

Effect of the local application of bupivacaine in early pain control following impacted mandibular third molar surgery: A randomized controlled study

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Abstract

Background. Postoperative pain is one of the main complications following impacted mandibular third molar (IMTM) surgery.

Objectives. The aim of this study was to assess the effect of the local application of bupivacaine on reducing early postoperative pain following IMTM surgery.

Material and methods. A prospective, single-blinded, randomized controlled study was conducted on 40 patients who had undergone the surgical removal of an IMTM under local anesthesia. In the study group ($n = 20$), absorbable gelatin sponge (AGS) soaked in 3 mL of 0.5% plain bupivacaine hydrochloride was locally applied in the post-extraction socket. In the control group ($n = 20$), AGS soaked in 3 mL of normal saline was used. Pain intensity was assessed using a pain numerical rating scale (NRS) 4 and 12 h postoperatively. The variables were compared between the 2 groups and probability values <0.05 were considered statistically significant.

Results. The pain scores in the study group were significantly lower than those recorded in the control group at 4 h postoperatively ($p = 0.003$), whereas the difference in the pain scores between the 2 groups 12 h after surgery was not statistically significant ($p = 0.443$).

Conclusions. The local application of bupivacaine is effective in reducing postoperative pain 4 h after the surgical extraction of IMTMs without any significant complications.

Keywords: third, postoperative, pain, bupivacaine, molar

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Introduction

The impaction of third molars is a common problem worldwide. Its prevalence has been estimated to range from about 3% to about 68%, with an average rate of 24.4%; it has significant geographic variation.¹ The surgical extraction of impacted mandibular third molars (IMTMs) is a common practice in oral surgery and it is usually accompanied by side effects, such as swelling, trismus and postoperative pain.²⁻⁵

Postoperative pain is the most common complication following dental surgery,³ and the patient's experience depends on the degree of surgical trauma, the need for bone removal and the periosteal extension. It is undoubtedly the most common symptom and can continue even 1 week after surgery, despite analgesic treatment, leading to increased morbidity and detrimental effects on the patient's well-being and quality of life.^{6,7} Inadequate management of early postoperative pain has been related to a wide range of negative outcomes, including delayed recovery and even an increased risk of developing chronic pain.^{8,9}

The development and use of local anesthetics for intraoperative anesthesia and postoperative analgesia is considered to be one of the most important advances in dentistry in the last century.¹⁰ Several researchers have credited bupivacaine with the ability to provide prolonged postoperative analgesia and to minimize analgesic requirements in the early postoperative hours, when pain is at its highest intensity. Its long duration of action and superior ability to decrease pain and discomfort have been reported in comparison with articaine and lidocaine. Therefore, bupivacaine is a common choice for pain control following IMTM extraction.¹¹

The delivery of a local anesthetic agent to the post-extraction socket has been described to alleviate postoperative pain.³ However, the use of local delivery therapeutics requires some mechanism to maintain the agent within the oral environment for an adequate period of time to prolong drug effectiveness and reduce its toxicity by slowing drug uptake into the systemic circulation.^{12,13}

Few studies have investigated the effect of the local application of bupivacaine in post-extraction sockets following the surgical removal of IMTMs. Therefore, the aim of this study was to assess the effect of the local application of bupivacaine on reducing early postoperative pain following IMTM surgery.

Material and methods

This study was designed and conducted as a prospective, single-blinded, randomized controlled study guided by the Consolidated Standards of Reporting Trials (CONSORT) statement.¹⁴ It included patients undergoing the surgical extraction of IMTMs at the Department of Oral and Maxillofacial Surgery of the College of Dentistry, University of Baghdad, Iraq.

The inclusion criteria were as follows: adults aged 18 years or older; with the American Society of Anesthesiologists physical status classification level I (ASA I); who had an IMTM indicated for surgical extraction; and reported no history of allergic reactions to the local anesthetic agents used in the study.

