10.21608/ADJC.2022.153497.1158 Advanced Dental Journal
Volume 4 (2022) | Issue 4| Pages 296 - 308

Original Article

Anaesthetic Efficacy of 4% Alexadricaine Versus 2% Mepecaine-L For Infiltration Anaesthesia in Extraction of Maxillary First Primary Molars in Children: A Randomized Controlled Pilot Study

Ghada Mohamed Mostafa Mahmoud[1]; Sara Ahmed Mahmoud[1]; Marwa Aly Elchaghaby[1]
[1]Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University

Email: ghada.mostafa@dentistry.cu.edu.eg

Submitted: 23-8-2022
Accepted: 28-10-2022

Abstract

Aim: This study aimed to evaluate the anaesthetic efficacy of 4% Alexadricaine versus 2% Mepecaine-L for infiltration anaesthesia in the extraction of maxillary first primary molars in children.
Subjects and Methods: The present study is a split-mouth study in which ten children aged from 5 to 7 years with bilateral badly decayed maxillary first primary molars indicated for extraction were selected from the outpatient diagnostic clinic in Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University. The children's teeth were randomly assigned to two groups. Group A received 4% Alexadricaine and group B received 2% Mepecaine-L for infiltration anaesthesia. The intra-operative pain during the extraction was assessed using the Visual Analogue Scale (VAS) and the Sound, Eyes and Motor Scale (SEM). Moreover, the onset and duration of soft tissue anaesthesia were objectively evaluated.
Results: Group A showed slightly higher values of VAS and SEM scale than group B regarding intra-operative pain during extraction with a statistically non-significant difference. Regarding the onset of soft tissue anaesthesia, both groups had the same mean value (0.25±0.00). Regarding the duration of soft tissue anaesthesia, group A (214.00±9.66 minutes) showed a significantly higher mean value than group B (162.50±16.87 minutes) with a statistically significant difference (P<0.001).
Conclusion: Regarding infiltration anaesthesia in the extraction of maxillary first primary molars in children, both 4% Alexadricaine and 2% Mepecaine-L can provide similar effective pain control with rapid onset of action. However, 4% Alexadricaine has a longer duration of soft tissue numbness than 2% Mepecaine-L.

Keywords: Alexadricaine; Mepecaine-L; Local Anaesthesia; Extraction; Primary Molars

Introduction

Dental extraction is considered one of the most feared and painful procedures in the dental field, during which effective pain control is needed to build a trusting relationship between the child and the dental practitioner **(Gazal, 2018; AAPD, 2020)**.

Unsuccessful pain control may result in increased sensitivity to pain, delay or avoidance

of medical or dental care, and traumatic memories that may last during adolescence and adulthood **(Gaglani and Gross, 2018)**.

Pain is a physiological phenomenon with a complex nature as it is affected by physiological, psychological, behavioural, and developmental factors. Pain in children was always under-evaluated due to its subjective nature. Therefore, pain assessment is important to detect a child's pain and evaluate the effectiveness of pain control **(Tawycross, 2017)**.

Local anaesthesia is the backbone of pain control in dentistry. Local anaesthetic agents temporarily block the action potential transmission along the nerve membrane, which in turn blocks pain sensation in a circumscribed part of the body without loss of consciousness **(Garmon and Huecker, 2021)**.

Local anaesthetic agents are considered the safest drugs to control pain. However, the local anaesthetic injection is found to be the most feared procedure by the majority of children. Therefore, finding the local anaesthetic agent with high potency, fast onset of action, and adequate duration of anaesthesia will minimize the number of injections required to achieve ideal pain control **(Singh, 2012; Kumar and Santhosh, 2015).**

Lidocaine, articaine, and mepivacaine are the world's most commonly used local anaesthetic drugs. To the best of our knowledge, up till now, there is not enough evidence in the literature about the superiority of articaine in comparison to mepivacaine in pain control in children **(Gaffen and Haas, 2009; Gazal, 2018)**. Therefore, this study aimed to evaluate the anaesthetic efficacy of 4% Alexadricaine versus 2% Mepecaine-L for infiltration anaesthesia to extract maxillary first prim ary molars in children.

Subjects and methods

Study Design:

This study is a randomized controlled triple-blinded pilot study with a split-mouth design and a 1:1 allocation ratio.

Trial Registration:

ClinicalTrial.gov **ID: NCT04477317**

Ethical Approval:

The Research Ethics Committee at the Faculty of Dentistry, Cairo University, Egypt, granted ethical approval, c**ode number (8-11-20)**.

Eligibility Criteria:

Inclusion Criteria:

- Medically fit (ASA I, II).
- Mentally capable of communication (Frankl 3,4).
- Children aged 5-7 years.
- First maxillary primary molar needs extraction due to root caries "beyond possible repair".
- First dental visit.
- The child must give assent prior to participation and approved parental informed written consent.

Exclusion Criteria:

- Children with acute or sub-acute dentoalveolar abscess.
- Children with a history of prolonged bleeding, platelet disorders, Hyperthyroidism, or hypersensitivity.
- Patients who had taken analgesics or antibiotics in the 12-hrs preceding the injection.

