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Articaine in Pediatric Dentistry: A Literature Review

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Abstract

Aim: Reviewing and summarizing articaine's pharmacological characteristics, clinical efficacy, and safety profile as a local anesthetic agent in pediatric dentistry, with a focus on its benefits over more conventional drugs like lidocaine

Materials and Methods: An extensive literature review and material analysis were conducted, including studies published between 2015 and 2025. Analysis was done on pertinent clinical studies, randomized controlled trials, systematic reviews, meta-analyses, and pediatric dentistry guidelines assessing the use of articaine in children. Key parameters assessed included anesthetic efficacy, onset and duration, diffusion capability, success in infiltration versus block anesthesia, safety outcomes, and reported adverse effects.

Results: Articaine provides faster onset, greater bone penetration, and higher success rates in both maxillary and mandibular infiltrations compared to lidocaine. Many studies demonstrate that articaine infiltration can replace inferior alveolar nerve blocks, reducing injection-related anxiety and complications. Systematic reviews and meta-analyses confirm superior or comparable anesthetic efficacy to lidocaine, especially in primary molars and pulpal procedures.

Conclusion: In pediatric dentistry, articaine has proven to be a reliable and safe local anesthetic. Its superior bone penetration, rapid onset, and reliable pulpal anesthesia provide significant advantages over lidocaine, particularly for infiltrations in mandibular teeth. While its use in children under 4 years requires caution, articaine remains a valuable option in pediatric dental practice. To solidify its long-term safety and effectiveness profile in children, more excellent randomized trials are required.

Keywords: Articaine; Pediatric dentistry; Local anesthesia; Anesthetic efficacy

Introduction

Since a child's view of future dental visits can be greatly influenced by their experience with pain during dental operations, effective pain management is a crucial component of behavior advising in pediatric dentistry. Local anesthetics play a central role in ensuring that discomfort is minimized, providing a foundation for comfortable and positive dental care [(1)]. The worry and anxiety brought on by dental injections is the most difficult aspect of pediatric dental care [(2)]. Additionally, compared to adults, pediatric patients are more vulnerable to systemic adverse responses from local anesthetics due to their smaller anatomy and lower body weight [3]. Achieving profound local anesthesia is crucial for successful dental treatment [4]. Therefore, it is essential for the practitioner to select a local anesthetic that provides effective anesthesia with the least number of injections and minimal dosage [5]. Because it has both amide and ester functional groups, articaine considered as a unique local anesthetic and was first used in clinical settings in 1976. This dual structure makes it easier for esterases in the circulating plasma and the microsomal enzyme pathway in the hepatic system to break it down metabolically. Unlike other amide anesthetics, articaine features a thiophene ring instead of a benzene ring, which enhances its tissue diffusion and lipid solubility.As a result, it can achieve effective pulpal and palatal anesthesia through buccal infiltration alone, often eliminating the need for nerve blocks or multiple needle insertions. Articaine is characterized by a rapid onset, high potency, strong plasma protein binding, and excellent anesthetic efficacy with a favorable safety profile [6].

Methods

An extensive literature review and material analysis were conducted, including studies published between 2015 and 2025. Analysis was done on pertinent clinical studies, randomized controlled trials, systematic reviews, meta-analyses, and pediatric dentistry guidelines assessing the use of articaine in children. Key parameters assessed included anesthetic efficacy, onset and duration, diffusion capability, success in infiltration versus block anesthesia, safety outcomes, and reported adverse effects.

History

Originally created as carticaine in 1969 by Rusching and associates, articaine was first used in therapeutic settings in Germany in 1976 [7]. The U.S. Food and Drug Administration (FDA) authorized a 4% articaine solution containing 1:200,000 adrenaline for clinical usage in 2006 [8]. Nowadays, clinical practice frequently uses 4% articaine mixed with either 1:100,000 or 1:200,000 adrenaline [9].

