



Topical Anesthetics and Reversal Agents

¹Dr Mohanaram Selvaraj, ²Prof. (Dr) Amarshree A Shetty , MDS , PhD

^{1,2}Department of Pediatric & Preventive dentistry, A B Shetty Memorial Institute of Dental Sciences

(Received: 16 September 2024

Revised: 11 October 2024

Accepted: 04 November 2024)

KEYWORDS

Topical, Anaesthetics,

EMLA,

Phentolamine mesylate,

Dental pain

ABSTRACT:

Topical anaesthesia is important to optimize pain control during dental injection. Despite the continuous development of new dental injection techniques, the injection of local anaesthesia still causes discomfort and pain for many patients and has been described as a major reason for dental anxiety. Topical anaesthesia should therefore be used to eliminate or minimize the pain caused by the needle. The methods used today for topical anaesthesia before dental injections mainly include different types of gel (e.g. lidocaine, prilocaine or benzocaine) available at various composition. In order to give our patients, the finest treatment possible at all times, we must continually update, assess, and adopt newer medications and procedures into our everyday practises. This is especially important in the present evidence-based age of dental practice.

1. Introduction

The anaesthetic components which are obtainable in gels, creams, lozenges, patches, and solutions, alongside other forms. ^[2] Mucosal unpleasantness of the oral tissues can be alleviated by 13 different forms of topical anaesthetics and analgesics encompassing various bases. There are numerous analgesic and anaesthetic combinations offered by various manufacturers, including:

- Combination of benzocaine, butamben and tetracaine (Cetacaine)
- Lidocaine and prilocaine (EMLA , Oraqix)
- Lidocaine and tetracaine (Synera)
- Methyl salicylate and menthol (BenGay,Icy Hot) ^[3]

These formulas reflect distinct anaesthetics that are used for varied purposes. ^[3] These formulations have been granted approval authorised for use as topical anaesthetic agents based on the US Food and Drug Administration Society. The majority of topical anaesthetics have little systemic side effects and few medication interactions. However, these medications must be prescribed carefully since they might be harmful in dosages that are not recommended. ^[4]

EUTECTIC MIXTURE OF LOCAL ANESTHETICS (EMLA)

2.5% prilocaine and 2.5% lidocaine rendering up the eutectic combination that constitutes local anaesthetics, or EMLA. It is composed of up of 2.5 percent lidocaine and 2.5 percent prilocaine, two low-melting-temperature crystalline powders in conjunction to formulate a liquid oil. It is capable of penetration intact skin or mucosa up to a depth of 5 mm in that way outlined above. For an array of inaccessible superficial procedures, which include venepuncture, cautery for condylomata, epilation, laser surgery, and superficial surgery, the extensive local anaesthetic that EMLA yields is beneficial. ^[5,6] Only mild and transient skin blanching has been demonstrated in the EMLA tolerance profile, which was equitably appealing. Erythema is said to be the most frequently seen unfavourable side effect of EMLA implementation to skin. ^[6] Some authors have asserted that EMLA is the most efficacious topical treatment in dentistry, despite acknowledging that it was previously contraindicated for the oral mucosa^[7,8]. Additionally, this technique has been harboured for an assortment of minor pre-operative procedures, notably rubber dam clamp, biopsies, and sinus puncture, with phenomenal outcomes in children who perceive pain during venipuncture. ^[9,10,11]

Moreover, EMLA does not hamper wounds from healing. ^[12] Lipophilic pharmaceuticals can be acquired with greater urgency via the oral mucosa owing to its



thinner structure and deeper blood supply when compared to cutaneous tissue. A research investigation investigated whether the plasma concentration of EMLA was below the permissible level of toxicity when it was infused to the oral mucosa. Their results show that following the application of EMLA is liberally applied to the oral mucosa to feed 30 minutes, safe plasma concentrations of lidocaine (418 ng/ml) and prilocaine (223 ng/ml) are attained. The aforementioned concentrations are significantly lower than the comprehended hazardous concentrations of the substances, which are 6.0 g/ml and 4.4 g/ml, respectively. ^[13] EMLA has been administered to reduce pain during dental injections, minor gingivectomy treatments, pocket scaling, and restorative operations, corresponding to a comprehensive investigation. ^[13] EMLA equates in concentrations ranging 2.5 and 5%. Reports demonstrate that the effective duration of 5% EMLA is 2 to 10 minutes ^[14, 15], which is comparable to prolonged intraoral implementation periods. Eutectic blend of topical anaesthetics for periodontal therapy.