Sample Size:

Within the scope of the current systematic search, to date, no clinical trials in literature have been performed to compare the anaesthetic efficacy of 4% articaine versus 2% mepivacaine regarding the intra-operative pain during extraction of badly decayed upper first primary molars using the Visual Analogue Scale as a numerical, not categorical scale.

In addition, the intervention (4% Alexadricaine) is new and was never used before. Therefore, a pilot study is recommended. In addition, estimated sample size was suggested with a total sample size of 20 teeth **(Hertzog, 2008)**.

Grouping:

The total sample was divided into two equal groups as follows:

Group A (Intervention group):

Ten children received an infiltration injection of 1.7 ml of 4% Alexadricaine (equivalent to 1 cartridge) (4% Articaine hydrochloride with 1:100,000 Epinephrine) at one maxillary quadrant.

Group B (Control group):

Ten children received another infiltration injection of 1.8 ml of 2% Mepecaine-L (equivalent to 1 cartridge) (2% Mepivacaine hydrochloride with 1:20,000 Levonordefrin) at the maxillary opposite quadrant.

Study Setting:

Children aged 5 to 7 years with bilateral badly decayed maxillary first primary molars indicated for extraction (20 maxillary first primary molars) were selected from the outpatient diagnostic clinic in Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University.

Informed Consent:

The aim of the study, a complete description of the study methods, and the potential adverse effects were explained to the parent or the legal guardian in clear language. They were allowed to ask any questions about the study and choose whether to participate or not. Signed informed consent was collected from the parent or the legal guardian, and verbal assent was obtained from each child participating in the study.

Diagnosis:

Personal and Medical History:

The principal investigator collected data regarding personal, medical, and dental histories from the child and his parent/ legal guardian, which were recorded in a specially designed diagnostic chart **(Newsome, Smales and Yip, 2012)**.

Clinical Examination:

The principal investigator performed an extra-oral and intra-oral examination. The right and left maxillary first primary molars were examined for the presence of any pathosis and to evaluate the clinical restorability of the tooth by assessing the extension of proximal caries apically **(Albannai, 2020)**.

Radiographic Examination:

The principal investigator used the x-ray machine to take preoperative intra-oral periapical x-rays to the suspected molar using bisecting angle technique to confirm that the tooth is beyond possible repair and there is no significant bone or root resorption **(Almeida *et al.*, 2021)**.

Randomization and Allocation concealment:

The assistant supervisor generated a random sequence using computer software (www.random.org). The assistant supervisor concealed the allocation sequence from the principal investigator in sequentially numbered opaque sealed envelopes. The envelopes were numbered from 1 to 10; each patient took an envelope in ascending order. In addition, the assistant supervisor assigned the research units to the intervention or control groups according to the sequence generation table while the principal investigator conducted enrollment.

Blinding:

The patient, the health care providers (including the principal investigator), the outcome assessor, and the statistician were all blinded in this study. Therefore, it was a triple-

blinded study. The printed labels on the anaesthetic carpules were masked with an adhesive opaque paper, and were handed by the assistant supervisor to the principal investigator after opening the patient envelope.

Intra-operative procedures:

1. For buccal infiltration, the principal investigator pulled the cheek outward to stretch the mucous membrane at the site of injection to facilitate needle penetration, the needle cap was removed, and the tip of the needle was positioned and inserted at the muco-buccal fold above the selected molar with the needle forming 45° with the long axis of the tooth. The needle bevel was facing the bone **(Malamed, 2019)**.
2. Aspiration was performed, and a few drops of the solution were deposited **(Ghavimi *et al.*, 2015)**. After pausing for a few seconds, the needle was advanced to touch the bone, then slightly withdrawn, and the rest of the anaesthetic solution was injected slowly for over 30 seconds till 1.5 ml of the solution was injected **(Abdellatif, 2011; Jung *et al.*, 2017; Jayakaran, Vignesh and Shankar, 2019).**
3. The intra-papillary injection was performed after ensuring numbness of the buccal mucosa. 0.2-0.3 of the anaesthetic solution was injected slowly into the mesial and the distal interdental papillae. The needle was inserted horizontally at the buccal side of the papillae 2 mm apical to the tip of the papillae parallel to the occlusal plane. It was advanced until reaching the papillae's palatal side, causing blanching of the tissues **(Abdellatif, 2011)**.
4. Immediately after injection, the onset of the soft tissue numbness was objectively assessed by probing the buccal and the palatal gingival sulci at intervals of 15 seconds using a stopwatch **(Gazal *et al.*, 2017)**. Another stopwatch was adjusted to calculate the duration **(Barath *et al.*, 2015)**.
5. The principal investigator held the upper primary molar forceps parallel to the long axis of the maxillary first primary molar. The initial movement was in the apical direction to obtain a solid apical grip through the engagement of the trifurcation of the molar. Then, buccal and palatal luxation movement was done steadily with reasonable force to expand the bony socket. After complete luxation of the tooth, the final move was to deliver the tooth in an occluso-buccal direction to avoid injuring the opposing teeth **(Albannai, 2020).**
6. After tooth delivery, the child was asked to bite on a small sterile piece of gauze placed at the extraction site for 30 minutes. Post extraction instructions were explained to the parent/ legal guardian in simple words **(AAPD, 2020)**.
7. Two weeks after the extraction visit, the child came to the clinic to anesthetize and extract the contra-lateral maxillary first primary molar using the other type of local anesthetic agent by the principal investigator with the same clinical steps **(Ege *et al.*, 2020)**.

