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Original Article

Comparison of the anesthetic effect of bupivacaine and articaine in third molar extractions: a split-mouth randomized controlled trial

Comparação do efeito anestésico da bupivacaína e da articaína em extrações de terceiros molares: um ensaio clínico randomizado e controlado em modelo de boca dividida

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Resumo

Introdução: A extração de terceiros molares é um dos procedimentos cirúrgicos mais executados na odontologia e exige anestesia eficaz para controle adequado da dor. Entre os anestésicos locais utilizados, a articaína e a bupivacaína se destacam por suas diferenças no início de ação, duração e perfil analgésico. Comparar essas substâncias pode contribuir para a escolha do protocolo mais adequado em cirurgias orais. **Objetivo:** Este ensaio clínico randomizado do tipo boca dividida teve como objetivo comparar a eficácia anestésica da bupivacaína e da articaína em exodontias de terceiros molares. **Material e método:** Trinta e dois pacientes foram submetidos à extração dos quatro terceiros molares, após aprovação pelo Comitê de Ética em Pesquisa da Universidade Federal de Uberlândia. Cada paciente recebeu dois agentes anestésicos diferentes: um lado com bupivacaína a 0,5% associada à epinefrina (1:200.000) e o outro lado com articaína a 4% associada à epinefrina (1:100.000). A anestesia foi realizada com a administração de três tubetes por hemi-arco, visando a obtenção de analgesia nos terceiros molares superiores e inferiores. As variáveis analisadas incluíram a necessidade de suplementação anestésica, o tempo de latência e a duração da anestesia, bem como a intensidade da dor avaliada por meio da Escala Visual Analógica (EVA) durante e após o procedimento cirúrgico. **Resultado:** A articaína apresentou início de ação significativamente mais rápido e menor duração anestésica em comparação à bupivacaína ($p < 0,05$). Apesar disso, o número de tubetes suplementares necessários foi semelhante entre os grupos. Os pacientes relataram intensidade de dor pós-operatória significativamente maior no lado anestesiado com bupivacaína ($p < 0,05$). **Conclusão:** Conclui-se que a articaína proporciona início de ação mais rápido e melhor controle da dor intraoperatória, enquanto a bupivacaína oferece um efeito anestésico prolongado no pós-operatório.

Descritores: Anestesia; controle da dor; terceiro molar; bupivacaína; articaína.

Abstract

Introduction: The extraction of third molars is one of the most frequently performed surgical procedures in dentistry and requires effective anesthesia for adequate pain control. Among the local anesthetics used, articaine and bupivacaine stand out for their differences in onset of action, duration, and analgesic profile. Comparing these agents may contribute to selecting the most appropriate protocol for oral surgeries. **Objective:** This split-mouth randomized controlled trial aimed to compare the anesthetic effectiveness of Bupivacaine and Articaine in third molar extraction. **Material and method:** Thirty-two patients underwent extraction of all four third molars after approval by the Research Ethics Committee of the Federal University of Uberlândia. Each patient received two different anesthetic agents: one side with Bupivacaine 0.5% plus epinephrine (1:200,000) and the other with 4% Articaine plus epinephrine (1:100,000). Anesthesia was administered using three cartridges per hemi-arch to achieve analgesia in both upper and lower third molars. Variables analyzed included the need for anesthetic

supplementation, onset and duration of anesthesia, and pain intensity assessed with the Visual Analog Scale (VAS) during and after surgery. **Result:** Articaine showed a significantly faster onset and shorter duration of anesthesia compared to Bupivacaine ($p < 0.05$). Despite this, the number of supplementary anesthetic cartridges required was similar for both groups. Patients reported significantly higher postoperative pain on the side anesthetized with Bupivacaine ($p < 0.05$). **Conclusion:** In conclusion, Articaine provides quicker onset and better intraoperative pain control, while Bupivacaine offers a prolonged postoperative anesthetic effect.

Descriptors: Anesthesia; pain management; third molar; bupivacaine; articaine.