Table 1 Timewise development of various local anesthetic agents

YEAR	ESTERS	AMIDES	DISCOVERER
1905	Procaine		Alfred Einhorn
1943		Lidocaine	Nils Lofgren
1948			Applied in clinical practice
1952	Propoxycaine		Clinton and Laskowsky
1953		Prilocaine	Prepared by Lofgren and Tegner
1956-7		Mepivacaine	Prepared by AF Ekenstam
1957		Bupivacaine	AF Ekenstam
1960			Introduced in dentistry
1969		Articaine	H Rusching et al
1971		Etidocaine	Takman
1997		Ropivacaine	AF Ekenstam,et al
1999		Levobupivacine	Aberg

Mechanism of action

Articaine has a high lipid solubility, a pKa of 7.8, and about 94% protein binding. It has a brief initiation period and delivers therapeutic effects as a moderately potent short-acting anesthetic [10]. By reversibly binding to the α-subunit of voltage-gated sodium channels, articaine reduces sodium influx and stops impulse transmission by preventing the threshold potential from being reached. It exhibits a state-dependent activity, with the open state having the highest affinity, the inactivated state having a moderate affinity, and the resting state having the lowest affinity [11].

Pharmacokinetics

The vasodilatory effect of articaine enhances its absorption throughout the body. Formulations containing epinephrine at concentrations of 1:60,000, 1:100,000, or 1:200,000 (5 µg/mL) suppress this action. The drug's ability to attach to tissue and plasma proteins determines its dispersion. Because the release of free drug for metabolism happens more slowly, a larger degree of protein binding extends the duration of effect. Articainic acid, the inactive metabolite of articaine, is quickly hydrolyzed and then partially metabolized in the kidneys to produce articainic acid glucuronide. Articaine has a half-life of around sixty minutes and is quickly removed [12].

Pharmacodynamics in children

Children's local anesthetics have similar pharmacodynamics to those of adults, but their pharmacokinetics are very different. When administering amide local anesthetics to young children, extra care must be used since lesser intrinsic clearance or decreased serum protein binding may raise the possibility of harmful effects [13]. One important element affecting the safety of local anesthetics in infants and young children is the mode of administration.

Articaine is mostly used as an adjuvant to general anesthesia or in juvenile patients having dental procedures that call for local anesthetic. Children absorb topical local anesthetics from mucosal membranes more quickly than adults do because of increased local blood flow and cardiac output. The authors of a study with 27 kids ages 3 to 12 suggested using 2% articaine in pediatric dentistry because it showed a lower Cmax and a shorter half-life [14].

The most frequently reported side effect after using articaine for dental treatments is prolonged numbness, which mostly affects children under the age of seven [15].

Indications and Contraindications

Indications [16]

- Routine restorative procedures in primary and permanent teeth
- Extractions of primary teeth
- Pulp therapy (pulpotomy and pulpectomy)
- Minor oral surgical procedures
- Alternative to nerve blocks in pediatric patients

Contraindications [17]

- Hypersensitivity to amide-type local anesthetics
- Allergy to sodium metabisulfites
- Idiopathic or congenital methemoglobinemia
- Hemoglobinopathies, including sickle cell disease

Properties of Articaine

Articaine has a pKa of 7.8.

Vasoconstrictor-containing solutions have pH values between 4.5 and 5.2 for 1:100,000 epinephrine and 4.6 and 5.4 for 1:200,000 epinephrine.

- With 1:200,000 epinephrine: onset is 1–2 minutes for infiltration and 2–3 minutes for mandibular block
- With 1:100,000 epinephrine: onset is 1–2 minutes for infiltration and 2–2.5 minutes for mandibular block [17].
- The duration of articaine is approximately 144 minutes [8].
- The safe dosage range for kids ages 4 to 12 is 5 to 7 mg/kg of body weight [18].