Assessment of outcomes:

1. Intra-operative pain assessment scales:

Visual analogue scale:

Immediately after the extraction procedure, the Visual Analogue Scale was shown and explained to the child as it is a 10 cm (100 millimetres) scale with two anchor words on its ends, the left end represents “no pain”, and the right end represents “the worst pain”. The child was asked to put a mark that indicated how much pain he felt during the extraction. The distance between the mark and the left end of the scale was measured and recorded in millimetres **(Langley and Sheppeard, 1985; Jain and Nazar, 2018)**.

Sound Eyes Motor scale:

The extraction procedure was videotaped by a trained assistant standing 1 meter away from the child. The principal investigator and the assistant supervisor blindly and objectively evaluated the child's reactions during the extraction to achieve inter-rater reliability. Both assessed the child's reactions on more than one occasion to ensure intra-rater reliability **(Abdul Khalek *et al.*, 2017)**.

The Sound, Eyes, and Motor Scale is an objective scale that evaluates the child's pain based on three aspects: sound, eyes, and movement. Each category ranged from 1 (comfort) to 4 (severe discomfort). The scores of the four categories were summed up to give the total score, which was then recorded and tabulated **(Wright *et al.*, 1991; Abdelmoniem and Mahmoud, 2016)**.

2. Onset of soft tissue anaesthesia:

Immediately after the buccal infiltration and palatal intra-papillary injection, a stopwatch was adjusted to evaluate the beginning of soft tissue numbness. The principal investigator used the dental probe to objectively assess the numbness of buccal and palatal gingival sulci immediately after injection and at 15-second intervals until the child feels no pain **(Gazal *et al.*, 2017; Afsal *et al.*, 2019)**.

3. Duration of soft tissue anaesthesia:

Immediately after the anaesthetic injection, another stopwatch was adjusted to evaluate the duration of soft tissue anaesthesia. The principal investigator assessed the duration objectively and blindly in the clinic. After extraction, the principal investigator probed the buccal and the palatal gingival sulci to check numbness. The probing testing was then repeated every 30 minutes until the child felt a blunt sensation, then repeated every 10 minutes until he felt slight pain. The duration of soft tissue anaesthesia was calculated from the onset of soft tissue anaesthesia to the time numbness disappeared **(Barath *et al.*, 2015)**.

Statistical Analysis:

Categorical data were presented as frequency and percentage values. Numerical data were presented as mean and standard deviation values. Parametric data were analyzed using paired t-test. Non-parametric data were analyzed using Wilcoxon signed-rank test. Associations were analyzed using the Mann-Whitney U test. Correlations were analyzed using Spearman's rank-order correlation coefficient. The significance level was set at $p \leq 0.05$ within all tests. Statistical analysis was performed with R statistical analysis software version 4.1.2 for Windows.

Results

1. Demographic data:

Age and gender distribution

Ten children were included in the present study. The mean age of the participants was (5.82±0.75) years. Among the participants, 8(80.0%) children were males, and 2(20.0%) were females.

2. Intra-operative pain:

Visual analogue scale (VAS)

Regarding the Mean and Standard deviation values for VAS, Group (A) had a higher score (18.50±15.99) than Group (B) (16.00±15.78), as shown in figure (1). Yet, the difference was not statistically significant (p=0.423).

Sound Eye Motor scale (SEM)

Regarding the Mean and Standard deviation values for SEM (average between the two assessors), Group (A) (6.40±2.86) had a higher score than group (B) (5.40±2.72), as shown in figure (2). Yet, the difference was not statistically significant (p=0.100).

Inter-Rater reliability

Regarding the Inter-Rater reliability, there was a strong agreement between both raters 0.987[0.968:0.995].

3. Onset of anaesthesia:

Regarding the Mean and Standard deviation values for the onset of anaesthesia, both groups had the same mean value (0.25±0.00), as shown in figure (3).

4. Duration of anaesthesia:

Regarding the Mean and Standard deviation values for the duration of anaesthesia, Group (A) (214.00±9.66) had a significantly higher value than group (B) (162.50±16.87) ($p<0.001$), as shown in figure (4).

5. Associations and correlations

Associations with gender:

Regarding the associations with gender, there was no significant association between gender and different parameters for both groups ($p>0.05$).

Correlations with age:

Regarding the correlations with age, for both groups, there was a significant moderate negative correlation between age and anaesthesia duration ($p<0.05$). However, for other parameters, there was no significant correlation ($p>0.05$).

Discussion

Local anaesthesia is the cornerstone of pain control in dentistry. The statistical analysis of the present study data showed no statistically significant difference in intra-operative pain during the extraction procedure between group A (4% Alexadricaine) and group B (2% Mepecaine-L) using the Visual Analogue Scale. This result is in line with **Almeida *et al.* (2020)**. They stated no statistically significant difference between 4% articaine and 2% mepivacaine regarding pain perception using VAS during third molar extraction.