INTRODUCTION

In a considerable portion of the population, the prospect of dental pain or the mere possibility of experiencing discomfort during a visit to the dental professional generates anxiety and fear in the patient, especially regarding procedures involving surgery[1]. One of the most commonly performed surgical procedures in dentistry is third molar extractions. This procedure is indicated due to the non-occurrence or partial occurrence of third molar eruption, which sometimes makes it necessary to remove these teeth, in order to avoid the possibility of complications inherent to their permanence in the oral cavity, such as caries cavities, pulp pathologies, pericoronitis, and odontogenic infections[2].

Adequate pain management during tooth extraction not only provides benefits to the patient, reducing anxiety and improving pain, but also improves working conditions for the dentist[3]. Additionally, as it is a complex procedure, in many cases, techniques such as osteotomy and odontosection are required, which can increase surgical time and demand greater anesthetic supplementation[4]. In this scenario, in-depth investigation of anesthetic solutions is crucial, aiming to determine the most appropriate anesthetic for each specific case[1].

An effective anesthetic need to offer analgesia during surgery, cause minimal discomfort during administration, be safe for the patient, and eliminate the need for high doses[5]. Local anesthetics act by blocking sodium channels in neuronal membranes, inhibiting the generation and conduction of action potentials and, thus, interrupting the transmission of nerve signals responsible for the sensation of pain[6]. The main differences between local anesthetics used in dentistry is in their formulation, concentration, and vasoconstrictor effect, which impact the duration of action[6]. The choice of local anesthetic may depend on the severity of the dental procedure, the anticipated duration of the anesthetic effect, and individual patient characteristics, such as allergies and systemic conditions that contraindicate the use of some anesthetics[7].

Articaine is classified as an amide-type anesthetic and stands out for its remarkable effectiveness in providing rapid and efficient pain relief. Furthermore, articaine has been shown to provide an adequate duration of analgesia for carrying out dental procedures[8]. Its distinctive features include effective diffusion through bone trabeculae, which contributes to the distribution of the anesthetic in the target region[6]. In fact, a previous study demonstrated that articaine had a faster onset of analgesia and required fewer tubes to supplement analgesia when compared to lidocaine in third molar extraction surgeries[9]. Bupivacaine is also classified as an amide-type anesthetic. This anesthetic is characterized by having a more gradual onset of action compared to other anesthetics[10]. Despite this slower onset, bupivacaine stands out for its prolonged duration of analgesia, resulting in a reduction in the need for frequent administration of anesthetics. This feature appears to be particularly beneficial as it offers an extended period of pain relief[10].

When comparing bupivacaine with articaine, it is noted that both demonstrate adequate efficacy for performing surgical procedures, including tooth extractions[11]. However, it is important to highlight that there is a scarcity of records in the literature that perform comprehensive comparisons between bupivacaine and other anesthetics, including articaine[12]. The low number of specific comparative studies may limit the availability of detailed information about the differences and similarities between these anesthetic agents in dental contexts. Therefore, the objective of the current study is to compare the efficiency of anesthesia with 2% bupivacaine associated with epinephrine (1:200,000) and with 4%

articaine associated with epinephrine (1:100,000) in the extraction of upper and lower third molars. The null hypothesis of this clinical experiment is that articaine and bupivacaine will not present differences in the analgesic effect for third molar extraction surgeries.

MATERIAL AND METHOD

Ethical considerations

This study was approved by the Research Ethics Committee of the Federal University of Uberlândia (CAAE: 49164821.0.0000.5152) and previously registered in the Brazilian Clinical Trials Registry (REBEC - U1111-1269-7450; RBR-103g7j28 – Approval date 19/01/2024). The study was conducted in accordance with the precepts of the Declaration of Helsinki. All the patients read, understand and agreed with the study protocol before the inclusion in this study.

Study design

This split-mouth, double-blind, randomized trial followed the CONSORT (Consolidated Standards of Replacing Trails) protocol. The study involved 32 patients from the School of dentistry at the Federal University of Uberlândia (FOUFU, Uberlândia, Brazil) from January 2024 to May 2024. To remove the third molars, the patients were anesthetized with two different types of local anesthetics, one side was anesthetized with bupivacaine/epinephrine (1:200,000) and the other side was anesthetized with articaine/epinephrine (1:100,000) (Figure 1).

