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Comparison of Efficacy of Articaine and Bupivacaine after Impacted Third Surgery: A Double-Blinded Randomized Controlled Trial

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ABSTRACT

Objective: This randomized controlled clinical trial(RCT) aims to compare the effect of bupivacaine and Articaine at normal doses on pain intensity and the requirement for analgesics after lower third molar extraction.

Materials and methods: The final study sample comprised 50 volunteers (26 males and 24 females; age range, 18-30 years) undergoing scheduled surgical extraction of the impacted lower third molar. A computer-generated random sequence was used to allocate participants to the articaine (4%) or bupivacaine (0.5%) group. Surgeons and patients were blinded by labeling the articaine and bupivacaine carpules with numbers (1 and 2, respectively). Postoperative pain intensity (primary outcome) was evaluated with a visual analog scale (VAS), while the requirement for and timing of rescue medication and the quality of intraoperative anesthesia were also measured (secondary outcomes).

Results: VAS-measured pain intensity was significantly higher ($p < 0.05$) in the articaine group than in the bupivacaine group at all-time points except for 8 h post-surgery ($p=0.052$). Rescue medication was required by 13 (52%) patients in the articaine group and 8 (32%) patients in the bupivacaine group, although the difference was not statistically significant ($p=0.252$). The groups did not significantly differ ($p=0.391$) in the quality of the intraoperative anesthesia.

Conclusions: Bupivacaine is a valid alternative to articaine in third molar surgery and may offer residual anesthesia as a means of reducing postoperative pain. However, further well-designed RCTs are required in larger study populations to verify the effectiveness of bupivacaine to achieve residual analgesia after oral surgery.

Key words: Articaine, Bupivacaine, Postoperative pain, Acute pain, Third molar surgery

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INTRODUCTION

Lower third molar extraction, one of the most frequent procedures in oral surgery [1,2], is commonly associated with postoperative complications such as pain, inflammation, or trismus, or, less frequently, by infectious complications such as alveolitis or surgical wound infection [1,3]. Pain from surgical trauma and release of pain mediators is not uncommon after oral surgery, and 90% of patients require analgesic treatment [4]. Pain is maximal during the first few hours after third molar extraction when there is an increase in the production of pain mediators and the effect of the local anaesthetic is lost. This postoperative pain is usually controlled with oral analgesics, although it is also possible to use long-acting anaesthetics during surgery [5]. Local anaesthetics reversibly block nerve conduction, while the patients remain conscious, producing a transient inhibition of the sensitive or motor function of nerve fibers around the anaesthetic injection site and neighboring area [6]. Administration of long-acting local anaesthetics was found to reduce pain during the first 6–8 h after oral surgery. In particular, bupivacaine offers strong anaesthetic potency and a prolonged action due to its high liposolubility and adhesion to plasma proteins [7,8]. Bupivacaine has an intermediate speed of onset and relatively long latency time, with a pk value of 8.11 [9], while its high liposolubility reduces its effectiveness in infiltrative techniques because a large amount is retained by soft tissues and only a small volume reaches the bone. It is mainly indicated for procedures of long duration and postoperative pain management [10]. For its part, articaine is an amide-type local anaesthetic widely used in oral surgery due to its rapid action, potency, and intermediate duration [6,10]. Authors have compared the analgesic efficacy of bupivacaine with that of other local anaesthetics in the extraction of impacted third molars, but few compared it with the analgesic efficacy of articaine after surgery in the maxillofacial area, and the results were largely inconclusive. The drawing of reliable conclusions is further hampered by differences in the characteristics (design, study population, and methodology) of these

clinical studies [8]. The study hypothesis was that residual analgesia produced by the longer-acting bupivacaine would reduce postoperative pain intensity in comparison to the use of articaine. The objective of this randomized controlled clinical trial (RCT) was to compare the effect of bupivacaine and articaine at habitual doses on pain intensity and the need for analgesics after lower third molar extraction [7,11].

MATERIALS AND METHODS

Study design and patient choice

This single-centre, double-blind RCT was conducted in 50 volunteers (23 males and 27 females; age range, 18–30 years) undergoing scheduled surgical extraction of impacted lower third molar at the department of Oral and Maxillofacial surgery at Saveetha dental College. Study exclusion criteria were as follows: age under 18 years, renal failure, pregnancy or breastfeeding, allergy to the study medication or related drugs, immunocompromised status, psychological disorder, epilepsy, receipt of medication with analgesic or anti-inflammatory properties less than 24 h before the surgery, preoperative inflammation and pain at the surgical site, and clinical or radiographic evidence of active oral disease. All participants signed their informed consent to participate in the study, This double-blinded RCT was done in 50 volunteers (23 males and 27 females; age extend, 18– 30 years) who were undergoing third molar surgery. Study rejection criteria were as per the following: age under 18 years, renal failure, pregnancy or malnourished patients, hypersensitivity to the examination prescription or related medications, immunocompromised status, epilepsy, receipt of drug with pain-relieving or mitigating properties under 24 h before the medical procedure, preoperative aggravation and torment at the careful site, and clinical or then again radiographic proof of dynamic oral illness. Surgeons and patients were blinded by labelling the articaine and bupivacaine vials with the numbers 1 and 2, respectively. A computer-generated random sequence was used to allocate participants to the articaine (4% articaine with 1:100,000 epinephrine) or bupivacaine (0.5% bupivacaine with 1:200,000 epinephrine) group. Each group finally included 25 patients.