The exclusion criteria embraced patients with systemic diseases, pregnant females, patients with a missing lower second molar on the side of the surgery, patients with impacted teeth due to any pathology, such as cysts or tumors, patients presenting with signs and symptoms of acute general infections, such as fever and lymphadenopathy, and patients who had taken any type of analgesic within 24 h prior to the surgery.

The study was approved by the institutional Research Ethics Committee (protocol No. 127119). The patients were informed about the nature of the study, the procedures, and the possible intra- and postoperative complications they might encounter. Every patient signed an informed consent form to participate in the study.

The patients were randomly assigned to 2 groups with the use of Microsoft Office Excel 2016 (Microsoft Corporation, Redmond, USA). Block randomization was performed to ensure a nearly equal distribution of patients in both groups. For the patients in the study group, a 10 × 10 × 10-mm piece of absorbable gelatin sponge (AGS) (SPONGOSTAN® Dental; Ferrosan Medical Devices, Søborg, Denmark) soaked in 0.5% plain bupivacaine hydrochloride (Marcaïne; AstraZeneca, Istanbul, Turkey) was applied in the post-extraction socket. The patients assigned to the control group received AGS soaked in normal saline as a placebo. The patients were blinded to the type of local treatment they received.

A preoperative panoramic radiograph was obtained for each patient to assess the angulation of the impacted tooth according to Winter's classification¹⁵ as well as the position and depth of impaction according to the Pell and Gregory classification.¹⁶ All procedures were scheduled to start at 9 a.m. and were performed by one operator under local anesthesia (2% lidocaine hydrochloride with epinephrine 1:80,000). The procedure consisted of reflecting a triangular flap and extracting the tooth with the use of elevators alone, or after bone removal with or without tooth sectioning with the use of a surgical handpiece and burs under copious irrigation with normal saline. The duration of the surgery was calculated in minutes starting from the first incision to the last suture.

Operative difficulty was determined by the surgical technique and the duration of extraction according to de Carvalho and Vasconcelos.¹⁷ With respect to the surgical technique, the degree of difficulty was considered low when the extraction was performed using elevators alone, moderate when bone removal was required, and high when bone removal and tooth sectioning were required to complete the extraction. For the duration of surgery, the difficulty was considered low when the duration

of the surgical extraction was less than 15 min, moderate when the duration was 15–30 min and high when the duration was more than 30 min.

After extraction, the socket was thoroughly irrigated with normal saline, all sharp edges were smoothed and hemostasis was achieved. In the study group, a piece of AGS was soaked in 3 mL of 0.5% plain bupivacaine hydrochloride for 5 min and applied in the post-extraction socket. In the control group, the same procedure was performed, but 3 mL of normal saline was used. The flap was repositioned to its original place and sutured with 3/0 black silk sutures, using the simple interrupted suturing technique. Antibiotics (amoxicillin 500 mg every 8 h for 5 days) and ibuprofen (400 mg every 8 h for 5 days) were prescribed to all patients, and the patients were instructed to record any extra analgesic drug use.

Pain intensity was reported by the patients on a pain numerical rating scale (NRS) 4 and 12 h postoperatively. The patients were instructed to write a number (0–10) to quantify their pain intensity, where 0 represented no pain and 10 represented the worst pain possible. The patients were aware that the scale served to analyze the presence and intensity of pain alone, and was not a representation of generalized postoperative discomfort.

The predictor variable was the local application of bupivacaine- or normal saline-soaked AGS in the post-extraction socket, while the outcome variable was the pain scores recorded 4 and 12 h after surgery. Other

variables included age, gender, indication for extraction, the angulation, position and depth of the IMTM, and the difficulty of extraction determined by the surgical technique and the duration of extraction.

Statistical analysis

The statistical analysis was performed using GraphPad Prism v. 6 for Windows (GraphPad Software, La Jolla, USA). The descriptive statistical analysis included the calculation of frequency as number (n), mean (M) and standard deviation (SD), and median (Me). The inferential analysis included the Shapiro–Wilk normality test, the Mann–Whitney U test, Cohen's d test, Fisher's exact test, and the χ^2 test. Probability values <0.05 were considered statistically significant.