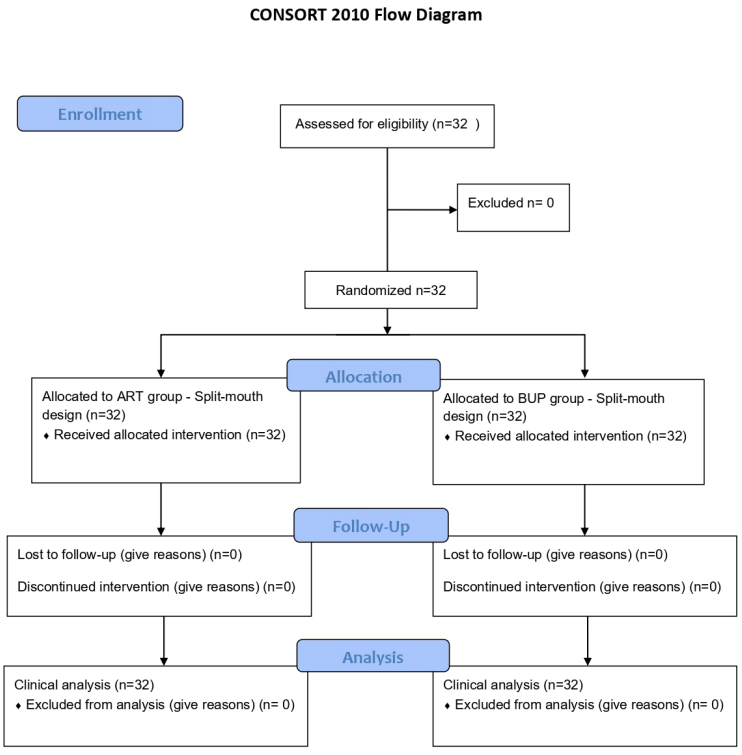

Figure 1. Flow diagram of the study.

Sample size calculation

The primary variable in this study was the painful sensation obtained using the VAS scale. This variable was used to calculate the sample size. To perform this calculation we used as a reference a study that applied the VAS scale to compare the sensation of pain associated with the extraction of upper molars to the previous application of local infiltrative anesthesia with articaine and lidocaine only in the vestibular region. Considering variations on the scale of 0.5 as being significant and predicting a mean standard deviation of 0.85[13] and a split-mouth model, it was determined that a sample size of 30 patients would be sufficient for a β power of 0.80 with type I error fixed at 0.05.

Eligibility criteria

For inclusion in this study, the patients were required to present the following characteristics: 1) Over 18 years of age; 2) Present the four third molars with indication for tooth extraction, and 3) Present good oral hygiene (Plaque index < 20%)

Exclusion criteria involved the following characteristics: 1) Patients with periodontal disease; 2) Patients with systemic diseases or conditions or users of medications that alter the inflammatory response; 3) Pregnant or lactating women; 4) Heavy smokers (more than 10 cigarettes daily); 5) Presence of periapical lesions or presence of acute pericoronitis lesions in teeth indicated for extraction.

Surgical procedure and study groups

A clinical and panoramic radiographic examination was performed on all patients during the screening. The third molars were classified according to the Pell & Gregory and Winter classification. The following maneuvers were performed sequentially at the time of the surgical procedure: Extraoral and intraoral asepsis with 2% and 0.12% Chlorhexidine Digluconate, respectively; placement of sterilized fields; and, subsequently, anesthesia in the region of the upper and lower third molars with bupivacaine with epinephrine (1:200,000), or 4% articaine with epinephrine (1:100,000) (DAP and MSB). The side on which each anesthetic solution was applied was allocated randomly by applying a randomization table (random.org) (GJO). The evaluators and patients were unaware of the type of anesthetic that was used at each site.

Preoperative care consisted of the administration of dexamethasone (8 mg) in a single dose one hour before the surgical procedure. In the postoperative phase, diclofenac sodium (50 mg) was prescribed for 3 days every 8 hours, and dipyrone sodium (500mg) for 3 days every 6 hours, all prescribed orally. Additionally, a mouthwash based on 0.12% chlorhexidine digluconate was prescribed for 7 days every 12 hours. The sutures were removed after 7 days.

