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Research Article

Analgesic Efficacy of Bupivacaine as an Infiltration Injection Technique after Extraction of Impacted Mandibular Third Molars: A Randomized Controlled Study

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Abstract

Background: Pain after surgery is a common adverse effect that patients experience after having their lower third molars surgically removed. ***Objective***: To assess how well local injection of bupivacaine reduces pain after surgical extraction of an impacted mandibular third molar. ***Methods***: A single-blinded randomized controlled clinical trial included a total of 56 patients that were randomly selected according to Microsoft Office Excel sheets and divided into two groups. The study includes 29 patients who received a 2 ml dose of bupivacaine 0.5% through local infiltration near the extraction site using an insulin syringe to avoid intravenous or intraneural infiltration. The other 27 patients who served as the control group received a 2 mL dose of normal saline using the same administration technique. Both groups underwent a surgical procedure to remove their impacted mandibular third molars while under the influence of local anesthesia. Pain was evaluated using a numeric rating scale (NRS) at 4, 8, 12, and 24 hours post-operatively. ***Results***: The study group exhibited significantly lower pain scores compared to the control group at 4, 8, 12, and 24 hours following the surgical procedure (p=0.0001). ***Conclusions***: There were no major problems associated with the local injection of bupivacaine; it lowers postoperative pain 4, 8, 12, and 24 hours after the surgical extraction of impacted mandibular third molars.

Keywords: Bupivacaine, Infiltration, Impaction, Third molar, Postoperative pain.

الفعالية المسكنة للبوبيفاكايين كتقنية حقن التسلل بعد استخراج الأضراس الثالثة المتأثرة بالفك السفلي: دراسة معشاة ذات شواهد

الخلاصة

الخلفية: الألم بعد الجراحة هو تأثير سلبي شائع يعاني منه المرضى بعد إزالة الأضراس الثالثة السفلية جراحيا. **الهدف**: تقييم مدى جودة الحقن الموضعي للبوبيفاكايين في تقليل الألم بعد الاستخراج الجراحي للضرس الثالث للفك السفلي المتأثر. **الطرق**: تضمنت تجربة سريرية معشاة ذات شواهد أحادية التعمية ما مجموعه 56 مريضا تم اختيارهم عشوائيا وتقسيمهم إلى مجموعتين. شملت الدراسة 29 مريضا تلقوا جرعة 2 مل من بوبيفاكايين 0.5٪ من خلال التسلل الموضعي بالقرب من موقع الاستخراج باستخدام حقنة الأنسولين لتجنب التسلل الوريدي أو العصبي. تلقى المرضى ال 27 الآخرون الذين عملوا كمجموعة مراقبة جرعة 2 مل من المحلول الملحي العادي باستخدام نفس التقنية. خضعت كلتا المجموعتين لعملية جراحية لإزالة الأضراس الثالثة المتأثرة بالفك السفلي تحت تأثير التخدير الموضعي. تم تقييم الألم باستخدام مقياس تصنيف رقمي في 4 و 8 و 12 و 24 ساعة بعد الجراحة. **النتائج**: أظهرت مجموعة الدراسة درجات ألم أقل بكثير مقارنة بالمجموعة الضابطة في 4 و 8 و 12 و 24 ساعة بعد الإجراء الجراحي. **الاستنتاجات**: لم تكن هناك مشاكل كبيرة مرتبطة بالحقن الموضعي للبوبيفاكايين. يقلل من آلام ما بعد الجراحة بعد 4 و 8 و 12 و 24 ساعة من الاستخراج الجراحي للأضراس الثالثة المتأثرة بالفك السفلي.