Results

Forty-three patients initially participated in this study, but 3 patients were lost to follow-up and excluded from the analysis. The remaining 40 patients ranged in age from 18 to 30 years, with a mean age of 23.6 ± 3.55 years. Among the patients there were 17 (42.5%) males and 23 (57.5%) females. They were randomly assigned to the control and study groups of 20 patients each. Figure 1 summarizes the phases of the study.

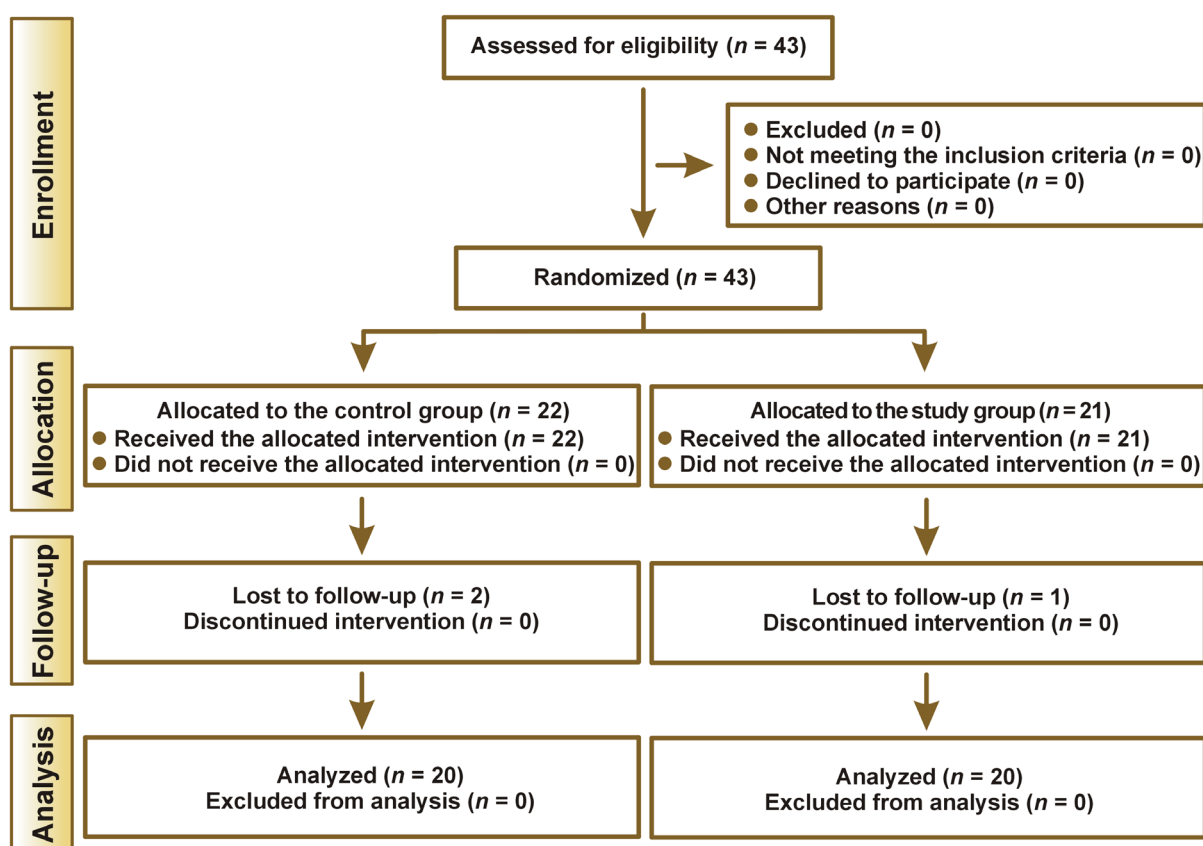


Fig. 1. Flow diagram of the randomized study

The comparisons of different independent variables between the 2 groups are summarized in Table 1. All differences were statistically non-significant, which indicates that none of these variables acted as a confounding factor for the outcome of interest (the pain score).

