Comparative study of the anaesthetic efficacy of 4% articaine versus 2% mepivacaine in mandibular third molar germectomy using different anaesthetic techniques: a split-mouth clinical trial.

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ABSTRACT

Aim: To compare the clinical efficacy of local anaesthetics with articaine 4% or mepivacaine 2% (both with epinephrine 1:100.000) using different anaesthetic techniques to perform germectomy of lower third molars and to assess patients' feelings and pain during surgery.

Methods: 50 patients (ranged 11-16 years) who required germectomy of mandibular third molars were recruited. Each patient received local anaesthesia on one side with articaine inoculated with plexus technique while on the other side with mepivacaine using inferior alveolar nerve block technique. The patients' evaluation was performed on pre and intraoperative tactile-pressure feelings and intraoperative pain with four levels on the analogic visual scale (VAS).

Results: Surgical operations lasted less with more efficient analgesia when articaine was used. The additional intraosseous injection was required mainly in the mepivacaine group intraoperatively. A few patients had tactile-pressure feelings while intraoperative pain sensation was absent in 90% of cases with articaine. Significant differences were found in the cases who reported "absent" and "moderate" VAS values, favoring the use of articaine.

Conclusion: Articaine injected with a plexus anaesthetic technique seems to be more clinically manageable than mepivacaine for the mandibular third molar germectomy. The discomfort of tactile-pressure feelings and pain experienced was lower using articaine anaesthetic technique used.

KEYWORDS

Local Anaesthetic, Articaine, Mepivacaine, Third Mandibular Molar, Germectomy

INTRODUCTION

The surgical extraction of a tooth that exhibits at least a third of its root in formation, with a periodontal ligament discernible on panoramic x-ray, is defined as germectomy. Early germectomy is a useful intervention to avoid several problematics caused by lower third molar retention and

impaction, and it is often required before or after orthodontic treatment [1-4]. This surgical technique would also allow to avoid complications, such as inferior alveolar and lingual nerve damage [3-6].

The control of the patient's pain and anxiety by using efficient anxiolytics and local anaesthesia is essential in oral surgery [7]. These aspects become important in adolescents, above all in the case of third molar germectomy [8]. Local anaesthetic (LA) injection is often the only painful part of the dental procedure, and the fear associated with this technique is the main reason that leads patients to avoid dental treatment [9]. A study by Kaufman [10] assessed and compared the pain, pressure and discomfort induced by four intraoral LA injection techniques. The results indicated that the inferior alveolar nerve block (IANB) is the most painful while the local infiltration is the least painful probably because the submucosa area has fewer number of free nerve endings compared to the oral mucosa and the periodontium. Among the possible ways to minimize the discomfort perceived at the time of injection, the distensibility of the tissues through short tremors (trembling) of the mucous membrane to be stung can be used [11].

During the execution of these surgical procedures, anaesthesia of the structures innervated by the mandibular nerve is necessary, and many local anaesthetic techniques are described in the literature [12]. Generally, infiltration plexus technique is usually performed for maxillary procedures while IANB is used for molar mandibular sites with 2% local anaesthetics [4-8]. Failure rates for IANB are high, sometimes reaching 80% for the lower incisors with this technique, and numerous approaches for the implementation of a new technique of IANB have been described [13]. Among them, the articaine 4% already has been successfully used to achieve local anesthesia [14-17] and facial infiltration anaesthetic technique in the mandible showed efficacy with encouraging result that can be overlapped to the IANB technique [13]. Articaine (4-methyl-3-[2-(propylamino)-propionamido]-2-thiophene-carboxylic acid, methyl ester hydrochloride) contains a thiophene ring instead of benzene and an ester group. The thiophene ring allows for higher lipid solubility so a greater portion of an administered dose can enter in neurons. Gazal et al. [17] found that a

combination of nerve block anaesthesia, buccal infiltration and intra-ligamentary injection resulted in more profound anaesthesia (P =0.003) and higher success rates compared to IANB alone in mandibular first molar pulp anaesthesia. Other studies reported the use of articaine in implantology interventions in which it was used with subperiosteal technique on the buccal and vestibular sides [18].

Thus, the literature showed several conflicting results on the mandibular facial plexus infiltration technique used with different anesthetics [6,8,14].