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INTRODUCTION

The third molars exhibit a higher incidence of impaction compared to other permanent teeth due to their delayed eruption in the oral cavity [1,2]. Most people don't even know they have an impacted third molar until it's detected accidentally during an imaging procedure. When an impacted third molar is found, it is usually removed to prevent further problems or pathological disorders, such as the development of distal caries in the second molar tooth [3,4]. Controlling the inflammatory process that happens after the surgical procedure is extremely important regarding pain and edema [5]. The effective management of post-operative dental pain is crucial in order to alleviate unnecessary patient distress, enhance overall quality of life, and mitigate healthcare expenses associated with subsequent clinical appointments [6]. Surgical trauma and the subsequent release of pain mediators are typical causes of postoperative pain. The metabolic response to surgical trauma is distinct and involves an increase in the circulatory hormones [7]. Extraction of impacted lower third molars (LTMs) causes the most discomfort three to five hours after surgery [8,9], when the effects of local anesthesia have worn off [10]. Mild oral analgesics or nonsteroidal anti-inflammatory medications are typically used to manage the associated pain and inflammation [11]. Orally administered medications of this nature necessitate ongoing self-administration and possess the capacity to induce unfavorable systemic consequences, such as disturbances in sleep patterns, feelings of nausea, impairment in neurological function, depression of the circulatory and respiratory systems, as well as the potential for addiction [12]. Bupivacaine hydrochloride has been suggested as a means of decreasing the need for postoperative painkillers and NSAIDs and was preferred over lignocaine due to the long-lasting effect of bupivacaine [13-15]. Furthermore, the amide anesthetic aids in relieving the pain post-op after lengthy procedures (often lasting between 8 and 12 hours) and was reported to have a blocking action on nerves in addition to the infiltrative action that was intended to be discovered in this study [16-18]. No research has previously looked into the effects of local bupivacaine injections into the sockets left behind after surgically extracting an impacted mandibular third molar. The purpose of this study was to evaluate whether local bupivacaine injections after impacted mandibular third molar surgery can reduce early postoperative pain.

METHODS

Study design and sample selection

To calculate the sample size, G Power 3.1.9.7 for Windows (Heinrich-Heine University, Dusseldorf, Germany) software was used. A priori sample size calculation was performed using the following parameters: α err prob 0.05, power (1-β err prob) 0.80, and effect size d 0.6. The calculation yielded a total sample size of 72. According to limitation factors (time, the provision of services in the dental center was stopped due to a lack of anesthetic materials), it was decided to include a total of 60 patients. The study initially included 60 patients (1 lost follow-up; 3 were excluded because of a lack of commitment to the prescribed medication). These patients were randomly allocated into two groups. The study was conducted in the Department of Oral and Maxillofacial Surgery, College of Dentistry, University of Baghdad. Additionally, data collection also took place at the Al-Amirya Specialized Dental Center. The study was conducted over a period spanning from December 2022 to May 2023.

Inclusion and exclusion criteria

Inclusion criteria included patients with an indication for extraction of mandibularly impacted molars (totally or partially impacted in the bone). Patients classified as Class I-II and positioned as A-B, according to Pell and Gregory's classification, were included in the study. These patients were medically fit, without any systemic diseases that could potentially affect the surgery. Only patients who expressed willingness to comply with the study requirements and were available for follow-up were included. Patients who had health problems or were under 18 years old, who were pregnant or nursing, who were getting chemotherapy or radiation therapy or had just had it, who had an acute infection at the surgical site at the time of the operation, who had cysts or tumors near the impacted teeth, who had CL III and position C according to the Pell and Gregory classification, and who had taken any kind of painkiller before a surgery were not eligible.

Ethical considerations

This study protocol adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines, and the outcomes will be assessed within the initial 24 hours following the surgical procedure. The study received approval from the Research Ethics Committee at the College of Dentistry, University of Baghdad (Project #768123 on January 19, 2023).