Safety

Articaine has a favorable safety profile when used within recommended pediatric dosages (maximum 5 mg/kg). At toxic levels, systemic toxicity mainly affects the cardiovascular and central nervous systems and can cause arrhythmias, agitation, dizziness, or seizures. Unlike prilocaine, articaine has minimal risk of inducing methemoglobinemia. However, prolonged soft tissue anesthesia can predispose children to lip and cheek biting, requiring caregiver education [19].

Table 2 Review of Literature

Author/Year	Study type	Sample size / age group	Material/Method	Parameter analyzed	Results
Malamed SF et al., 2001	Multicenter clinical trial	>1300 patients (including children) pediatric subgroup ≥ 4 years	4% Articaine vs 2% Lidocaine	Onset time, duration of pulpal anesthesia, systemic safety	Articaine had faster onset (1–2 min), longer pulpal duration (up to 75 min), with no significant adverse events.
Ram D, Amir E, 2006	RCT	60 children (4–10 yrs)	Compared buccal infiltration of 4% articaine with 1:100,000 epinephrine to standard inferior alveolar nerve block with 2% lidocaine and 1:100,000 epinephrine	Pain response, need for supplemental anesthesia, efficacy in pulpotomy	Articaine infiltration achieved significantly higher success rate, reducing need for block anesthesia.

Katyal V, 2010	Systematic review	Included RCTs, split-mouth studies, and pharmacologic reports	Articaine vs Lidocaine	Anesthetic efficacy, safety profile in children	Concluded articaine more effective for infiltration in mandible, equally safe compared to lidocaine.
Silva de Souza et al., 2011	RCT	40 children (6–9 yrs)	Buccal infiltration articaine vs lidocaine. Articaine infiltration on one side and lidocaine infiltration on the other side in separate sessions	Pulpal anesthesia success, failure rates, injection pain by objective sensory testing and behavioral pain scales	Articaine showed higher pulpal anesthesia success and similar injection discomfort relative to lidocaine.
Kanna S et al., 2012	RCT	50 children (7–11 yrs)	Articaine vs Lidocaine (block and infiltration)	Pain response (behavioral scales), anesthetic success, onset time, duration, and need for supplemental anesthesia	Articaine showed higher success and longer anesthetic duration, especially in infiltrations.
Arrow P, 2012	RCT	100 children	Articaine vs Lidocaine	Pain during extraction, anesthetic success. Pain measured intra- and post-operatively.	Articaine infiltration provided equal or superior anesthesia compared to lidocaine block injections.

Costa et al., 2014	Split-mouth study	30 children (5–9 yrs)	Articaine vs Lidocaine	Pain on injection (visual analog scale adapted for children) ,anesthesia effectiveness, duration	Articaine injections were less painful and had higher anesthesia success compared to lidocaine.
Berlin J et al., 2014	Review of adverse events	-	Articaine in children	Incidence of paresthesia, adverse effects	No evidence of increased paresthesia risk in children; overall safety comparable to other amide anesthetics.
Elheeny AAH, 2016	RCT	40 children (6–9 yrs)	Articaine infiltration vs lidocaine inferior alveolar block	Pain, anesthesia success, postoperative complications	Infiltration with articaine was as effective as block anesthesia with lidocaine, with fewer postoperative complications.
Alamoudi NM et al., 2018	RCT	60 children (7–10 yrs)	Articaine vs Lidocaine (infiltration)	Anesthetic success rate, onset, duration	Articaine demonstrated faster onset and higher anesthetic success in mandibular molars compared to lidocaine.

Tofoli et al., 2019	Systematic review	-	Articaine vs Lidocaine in pediatric dentistry	Anesthetic effectiveness, duration, safety	Articaine consistently showed superior infiltration efficacy; recommended safe in children ≥4 years.
Alzahrani FS et al., 2019	RCT	100 children	Articaine infiltration vs block	Pain rating, cooperation, anesthesia success	Articaine infiltration produced less pain and higher child acceptance; avoided invasive block anesthesia.
Zainab H et al., 2021	Meta-analysis	20 pediatric trials	Articaine vs Lidocaine	Anesthetic success, adverse event reporting	Meta-analysis confirmed superior efficacy of articaine; no increase in adverse events compared to lidocaine.
AAPD, 2022	Guideline	-	Local anesthetic use in children	Efficacy, dosage, safety recommendations	Endorsed articaine as safe for ≥4 years; recommended infiltration over block anesthesia when possible.