In contrast to the previous finding, **Bortoluzzi *et al.*(2008)** stated that 4% articaine was better than 2% mepivacaine regarding the depth of anaesthesia using VAS. **Gao and Meng (2020)** found that articaine was superior to mepivacaine and lidocaine as a supplemental buccal infiltration after Inferior Alveolar Nerve Block for endodontic treatment using VAS. On the other hand, another study by **Bortoluzzi *et al.* (2018)** revealed that 2% mepivacaine was better than 4% articaine regarding anaesthetic depth and extent using VAS.

Regarding the evaluation of intra-operative pain during extraction using the Sound, Eyes, and Motor scale, there was no statistically significant difference between group A (4% Alexadricaine) and group B (2% Mepecaine-L), which is consistent with **Wright *et al.* (1991)** who stated that the difference of intra-operative pain scores using SEM scale between 4% articaine and 2% mepivacaine for infiltration anaesthesia in mandibular primary molars was statistically insignificant. Moreover, **Hosny**, **Abd Al Gawad, and Aly (2021)** revealed no statistically significant difference in intra-operative pain, using the SEM scale, between 4% Artpharmadent and 2% Mepecaine-L for infiltration in the extraction of mandibular primary first molars.

The inter-rater reliability of the SEM values was statistically calculated using the Intra-class Correlation Coefficient (ICC) and Cohen's Kappa. Concerning the inter-rater reliability, there was a strong agreement (0.987) between the first and the second assessors regarding SEM scores of the intra-operative pain, indicating the high reliability of the findings. This can be attributed to the training of the two assessors before study enrollment **(Abdul Khalek et al., 2017)**.

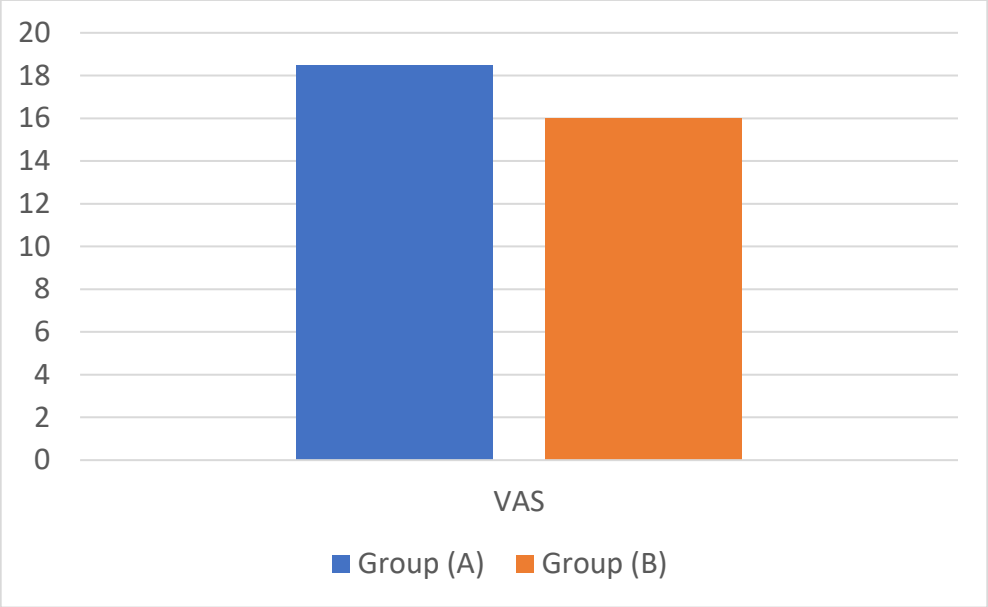

Figure (1) Bar chart showing the average VAS in both groups.

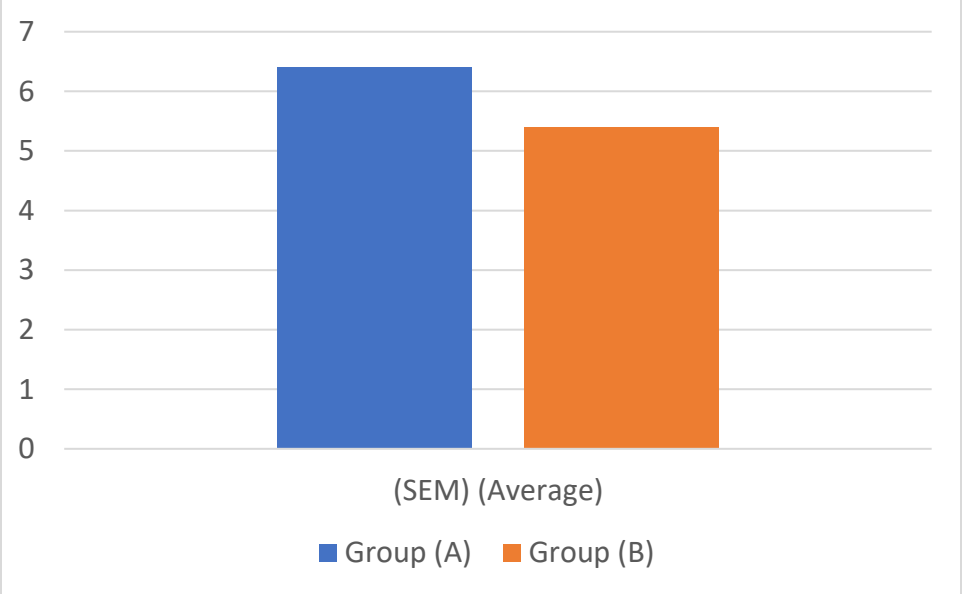

Figure (2) Bar chart showing average (SEM) (Average) in both groups.