Outcome measurements

A preoperative panoramic radiograph (OPG) or, in certain circumstances, a cone beam computed tomography (CBCT) was done to examine the knocked-out third molar, the essential structures surrounding it, and any concerns that were present. Radiographs were utilized to examine the impacted tooth's direction, position, and depth in respect to the second molar adjacent to it, as well as the creation, shape, number, and pattern of the roots. This was done in accordance with the classifications of Winter, Pell, and Gregory. The patients were subjected to surgical operations done by a single

consultant surgeon while under the effect of local anesthetic provided via injections into the inferior alveolar, lingual, and long buccal nerves. The exact anesthetic used was a 2% lidocaine hydrochloride solution in a 1.8-ml cartridge with a 1:80,000 adrenaline concentration. A No. 15 surgical blade was used to make the incision, and a periosteal elevator was used to reflect the two-sided buccal mucoperiosteal flap. The incision began distolateral to the third molar tooth on the external oblique ridge and continued buccally until it reached the distal side of the first molar, where it joined a vertical incision that extended downwards toward the muco-buccal fold, without involving the papilla between the first and second molars. The bone was removed using a fissure or round bur in a surgical straight hand piece with extensive saline irrigation to expose the cervical line of the lower third molar tooth occlusally, buccally, and distally. For the lower third molar, the impacted tooth was extracted with a straight elevator, Coupland's chisel, Cryer, and/or forceps. If necessary, the tooth was sectioned with a turbine handpiece and fissure burs. Following the evacuation of the impacted tooth, the incision was thoroughly examined to determine the presence of bone pieces, tooth follicles, and/or granulation tissues. The flap was relocated, and the incision edges were sutured with a 3/0 black silk suture and an interrupted suturing technique. After attaining hemostasis, the study group got a 2 ml injection of 0.5% bupivacaine (infiltration) buccally around the socket area. The identical technique was performed on the control group, but with 2 ml of normal saline as a placebo. The wound was covered with a sterile gauze pack, and the patient was instructed to bite on it. The duration of the surgical process was recorded in minutes, spanning the time from the initial incision and the final suture. The sort of drug utilized was unknown to the patient. The Pederson index [19] was used to calculate surgical complexity. A score was assigned to each of the following relationships: spatial relationship, depth, ramus relationship, and accessible space. The score was then calculated in such a way that it corresponded to the following index scores: 3-4 are somewhat challenging, 5-6 are slightly difficult, while 7-10 are quite difficult. Upon their departure, patients were given a survey about patient satisfaction, as well as a paper with a Numerical Rating Scale (NRS). Patients were asked to record their perceived pain levels at four different time intervals following their surgical procedure: four, eight, twelve, and twenty-four hours. Participants were instructed to indicate a number value ranging from 0 to 10 related to their perceived level of pain intensity. A pain rating of 0 signified no pain, while a pain rating of 10 indicated extreme discomfort. After filling out the details as indicated, patients were prompted to send an image of the completed form to the principal author.

Statistical analysis

SPSS software version 26 (SPSS® Inc., Chicago, USA) was used to analyze the data. Continuous data were expressed as mean±standard deviation (SD) and categorical data as count and percentage. For discrete variables, associations between distinct parameters were evaluated using the Mann-Whitney, Chi-square, or Fisher exact tests. For continuous variables, however, an independent sample *t*-test was utilized. A p-value less than 0.05 was judged statistically significant.

RESULTS

The study included 56 patients (18–30 years old) with a mean age of 22.3±3.4 years, consisting of 28 (50%) females and 28 (50%) males. The level of education of patients was between that of undergraduate students and that of those who got their bachelor's degree. They were assigned into two groups: (n = 29) for the study group and (n = 27) for the control group. While comparing the independent variables between the two groups, none of the independent variables acted as a confounding factor for the outcome of interest (pain score) (Table 1).