Analysis of the anesthesia procedure

Anesthesia was performed with 3 anesthetic tubes per hemi-arch, aiming at the upper and lower third molars. Each tube had a volume of 1.8ml. Subsequently, the number of tubes used for anesthetic supplementation, the time of the beginning and end of anesthesia, as well as reports of pain during and after surgery using the VAS scale were recorded. The effect of analgesia was evaluated when the patient reported changes in the sensitivity of the lower lip and by applying pressure to the buccal and palatal region of the upper third molar. When the patient reported discomfort when handling the area to be operated on, anesthetic supplementation was indicated. The analysis were performed by blinded evaluators (SSS and PGJM)

Statistical analysis

GraphPad Prism 8.4 software (San Diego, CA, USA) was used to perform the statistical analysis. The normal distribution of the numerical data in this study was demonstrated using the Shapiro-Wilk normality test. The comparison of data obtained with the application of bupivacaine and articaine was performed using the paired t-test. All statistical tests used in this study were applied at a significance level of 5%.

RESULT

There was no difference between the groups in relation to the complexity of the position in which the teeth were located before the procedure (Tables 1, 2). The average surgery time was 62.08 ± 15.04 minutes.

Table 1. Distribution of tooth position according to Winter's classification (Winter)[14]

Groups	Bupivacaine		Articaine	
Position/Locations	Upper	Lower	Upper	Lower
Vertical	27	20	27	17
Mesio-angulated	1	7	2	7
Disto-angulated	4	2	3	2
Horizontal		3	-	6
Total	32	32	32	32

Table 2. Distribution of tooth position according to Pell & Gregory classification (Pell, Gregory)[15]

Position/Group	Bupivacaine		Articaine	
	Upper	Lower	Upper	Lower
A	22	21	21	18
B	2	10	3	14
C	8	1	8	0
Total	32	32	32	32

It was found that the sides anesthetized with articaine had a shorter time to the start of analgesia than the sides anesthetized with bupivacaine ($p < 0.05$), as well as a shorter time to the end of analgesia ($p < 0.01$). However, the number of tubes applied to supplement analgesia was similar between the two groups. Patients reported greater painful discomfort on the sides that were anesthetized with bupivacaine ($p<0.05$). No complications were observed, such as paresthesia or toxicity reactions, associated with the use of the anesthetic solutions tested. The mean and standard deviation data from clinical analyses related to the use of anesthetics in third molar extraction surgeries are shown in Table 3.

Table 3. Mean and standard deviation values of clinical data related to the use of anesthetics in third molar. extraction surgeries

Parameter	Bupivacaine	Articaine
Number of tubes used (n)	3	3
Anesthetic supplementation (n)	1.68 ± 1.30	1.31 ± 1.37
Analgesia onset time (s)	190.2 ± 50.77*	136.5 ± 68.12
Analgesia end time (m)	555.4 ± 356.2*	339.1 ± 253.0
VAS Scale	2.53 ± 2.42*	1.56 ± 2.35

*p<0.05 – Higher time values for the onset of analgesia, end of analgesia, and pain sensation compared to the articaine group – Paired t-test.

DISCUSSION

The results of the current study demonstrated that the side anesthetized with articaine had a shorter time to onset of analgesia when compared to the side anesthetized with bupivacaine. Another important finding is that the number of tubes needed for anesthetic supplementation was similar between the two solutions, and there were no complications (paresthesia or toxicity reactions) in the two comparative groups. The discomfort felt by patients during the application of bupivacaine anesthesia was greater, however, patients noted a longer period of analgesia sensation compared to the side anesthetized with articaine. Therefore, based on the results of this study, the null hypothesis was rejected.

The shorter time for the onset of the sensation of analgesia promoted by articaine observed in this study was also noted in previous studies. Pellicer-Chover et al.[16], demonstrated that the application of articaine was related to a shorter time for the onset of analgesia sensation compared to bupivacaine in lower third molar extraction surgeries. On the other hand, in Sancho-Puchades et al.[17], it was observed that the beginning of the sensation of analgesia between bupivacaine and articaine in lower third molar extraction surgeries was similar, however, measurements for this outcome were started 10 minutes after the application of the anesthetic solution, which may explain the differences between the findings of that study and those presented in the current study. It is also worth noting that the present study evaluated the joint extraction of upper and lower molars, which may also have interfered with the findings, since this fact is associated with the greater amount of anesthetic used. The high capacity for diffusion and distribution through bone trabeculae, due to its high lipid solubility and pKa closer to the blood pH, facilitates the penetration of articaine into nerve fibers in the target region, and may justify its earlier effect in promoting analgesia compared to bupivacaine[18].