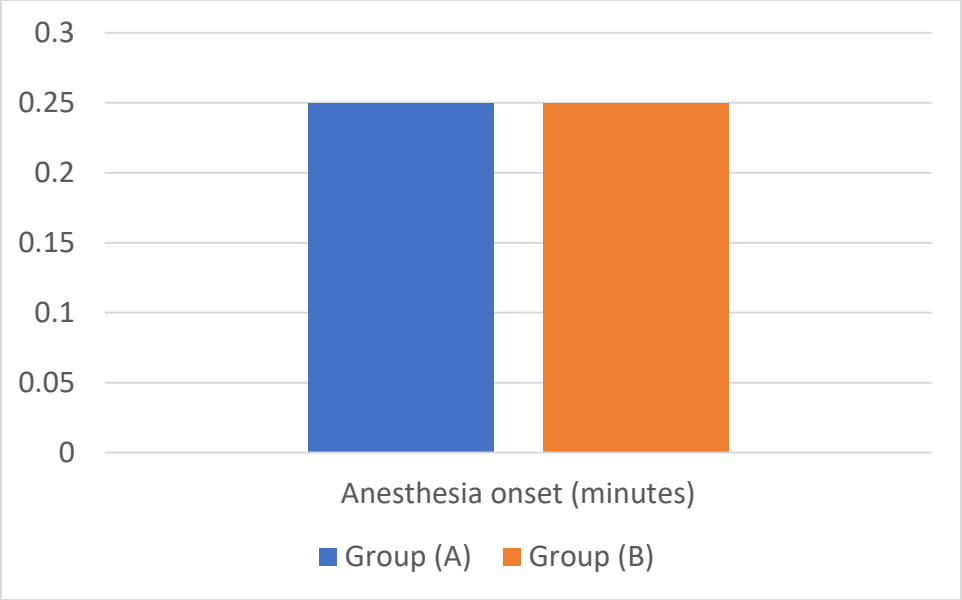

Figure (3) Bar chart showing average anesthesia onset (minutes) in both groups.

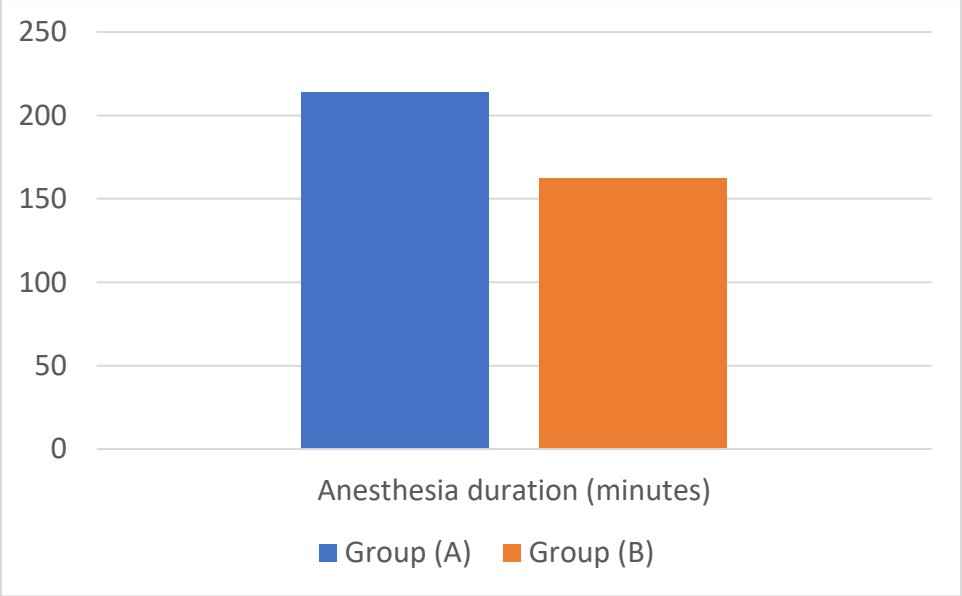

Figure (4) Bar chart showing the average anesthesia duration (minutes) in both groups.