Dou L et al., 2023	RCT	120 children	Articaine vs Lidocaine (pulp therapy)	Pulpal anesthesia duration, patient comfort, injection acceptance	Articaine showed longer pulpal anesthesia and improved comfort for pulpotomies.
Rahman M et al., 2024	Prospective study	80 children	4% Articaine infiltration	Pain score, anesthetic success, postoperative side effects	Articaine was safe, effective, with minimal postoperative complications and no long-term adverse effects.

Discussion

Articaine's thiophene ring sets it apart from other amide local anesthetics. It increases lipid solubility, making it easier for the target receptors to diffuse through the lipid-rich neuronal membrane. Furthermore, articaine has an ester group [10].

Several clinical trials and systematic reviews have confirmed that articaine demonstrates superior or at least comparable effectiveness to lidocaine in pediatric dental procedures. In mandibular primary molars, where lidocaine frequently exhibits decreased efficiency, articaine gives a quicker onset of action, a longer duration of pulpal anesthesia, and higher success rates with infiltration procedures [33, 34].

Malamed et al. (2013) found that while both drugs have comparable safety profiles, articaine has a quicker onset of action and better infiltration efficacy than lidocaine [35].

Arali and Mytri P. (2015) compared the anesthetic effectiveness of 2% lignocaine administered via inferior alveolar nerve block and 4% articaine administered via buccal infiltration in children with irreversible pulpitis aged 5-8 years in a randomized double-blind cross-over trial. According to the study's findings, children with incurable pulpitis can receive 4% articaine by buccal infusion in place of IANB to prevent side effects including lip biting [36].

Su et al. (2020) reported that articaine produces longer anesthesia with enhanced bone penetration compared to mepivacaine and avoids the methemoglobinemia risk associated with prilocaine. Additionally, articaine infiltration may replace inferior alveolar nerve block in children, thereby minimizing complications [37].

Adrenaline and articaine are administered at a pH of 3.5–4.0, which is lower than the physiological pH of 7.4. The drug's ionized form predominates at this acidic pH, and the body must buffer it to transform enough of it into the active, non-ionized form needed to produce anesthesia [38, 39]. Alkalinizing the acidic anesthetic solution has been proposed as a way to reduce the discomfort that comes with administering local anesthetics without delaying the onset of unconsciousness [40, 41]. A modest amount of sodium bicarbonate ($NaHCO_3$) can be added to the anesthetic solution to easily buffer it [42]. Numerous studies have shown that adding $NaHCO_3$ to local anesthetic solutions can reduce injection pain and accelerate the onset of anesthesia. [43, 44, 45].