Recent studies of this anaesthetic technique found that 1.8 cc of 4% articaine facial infiltration in the mandible can be effective when the thickness of mandibular facial cortex is < 2.0-3.0 mm, with 5-10 minutes needed for the adequate anaesthesia, and often an additional 1.8 cc of the dose was required to obtain anaesthesia in adult patients [13-15].

It was reported that many dental procedures on deciduous molars could be accomplished with infiltration of articaine alone in the pediatric population [19].

As above mentioned, the difficulty in achieving reliable anaesthesia in the third mandibular molars in adults with facial infiltration of local anaesthetic is related to the thickness of the cortical bone and inability to achieve consistently inferior alveolar nerve [12]. An ideal local anaesthetic should have the following characteristics: a) short latency time; b) strength of the intense effect; c) duration of prolonged action; d) lack of harmful local and systemic effects [19-20].

Currently, mepivacaine is among the most used and studied anaesthetics in dentistry [17]; however, articaine is nowadays increasingly used for its manageability, lack of side effects and high anaesthetic potency [13,21,22]. Mepivacaine is an amide-type anaesthetic with fast action from the beginning and 30-120 minutes duration. Its maximum allowed dose is 300 mg with epinephrine or 500 mg alone. The dose for children is 4-6 mg/kg/dose (maximum: 270 mg) without epinephrine [19].

Articaine, due to its chemical characteristics, is quickly soluble and rapidly released from adipose/lipid tissue. The ester side chain of articaine is hydrolyzed by plasmaesterases rendering

the molecule inactive. Evidence suggests that it is the local anaesthetic that best spreads within soft and hard tissues [23]. Then, it has a non-conducive effect on extended operations having a shorter half-life of 25 minutes compared to approximately 90 minutes of other amides (115 minutes for mepivacaine) that require hepatic clearance [24]. Accordingly, it was suggested that articaine does not own any relevant side effects or systemic toxicities [25].

For this reason, articaine has been used at higher concentrations (4%), associated with epinephrine, compared to other local dental anesthetics [26]. This higher concentration ensures an excellent spread both in hard and soft tissues, also promoted by a pKa (7,8) very similar to the physiological pH of tissues. Its great liposolubility allows a rapid diffusion in adipose tissue (spread coefficient = 17,0) and involves a lower adherence to the nerve membranes and, above all, lower toxicity for the tissues. Moreover, articaine has a high protein-based bond (94%) which allows a better affinity for the protein-based membrane receptors, and it is a direct sign of its increased anaesthetic potency [19,27-29].

Dental local anaesthetics are often combined with vasoconstrictors, such as epinephrine, to increase the depth and duration of analgesia [24,29]. Clinical experiments, in which articaine without vasoconstrictor was used, did not show any satisfying results [30], whereas the use of articaine combined with low concentrations of vasoconstrictors produced better anaesthetic effects than other common local anaesthetics such as bupivacaine [31] and mepivacaine [32]. It is well documented that vasoconstrictors have a safety range [33] if used at low doses, and not directly injected in the blood vessels, even in particular care patients [34,35].

The present study aimed to compare the clinical efficacy of articaine 4% (epinephrine 1:100.000) versus mepivacaine 2% (epinephrine 1:100.000) for the surgical germectomy of mandibular third molars with two different conventional anaesthetic techniques in young patients whom jawbone is not completely mineralized yet and more penetrable by the articaine molecule.

MATERIALS AND METHODS

This observational prospective split-mouth clinical trial was performed at the Oral Surgery of the University of Campania "Luigi Vanvitelli". Fifty patients, aged between 11 and 16 years old, requiring bilateral germectomy of mandibular third molars before orthodontic treatment, after evaluating their panoramic x-ray, were consecutively recruited between June 2018 and October 2019 (Table 1). The subjects were children undergoing orthodontic treatment in whom early extraction was indicated to facilitate their treatment in some specific conditions (i.e. posterior crowding, altered second molar eruption, non-extraction approach) [1,2]. Thus, patients were checked for the fulfilment of inclusion criteria through medical history collection and clinical examinations, then routine blood tests were made before intervention. All included patient's parents gave informed written consent after providing them with detailed information and the guidelines approved by the Ethics Committee of the University of Campania "Luigi Vanvitelli" (Prot. number 6251) were followed in this investigation. At the preliminary visit, a good explication on the surgical procedures was provide to encourage the compliance of young patients and their parents.

