



Recent advances in topical anesthesia

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Topical anesthetics act on the peripheral nerves and reduce the sensation of pain at the site of application. In dentistry, they are used to control local pain caused by needling, placement of orthodontic bands, the vomiting reflex, oral mucositis, and rubber-dam clamp placement. Traditional topical anesthetics contain lidocaine or benzocaine as active ingredients and are used in the form of solutions, creams, gels, and sprays. Eutectic mixtures of local anesthesia cream, a mixture of various topical anesthetics, has been reported to be more potent than other anesthetics. Recently, new products with modified ingredients and application methods have been introduced into the market. These products may be used for mild pain during periodontal treatment, such as scaling. Dentists should be aware that topical anesthetics, although rare, might induce allergic reactions or side effects as a result of an overdose. Topical anesthetics are useful aids during dental treatment, as they reduce dental phobia, especially in children, by mitigating discomfort and pain.

Keywords: Administration, Topical; Anesthetics; Benzocaine; EMLA; Lidocaine.

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INTRODUCTION

The word anesthesia is a compound word from the Greek words an- (“without”) and aesthesis (“sensation”). Anesthesia is broadly divided into general and local anesthetics. Local anesthesia refers to a loss of sensation caused by a reversible blockade of nerve conduction around the site of application. In dentistry, local anesthetics are administered via a variety of anesthetic techniques that are classified according to their specific effects as (1) conduction anesthesia, (2) infiltration anesthesia, (3) topical anesthesia or surface anesthesia [1].

Although conduction anesthesia and infiltration anesthesia produce a deep anesthesia, the use of needles may arouse fear and pain in patients. On the other hand, although the intensity of the anesthesia is weak, topical

anesthetics have little side effects with easy administration and reduces pain caused by needle injections and can thus generate positive responses towards dental treatment in patients. There are ongoing efforts to develop various forms of topical anesthetics with more potent effects in order to facilitate the provision of quality care by dentists, upon a thorough understanding of the products [2].

In this article, we aim to review the uses of and recent advances in topical anesthetics in dentistry. We also review traditional topical anesthetics and recently developed products, as well as discuss the rare but possible adverse reactions of topical anesthetics.

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USE OF TOPICAL ANESTHETICS IN DENTISTRY

Topical anesthetics alter pain thresholds by controlling pain sensations through a blockade of signals that are transmitted from the peripheral sensory nerve fibers. However, they are only effective in blocking the pain stimuli in the superficial layer of the mucosa. Local anesthetics that are used for topical anesthesia must have superior mucosal permeability in order to easily reach free nerve terminals [1]. Vasoconstrictors are not added to topical local anesthetics because they undermine mucosal permeability. Furthermore, topical local anesthetics are typically more concentrated than injectable anesthetics in order to promote diffusion after passing through the mucosa [3].

Cocaine has been used as a topical anesthetic agent in the past for its potent anesthetic effect and local vasoconstrictive properties, but its use is currently very limited because of high toxicity and risk of acute addiction [2]. Lidocaine and benzocaine are widely used for their low toxicity and potent topical anesthetic effects and several products with mixed ingredients have been introduced in the market recently [3].

Topical anesthetic products are in the form of sprays, solutions, gels, and ointments. There is a wide range of indications for topical anesthesia in dentistry and a specific agent should be chosen in accordance with the purpose of its use (Table 1) [4]. Sprays can effectively block a wide surface, but prolonged exposure increases the risk for absorption into the circulatory system. It is known that spray anesthetics are good for use prior to

Table 1. Indications for surface anesthesia in dentistry

- Needle insertion for conduction or infiltration anesthesia
- Control of pain in a wounded area
- Placement of orthodontic bands
- Inhibition of vomiting (for radiographic imaging or impression)
- Dry socket
- Simple extraction of primary tooth
- Rubber-dam clamp placement
- Surgical treatment of the mucosal surface, such as superficial submucosal abscess incision
- Inhibition of reflexes during endotracheal intubation
- Root planning or scaling

oral radiographs and prior to taking impressions for dentures in patients with an excessive vomiting reflex. Solutions are effective when anesthesia is needed to cover a wide surface area without the risk of aspiration. Gels or ointments are effective for pain relief caused by a laceration or abrasion and can alleviate pain at the point of injection of local anesthetics [4].