Four hours postoperatively, the study group recorded a mean pain score of 2.90 ± 2.43 and a median of 3.0, while the control group recorded a mean pain score of 5.95 ± 3.14 and a median of 5.5. The difference in the pain scores between the 2 groups was statistically significant ($p = 0.003$) (Fig. 2). The effect size of the intervention was 0.9723 (Glass's delta), which can be interpreted as a large effect (large effect: 0.8 or more).

Twelve hours after surgery, the pain scores recorded by the study group presented a mean of 3.80 ± 3.09 and a median of 3.0, while the control group had a mean of 4.25 ± 2.71 and a median of 3.0. The difference between the 2 groups for this time interval was not statistically significant ($p = 0.443$) (Fig. 2).

None of the patients in either group required extra analgesics other than those prescribed during the first 24 h postoperatively. The sutures were removed 7 days postoperatively. Five patients in the control group developed

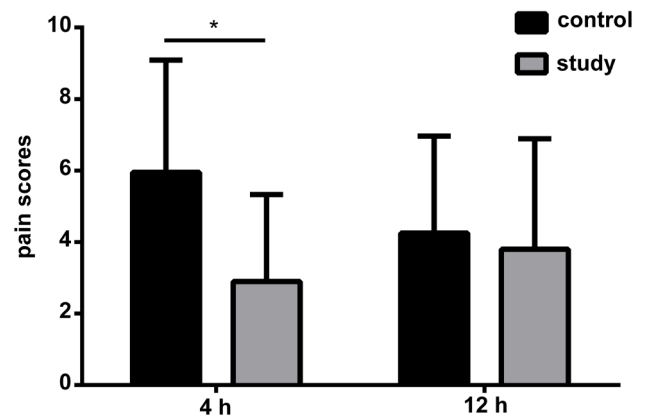


Fig. 2. Bar chart illustrating the difference in the pain scores between the 2 groups 4 and 12 h postoperatively

* statistically significant.

complications (a dry socket in 2 patients and wound dehiscence in 3 patients). Three patients in the study group developed complications (a dry socket in 2 patients and wound dehiscence in 1 patient). The difference in complication rates between the 2 groups was not statistically significant ($p = 0.695$).

Table 1. Comparison of independent variables between the 2 groups

Variable		Control group <i>n</i> = 20	Study group <i>n</i> = 20	<i>p</i> -value
Age [years] <i>M</i> ± <i>SD</i>		24.8 ± 3.61	23.4 ± 3.57	0.6619 [†]
Gender <i>n</i>	male	10	7	0.5231 ^{††}
	female	10	13	
Side of extraction <i>n</i>	right	9	13	0.3406 ^{††}
	left	11	7	
Angulation (Winter's classification) <i>n</i>	mesioangular	8	6	0.2502 [‡]
	vertical	7	4	
	horizontal	5	10	
Position (Pell and Gregory classification) <i>n</i>	A	7	9	0.7475 ^{††}
	B	13	11	
Indication for extraction <i>n</i>	dental caries	3	6	0.5177 [‡]
	orthodontic treatment	9	7	
	pericoronitis	8	7	
Duration of extraction [min] <i>M</i> ± <i>SD</i>		27.55 ± 12.21	30.55 ± 14.18	0.6054 [†]
Difficulty/duration <i>n</i>	low	1	0	0.5378 [‡]
	moderate	10	12	
	high	9	8	
Difficulty/technique <i>n</i>	low	4	4	0.7788 [‡]
	moderate	9	7	
	high	7	9	

n – number; *M* – mean; *SD* – standard deviation; [†] Mann–Whitney *U* test; ^{††} Fisher's exact test; [‡] χ^2 test. All patients demonstrated class II according to the Pell and Gregory classification.