Exclusion criteria were patients presenting systemic and oral diseases, overweight, and allergy to the drugs and substances used during the surgical intervention. If the anaesthesia was not adequate with one of the two techniques, or if the patient, already included in the study, presented an excessive anxiety state, the patient was also excluded from the analysis.

Germectomy, defined as the removal of an impacted tooth with at least a third of its root information with a periodontal ligament discernible on panoramic x-ray, was the surgical operation planned in the present study.

The type of local anaesthesia (solution containing mepivacaine 2% with 1:100.000 epinephrine or solution containing articaine 4% with 1:100.000 epinephrine) and the related technique to be used on the right or left side were randomly selected using a computerized randomization program before starting the protocol. In Table 2 are shown the pharmacokinetic parameters of the two anaesthetics.

For each subject, the first germectomy was scheduled 15 days apart. The same senior operator, assisted by the same practitioner, completed all the surgical procedures. All interventions made with mepivacaine were performed with the same anaesthetic technique routinely used in Oral surgery (IANB). The technique was complemented with anaesthesia of the buccal nerve, as routine for this technique, administering another 1.8 ml of the same anaesthetic used in each intervention. On the other hand, the surgical procedures in articaine cases were made practising a plexus technique, performing a deep buccal injection distally to the second mandibular molar.

At the first intervention, patients received mepivacaine 2% with 1:100.000 epinephrine or articaine 4% with 1:100.000 epinephrine. In the articaine group, an alternative procedure was applied to perform a plexus technique on the buccal side distal to the second mandibular molar region. Two injections of articaine were performed. Firstly, equivalent to one-quarter of the cartridge was injected in the buccal fornix in the sovraperiosteal area of the lower third molar. It was asked to practice a trembling manoeuvre to prevent patients from perceiving the discomfort of the first puncture, avoiding the pain by the next injection in the deeper tissues. Secondly, it was used the rest of the cartridge, approximately after three minutes deeper in the subperiosteal area at the same point with direct contact to the mandibular cortical bone. It was not necessary to provide an additional injection of anaesthetic to obtain lingually anaesthesia in the articaine groups. During the surgical procedures, an additional injection of anaesthesia was requested mainly in the mepivacaine group.

Once performed the injections, patients were asked to notice on a visual analogue scale (VAS) [7], how much discomfort they felt due to the anaesthetic injections. Moreover, patients were asked to notice, after 6-8 minutes from the injection, the tactile and pressure feelings on the same VAS scale. These perceptions were stimulated using a periodontal probe applied distal to gingiva of the second mandibular molar on the same side of the intervention. The same pressure and tactile tests were repeated intraoperatively directly on the exposed bone using the same method. Finally, a mucoperiosteal flap was lifted, without vertical releasing incisions were not required, followed by

germectomy of the third mandibular molar.

At the end of each surgical operation, patients were asked to notice intra-operative pain on another visual analogue scale (VAS) with four different levels of pain: absent (0), mild (1), moderate (2), high (3) [7]. All interventions were performed with the same surgical technique and completed with satisfactory results without any intra-operative and post-operative complications. All patients were discharged after nearly 2 hours from the end of the intervention giving home instructions, and antibiotic and anti-inflammatory medical coverage. The suture applied at the end of surgery was removed seven days after surgery. Student t-test statistical analyses were performed to compare the VAS results.

RESULTS

In the mepivacaine group, the mean time between injection and full anaesthetic effect ranged between about 7 minutes. In 40 patients (82%) additional intraosseous injection (Table 3) (0.5 ml, 45% of one cartridge) was requested intraoperatively on the bone, limited to the duration of the intervention on the bone. The average time of surgical procedures was 25 minutes, with a minimum of 20 minutes and a maximum of 30 minutes.

In the articaine group, it took about 4 minutes to achieve full anaesthesia after the second inoculation. In 21 cases (mild/moderate pain), additional intraosseous injections were needed (42%): it was practiced because patients asked for maximum comfort (0.2 ml). The average time of the operations was approximately 20 minutes, with a minimum of 15 and a maximum of 25 (Table 3).

After 6-8 minutes from IANB anaesthesia/buccal nerve block and plexus technique, tactile-pressure feelings were recorded, as in a previous study [25]: in the mepivacaine group no patients experienced severe tactile-pressure feelings, but 40% had them in other categories, whereas in the articaine group, 70% of patients did not experience any tactile-pressure feelings (Tables 4, 5).