Generally, topical anesthesia is applied by after drying the mucous membrane or skin where the anesthesia will be administered and spraying or using a cotton swab to apply the minimal amount required to produce an adequate effect. Since the duration of action of the topical anesthetic is about 10 minutes, the subsequent procedure should be performed in approximately two minutes after administration [5]. Methods of use vary for each product, so adhering to the manufacturer's instructions is recommended. Furthermore, the effects of topical local anesthetic agents are enhanced when the mucosal surface is dry; therefore, surfaces should be adequately dried prior to administration. Topical anesthetic agents are generally concentrated to facilitate infiltration; hence, they should be applied as a thin layer over a small area to avoid toxicity. Although topical anesthetics are safer than injections, practitioners should beware of allergic reactions in all patients with hypersensitivities or neuropathies [4,5].

COMPOSITION OF TOPICAL ANESTHETICS (Table 2)

1. Benzocaine

Benzocaine is an ester-based local anesthetic agent (ethyl ester of p-aminobenzoic acid [PABA]). Compared to amide-based local anesthetics, ester-based local anesthetics are commonly associated with allergic reactions

Table 2. Types of topical anesthetics

Non-aqueous	Ethyl aminobenzoate (benzocaine)
	Lidocaine base
Aqueous	Benzyl alcohol
	Tetracaine hydrochloride
	Lidocaine hydrochloride

due to the structure of PABA. Its poor water solubility hinders cardiovascular absorption and benzocaine residues remain on the applied surface for relatively prolonged periods. It is generally produced in the form of a spray, gel, gel patch, ointment, or solution as a 6-20% concentration, depending on the manufacturer [6]. Aerosol agents may be used on the soft palate to reduce the vomiting reflex when taking impressions, while gel agents may be used prior to infiltration anesthesia to minimize pain and discomfort caused by the needle injection. Ointments and solutions are used for patients with aphthous ulcers [7]. Twenty-percent polyethylene glycol-based agents are most commonly used for topical anesthesia and low-concentration agents are used for surgical dressings.

Agents that are made to 20% concentration typically produce an effect within 30 seconds, but about two to three minutes are required until an adequate depth and intensity are achieved. Benzocaine reduces pre-injection pain in the alveolar mucus and is effective for anesthesia of the tongue. However, it is hardly effective for inducing anesthesia in the palatal mucous membrane because it is thick and firm with densely packed nerves. Once anesthesia is achieved, the duration of action is approximately 5 to 15 minutes [8].

2. Tetracaine hydrochloride

Tetracaine is an ester derivative of PABA. Its lipid solubility and anesthetic efficacy was elevated by replacing a hydrogen of the p-amino group with a butyl. In fact, tetracaine is 5 to 8 times more efficacious than cocaine and is the most potent among dental topical anesthetics. Products are available in the form of a spray solution or ointment in concentrations ranging from 0.2 to 2.0%. Products with 0.15% concentrations are sold as injectable agents [9-11].

The onset of action is 2 minutes and duration of action ranges from 20 minutes to 1 hour. Tetracaine is quickly absorbed into the mucous membrane, especially in the respiratory mucosa; hence, doses should be limited to 20 mg (1 ml for 2% solutions) per session even in healthy adults. An overdose may induce various adverse reactions.

3. Lidocaine and Lidocaine hydrochloride

Lidocaine is the only amide-based local oral topical anesthetic that is also used as an injectable anesthetic. In dentistry, lidocaine is used as a 2% or 5% gel, 2% solution, 4% or 5% solution, 5% ointment, or 10% spray [12]. The onset of action is approximately 1 to 2 minutes