An injection of local anaesthetic needs to be administered for scaling and root planing interventions, although there is substantial proof to support this method of treatment. ^[16,17] Unfortunately, there's no way to completely eliminate anxiety and aversion to needles when dispensing local anaesthetic. ^[18] As a consequence of this, some patients are a lot more inclined to expertise the discomfort experienced with scaling and root planing than refrain from keeping up with their injection-related anxiety and apprehension. ^[19] Comparing EMLA, the lidocaine patch equivalent, to a placebo, individuals who had moderate chronic periodontitis endured less pain and discomfort despite intervention. ^[20,21] The effects of topical 2% benzocaine, injectable 2% lidocaine, EMLA 25 mg/g, and a placebo on pain alleviation was evaluated in this study. It emerged that EMLA was more effective than the other two categories and on par with injectable lidocaine. ^[22] Due to the topical anaesthetic's shorter duration of pain, discomfort, and numbness, 70% of research participants preferred it. Furthermore, 6.2% of the EMLA group, 25% of the benzocaine group, and 50% of the placebo group acknowledged experiencing pain intolerance. ^[24]

In accordance with experts, there is an association between the depth of the pocket and the magnitude of

discomfort experienced whilst on root planing and scaling. The clinical efficacy of EMLA intra-pocket on 638 individuals complied with for root planing and scaling was examined in a remarkable study. Results revealed that 72% of participants chose to use EMLA for scaling and root planing, even in cases with extensive periodontal pockets. ^[24] In distinct perspectives trial, 25 patients with a 5 mm periodontal pocket depth underwent scaling and root planing procedures executed while the therapeutic benefits of EMLA, a 20% lignocaine patch, and electronic dental anaesthesia were investigated. The results showed that an electronic dental anaesthetic was significantly inferior to a 20% lignocaine patch and a 5% EMLA among the medications under evaluation. ^[25] a study to determine how well EMLA influences patients' perceptions of pain during root planing and scaling. Additionally, they analysed the frequency and intensity of discomfort generated by manual and ultrasonic tools. ^[23] They claimed that there are notable improvements in patient comfort when EMLA is used in conjunction with ultrasonic devices.

Implement a topical eutectic mixture of local anaesthetics prior to administering a needle injection. The palatal mucosa, especially in the anterior region, is resistive to the effects of topical anaesthetics due to its thick, keratinized layer, which sets it apart from other intraoral locations. The insertion of needles during local anaesthetic infiltration can trigger discomfort for the preceding indicated reason. ^[24, 25] Less frequently than nonetheless, palatal injection discomfort correlates with the repositioning of the mucoperiosteum in lieu of the puncture. ^[26] Furthermore, considering the palatal mucosa is among the most uncomfortable regions to puncture, an individualised test can be performed to assess how effectively various topical anaesthetic drugs work. ^[27] Before palatal injection, the effectiveness of liposome-encapsulated 2% ropivacaine, liposome-encapsulated 1% ropivacaine, and EMLA had been evaluated. Local anaesthetic gets eliminated incrementally by drug delivery phospholipid vesicles which are referred to as liposomes, which additionally enhances cutaneous and percutaneous penetration. ^[27] Although EMLA emerged to be a more effective analgesic than the other drugs examined, no statistically significant differences were witnessed. ^[27]



