	0.23/0.87
p values	0.3480	0.2190	0.8388	0.8920	0.5261	0.3333	0.1502
Dr. B vs. Dr. C-L							
VAS scores	0.21/0.27	1.11/1.18	0.79/1.72	0.80/2.22	0.76/2.86	1.14/3.06	0.26/0.87
p values	0.5899	0.0133	0.0007	0.0001	<0.0001	0.0058	0.0092

This table shows mean VAS scores during each particular step of BMBA and the p values when comparing doctors. Doctor A and doctor B have similar background regarding experience and number of biopsies performed.

¹ Local anesthesia application.

² Biopsy needle penetration through soft tissue.

³ Biopsy needle penetration through bone.

⁴ Bone marrow aspiration.

⁵ Bone extraction.

differences between the doctors who performed the BMBA. Moreover, the physician can use the survey questions to address the pain that patients experience at the various stages of the biopsy and then use the data as constructive feedback for improving his or her operating technique. This tool may reduce pain for patients undergoing BMBA. The study also shows that 2 very experienced doctors (each of whom had performed more than 3000 biopsies) differ significantly in their techniques used to perform biopsies. This finding indicates that the technique and behavior of the operator during the biopsy is a decisive factor in the biopsy experience of the patient. The patients of doctor A, whose pain scores were significantly lower, also reported better communication with the doctor and having received more adequate information. Surprisingly, the aspiration is not the most painful part of the procedure – this can be easily explained once the technique of aspiration is watched. The speed of the suction and the volume of the obtained marrow influence the pain of the patient. As our center has very strict policy on minimal volumes of marrow samples they remain low (usually 2–10 ml) compared to other centers where quite often much higher volumes of marrow are sampled for scientific use or biobanking. This could explain that the aspiration was usually not the most painful part of the procedure in contrast to experience in other centers.

Another question is how the technique of the operator with classical BMBA needle will compare to the powered BMBA devices. One recent systematic review and meta-analysis of 5 randomized clinical trials indicated an advantage of powered devices over manual techniques. One of the conclusions of this review was that powered systems could offer an alternative for patients with high anxiety and sensitivity to pain [15]. However, when we indirectly compare the VAS scores belonging to the patients treated by the most skilled doctor in performing BMBA with minimal pain, he surpasses with a clear margin the results of the trials with powered devices. In our opinion this fact questions the data presented in studies exploring the effectiveness and impact of powered BMBA devices on pain scores, as they can clearly be biased by comparing the pain scores of powered devices with physicians who did not yet achieve excellence in minimizing the BMBA associated pain. Therefore, a comparison of the top performing physicians using classical BMBA needles with physicians using powered BMBA devices would be more conclusive in exploring and answering the question to what extent the technique chosen and applied by the physician influences the pain level.

The study has some obvious limitations. This is a single center study and there was no randomization. The patients mostly knew the doctors and this could have an influence on pain assessment – there could be possible effect on giving better “grades” to the doctors that the patients like. The only possibility to dissect this effect would be to randomly assign the patients to different doctors who they do not know – which is rather hard to accomplish given the multiple chances that the patient has to get acquainted with different doctors at the center. Given these limitations, the pool of 125 biopsies is one of the biggest published so far

and it is the first study that tried to dissect the pain felt on different stages of biopsy – to show where improvements could be made, and also provide the doctors instant feedback on when their patients feel the pain. The study shows differences in BMBA skills between the doctors at one center. We were only limited to 2 doctors performing enough biopsies to allow for valid analysis and we had to use pooled results of the rest of the doctors to show how those results compare to the practice at the center. This is not objective test, still it points to differences in skills that can be assessed and later used for education and training purposes.

A general misconception by physicians is that there is no difference in pain intensity experienced during bone marrow aspirations of the sternum versus bone marrow aspirations of the spina iliaca. Our study results demonstrate that an aspiration of the sternum is more painful at each step of the procedure. Moreover, the sternum and spina iliaca show significant differences in the pain scores during the application of local anesthesia and bone marrow needle insertion through soft tissue. Increased anxiety served as an underlying factor that increased the sensation of pain [16–18] during sternal aspirations. The sight of the needle that delivers the syringe filled with local anesthetic can be a stressful moment for many patients, as can the sight of the biopsy needle, which is inserted after applying the local anesthetic.

We also asked patients to report their perspectives on important pain influencing factors. They mentioned proper anesthesia, the technique of the operator and their own stress levels prior to the BMBA. These data and the findings from this study are congruent with those of other studies in the field [9]. Therefore, 3 ways the operator can influence the patient's experience include taking care to anesthetize the biopsy site fully, using biopsy techniques that reduce pain and reducing stress by adequately communicating with the patient. Our study also shows clear directions for further research on this topic. We are open to sharing our questionnaire with any center involved in research of the standardization of BMBA technique.