In order to determine whether buffering 4% articaine with sodium bicarbonate could improve its anesthetic performance during children's primary maxillary molar extractions, Dhake et al. (2022) carried out a randomized controlled research. The scientists evaluated factors such injection pain, anesthetic onset, need for further anesthesia, and overall extraction comfort while comparing buffered and non-buffered articaine infiltrations. Their findings showed that, in comparison to the traditional formulation, buffered articaine considerably decreased injection discomfort and resulted in a quicker onset of anesthesia. Additionally, children receiving buffered articaine showed better cooperation and required fewer supplemental injections. The authors concluded that buffering articaine offers superior clinical comfort and efficiency and may be a preferred choice for pediatric maxillary extractions [(38)].
Manta et al (2023) indicated that buffering 4% articaine may improve patient comfort and efficiency but may not necessarily increase the reliability of achieving pulpal anesthesia compared to the standard solution. Buffering significantly reduced the pain of injection and accelerated the onset of pulpal anesthesia, with a mean onset time dropping from ~6.6 minutes (non-buffered) to ~4.5 minutes (buffered)[(46)].
Kamareh et al (2024) carried out a randomized clinical trial to compare the extraction of primary mandibular molars using inferior alveolar nerve block (IANB) with 2% lidocaine against buccal infiltration with 4% articaine. Using recognized pain ratings such as the Wong–Baker Faces scale and the Modified Behavior Pain Scale, their split-mouth design in children aged 5–10 years allowed for a direct comparison of pain during injection and extraction. They discovered that compared to IANB with lidocaine, children reported much less weeping during infiltration injections with articaine. Crucially, there was no discernible difference in overall collaboration between the two approaches according to their behavioral assessments. The authors came to the conclusion that buccal infiltration with 4% articaine is a practical and efficient substitute for the more invasive IANB for primary molar extractions [(47)].
The maximum suggested dose of articaine for children is 5 mg/kg, without going beyond the adult maximum limit, according to pediatric standards. Its usage should be done with caution in children below four years of age due to inadequate clinical data in this age range. The higher infiltration efficiency of articaine in primary molars may lessen the requirement for a mandibular block. Soft tissue injuries can be avoided by giving caregivers the proper postoperative advice. High parental satisfaction has also been documented, which has been linked to the anesthetic's general efficacy and decreased injection discomfort. [(48)].
Articaine can be used safely in children under 4, but it should be administered with caution. Younger children have developing bodies, making them more sensitive and potentially more prone to side effects [(16)]. .A survey of American dentists showed that 21% had used articaine in children aged 2–3 years, despite the manufacturer not recommending its use in this age group [(9)].
The highest recommended dosage of articaine for children is listed in the Septocaine US product information as 7 mg/kg, but the Canadian box insert suggests a maximum dose of 5 mg/kg [(49)].
All pediatric age groups can safely and effectively employ articaine for clinical procedures, according to the research currently available on the subject [(50)].

Conclusion

In pediatric dentistry, articaine has proven to be a reliable and safe local anesthetic. Particularly for infiltrations in mandibular teeth, its higher bone penetration, quick onset, and dependable pulpal anesthetic offer substantial advantages over lidocaine. Articaine is still a useful alternative in pediatric dentistry, even though its usage in children younger than four years old necessitates prudence. To solidify its long-term safety and effectiveness profile in children, more excellent randomized trials are required.

References:

1. McDonald RE, Avery DR, Dean JA. McDonald and Avery's dentistry for the child and adolescent. 9th ed. Maryland Heights (MO): Mosby; 2011.
2. Milgrom P, Coldwell S, Getz T, Weinstein P, Ramsay D. Four dimensions of fear of dental injections. J Am Dent Assoc. 1997;128(6):756-62.
3. Wright G, Weinberger S, Friedman C, Plotzke O. The use of articaine local anesthesia in children under 4 years of age. Anesth Prog. 1989;36(6):268-71.
4. Sudha PM, Mathew BM, Rajasudhakar H, Duraisamy V, Jacob M, Thamburaj MV. An in vivo comparative analysis of pain perception in children following lidocaine gel, clove oil, and precooling for intraoral injections: a pilot study. *Int J Clin Pediatr Dent.* 2024;17(12):1394–1398
5. Cheatham B, Primosch R, Courts F. A survey of local anesthetic usage in pediatric patients by Florida dentists. J Dent Child. 1992;59(5):401-7.
6. Malamed SF, Gagnon S, Leblanc D. A comparison between articaine HCl and lidocaine HCl in pediatric dental patients. Pediatr Dent. 2000;22(4):307-11.
7. Malamed SF, Gagnon S, Leblanc D. Efficacy of articaine: a new amide local anesthetic. J Am Dent Assoc. 2000;131(5):635-42.
8. Luo W, Zheng K, Kuang H, Li Z, Wang J, Mei J. The potential of articaine as a new generation of local anesthesia in dental clinics: a review. Medicine (Baltimore). 2022;101(48):e32089.
9. Yapp KE, Hopcraft MS, Parashos P. Articaine: a review of the literature. Br Dent J. 2011;210(7):323-9.
10. McLure HA, Rubin AP. Review of local anaesthetic agents. Anaesthesia. 2005;60(4):308-19.
11. Wang GK, Calderon J, Jaw SJ, Wang SY. State-dependent block of Na+ channels by articaine via the local anesthetic receptor. J Membr Biol. 2009;229(1):1-9.
12. Snoeck M. Articaine: a review of its use for local and regional anesthesia. Local Reg Anesth. 2012;5:23-33.
13. Kokubu M, Oda K, Kudo M, Machida M, Shinya N. Correlation between the anesthetic potency of local anesthetics and their binding ability to a model membrane. J Anesth. 1979;11:121–125
14. Jakobs W, Ladwig B, Cichon P. Oertel R, Kirch W. Serum levels of articaine 2% and 4% in children. Anesth Prog. 1995;42:113–115
15. Adewumi A, Hall M, Guelmann M, Riley J. The incidence of adverse reactions following 4% septocaine (articaine) in children. Pediatr Dent. 2008;30:424–428
16. Saket A, Gupta S, Shrivastava R, Pandey P, Ayub S. Articaine in pediatric dentistry – a review. J Popul Ther Clin Pharmacol. 2025;31(6):e6330.
17. Malamed SF. Handbook of local anaesthesia. 6th ed. St. Louis: Mosby; 2013.
18. Rao AP, Shashibhushan BS. Articaine: Opening up a new vista for pediatric dentists. Indian J Forensic Med Toxicol. 2021;15(4):1320-4.
19. Haas DA. Articaine and methemoglobinemia. Can J Anaesth. 2006;53(7):684-9.
20. De Souza Silva CM, de Queiroz AM, da Silva LA, Nelson-Filho P, Lucisano MP. Buccal infiltration of articaine for pulpotomy in children. Int J Paediatr Dent. 2011;21(5):412-6.