Study variables were classified as the primary outcome, and secondary outcome variables. The primary outcome variable was the postoperative pain intensity. During the 48-h postoperative period, each patient completed a data collection form on the postoperative pain intensity at 2, 4, 6, 8, 10, 12, 24, and 48 h, using a horizontal 100-mm visual analog scale (VAS) with no pain^ and worst pain imaginable^ as endpoints. Secondary outcome variables were as follows: the need for rescue analgesia with 1 g Paracetamol (yes/no) and its timing, and the quality of intraoperative anesthesia, which was classified as no discomfort during surgery, discomfort/pain not requiring additional anesthesia, or discomfort/pain requiring additional anesthesia. Patients returned 7 days after the surgery for a postoperative follow-up and suture removal and to hand in their questionnaires after receiving any necessary clarification of items.

Sample size

The primary outcome of this study was VAS-measured postoperative pain intensity. The sample size was calculated using the G power 3.1.2 version with an alpha value of 0.05, the statistical power of 80%, and the assumed loss to the follow-up of 15%. According to this calculation, the number of patients required per group was 24, and we finally included 25 patients in each group.

RESULTS

The mean ± standard deviation (SD) age of participants was 21.06 ± 5.69 years in the articaine group and 22.17 ± 6.10 years in the bupivacaine group; 26 participants were male and 24 female. No significant differences were found between the articaine and bupivacaine groups in mean age or sex or any tooth-related or surgical variable. As shown in Figure 1, VAS-measured pain intensity was significantly higher ($p<0.05$) in the articaine group than in the bupivacaine group at all-time points except for 8 h post-surgery ($p=0.052$). Among the patients who did not consume rescue medication, which did not affect pain levels, higher pain intensity was also observed in those treated with articaine at all times except for 8 h post-surgery ($p=0.12$) (Figure 2). Among the patients who had consumed rescue medication, the pain intensity was higher in those treated with articaine at 2, 4, and 6 h, but there was no significant difference between the groups from 8 h onwards. Rescue medication was required by 13 patients in the articaine group and 8 patients in the bupivacaine group, although the difference did not reach statistical significance ($p=0.252$). There was also a non-significant tendency ($p =0.183$) towards greater consumption of rescue medication by the articaine group during the immediate postoperative period (48 h post-surgery). The groups did not significantly differ ($p=0.391$) in the quality of the intraoperative anesthesia according to the discomfort/pain reported by the patients or their need for additional anesthesia.

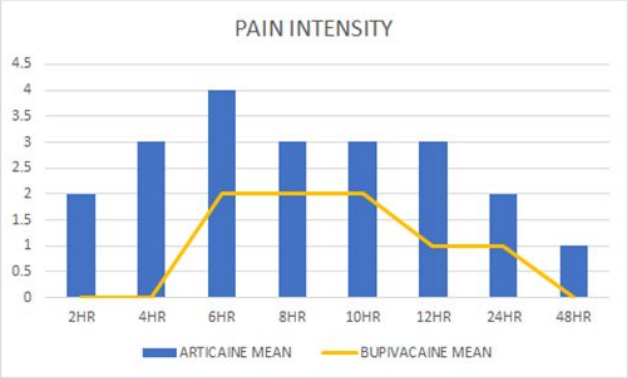

Figure 1: VAS-measured pain intensity in articaine and bupivacaine groups at all time points.

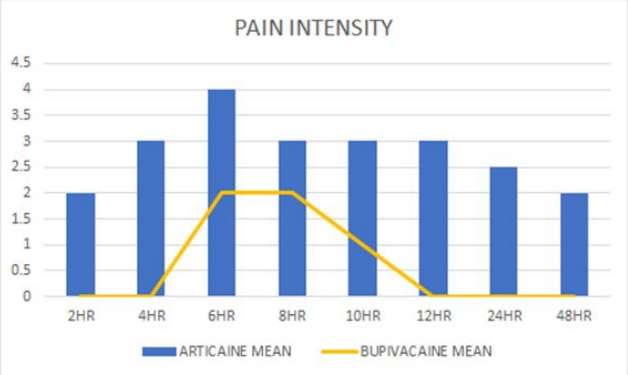

Figure 2: VAS-measured pain intensity in Articaine and bupivacaine groups at all-time points among the patients who did not consume rescue medication.