Table 1: Difference between study and control group regarding clinical characteristics

Variable	Bupivacaine Frequency (%) n=29	Saline Frequency (%) n=27	p-value
Gender			
Male	13(44.8)	7(25.9)	0.140[1]
Female	16(55.2)	20(74.1)	
Technique			
Osteotomy	10(34.5)	14(51.9)	
Elevator	8(27.6)	2(7.4)	0.122[1]
Osteotomy and tooth sectioning	11(37.9)	11(40.7)	
Depth			
A	7(24.1)	4(14.8)	0.380[1]
B	22(75.9)	23(85.2)	
Duration of operation			
Mean±SD	31.9±14.3	32.7±11.9	0.762[2]
Relation with ramus			
Class I	6(20.7)	3(11.1)	0.472[3]
Class II	23(79.3)	24(88.9)	
Winter classification			
Mesio angular	8(27.6)	13(48.1)	
Vertical	12(41.4)	7(25.9)	0.261[3]
Horizontal	9(31)	7(25.9)	
Pederson index			
Slightly difficult	8(27.6)	2(7.4)	
Moderately difficult	13(44.8)	14(51.9)	0.132[1]
Severely difficult	8(27.6)	11(40.7)	

[1]Chi-square test; [2]Independent *t*-test; [3]Fisher's exact test.

There was a highly significant result (p<0.0001) in all of (4, 8, 12, and 24 hours) with a difference in mean pain score between the study and control groups, indicating lower pain scores in the study group (Table 2) (Figure 1).

Table 2: Difference between groups regarding every assessment time point

Variable	Bupivacaine mean±SD	Normal saline mean±SD	*p*-value
NRS 4h	1.3±1.4	3.8±1.2	0.000[1]
NRS 8h	3.3±1.4	6.9±1.5	0.000[1]
NRS 12H	3.2±1.6	6.8±1.5	0.000[2]
NRS 24H	1.2±1.1	3.2±0.9	0.000[1]

[1]Independent t-test; [2]Mann-Whitney test

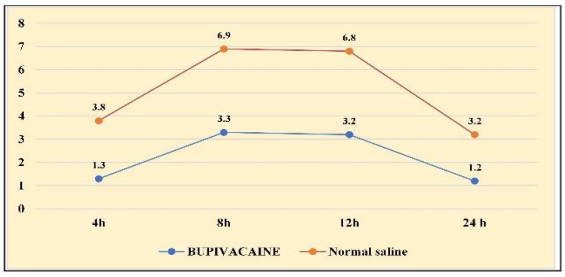

Figure 1: Mean distribution of the participants according to study and control group with subsequent time points.

Relationship of NRS with gender at 4 and 8 hours: the difference was statistically significant with *p*=0.009 and 0.014, respectively, for the study group (Table 3), and *p*=0.013 and 0.028 for the control group, indicating higher scores of pain in females (Table 4). A statistically significant result between the study and control groups indicates increased consumption of analgesics for the control group (71.4%) (Table 5). Neither the study group nor the control group experienced any major difficulties. In particular, none of the patients displayed any symptoms of bupivacaine toxicity, such as cardiovascular abnormalities causing changes in blood pressure or vomiting.

DISCUSSION

This study looks at how well Bupivacaine works as a painkiller when injected locally after the removal of an impacted mandibular third molar. The goal is to reduce the number of painkillers people need to take. In the first 12 hours following third molar surgery, moderate to severe discomfort is typical [20].

Table 3: Relationship of NRS with gender in Bupivacaine group

Variable	NRS 4h	*p*-value	NRS 8h	*p*-value	NRS 12h	*p*-value	NRS 24h	*p*-value
Gender								
Male	0.7±1.5	0.009[1]	0.8±1.4	0.014[2]	0.7±1.7	0.038[1]	1.2±1.3	0.722[2]
Female	2.9±1.3		2.8±1.4		2.6±1.5		1.4±0.9	

[1]Mann-Whitney test; [2]Independent test

Table 4: Relationship of NRS with gender in Normal saline group

Variable	NRS 4h	*p*-value	NRS 8h	*p*-value	NRS 12h	*p*-value	NRS 24h	*p*-value
Gender								
Male	2.8±1.4	0.013[1]	3.6±1.6	0.028[1]	3.8±0.8	0.870[1]	3.5±0.9	0.456[1]
Female	4.9±1.2		5.1±1.5		3.9±1.7		4.2±0.9	