Bupivacaine had a longer duration of anesthetic effect and postoperative analgesia, which has been previously described. A clinical study observed that the side anesthetized with bupivacaine presented a more effective reduction in postoperative pain, while in the side anesthetized with articaine the sensation of analgesia ended more quickly[11]. The reason for this effect has been related to bupivacaine's ability to promote protein binding with high affinity and a pKa that is more distant in relation to plasma pH[17]. The high diffusion of articaine through tissues may be the reason for the faster metabolism of this anesthetic[19,20]. Despite these findings, the increase in analgesia time in controlling postoperative pain seems to have a less significant impact than the reduction in time to obtain analgesia and the comfort during surgery provided by articaine, as verified in the current study, since patients reported higher levels of pain on the side anesthetized with bupivacaine.

The findings of the current study demonstrate that it is necessary to consider the use of both solutions in third molar extraction procedures. It can be assumed that due to bupivacaine's longer duration of action, it would be indicated for longer surgical procedures, such as extractions of teeth with a horizontal position and impacted, or requiring osteotomy and odontosection. However, although not statistically significant, bupivacaine required greater anesthetic supplementation than articaine in this study. The cardiotoxic effects of bupivacaine in large anesthetic doses must be taken into account[21], as well as that bupivacaine supplementation may be unsafe for patients with heart disease[22]. Another issue is that the long-term effect of bupivacaine on children and older adults can cause these patients to experience self-inflicted trauma to the oral cavity, arising from bites due to the difficulty these patients have in identifying the analgesic effect[19]. In short-term procedures, such as endodontic treatments, restorative procedures, and extraction of third molars in non-challenging positions, it does not seem necessary to use an anesthetic with a long duration, so articaine may be sufficient to promote analgesia throughout the clinical procedure in these situations.

Some factors may have interfered with the results of this study and must be taken into consideration when analyzing the data presented herein. All patients received dexamethasone

8mg preoperatively, and this anti-inflammatory may have helped to enhance the effect of the anesthetics. An et al.[23], showed in a laboratory study that dexamethasone prolonged the duration of sensory and motor blockade of the sciatic nerve, but also prevented the reversible neurotoxicity of bupivacaine. Rodrigues et al.[24], in a randomized clinical study, found that the use of dexamethasone or diclofenac potassium associated with 4% articaine (epinephrine 1:200,000) was favorable in increasing the success rate of inferior alveolar nerve block in cases of molars with irreversible symptomatic pulpitis, and reduced the occurrence of postoperative pain when compared to the use of placebo. The current study was conducted in a split-mouth model, and thus, the effect of dexamethasone on the effects of the anesthetics used occurred similarly between the groups. However, this model also creates difficulty in determining the values of the VAS scale for patients, which can generate confusion in the assessment. Another important factor is that the surgeries were conducted by experienced surgeons who perform these procedures more conservatively and, in less time, than dentists who do not have experience in this type of procedure.

It can be concluded that articaine achieves the anesthetic effect more quickly than bupivacaine, as well as providing better pain control during the surgical procedure. However, bupivacaine maintains the anesthetic effect for longer after the surgical procedure.

AUTHORS' CONTRIBUTIONS

Guilherme José Pimentel Lopes de Oliveira, Davisson Alves Pereira, Mariana da Silva Bonatto: Study design and concept.

Samara de Souza Santos, Pedro Gomes Junqueira Mendes, Gustavo Barcellos Lima, Davisson Alves Pereira, Mariana da Silva Bonatto: Methodology. Samara de Souza Santos, Pedro Gomes Junqueira Mendes, Gustavo Barcellos Lima: Data obtention. Guilherme José Pimentel Lopes de Oliveira: Data curation. Samara de Souza Santos, Davisson Alves Pereira, Guilherme José Pimentel Lopes de Oliveira: Writing of the paper. Guilherme José Pimentel Lopes de Oliveira: Approval of the final version: all the authors; Project supervision. All authors read and approved the final version of the manuscript.