A subsequent research investigation appraised the efficacy of a multitude of topical anaesthetics preceding palatal injection, such as 2.5% lidocaine, 5% xylocaine, 2.5% EMLA, and liposome-encapsulated 2.5% lidocaine. The outcomes concurred with the earlier research, which revealed that when compared to other medications, 5% liposome-encapsulated lidocaine and EMLA produced the best anaesthetic effects.^[28] Another way to assess the therapeutic value of the aforementioned topical anaesthetics in a clinical study was to place 20 mg, 60 mg, 60 mg, and 20 mg of ropivacaine gel, all at 1% each, in the buccal fold of the maxillary canine tooth prior to local anaesthetic infiltration. The end outcomes demonstrated that all topical anaesthetics reduced needle penetration pain in a comparable manner, although EMLA 60 mg promoted a longer duration of soft tissue paresthesia.^[29] Another study investigated 40 patients who underwent palatal anaesthetic infusion and the anaesthetic efficacy of 20% benzocaine gel and EMLA. They predicted that the EMLA group's pain scores were significantly reduced than those of the other groups.^[30] Moreover, analysing the differences between EMLA and lignocaine gel revealed that EMLA had more effective anaesthetic efficacy.^[8]

Limitations:

There are a couple of minor adverse reactions to be cognizant of when utilising EMLA, however no significant side effects or contraindications emerge. Oedema, erythema, and transient pallor are the most commonly encountered challenges experienced when EMLA is applied externally.^[30] Furthermore, an EMLA overdose could result in methemoglobinemia and seizures.^[30] In allusion to oral administration, another investigation reported cases in which topical EMLA use was confirmed by gingival desquamation and ulceration.^[31]

Reversing local anesthesia:

A common unintentional side effect of intraoral local anaesthetic is the development of long-lasting lingual and facial numbness. Many dental patients contend that long-term soft tissue anaesthesia makes it difficult for them to talk normally. Self-inflicted injuries can occur. To alleviate functional abnormalities brought on by soft tissue anaesthesia after using a local anaesthetic, the FDA approved Oraverse (phentolamine mesylate) in

May 2009. When used by adults and kids as young as 6 years old, Whenever it comes to shortening the time required for recovery implementing soft tissue local anaesthetic, phentolamine appeared to be effective as well as safe.^[32,33,34] According to a few studies, children as young as four have a good safety profile.^[35] Recent investigations^[36] investigated Oraverse consumers' usage tendencies and queries from dentists and patients. 51 dentists who provided data on 390 patients ranging in age from 4 to 90 were approached for information. Patients reported shorter mouth numbness multiple times (92%), and better dental experiences (84%). Patients as a whole said that 79% would pick Oraverse in the future and 83% would recommend the medication to others. Dentists said that the medicine exceeded their expectations (82%), met their demands (86%), helped them stand out from the competition (55%), helped them expand their businesses (45%), and improved scheduling (29%). Both patients and dentists reported feeling very satisfied.

pH buffering of local anaesthesia

It is now feasible, according to recent technological advancements, to alkalize dental anaesthetic cartridges at the injection site. For dentists interested in local anaesthesia that is quicker, more effective, and more predictable while also being more pleasant for the patient, it is worthwhile to take into account the science of buffering local anaesthetic. Alkalinisation reduces injection discomfort and hastens the onset of analgesia. Clinicians are instructed by research to buffer each injection and the cartridge shortly prior to administration.^[37]

FUTURE TRENDS

The development of more sophisticated tools and methods to manufacture profound anaesthesia nasal spray, that somewhat has been highlighted in an FDA Phase 3 trial that can completely numb the six maxillary front teeth, should be the primary goal of future research. This is in contrast to the uncomfortable anaesthetic injections that are momentarily the "gold standard" of care. A state-of-the-art dental equipment called the Syringe Micro Vibrator (SMV) [38] is used for alleviating injection-related apprehension and anxiety.



CONCLUSION

The aim of pain-free dentistry has not yet been achieved due to the practitioner's constraints in updating about current medication formulations and novel procedures to deliver the treatments. When the advantages outweigh the drawbacks, availability and cost concerns are not justifications for not implementing newer, more effective approaches. In order to give our patients the finest treatment possible at all times, we must continually update, assess, and adopt newer medications and procedures into our everyday practises. This is especially important in the present evidence-based age of dental practise.