The contradicting findings concerning the difference in intra-operative pain between 4% articaine and 2 % mepivacaine could be justified as each agent has distinct properties which can make it superior to the other in different studies. The better performance of articaine in some studies could be attributed to its greater lipid solubility as it includes a thiophene ring in its chemical structure which facilitates the diffusion of articaine molecules across the lipid membrane of the nerve cell, giving it high potency and depth. Another cause could be the higher concentration of articaine solution than mepivacaine. The superiority of mepivacaine in some studies could be explained that there are more mepivacaine molecules in the unionized soluble form, which means that more molecules can travel through the nerve cell membrane **(Gazal, 2018; Gao and Meng, 2020).**

Regarding the anaesthetic onset of action, both groups had the same onset (0.25±0.00 minute). No statistically significant difference was found between group A (4% Alexadricaine) and group B (2% Mepecaine-L) (0.25±0.00 minute). This was in the same line as **Odabaş *et al.* (2012)**. They found that the difference in onset of anaesthesia between 4% articaine and 3% mepivacaine (epinephrine free) was statistically insignificant in children aged from 7 to 13 years.

On the other hand, **Gazal (2015)** stated that 4% articaine group showed earlier numbness of the lip and teeth than 2% mepivacaine group in supplemental buccal infiltration anaesthesia in mandibular teeth in adults. **Yekta-Michael, Stein and Marioth-Wirtz (2015)** found that plain articaine has a faster onset than plain mepivacaine in anaesthesia of maxillary canine. **Gazal et al., (2017)** and **(2018)** declared that the onset of teeth and palatal soft tissue anaesthesia was faster in the 4% articaine group than the 2% mepivacaine group using buccal infiltration for extraction of maxillary teeth in adults.

These contradicting results regarding onset could be attributed to specific characteristics of each local anaesthetic agent. For example, Mepivacaine has the lowest pKa (7.6) of all local anaesthetic agents, which is very close to the physiological pH (7.4). Therefore, in the normal tissue pH, more drug molecules are available in unionized form (lipid-soluble form), which can diffuse easily through the nerve cell membrane (lipid in nature) and fasten the onset of action **(Malamed, 2019)**. On the other hand, articaine has a unique chemical structure since it contains a thiophene ring which increases lipid solubility and enhances the diffusion through the nerve cell membrane resulting in faster onset. Additionally, the articaine used was higher in concentration (72 mg) than mepivacaine (36 mg) **(Gazal, 2015)**.

Regarding the duration of soft tissue numbness, the duration was longer for group A (4% Alexadricaine) (214.00±9.66 minutes) than for group B (2% Mepecaine-L) (162.50±16.87 minutes), and the difference was statistically significant ($P<0.001$). This was consistent with **Colombini *et al.* (2006)**, who declared that 4% of articaine has a longer duration of anesthesia than 2% mepivacaine in mandibular third molar extraction. **Odabaş *et al.* (2012)** found that 4% articaine has a longer duration than 3% mepivacaine (epinephrine free) in 7–13-year-old children.

The result of this study was inconsistent with **Bortoluzzi *et al.* (2018),** who stated that 2% mepivacaine showed longer duration than 4% articaine.

The longer duration of articaine in some studies could be justified that articaine has the highest protein binding percentage (94%) of all amides based on its chemical properties. Therefore, it takes more time for the drug to be in its free form to undergo metabolism. Moreover, articaine is highly lipid-soluble because of the thiophene ring, which allows more drug

molecules to pass through the lipid layer of the nerve membrane **(Kambalimath *et al.*, 2013; Mumba, Kabambi and Ngaka, 2017)**.

The longer duration of mepivacaine in a few studies could be explained that the mepivacaine itself has the mildest vasodilating effect of all local anesthetic agents. The higher the vasoconstriction; the longer the duration since drug absorption into blood circulation decreases with increasing constriction of the blood vessels **(Bortoluzzi *et al.*, 2018)**.

For both groups, there was a significant, moderate, negative correlation between the child's age and anesthesia duration, which means that the duration of the local anesthesia increased with decreasing age. This could be explained as many anatomical and physiological changes occur during childhood which may affect the pharmacokinetics of the drug regarding drug absorption, distribution, and metabolism **(Batchelor and Marriott, 2015)**.

Limitation of the study:

Generalizing the study results is difficult and should be performed with caution as this is a pilot study with a limited number of participants.

CONCLUSIONS:

1. Both 4% Alexadricaine and 2% Mepecaine-L can be used effectively in pain control during the extraction of maxillary primary molars in children.
2. 4% Alexadricaine has a longer duration of soft tissue numbness than 2% Mepecaine-L.
3. The child's age was found to have a significant, moderate and negative correlation with the duration of anesthesia for both local anesthetic agents.

Conflict of Interest:

The authors declare no conflict of interest.

Source of Funding:

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES:

AAPD (2020) "American Academy of Pediatric Dentistry reference manual," *Pediatr. Dent.*, 36, pp. 1–140.

Abdellatif, A. M. (2011) "Pain assessment of two palatal anesthetic techniques and their effects on the child's behavior," *Pediatric Dental Journal*, *21*(2), pp. 129–137. Available at: https://doi.org/10.1016/S0917-2394(11)70239-7

Abdelmoniem, S.A. and Mahmoud, S.A. (2016) "Comparative evaluation of passive, active, and passive-active distraction techniques on pain perception during local anesthesia administration in children," *Journal of Advanced Research*, 7(3), pp. 551–556. Available at: https://doi.org/10.1016/J.JARE.2015.10.001.