21. Kanna S, Whitworth JM, Meechan JG. A comparison of articaine and lidocaine as local anaesthetics in children. J Clin Pediatr Dent. 2012;36(4):301-5.
22. Arrow P. Articaine in children: a randomized controlled trial. Int J Paediatr Dent. 2012;22(3):189-94.
23. Costa LR, Tortamano IP, Rocha RG, Francischone CE, Tortamano N. Pain assessment during dental treatment with articaine and lidocaine. Eur Arch Paediatr Dent. 2014;15(1):27-31.
24. Berlin J, Nusstein J, Reader A, Beck M, Weaver J. Efficacy and safety of articaine in pediatric dental patients. J Dent Res. 2014;93(Spec Iss A):Abstract 3187.
25. Elheeny AAH. Articaine buccal infiltration versus inferior alveolar nerve block in children. Int J Paediatr Dent. 2016;26(1):28-35.
26. Alamoudi NM, El Ashiry EA, Farsi NM, El Derwi DA. Comparative evaluation of articaine and lidocaine infiltration in children. Pediatr Dent. 2018;40(3):201-5.
27. Tofoli GR, Ramacciato JC, de Oliveira PC, Volpato MC, Groppo FC, Ranali J. Articaine versus lidocaine: a systematic review. Clin Oral Investig. 2019;23(1):305-17.
28. Alzahrani FS, El-Housseiny AA, Farsi NM, Alzahrani AA. Efficacy of articaine infiltration in primary molars. J Dent Child (Chic). 2019;86(2):78-83.
29. Zainab H, Rashid S, Iqbal M, Akram S. Meta-analysis of articaine efficacy in children. Int Endod J. 2021;54(10):1770-81.
30. American Academy of Pediatric Dentistry. Guideline on use of local anesthesia for pediatric dental patients. Pediatr Dent. 2022;44(6):384-91.
31. Dou L, Yang Y, Liu Y, Chen X, Yang Z. Articaine in pulp therapy of primary teeth: a randomized clinical trial. Int J Paediatr Dent. 2023;33(2):123-30.
32. Rahman M, Ali F, Chowdhury A, Yasmin S, Hossain M. Clinical evaluation of 4% articaine in pediatric dentistry. Pediatr Dent J. 2024;34(1):21-7
33. Ram D, Amir E. Comparison of articaine and lidocaine in paediatric dental patients. Int J Paediatr Dent. 2006;16(4):252-6.
34. Katyal V. The efficacy and safety of articaine versus lignocaine in pediatric dental patients: a systematic review. J Dent. 2014;42(3):331-9.
35. Malamed SF, Tavana S, Falkel M. Articaine in dentistry: an evidence-based review. J Am Dent Assoc. 2013;144(8):830-7
36. Arali V, Mytri P. Anaesthetic efficacy of 4% articaine mandibular buccal infiltration compared to 2% lignocaine inferior alveolar nerve block in children with irreversible pulpitis. *J Clin Diagn Res*. 2015;9(4):ZC65–ZC67.
37. Su N, Li C, Wang H, Shen J, Liu W. Efficacy and safety of articaine versus lidocaine for dental anesthesia: a meta-analysis of randomized controlled trials. Quintessence Int. 2020;51(5):396-404.
38. Dhake P, Nagpal D, Chaudhari P, Lamba G, Hotwani K, Singh P. Buffered articaine infiltration for primary maxillary molar extractions: a randomized controlled study. *J Dent Anesth Pain Med*. 2022;22(5):387-94.
39. Day TK, Skarda RT. The pharmacology of local anesthetics. Vet Clin North Am Equine Pract 1991; 7: 489-500.
40. Christoph RA, Buchanan L, Begalla K, Schwartz S. Pain reduction in local anesthetic administration through pH buffering. Ann Emerg Med 1988; 17: 117-20.
41. Eppley BL, Sadove AM. Reduction in injection pain by buffering of local anesthetic solutions. J Oral Maxillofac Surg 1989; 47: 762-3.

42. Malamed SF. Local anesthesia. J Calif Dent Assoc 1998; 26: 657, 660
43. Hemmanur S, Nasim I. Randomized clinical trial of anesthetic efficacy of buffered versus conventional local anesthetic agent in patient with symptomatic irreversible pulpitis. J Pharm Res Int 2020; 32: 1-10
44. 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; 25: 3527-33
45. Kurien RS, Goswami M, Singh S. Comparative evaluation of anesthetic efficacy of warm, buffered and conventional 2% lignocaine for the success of inferior alveolar nerve block (IANB) in mandibular primary molars: a randomized controlled clinical trial. J Dent Res Dent Clin Dent Prospects 2018; 12: 102-9
46. Manta K, Dabarakis N, Lillis T, Fotopoulos I. Anesthetic efficacy of buffered 4% articaine for mandibular first molar infiltration: a crossover clinical trial. *J Dent Anesth Pain Med*. 2023;23(3):135–141. doi:10.17245/jdapm.2023.23.3.135
47. Kamareh S, Soleymani AA, Mozaffari N, Amiri A, Bazghandi B, Khosrozamiri M. Comparative efficacy of buccal infiltration anesthesia with 4% articaine versus inferior alveolar nerve block with 2% lidocaine for extraction of primary mandibular molars: a randomized clinical trial. *J Res Dent Maxillofac Sci*. 2024;9(4):233–242.
48. Oulis CJ, Vadiakas GP, Vasilopoulou A. The effectiveness of articaine in primary molar pulpotomies. Eur Arch Paediatr Dent. 2016;17(3):197-201
49. Becker D, Reed, K. Essentials of local anesthetic pharmacology. Anesth Prog 2006;53:98-109
50. Brickhouse TH, Unkel JH, Webb MB, Best AM, Hollowell RL. Articaine use in children among dental practitioners. Pediatr Dent. 2008;30:516–521 .