DISCUSSION AND CONCLUSION

Few studies have compared the effectiveness of articaine versus bupivacaine for analgesia after surgery in the maxillofacial area, and most of them have not reached clear conclusions [8,12,13]. In this RCT, the postoperative pain intensity was significantly lower ($p < 0.05$) in the bupivacaine group than in the articaine group at all-time points during the first 48 h post-surgery except at 8 h ($p=0.052$). Among the patients requiring rescue medication (Paracetamol), pain intensity was higher in those receiving articaine during the first 8 h post-surgery, but there was no difference between the groups after this time, likely attributable to the effect of the Paracetamol. Among the patients with no need for rescue medication, pain intensity was significantly higher in those receiving articaine versus bupivacaine at all-time points during the first 48 h post-surgery except for 8 h. This finding suggests that bupivacaine offers residual analgesia that enhances pain relief after impacted third molar extraction. Our results agree with those obtained by [14], who reported lower pain levels in patients treated with bupivacaine for impacted third molar extraction between 5 and 9 h post-surgery. Studies by, [15,16] in the setting of third molar extraction all reported the superior analgesic effect of bupivacaine in comparison to other anaesthetics such as lidocaine or mepivacaine. In contrast [8,15] observed lower pain levels at 6 and 12 h post-surgery in patients injected with articaine versus bupivacaine, while [8,12,15] found no significant differences in postoperative pain levels between patients treated with these anaesthetics for the extraction of impacted third molars. The analgesic efficacy of 4% articaine plus 1:100,000 epinephrine was recently compared with that of 0.5% bupivacaine plus 1:200,000 epinephrines in patients with symptomatic irreversible pulpitis [17], using the Heft-Parker VAS to measure pain during treatment and finding similar results in both study groups. In contrast [18], reported that 4% of articaine acted more quickly and obtained lower pain scores in comparison to 0.5% bupivacaine in a tooth extraction model. The third molar extraction analgesia model employed in this study is robust and well-validated. It is one of the main models used to test and develop anaesthetic drugs because it provides a readily available healthy population and involves a relatively uniform surgical procedure confined to a single anatomic area. Further strengths of this well-designed RCT include the blinding of both dentist and patient to the anaesthetic used and the performance of all surgeries by a single experienced surgeon, avoiding between-surgeon variability. Furthermore, no significant difference in any predictor variable was found between the study groups, allowing a reliable comparison of outcome variables. However, although the sample size was estimated appropriately, studies of larger populations are warranted to verify the effectiveness of bupivacaine to achieve residual analgesia after oral surgery. The two groups significantly differed in postoperative pain intensity but did not significantly differ in the need for rescue medication, which was higher in the articaine (13/25 patients) versus bupivacaine (8/25 patients) group but without reaching statistical significance ($p=0.252$), which may be attributable to the limited sample size. Other authors found no statistically significant difference in rescue analgesic consumption between groups treated with articaine or bupivacaine [8,12]. We also observed a non-significant tendency ($p=0.183$) towards the earlier consumption of rescue analgesic in the articaine group than in the bupivacaine group. The groups did not differ in intraoperative bleeding, as also reported by [8]. Observed higher intraoperative bleeding with bupivacaine than with articaine, probably because a higher vasoconstrictor (epinephrine) concentration was used with articaine (1:100,000) than with bupivacaine (1:200,000) [12]. The two groups in the present study did not differ in the need for supplementary anesthesia, as also observed in the studies by [8,14]. However, [8,12] reported that the anesthesia quality was significantly superior with bupivacaine than with articaine. Many complications associated with lower third molar removal are described in the literature, including pain, swelling, trismus, infection, inflammation, and nerve damage. One of the most common complications is alveolar osteitis (alveolitis sicca dolorosa, dry socket, or localized osteitis), which has been reported in 0 to 68% of cases [19,20]. All patients received post-extraction anti-biotherapy with the aim of minimizing these complications, despite the limited evidence supporting the efficacy of commonly used antibiotics for this purpose. Achievement of a final consensus on the efficacy of antibiotic prophylaxis in this context requires well-designed randomized trials that take full account of known risk factors and clinical outcomes [20]. No statistically significant between-group differences were found in predictor variables, indicating that the outcome variables were not influenced by differences in patient-related, surgery-related, or tooth-related variables. It should be borne in mind that an anaesthetic of a shorter duration may be preferred by some patients who are discomforted by the feeling of anesthesia in soft tissues. For the sample size estimation, a reduction of 20 mm in VAS-measured postoperative pain intensity was considered a clinically relevant value for our primary

outcome. This decision was based on previous research published by our group and a review of RCTs with a comparable structure to our study that also considered similar variables. However, further high-quality RCTs are required in larger study populations to verify the effectiveness of bupivacaine to achieve residual analgesia after oral surgery. In conclusion, the results of this study indicate that bupivacaine is a valid alternative to articaine in third molar surgery and may offer residual anesthesia as a means of reducing postoperative pain.

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