[1]Mann-Whitney test

Table 5: Comparison between the patients who used analgesic

Variable	Bupivacaine Frequency (%) *n*=28	Normal saline Frequency (%) *n*=28	*p*-value
Analgesic use			
Yes	3(10.7)	20(71.4)	0.001[1]
No	25(89.3)	8(28.6)	

[1]Chi-square test

This frequently necessitates the use of oral opioid analgesics for pain management. Since the late 19th century, local injection of an anesthetic agent has been a well-known alternative to the oral administration of drugs for the purpose of producing analgesia. During the first 6–8 hours following oral surgery, pain can be minimized with the help of long-acting local anesthetics. Because of its high lipid solubility and adherence to plasma proteins, bupivacaine provides powerful anesthetic potency and sustained action [21,22]. After a third molar is surgically extracted, patients often experience the most severe pain between 6 and 8 hours postoperatively [10,23]. There was no difference in gender propensity for the occurrence of third molar impaction; the study is in line with other studies [24–27]. The duration mean for surgical operations is 32.3±13.7, which is within the range of Bede's study [28]. In this study, the peak of pain was meticulously documented, occurring precisely 8 hours subsequent to the surgical procedure. The mean pain score during this critical period was calculated to be 5.6±2.1, a value that aligns harmoniously with the findings of previous investigations. These studies, conducted with the utmost care and precision, have consistently demonstrated that the intensity of pain reaches its peak within the initial 8 hours following surgery. This phenomenon can be attributed to a greater production of pain mediators, coupled with a decreasing efficacy of the local anesthetic [29]. According to another study conducted to evaluate the efficacy of bupivacaine while delivering the solution by socket irrigation after completing the surgical operation [30], there was a statistically significant

($p< 0.05$) difference in pain levels between the two groups at 1, 6, 12, and 24 hours after surgery. Both groups experienced a peak in postoperative pain around 12 hours after surgery, with subsequent improvements being statistically significant. The observations of this study are in line with those of previous authors who recognized a significant difference and a lower pain level for the study group at 4, 8, 12, and 24 hours, and are in slight difference with some others [31]. When a piece of absorbable gelatin sponge (AGS) was soaked in 3 mL of 0.5% plain bupivacaine hydrochloride and applied in the post-extraction socket, this study recorded lower pain scores than the control group at 4 hours only, whereas the difference between the two groups at 12 hours after operation wasn't statistically significant. This difference between the results according to time may be caused by a difference in the route of delivery of the bupivacaine solution to the operation field. A statistical difference between the control and study groups indicated more pain perception for the normal saline group, which led to analgesic consumption in most of the patients, while regarding the bupivacaine group, generally there was less pain sensation. Even though no complications appeared in any of the patients, precautions were prepared to be taken in case of any complications, such as those seen in studies that presented with dry socket, postoperative hemorrhage, and wound infection [31,32]. Dry sockets, as an example, were planned to be treated by washing out any food or bacteria particles using saline and applying medicament to the socket [33]. Postoperative hemorrhage, on the other hand, would be treated by applying digital pressure and perhaps even a vasoconstrictor with local anesthetic ability if hemorrhage couldn't be controlled [34]. A wound infection would be treated using Augmentin or Clindamycin [35].

Study limitations

There are some limitations in the study, including the use of the Pederson index, which is a difficult measure and depends on the radiographic data only for difficulty assessment. The operator of the current study assessed the outcome variables without being unaware of the patients' placement in either of the trial's two arms. Additionally, the sample size is higher than 43 patients but still lower than the estimated number according to G power [36].

Conclusion

The analgesic method utilized in this study for third-molar extraction was demonstrated to be reliable and accurate. Gender, side, technique, depth, relationship with the ramus, angulation, time, and difficulty of extraction did not differ significantly between the two groups. There were no serious complications with the local injection of bupivacaine, and it was effective in reducing postoperative pain for up to 24 hours following the surgical extraction of IMTMs.

Conflicts of interest

There are no conflicts of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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