References

- 1) Daneshkazemi A, Abrisham SM, Daneshkazemi P, Davoudi A. The efficacy of eutectic mixture of local anesthetics as a topical anesthetic agent used for dental procedures: A brief review. *Anesthesia, essays and researches*. 2016 Sep;10(3):383.
- 2) Chan SK, Karmakar MK, Chui PT. Local anaesthesia outside the operating room. *Hong Kong Med J*.2002;8:106–13
- 3) McLure HA, Rubin AP. Review of local anaesthetic agents. *Minerva Anesthesiol*. 2005;71:59–74.
- 4) Kaweski S. Plastic Surgery Educational Foundation Technology Assessment Committee. Topical anesthetic creams. *Plast Reconstr Surg*. 2008;121:2161–5
- 5) Parker JF, Vats A, Bauer G. EMLA toxicity after application for allergy skin testing. *Pediatrics*.2004;113:410–1.
- 6) Buckley MM, Benfield P. Eutectic lidocaine/prilocaine cream. A review of the topical anaesthetic/analgesic efficacy of a eutectic mixture of local anaesthetics (EMLA) *Drugs*. 1993;46:126–51.
- 7) Vickers ER, Punnia-Moorthy A. Pulpal anesthesia from an application of a eutectic topical anesthetic. *Quintessence Int*. 1993;24:547–51.
- 8) McMillan AS, Walshaw D, Meechan JG. The efficacy of Emla and 5% lignocaine gel for anaesthesia of human gingival mucosa. *Br J Oral Maxillofac Surg*. 2000;38:58–61.
- 9) Manner T, Kanto J, Iisalo E, Lindberg R, Viinamäki O, Scheinin M. Reduction of pain at venous cannulation in children with a eutectic mixture of lidocaine and prilocaine (EMLA cream): Comparison with placebo cream and no local premedication. *Acta Anaesthesiol Scand*. 1987;31:735–9.
- 10) Hopkins CS, Buckley CJ, Bush GH. Pain-free injection in infants. Use of a lignocaine-prilocaine cream to prevent pain at intravenous induction of general anaesthesia in 1-5-year-old children. *Anaesthesia*. 1988;43:198–201.
- 11) Halperin DL, Koren G, Attias D, Pellegrini E, Greenberg ML, Wyss M. Topical skin anesthesia for venous, subcutaneous drug reservoir and lumbar punctures in children. *Pediatrics*. 1989;84:281–4.
- 12) Al-Asfour A, Al-Melh M, Andersson L, Joseph B. Healing pattern of experimental soft tissue lacerations after application of novel topical anesthetic agents – An experimental study in rabbits. *Dent Traumatol*. 2008;24:27–31
- 13) Vickers ER, Marzbani N, Gerzina TM, McLean C, Punnia-Moorthy A, Mather L. Pharmacokinetics of EMLA cream 5% application to oral mucosa. *AnesthProg*. 1997;44:32–7.
- 14) Tulga F, Mutlu Z. Four types of topical anaesthetic agents: Evaluation of clinicaeffectiveness. *J Clin Pediatr Dent*. 1999;23:217–20.
- 15) Barcohana N, Duperon DF, Yashar M. The relationship of application time to EMLAefficacy. *J Dent Child (Chic)* 2003;70:51–4.
- 16) van Steenberghe D, Garmyn P, Geers L, Hendrickx E, Maréchal M, Huizar K, et al. Patients' experience of pain and discomfort during instrumentation in the diagnosis and non-surgical treatment of periodontitis. *J Periodontol*. 2004;75:1465–70.
- 17) Canakci V, Canakci CF. Pain levels in patients during periodontal probing and mechanical non-surgical therapy. *Clin Oral Investig*. 2007;11:377–83.
- 18) Kumar PS, Leblebicioglu B. Pain control during nonsurgical periodontaltherapy. *Compend Contin Educ Dent*. 2007;28:666–9.
- 19) van Steenberghe D, Bercy P, De Boever J, Adriaens P, Geers L, Hendrickx E, et al. Patient evaluation of a novel non-injectable anesthetic gel: A multicenter crossover study comparing the gel to infiltration anesthesia during scaling and root planing. *JPeriodontol*. 2004;75:1471–8.