Abdul Khalek, A.M.G. *et al.* (2017) "Effect of Papacarie and Alternative Restorative Treatment on Pain Reaction during Caries Removal among Children: A Randomized Controlled Clinical Trial," *Journal of Clinical Pediatric Dentistry*, 41(3), pp. 219–224. Available at: https://doi.org/10.17796/1053-4628-41.3.219.

Afsal, M.M. *et al.* (2019) "Pain perception and efficacy of local analgesia using 2% lignocaine, buffered lignocaine, and 4% articaine in pediatric dental procedures," *Journal of Dental Anesthesia and Pain Medicine*, 19(2), p. 101. Available at: https://doi.org/10.17245/JDAPM.2019.19.2.101.

Albannai, H. A. (2020) "Exodontia: Tips and Pearls. *ARC Journal of Dental Science*," *5*(2), pp. 4–10. Available at: https://doi.org/10.20431/2456-0030.0502002

Almeida, H.C.R. de *et al.* (2021) "Clinical and radiographic evaluation of caries depth, root

resorption and furcation lesion in primary molars," *Research, Society and Development*, 10(5), p. 1_10. Available at: https://doi.org/10.33448/RSD-V10I5.14818.

Almeida, P.C. *et al.* (2020) "Volume and effectiveness assessment of articain 4% versus mepivacaine 2% used in third molar surgery: randomized, double-blind, split-mouth controlled clinical trial," *Medicina oral, patologia oral y cirugia bucal*, 25(6), pp. e762–e768. Available at: https://doi.org/10.4317/MEDORAL.23780.

Barath, S. *et al.* (2015) "Efficacy of 2% mepivacaine and 2% lignocaine in the surgical extraction of mesioangular angulated bilaterally impacted third molars: A double-blind, randomized, clinical trial," *Journal of Pharmacy & Bioallied Sciences*, 7(Suppl 2), p. S600_S606. Available at: https://doi.org/10.4103/0975-7406.163564.

Batchelor, H.K. and Marriott, J.F. (2015) "Paediatric pharmacokinetics: key considerations," *British Journal of Clinical Pharmacology*, 79(3), p. 395. Available at: https://doi.org/10.1111/BCP.12267.

Bortoluzzi, M.C. *et al.* (2008) "Comparative Study Of The Efficacy Of Articaine And Mepivacaine: A Double-Blind, Randomized, Clinical Trial," *The Internet Journal of Dental Science*, 7(1). Available at: https://doi.org/10.5580/A7779.

Bortoluzzi, M.C. *et al.* (2018) "Anaesthetic efficacy of 4% articaine compared with 2% mepivacaine: a randomized, double-blind, crossover clinical trial," *International Journal of Oral and Maxillofacial Surgery*, 47(7), pp. 933–939. Available at: https://doi.org/10.1016/J.IJOM.2017.11.011.

Colombini, B.L. *et al.* (2006) "Articaine and mepivacaine efficacy in postoperative analgesia for lower third molar removal: a double-blind, randomized, crossover study," *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 102(2), pp. 169–174. Available at: https://doi.org/10.1016/J.TRIPLEO.2005.09.003 .

Ege, B. *et al.* (2020) "Comparison of the Anesthetic Efficiency of Lidocaine and Tramadol Hydrochloride in Orthodontic Extractions: A Split-Mouth, Prospective, Randomized, Double-Blind Study", *Journal of Oral and Maxillofacial Surgery*, 78(1), pp. 52–62. Available at: https://doi.org/10.1016/J.JOMS.2019.07.010.

Gaffen, A. and Haas, D. (2009) "Survey of Local Anesthetic Use by Ontario Dentists," *Journal (Canadian Dental Association)*, 75(9), p. 649. Available at: https://www.researchgate.net/publication/38077217_Survey_of_Local_Anesthetic_Use_by_Ontario_Dentists.

Gaglani, A. and Gross, T. (2018) "Pediatric Pain Management," *Emergency medicine clinics of North America*, 36(2), pp. 323–334. Available at: https://doi.org/10.1016/J.EMC.2017.12.002.

Gao, X. and Meng, K. (2020) "Comparison of articaine, lidocaine and mepivacaine for buccal infiltration after inferior alveolar nerve block in mandibular posterior teeth with irreversible pulpitis," *British dental journal*, 228(8), pp. 605–608. Available at: https://doi.org/10.1038/S41415-020-1434-9.

Garmon, E.H. and Huecker, M.R. (2021) "Topical, Local, and Regional Anesthesia and Anesthetics," *StatPearls* [Preprint]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK430894/.

Gazal, G. (2015) "Comparison of speed of action and injection discomfort of 4% articaine and 2% mepivacaine for pulpal anesthesia in mandibular teeth: A randomized, double-blind cross-over trial," 9(2), pp. 201–206. Available at: https://doi.org/10.4103/1305-7456.156811.

Gazal, G. *et al.* (2017) "Comparison of onset anesthesia time and injection discomfort of 4% articaine and 2% mepivacaine during teeth extractions," *Saudi Journal of Anaesthesia*, 11(2), p. 152. Available at: https://doi.org/10.4103/1658-354X.203017.