REFERENCES

1. Gülnahar Y, Alpan AL, Gülnahar E. Articaine versus lidocaine inferior alveolar nerve block in posterior mandible implant surgeries: a randomized controlled trial. Med Oral Patol Oral Cir Bucal. 2023 Mar;28(2):e108-15. http://doi.org/10.4317/medoral.25475. PMid:36806026.

2. Zaman MU, Almutairi NS, Abdulrahman Alnashwan M, Albogami SM, Alkhammash NM, Alam MK. Pattern of mandibular third molar impaction in nonsyndromic 17760 patients: a retrospective study among saudi population in central region, Saudi Arabia. BioMed Res Int. 2021 Aug;1:1880750. http://doi.org/10.1155/2021/1880750. PMid:34493976.

3. Sawadogo A, Coulibaly M, Quilodran C, Bationo R, Konsem T, Ella B. Success rate of first attempt 4% articaine para-apical anesthesia for the extraction of mandibular wisdom teeth. J Stomatol Oral Maxillofac Surg. 2018 Dec;119(6):486-8. http://doi.org/10.1016/j.jormas.2018.06.005. PMid:29936238.

4. Gay-Escoda C, Sánchez-Torres A, Borrás-Ferreres J, Valmaseda-Castellón E. Third molar surgical difficulty scales: systematic review and preoperative assessment form. Med Oral Patol Oral Cir Bucal. 2022 Jan;27(1):e68-76. http://doi.org/10.4317/medoral.24951. PMid:34874928.

5. Bataineh AB, Nusair YM, Al-Rahahleh RQ. Comparative study of articaine and lidocaine without palatal injection for maxillary teeth extraction. Clin Oral Investig. 2019 Aug;23(8):3239-48. http://doi.org/10.1007/s00784-018-2738-x. PMid:30417227.

6. Amorim KS, Fontes VTS, Gercina AC, Groppo FC, Souza LMA. Buffered 2% articaine versus non-buffered 4% articaine in maxillary infiltration: randomized clinical trial. Clin Oral Investig. 2021 Jun;25(6):3527-33. http://doi.org/10.1007/s00784-020-03674-x. PMid:33151422.

7. Yamashita IC, Yamashita FC, Yamashita AL, Guimarães JC, Peixoto IF, Bispo CGC. Observational study of adverse reactions related to articaine and lidocaine. Oral Maxillofac Surg. 2020 Sep;24(3):327-32. http://doi.org/10.1007/s10006-020-00866-3. PMid:32524211.

8. Santos-Sanz L, Toledano-Serrabona J, Gay-Escoda C. Safety and efficacy of 4% articaine in mandibular third-molar extraction: a systematic review and meta-analysis of randomized clinical trials. J Am Dent Assoc. 2020 Dec;151(12):912-923.e10. http://doi.org/10.1016/j.adaj.2020.08.016. PMid:33228884.

9. de Souza Santos S, Bonatto MS, Mendes PGJ, Martins AVB, Pereira DA, de Oliveira GJPL. Efficacy of analgesia promoted by lidocaine and articaine in third molar extraction surgery. A split-mouth, randomized, controlled trial. Oral Maxillofac Surg. 2024 Jun;28(2):919-24. http://doi.org/10.1007/s10006-024-01223-4. PMid:38355872.

10. Bhattarai BP, Bijukchhe SM, Reduwan NH. Anesthetic and analgesic efficacy of bupivacaine in mandibular third molar surgery: a systematic review and meta-analysis. Quintessence Int. 2020;51(7):586-97. http://doi.org/10.3290/j.qi.a44633. PMid:32500866.

11. Tokuç B, Coşkunses FM. Comparison of the effects of articaine and bupivacaine in impacted mandibular third molar tooth surgery: a randomized, controlled trial. J Dent Anesth Pain Med. 2021 Dec;21(6):575-82. http://doi.org/10.17245/jdapm.2021.21.6.575. PMid:34909475.

12. Rossi MT, de Oliveira MN, Vidigal MTC, de Andrade Vieira W, Figueiredo CE, Blumenberg C, et al. Effectiveness of anesthetic solutions for pain control in lower third molar extraction surgeries: a systematic review of randomized clinical trials with network meta-analysis. Clin Oral Investig. 2021 Jan;25(1):1-22. http://doi.org/10.1007/s00784-020-03675-w. PMid:33161499.

