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Warmed and buffered lidocaine for pain relief during bone marrow aspiration and biopsy. A randomized and controlled trial

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HIGHLIGHTS

- Bone marrow aspiration and biopsy is a painful procedure despite local infiltration anaesthesia.
- Warming and buffering the local anaesthetic solution alleviates pain during infiltration.
- Processed solution does not ease pain during next steps of bone marrow sampling.
- Especially anxious patients may benefit from additional pain relieving methods.

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ABSTRACT

Background and purpose: Local infiltration anaesthesia is frequently painful due to low pH of the used anaesthetics, such as lidocaine. Usually pH of the solution is near 4.0, which causes tissue irritation and excitation of the pain mediating nerve endings. Warming and buffering the local anaesthetic solution have been shown to reduce the patient's experience of pain and unpleasantness during infiltration. Buffering reduces the dissociation of the local anaesthetic molecule and may enhance the anaesthetic's entrance into nerve cells. In this randomized placebo-controlled trial warmed and buffered lidocaine with adrenaline was compared to room temperature unbuffered lidocaine with adrenaline infiltrated before bone marrow aspiration and/or biopsy (BMAB). The aim was to find out to what extent warming and buffering would diminish pain during infiltration and whether this would be reflected in less pain also during subsequent steps of the BMAB procedure.

Methods: One hundred patients scheduled to undergo BMAB were interviewed regarding subjective experiences from previous medical procedures, current chronic and temporary medications, and their present state of anxiety before the BMAB procedure. They received local anaesthetic infiltration of lidocaine prior to BMAB. The solution used was either warmed lidocaine 20 mg/ml with adrenaline buffered with sodium bicarbonate 75 mg/ml (warmed and buffered group, 50 patients, pH approximately 7.3, 32 °C) or unbuffered lidocaine 20 mg/ml with adrenaline mixed with NaCl 0.9% solution (control group, 50 patients, pH approximately 3.7, room temperature). The lidocaine concentration was similar in both groups. The bone marrow sampling needle was inserted 2 min after local anaesthetic infiltration. The grade of preprocedural anxiety, and pain sensations during the BMAB, both rated on NRS (numeral rating scale, 0–10) were compared between the groups.

Results: In comparison with the use of an unbuffered solution at room temperature warmed and buffered lidocaine with adrenaline caused less pain during infiltration (median NRS 4.0 vs. 2.0, $P < 0.002$) but it did not make performing the other phases of BMAB any less painful. As expected, painful experiences from previous medical, other than BMAB, or dental procedures and anxiety were associated with local anaesthetic infiltration pain during BMAB. Patients' own pain or anxiolytic medication did not lessen pain during BMAB.

Conclusions: By warming and buffering the lidocaine solution containing adrenaline it is possible to make the pain during infiltration less intense. Unfortunately, such benefit was not detected during the following steps of BMAB, initiated 2 min later. Preprocedural anxiety made procedural pain more intense including that of the local anaesthetic infiltration.

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Implications: Warming and buffering the local anaesthetic prior to its administration is an effective and simple way of diminishing pain during infiltration. This benefit seems to be underutilized in the BMAB procedure. However, warming and buffering are not sufficient enough to diminish pain during bone marrow sampling and thus additional pain alleviating methods should be used, particularly in patients showing preprocedural anxiety.

1. Introduction

Bone marrow aspiration and/or biopsy (BMAB) in adults is usually performed after local anaesthetic infiltration, occasionally supplemented with a sedative or an opioid. In spite of infiltration of adequate amount and concentration of the local anaesthetic (usually lidocaine) the subsequent sampling procedures can be painful [1–3]. Since the local anaesthetic solutions are acidic, the subcutaneous and periosteal infiltration may itself cause discomfort and pain. For BMAB, adrenaline containing local anaesthetic solutions are preferred because the vasoconstrictor may reduce the size of postpuncture haematomas, in particular in patients with disturbed coagulation. However, the commercial adrenaline containing solutions are manufactured very acidic (approximately pH 4) by adding hydrochloric acid for adequate preservation of adrenaline, resulting in even more tissue irritation than with plain solutions (pH 5–7). Buffering the acidic local anaesthetic solution to near physiological pH by adding sodium bicarbonate just prior to administration has been found to reduce the pain from infiltration in a variety of clinical situations [4–6] as well as in one BMAB study [7]. In addition, by reducing the dissociation of the basic local anaesthetic molecule (p*K*a 7.9) through a pH rise, the molecules can enter into nerve cells more easily and act more rapidly and strongly [8,9].