In conclusion, this is the first study to address the pain experienced by the patient at each step of a BMBA. The experience of pain can be reduced by simple measures, such as properly communicating and providing appropriate and adequate information. Further research should be undertaken to establish clear and standardized evidence-based guidelines on how to perform a BMBA with minimal pain. Medical personnel underestimate the significance and severity of the pain felt by patients, and a greater awareness should be raised via staff education. Especially cooperation with specialist outside hematology, such as anesthesiology and intensive care might improve the pain prevention during the BMBA. Neglecting proper communication can lead to unjustified fear and increased stress levels in patients, which in turn can affect the patient's attitude toward further treatment. Currently, no mechanical device has surpassed the best skills of our doctors; it is the individual physician's technique that plays a crucial role and that needs to be improved.

Informed consent

Informed consent was obtained from all patients for being included in the study.

Authors' contributions/Wkład autorów

ES, NH – study design, data collection and data interpretation, manuscript preparation, literature search. EJ – study design, data collection and data interpretation, statistical analysis, manuscript preparation, literature search.

Conflict of interest/Konflikt interesu

None declared.

Financial support/Finansowanie

None declared.

Ethics/Etyka

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

REFERENCES / PIŚMIENNICTWO

- [1] Parapia LA. Trepanning or trephines: a history of bone marrow biopsy. *Br J Haematol* 2007;139:14–19.
- [2] Bain BJ. Bone marrow trephine biopsy. *J Clin Pathol* 2001;54:737–742.
- [3] Burt RK, Loh Y, Pearce W, Beohar N, Barr WG, Craig R, et al. Clinical applications of blood-derived and marrow-derived stem cells for nonmalignant diseases. *JAMA* 2008;299:925–936.
- [4] Kuball J, Schüz J, Gamm H, Weber M. Bone marrow punctures and pain. *Acute Pain* 2004;6:9–14.
- [5] Talamo G, Liao J, Joudeh J, Lamparella NE, Dinh H, Malysz J, et al. Perceived levels of pain associated with bone marrow aspirates and biopsies. *J Support Oncol* 2012;10(4):166–170.
- [6] Watmough S, Flynn M. A review of pain management interventions in bone marrow biopsy. *J Clin Nurs* 2011;20:615–623.
- [7] Lidén Y, Olofsson N, Landgren O, Johansson E. Pain and anxiety during bone marrow aspiration/biopsy: comparison of ratings among patients versus health-care professionals. *Eur J Oncol Nurs* 2012;16:323–329.
- [8] Riley RS, Hogan TF, Pavot DR, Forysthe R, Massey D, Smith E, et al. A pathologist's perspective on bone marrow aspiration and biopsy: I. Performing a bone marrow examination. *J Clin Lab Anal* 2004;18:70–90.
- [9] Hjortholm N, Jaddini E, Hałaburda K, Snarski E. Strategies of pain reduction during the bone marrow biopsy. *Ann Hematol* 2013;92:145–149.
- [10] Talamo G, Liao J, Bayerl MG, Claxton DF, Zangari M. Oral administration of analgesia and anxiolysis for pain associated with bone marrow biopsy. *Support Care Cancer* 2010;18:301–305.
- [11] Hudziak B, Krasnow RW. Contralateral ice massage during bone marrow aspiration. *PRN Forum* 1983;2:5.
- [12] Kuivalainen AM, Ebeling F, Rosenberg PH. Pre-medication with sublingual fentanyl did not relieve pain associated with bone marrow aspiration and biopsy: a randomized feasibility trial. *Eur J Pain* 2013;17:1357–1364.
- [13] Briggs M, Closs JS. A descriptive study of the use of visual analogue scales and verbal rating scales for the assessment of postoperative pain in orthopedic patients. *J Pain Symptom Manage* 1999;18:438–446.
- [14] Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimeters? *Pain* 1997;72:95–97.
- [15] Voight J, Mosier M. A powered bone marrow biopsy system versus manual methods: a systematic review and meta-analysis of randomized trials. *J Clin Pathol* 2013;66(9):792–796.
- [16] Johnson H, Burke D, Plews C, Newell R, Parapia L. Improving the patient's experience of a bone marrow biopsy – an RCT. *J Clin Nurs* 2008;17:717–725.
- [17] Brunetti GA, Tendas A, Meloni E, Mancini D, Maggiore P, Scaramucci L, et al. Pain and anxiety associated with bone marrow aspiration and biopsy: a prospective study on 152 Italian patients with hematological malignancies. *Ann Hematol* 2011;90:1233–1235.
- [18] Kuivalainen AM, Niemi-Murola L, Widenius T, Elonen E, Rosenberg PH. Comparison of articaine and lidocaine for infiltration anaesthesia in patients undergoing bone marrow aspiration and biopsy. *Eur J Pain* 2010;14:160–163.