- 20) Antoniazzi RP, Cargnelutti B, Freitas DN, Guimarães MB, Zanatta FB, Feldens CA. Topical intrapocket anesthesia during scaling and root planing: A randomized clinical trial. *Braz Dent J.* 2015;26:26–32.
- 21) Chung JE, Koh SA, Kim TI, Seol YJ, Lee YM, Ku Y, et al. Effect of eutectic mixture of local anesthetics on pain perception during scaling by ultrasonic or hand instruments: A masked randomized controlled trial. *J Periodontol.* 2011;82:25966.
- 22) Derman SH, Lowden CE, Kaus P, Noack MJ. Pocket-depths-related effectiveness of an intrapocket anaesthesia gel in periodontal maintenance patients. *Int J Dent Hyg.* 2014;12:141–4.
- 23) Pandit N, Gupta R, Chandoke U, Gugnani S. Comparative evaluation of topical and electronic anesthesia during scaling and root planing. *J Periodontol.* 2010;81:1035–40.
- 24) Meechan JG. Effective topical anesthetic agents and techniques. *Dent Clin NorthAm.* 2002;46:759–66.
- 25) Abu Al-Melh M, Andersson L, Behbehani E. Reduction of pain from needle stick in the oral mucosa by topical anesthetics: A comparative study between lidocaine/prilocaine and benzocaine. *J Clin Dent.* 2005;16:53–6.
- 26) Franz-Montan M, de Paula E, Groppo FC, Silva AL, Ranali J, Volpato MC. Liposomal delivery system for topical anaesthesia of the palatal mucosa. *Br J OralMaxillofac Surg.* 2012;50:60–4.
- 27) Svensson P, Petersen JK. Anesthetic effect of EMLA occluded with Orahesive oral bandages on oral mucosa. A placebo-controlled study. *Anesth Prog.* 1992;39:79–82.
- 28) Franz-Montan M, Baroni D, Brunetto G, Sobral VR, da Silva CM, Venâncio P, et al. Liposomal lidocaine gel for topical use at the oral mucosa: Characterization, in vitro assays and in vivo anesthetic efficacy in humans. *J Liposome Res.* 2015;25:11–9.
- 29) Rincon E, Baker RL, Iglesias AJ, Duarte AM. CNS toxicity after topical application of EMLA cream on a toddler with molluscum contagiosum. *Pediatr Emerg Care.* 2000;16:252–4.
- 30) Hahn IH, Hoffman RS, Nelson LS. EMLA-induced methemoglobinemia and systemic topical anesthetic toxicity. *J Emerg Med.* 2004;26:85–8.
- 31) Franz-Montan M, Ranali J, Ramacciato JC, de Andrade ED, Volpato MC, Groppo FC. Ulceration of gingival mucosa after topical application of EMLA: Report of four cases. *Br Dent J.* 2008;204:133–4.
- 32) Hochman MN. Single-tooth anesthesia: Pressuresensing technology provides innovative advancement in the field of dental local anesthesia. *Compend Contin Educ Dent.* 2007;28:186–93.
- 33) Hersh EV, Moore PA, Papas AS, Goodson JM, Navalta LA, Rogy S, et al. Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults. *J Am Dent Assoc.* 2008;139:1080–93.
- 34) Laviola M, McGavin SK, Freer GA, Plancich G, Woodbury SC, Marinkovich S, et al. Randomized study of phentolamine mesylate for reversal of local anesthesia. *J Dent Res.* 2008;87:635–9.
- 35) Tavares M, Goodson JM, Studen-Pavlovich D, Yagiela JA, Navalta LA, Rogy S, et al. Reversal of soft-tissue local anesthesia with phentolamine mesylate in pediatric patients. *J Am Dent Assoc.* 2008;139:1095–104.
- 36) Rafique S, Fiske J, Banerjee A. Clinical trial of an air-abrasion/chemomechanical operative procedure for the restorative treatment of dental patients. *Caries Res.* 2003;37:360–4.
- 37) Saunders TR, Psaltis G, Weston JF, Yanase RR, Rogy SS, Ghalie RG. In-practice evaluation of OraVerse for the reversal of soft-tissue anesthesia after dental procedures. *Compend Contin Educ Dent.* 2011;32:58–62.
- 38) Malamed SF, Falkel M. Advances in local anesthetics: pH buffering and dissolved CO₂. *Dent Today.* 2012;31:88–93.