About the intraoperative tactile-pressure feelings, in the mepivacaine group in 60% of cases a

moderate/severe solicitation was experienced, mild in 16% of cases and absent only in 24% of interventions; in the articaine group, tactile-pressure feelings were absent in almost all interventions (43 cases) (Tables 4, 5).

According to VAS during intraoperative pain sensation, the results were more homogeneous in the articaine group than in the mepivacaine one: in the articaine group, it was absent in 90% of cases (Tables 4, 5).

One of the most exciting aspects was that the youngest patients of our sample (11-13 years old, 50%) reported the best comfortable feelings, either post-operative.

The results of patients' feelings and pain after the use of the two different anaesthetics present statistically significant differences ($P < 0.05$) in the cases that were reported "absent" and "moderate" VAS values, favoring the use of articaine (Table 6).

Additionally, patients who received supplementary articaine injections verbally reported that the sufficient anaesthetic period was prolonged for approximately 2-3 hours. All patients experienced a high degree of discomfort with intraoral IANB due to the anaesthetic injection puncture performed through the internal pterygoid muscle. Conversely, as expected, the buccal plexus anaesthesia realized with the technique of the two subsequent injections of progressive depth did not leave in the patients any memory of discomfort injection.

DISCUSSION

Our preliminary results showed how it could be possible to avoid the painful and unpleasant sensation due to the traditional IANB technique injection through the internal pterygoid muscle taking advantage of the plexus technique allowed by the use of articaine. Moreover, this plexus technique avoids the need for a double injection that is performed typically in IANB technique, when a supplementary puncture is requested to block the buccal nerve and often on the lingual side. Lastly, no additional injection of anaesthetic was needed to obtain lingual anaesthesia in the articaine cases.

In our opinion, these data are clinically crucial for all patients, particularly for the younger and for all those patients that never experienced any dental treatment before, often generating the well-known "odontophobia". These shreds of evidence could lead to reducing the number of patients requiring dental care under general anaesthesia with less risk of damage to their health, the chance of unpleasant anaesthetic complications, respecting the cost-containment social. In addition, trismus and nonsurgical paresthesia, as results of damage caused by the needle to the inferior alveolar and lingual nerves, could be avoided.

The faster activation of drugs could explain the difference in latency time between articaine and mepivacaine that we experienced in our study with lower pKa and by the strong aptitude of articaine in bonding proteins, especially those of nervous tissue [19].

Moreover, these peculiarities promote deep anaesthesia that makes more comfortable performing the surgical germectomy of third mandibular molars, favoring more tranquility and collaboration from young patients: this can be related to shorter interventions (15-25 minutes) compared to mepivacaine (20-30 minutes). On the other hand, patients who received supplementary articaine intraosseous injections reported that the sufficient anaesthetic period was prolonged for approximately 3-4 hours, agreeing with results retrieved in literature [35,36]. Moreover, in our study it was never necessary to practice the IANB in the articaine group before starting the surgical procedures.

These data, combined with the lack of need for additional anaesthesia, represent an unquestionable benefit for using articaine as this reduced the waiting time between one patient and another and the psychological stress for patients undergoing surgical interventions, also avoiding the lower lip anesthesia [25].

Our choice of articaine instead of mepivacaine is widely supported in the literature, whereas the choice of a buccal plexus injection is justified by other experiences that confirmed the anaesthetic effect in case of pulpitis [37,38]. Borchard [39] believes that a local anaesthetic at the concentration of 4% is more long-lasting and has a higher effect than a concentration of 2%, denying the

hypothesis of a higher toxicity. Dudkiewicz [40] reported that, in the mandible, articaine HCl owns a partition coefficient higher than lidocaine (123.0 versus 10.0) that provides the physiochemical evidence to support the contention of better penetration and diffusion of articaine HCl. Significant differences were detected in time of onset and duration of action. The onset described in literature [41] as well as the anaesthetic duration of 4% articaine with 1:100.000 epinephrine is per our results. Articaine affinity for the membrane receptors of nerve cells is confirmed by anatomical studies on the trigeminal nerve and its selective block, which reported how the anaesthetic diffusion is related to the different diameters of different nervous fibres [42]. First fibres to be blocked are C-ones with the related lifting of the thermal sensitivity and burning pain, then A-□ fibres with loss of the cold+ sensitivity and stinging pain. At last, also A-□ fibres, that have the largest diameter, are blocked, losing tactile-pressure feelings [21,23,29].