Another simple and inexpensive manoeuver to make the local anaesthetic infiltration more comfortable is warming the solution to a temperature near body temperature [10]. Warming and buffering may act synergistically in alleviating infiltration pain [11,12], but experience from this combination for BMAB seems to be lacking. A pleasant experience from the first step of the BMAB procedure, i.e. local anaesthetic infiltration, may be reflected in reduced discomfort from the following steps of BMAB.

Therefore, in the present study we warmed the adrenaline containing lidocaine solution (32 °C) and added warm bicarbonate just before infiltration. The primary outcome was the intensity of pain during infiltration in comparison with the infiltration of the non-buffered solution at room temperature. The secondary aim was to find out whether pain during the subsequent steps (puncture, aspiration, biopsy) would be influenced by the pain experience from the local anaesthetic infiltration performed 2 min earlier.

2. Methods

The ethics committee of Helsinki and Uusimaa hospital district accepted the protocol (diary number 306/13/03/01/11). All patients gave informed consent before recruitment.

2.1. Patients

We included 100 patients in this randomized study; 50 patients received warmed and buffered lidocaine with adrenaline and the other 50 patients received non-buffered lidocaine with adrenaline at room temperature. The power analysis was based on a study comparing intradermal infiltration of unmanipulated lidocaine to warmed and buffered lidocaine in volunteers [11]. In that study, the VAS score for unmanipulated lidocaine infiltration was 44.2, and for warmed, buffered lidocaine it was 29.2. Thus, warming and buffering decreased the VAS score by 34%. In our previous study [2] mean NRS score for local anaesthetic infiltration was 3.5 (SD 2.08). A reduction in pain intensity during infiltration by 34% would be expected to yield a NRS score of 2.3 in our BMAB patients. When the alfa is set to 0.05 and power to 80%, we need 44 patients to both study groups. Due to the medical complexity of haematological patients we decided to recruit 100 patients to the study. Half of the patients were randomized to receive warmed and buffered lidocaine and the other half served as a control group receiving non-warmed and non-buffered lidocaine. Furthermore, approximately half of patients in each group had the bone marrow sampling performed from the sternum and the other half from the posterior iliac crest. The exclusion criteria were allergy to local anaesthetics, obesity (BMI, body mass index >32 kg/m^2) and unstable coronary heart disease. The flow chart is presented in Fig. 1.

2.2. Blinding

This study was single-blinded. The randomization was performed beforehand with sealed envelopes. Before the BMAB begun, the research assistant opened the envelope and prepared the local anaesthetic solution for the patient. The physician performing the BMAB was not told which group the patient belonged to. The non-blinded research assistant performed interviews using a designated

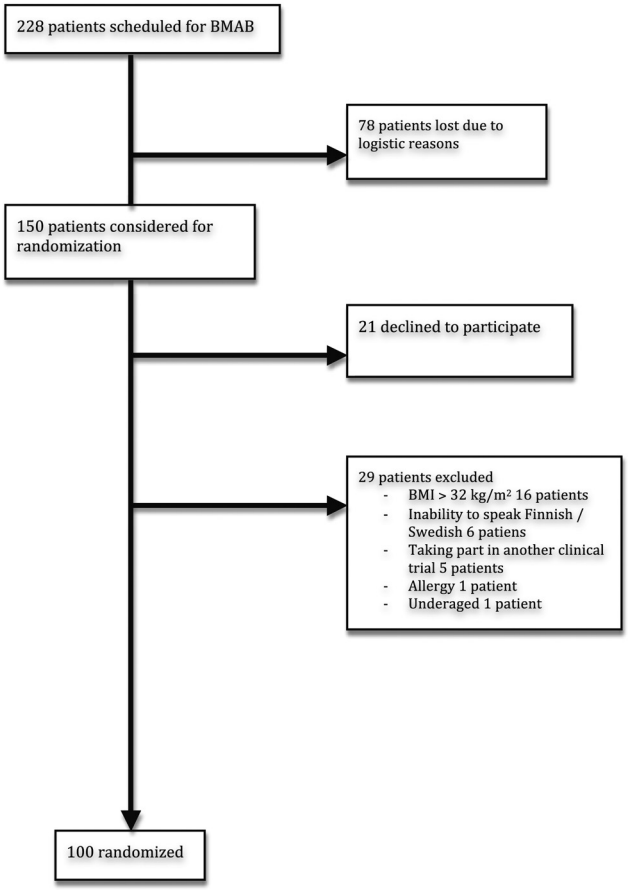

Fig. 1. Flow chart.