13. Majid OW, Ahmed AM. The anesthetic efficacy of articaine and lidocaine in equivalent doses as buccal and non-palatal infiltration for maxillary molar extraction: a randomized, double-blinded, placebo-controlled clinical trial. J Oral Maxillofac Surg. 2018 Apr;76(4):737-43. http://doi.org/10.1016/j.joms.2017.11.028. PMid:29257943.

14. Winter G. *Impacted mandibular third molar*. St. Louis: American Medical Book Co.; 1926.

15. Pell G, Gregory B. Impacted third molars: classification and modified techniques for removal. Dent Dig. 1933;39:330.

16. Pellicer-Chover H, Cervera-Ballester J, Sanchis-Bielsa JM, Peñarrocha-Diago MA, Peñarrocha-Diago M, García-Mira B. Comparative split-mouth study of the anesthetic efficacy of 4% articaine versus 0.5% bupivacaine in impacted mandibular third molar extraction. J Clin Exp Dent. 2013 Apr;5(2):e66-71. http://doi.org/10.4317/jced.50869. PMid:24455059.

17. Sancho-Puchades M, Vílchez-Pérez MÁ, Valmaseda-Castellón E, Paredes-García J, Berini-Aytés L, Gay-Escoda C. Bupivacaine 0.5% versus articaine 4% for the removal of lower third molars. A crossover randomized controlled trial. Med Oral Patol Oral Cir Bucal. 2012 May;17(3):e462-8. http://doi.org/10.4317/medoral.17628. PMid:22143739.

18. Skjevik AA, Haug BE, Lygre H, Teigen K. Intramolecular hydrogen bonding in articaine can be related to superior bone tissue penetration: a molecular dynamics study. Biophys Chem. 2011 Feb;154(1):18-25. http://doi.org/10.1016/j.bpc.2010.12.002. PMid:21227568.

19. Thakare A, Bhate K, Kathariya R. Comparison of 4% articaine and 0.5% bupivacaine anesthetic efficacy in orthodontic extractions: prospective, randomized crossover study. Acta Anaesthesiol Taiwan. 2014 Jun;52(2):59-63. http://doi.org/10.1016/j.aat.2014.04.006. PMid:25016509.

20. Chandrasekaran D, Chinnaswami R, Shanthi K, Dhiravia Sargunam AE, Kumar KS, Satheesh T. A prospective study to assess the efficacy of 4% articaine, 0.5% bupivacaine and 2% lignocaine using a single buccal supraperiosteal injection for maxillary tooth extraction. J Pharm Bioallied Sci. 2021 Jun;13(Suppl 1):S721-4. http://doi.org/10.4103/jpbs.JPBS_659_20. PMid:34447189.

21. Cox B, Durieux ME, Marcus MA. Toxicity of local anaesthetics. Best Pract Res Clin Anaesthesiol. 2003 Mar;17(1):111-36. http://doi.org/10.1053/bean.2003.0275. PMid:12751552.

22. Wilson IH, Richmond MN, Strike PW. Regional analgesia with bupivacaine in dental anaesthesia. Br J Anaesth. 1986 Apr;58(4):401-5. http://doi.org/10.1093/bja/58.4.401. PMid:2420347.

23. An K, Elkassabany NM, Liu J. Dexamethasone as adjuvant to bupivacaine prolongs the duration of thermal antinociception and prevents bupivacaine-induced rebound hyperalgesia via regional mechanism in a mouse sciatic nerve block model. PLoS One. 2015 Apr;10(4):e0123459. http://doi.org/10.1371/journal.pone.0123459. PMid:25856078.

24. Rodrigues GA, Hizatugu R, Bronzato JD, de-Jesus-Soares A, Frozoni M. Effect of preemptive use of a nonsteroidal anti-inflammatory drug and a corticosteroid on the efficacy of inferior alveolar nerve blockade and postoperative pain control in endodontic treatment of molars with symptomatic pulpitis: a randomized double-blind placebo-controlled clinical trial. Int Endod J. 2024 May;57(5):520-32. http://doi.org/10.1111/iej.14030. PMid:38279778.

CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

DATA AVAILABILITY

The data will be open access in the UFU - Universidade Federal de Uberlândia repository after Samara De Souza Santos' master's thesis defense.

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