Hence, after combining our results with the literature data on the physiology of the trigeminal nerve, it is possible to state the efficacy and depth of articaine in its selective and complete block action of nervous fibres, which resulted in being higher than with mepivacaine [43].

Authors of a recent systematic review with meta-analysis investigated and compared the efficacy and safety of articaine with lidocaine [44]. They found out that 4% articaine with 1:100.000 epinephrine showed a higher success rate in anaesthesia, lower VAS scores during injection phase and treatment phase, shorter onset time of pulpal anaesthesia and a lower percentage of patients experiencing adverse events. This study also confirmed other advantages with the use of articaine described in literature, such as less painful injection, faster onset of effect, with fewer adverse events, also avoiding pre-sedations used to reduce the intensity of anxiety in young patients during third lower molar extractions [45].

CONCLUSIONS

This study showed the differences in terms of tactile pressure and pain feelings, between the two anaesthetic drugs used with different anesthesiological techniques, which were assessed with VAS

encouraging the choice of articaine versus mepivacaine in the third molar germectomy in young patients. It should also be noted that the most effective anaesthetic effect was obtained by using articaine with a more comfortable and less painful anaesthetic technique, thanks to its intrinsic chemical characteristics, that reduce the unpleasant feelings due to classic IANB that involves a crossing of muscle fibres of the internal pterygoid muscle.

In conclusion, articaine has been found to provide significant clinical efficacy compared to mepivacaine. Moreover, it was observed shorter latency times, better anaesthetic quality, both pre and intraoperatively. Articaine requires less additional anaesthetic than mepivacaine and presents better patient compliance with a less unpleasant memory of the intervention. Further studies are necessary to determine clinical efficacy using articaine without IANB.

AUTHOR CONTRIBUTIONS

Conceptualization, D.M., B.R.; Methodology, L.L., F.D.; Validation, M.B., D.M.; Investigation, L.N., M.G., M.M.; Data Curation, L.N., M.G.; Writing – Original Draft Preparation, M.B., M.M.; Writing – Review & Editing, F.D., A.P.R.S.; Supervision, A.D.R.; B.R.; Funding Acquisition, A.D.R.

All Authors have approved the submitted version and agree to be personally accountable for the author's own contributions and for ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved, and documented in the literature.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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TABLES

Age of patients (yrs)	n° of cases
11-13	25
14-15	15
15-16	10

Table 1. Age distribution of cases.

Formulation	Maximum Dose mg/kg (Total)	Elimination T ½ (min)	Duration of Anesthesia Infiltration
2% Mepivacaine 1:100.000 epinephrine	7 (550)	114	40-60 min
4% Articaine 1:100.000 epinephrine	5-7 (500)	20	60-75 min

Table 2. Anesthetics pharmacokinetics parameters.

Type of anaesthesia	n° of cases	(%)
Mepivacaine	40	80
Articaine	21	42

Table 3. Request for additional anesthetic injection

	Tactile-pressure feelings after 6-8' since injection (n° of cases)	(%)	Intraoperative tactile-pressure feelings (n° of cases)	(%)	Intraoperative pain (n° of cases)	(%)
Absent (0)	20	40	12	24	10	20
Mild (1)	10	20	8	16	9	18
Moderate (2)	20	40	15	30	15	30
Severe (3)	0	0	15	30	16	32

Table 4. Mepivacaine-related tactile-pressure and pain feelings

	Tactile-pressure feelings after 6-8' since injection (n° of cases)	(%)	Intraoperative tactile-pressure feelings (n° of cases)	(%)	Intraoperative pain (n° of cases)	(%)

Absent (0)	35	70	43	86	45	90
Mild (1)	15	30	7	14	5	10
Moderate (2)	0	0	0	0	0	0
Severe (3)	0	0	0	0	0	0

Table 5. Articaine-related tactile-pressure and pain feelings

Feelings and pain Mepivacaine *vs* Articaine	**Absent**	**Mild**	**Moderate**	**Severe**
P-value	0.048 (*)	1.000	0.010 (*)	0.184

(*) $P < 0.05$

Table 6. Comparison between the patients' feelings and pain after mepivacaine or articaine use.