Discussion

This study evaluated the efficacy of AGS soaked in plain bupivacaine or normal saline, applied in the post-extraction socket, in reducing the early postoperative pain associated with IMTM surgery. This approach is in line with Shepherd et al., who maintained that the treatment of postoperative pain following dental extraction requires a formulation that would simultaneously serve as a hemostatic agent as well as a vehicle for controlled anesthetic delivery.¹³ The authors tested a biodegradable dental material containing bupivacaine combined with an absorbable hemostat Gelfoam® in a rat animal model, where it was packed in post-extraction sockets, and they observed reduced post-extraction pain by assessing food consumption, body weight, and sensitivity to mechanical and thermal stimuli.¹³

The present study indicates that the local application of 0.5% bupivacaine hydrochloride in the manner described above provided effective pain relief in the first 4 h after IMTM surgery. Studies have shown that the maximum postoperative dental pain after the surgical extraction of IMTMs is usually experienced during the first 6–12 h,^{3,18} so the use of bupivacaine in this simple-to-apply method can be helpful for patients in the early postoperative period.

Khiavi et al. used 4 mL of 0.5% plain bupivacaine hydrochloride to irrigate the post-extraction sockets of IMTM patients once, before flap suturing, and compared it with normal saline irrigation in a randomized clinical study with a crossover design.³ Pain was assessed at 4 time intervals – 1, 6, 12, and 24 h postoperatively. The authors reported significant pain alleviation at all time intervals, with no complications.³

In their study, Talimkhani et al. used the intra-socket administration of bupivacaine with a prepared catheter fixated to a mandibular second molar, with its cannula inserted into the socket of the extracted third molar so that the patients could directly administer drugs (bupivacaine or saline as a placebo) into the tooth socket.¹⁹ They compared it with oral mefenamic acid capsules or capsules filled with milk powder (as a placebo) in a randomized clinical study. The patients recorded the perceived pain intensity on a visual analogue scale (VAS) every 2 h before and after drug administration for 24 h. The authors found that bupivacaine significantly relieved postoperative pain after the surgical extraction of IMTMs.¹⁹

To assess the clinical effectiveness of the local application of bupivacaine in relieving early post-extraction pain, the amount of improvement that is important to patients must be determined. It is not enough to consider only the statistical significance, but also whether the observed change is meaningful to patients.²⁰ The distribution-based method was used in the present study to determine whether the pain relief achieved with the local application of bupivacaine 4 h after surgery was more than would be

expected by chance alone, and it demonstrated that the local application of bupivacaine, as described in the present study, had a considerable clinical effect.

The difference in the pain intensity recorded 12 h after surgery was not statistically significant, which indicates that this method of local application of bupivacaine provided only temporary relief of postoperative pain. In the present study, postoperative pain during the first 24 h was assessed at 2 time intervals only (4 and 12 h after surgery) to ensure better patient compliance. Talimkhani et al. reported more prolonged pain relief at 6 time points with the use of their method of multiple intra-socket administration, which required more patient compliance,¹⁹ while Khiavi et al. reported pain relief that lasted for 24 h from a single irrigation of the post-extraction socket at the end of surgery.³

No major complications were encountered in this study and the difference between the 2 groups in this regard was not statistically significant, indicating that this method of local application of bupivacaine is safe to use.



Limitations

The main limitations of this study are its small sample size and the fact that the sample size estimation was not performed. However, the total number of patients in this study (40) is close to that reported in 2 other studies that investigated the local application of bupivacaine after IMTM extraction.^{3,19} Other limitations of the study are the fact that the operator was not blinded to the intervention and the fact that the assessment of postoperative pain during the first 24 h was performed at only 2 time intervals to ensure better patient compliance.

Conclusions

The local application of AGS soaked in plain bupivacaine hydrochloride significantly reduces postoperative pain 4 h following IMTM surgery without significant complications.

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