Gazal, G. (2018) "Is Articaine More Potent than Mepivacaine for Use in Oral Surgery?," *Journal of Oral & Maxillofacial Research*, 9(3). Available at: https://doi.org/10.5037/JOMR.2018.9305.

Ghavimi, M. A. *et al.* (2015) "Overview of Local Anesthesia Techniques," *A Textbook of Advanced Oral and Maxillofacial Surgery Volume 2*. 1-18 IntechOpen. Available at: https://doi.org/10.5772/59214

Hertzog, M.A. (2008) "Considerations in determining sample size for pilot studies," *Research in Nursing & Health*, 31(2), pp. 180–191. Available at: https://doi.org/10.1002/NUR.20247.

Hosny, N.H., Abd Al Gawad, R.Y. and Aly, M.M. (2021) "ANESTHETIC EFFICACY OF 4% ARTPHARMADENT VERSUS 2% MEPECAINE-L FOR INFILTRATION ANESTHESIA IN EXTRACTION OF BADLY DECAYED LOWER FIRST PRIMARY MOLARS: A PILOT STUDY," *Egyptian Dental Journal*, 67(4), pp. 2875–2884. Available at: https://doi.org/10.21608/EDJ.2021.78818.1658.

Jain, M. and Nazar, N. (2018) "Comparative Evaluation of the Efficacy of Intraligamentary and Supraperiosteal Injections in the Extraction of Maxillary Teeth: A Randomized Controlled Clinical Trial.," *The Journal of Contemporary Dental Practice*, 19(9), pp. 1117–1121. Available at: https://doi.org/10.5005/JP-JOURNALS-10024-2391.

Jayakaran, T.G., Vignesh, R. and Shankar, P. (2019) "Local anesthetics in pediatric dental practice," *Research Journal of Pharmacy and Technology*, 12(8), pp. 4066–4070. Available at: https://doi.org/10.5958/0974-360X.2019.00700.5.

Jung, R.M. *et al.* (2017) "Local anesthetics and advances in their administration – an overview," *Journal of Pre-Clinical and Clinical Research*, 11(1), pp. 94–101. Available at: https://doi.org/10.26444/JPCCR/75153.

Kambalimath, D.H. *et al.* (2013) "Efficacy of 4 % Articaine and 2 % Lidocaine: A clinical study," *Journal of Maxillofacial & Oral Surgery*, 12(1), p. 3. Available at: https://doi.org/10.1007/S12663-012-0368-4.

Kumar, M. and Santhosh, M. (2015) "Newer Delivery Systems for Local Anesthesia in Dentistry," *Journal of Pharmaceutical Sciences and Research*, 7(5), pp. 252–255.

Langley, G. B. and Sheppeard, H. (1985) "The visual analogue scale: Its use in pain measurement," *Rheumatology International 1985 5:4*, *5*(4), pp. 145–148. Available at: https://doi.org/10.1007/BF00541514

Malamed, S.F. (2019) *HANDBOOK OF LOCAL ANESTHESIA*, seventh ed. Edinburgh London New York Oxford Philadelphia St Louis Sydney 2020: Elsevier Inc.

Mumba, J.M., Kabambi, F.K. and Ngaka, C.T. (2017) "Pharmacology of Local Anaesthetics and Commonly Used Recipes in Clinical Practice," *Current Topics in Anesthesiology* [Preprint]. Available at: https://doi.org/10.5772/67048.

Newsome, P., Smales, R., and Yip, K. (2012). "Oral diagnosis and treatment planning: part 1. Introduction," *British Dental Journal*, *213*(1), pp: 15–19. Available at: https://doi.org/10.1038/sj.bdj.2012.559

Odabaş, M.E. *et al.* (2012) "Comparison of the Anesthetic Efficacy of Articaine and Mepivacaine in Pediatric Patients: A Randomized, Double-blind Study," *Pediatric*

Dentistry, 34(1), pp. 42–45. Available at: https://www.ingentaconnect.com/content/aapd/pd/2012/00000034/00000001/art00010

Singh, P. (2012) "An emphasis on the wide usage and important role of local anesthesia in dentistry: A strategic review," *Dental Research Journal*, 9(2), p. 127. Available at: https://doi.org/10.4103/1735-3327.95224.

Tawycross, A. (2017) "Guidelines, strategies and tools for pain assessment in children | Nursing Times," pp. 18–21. Available at: https://www.nursingtimes.net/clinical-archive/pain-management/guidelines-strategies-and-tools-for-pain-assessment-in-children-18-04-2017/

Wright, G.Z. *et al.* (1991) "The effectiveness of infiltration anesthesia in the mandibular primary molar region.," *Pediatric Dentistry*, 13(5), pp. 278–283. Available at: https://europepmc.org/article/med/1815200

Yekta-Michael, S.S., Stein, J.M. and Marioth-Wirtz, E. (2015) "Evaluation of the anesthetic effect of epinephrine-free articaine and mepivacaine through quantitative sensory testing," *Head & Face Medicine*, 11(2), pp. 1–13. Available at: https://pubmed.ncbi.nlm.nih.gov/25889698/