Table 3. Ingredients of topical anesthetics and topical anesthetic products

Category	Ingredient	Product	Features
Single	20% Benzocaine	Hurricane (Beutlich LP Pharmaceuticals, USA)	Various types and scents (Gel, solution, etc.)
		HurriPAK (Beutlich LP Pharmaceuticals, USA)	Syringe applicable on gingival sulcus
		Topex (Sultan Healthcare, USA)	Gel and spray
		Orabase (Colgate Oral Pharmaceuticals, USA)	Ointment
		Ultracare (Ultradent, USA)	Gel
	5% Lidocaine	Xylonor Gel (Septodont, Canada)	Gel
		Xylocaine (Astrazeneca, USA)	Ointment
	10% Lidocaine	Xylocaine (Astrazeneca, USA)	Spray
		Xylonor Spray (Septodont, Canada)	Spray
		EMLA cream (Astrazeneca, USA)	Cream
Mixed	2.5% Lidocaine	OraQix (Dentsply, USA)	Syringe applicable on gingival sulcus
	2.5% Prilocaine	Cetacaine (Cetylite, USA)	Spray
	20% Benzocaine		Syringe applicable on gingival sulcus
	2% Aminobenzoate		
	2% Tetracaine		
	18% Benzocaine	One Touch (Hager Worldwide, USA)	Gel
	15% Tetracaine		
10% Lidocaine	Profound (Woodland Hills Compounding Pharmacy, USA)	Gel	
4% Tetracaine			
10% Prilocaine			

and duration of action is approximately 15 minutes, with peak efficacy occurring at 5 minutes. Although 5% ointments have a similar potency to 20% benzocaine, its onset of action is more delayed, requiring at least 3 minutes to achieve adequate anesthesia. It is effective on alveolar mucus, but not on the palatal mucous membrane. Lidocaine solution is an ingredient of Magic Mouth Wash rinse and may be used for patients with oral mucositis caused by radiation and chemotherapies [13].

4. Prilocaine

Prilocaine is the most popular amide-based local anesthetic agent used for infiltration anesthesia in dental procedures. It is used in combination with other topical anesthetics [14]. Prilocaine is a secondary amide, unlike mepivacaine and lidocaine. Prilocaine is used as two types of formulations, 4% prilocaine or 4% prilocaine with 1:200,000 epinephrine. Regardless of the presence of epinephrine, the maximum dose of prilocaine for adults is 2.7 mg/lb or 6 mg/kg. The total dose should not exceed 400 mg in adults. Prilocaine is relatively safe for use in pregnant women, with a Pregnancy Category B status.

EUTECTIC MIXTURES OF LOCAL ANESTHESIA (EMLA) CREAM

Mixtures of topical anesthetic agents used for local anesthesia are called eutectic mixtures of local anesthesia (EMLA). Mixing refers to the process of combining drugs or replacing an ingredient to prepare a commercial drug. The ultimate goal is to produce potent mixtures of local anesthetics to be used in procedures or surgeries that cause minimal or considerable pain. Such mixtures have lower melting points, which in turn promotes easier absorption of the EMLA into the oral mucous membrane [15].

EMLA cream, a 1:1 mixture of 2.5% prilocaine and 2.5% lidocaine, was first used as a cutaneous topical anesthetic in dermatology in the 1980's [16]. Holst and Evers were the first to attempt the administration of

EMLA cream within the oral cavity. Their results showed high efficacy in the attached gingiva [17]. Since this study, multiple studies have documented the application of EMLA cream on mucosal surfaces. In addition, several reports have noted that the use of EMLA cream reduced pain during probing, hand scaling, ultrasonic scaling, rubber-dam clamp placement, and palatine nerve block [18-25].

Nayak and Sudha suggested that the low viscosity of EMLA cream renders it difficult to handle, which in turn makes it difficult to administer locally as a topical anesthetic at the site of the needle injection [26]. To overcome this setback, Svensson and Peterson used an Orahesive bandage, which improved the pain relief effects of the topical anesthetic [27]. Despite various findings pertaining to the potential of EMLA cream for use in dentistry, the manufacturer does not recommend the use of the cream on mucous membranes. Further, additional studies are needed to identify the appropriate dose and duration of exposure in children to prevent overdose and side effects.

RECENT DEVELOPMENTS IN TOPICAL ANESTHETIC AGENTS FOR PERIODONTAL PROCEDURES

About two-thirds of all patients find scaling procedures to be painful. Approximately 30% of patients have been reported to feel pain during scaling and root planing [28,29]. However, infiltration anesthesia for the purpose of controlling such pain may actually cause pain and fear. Furthermore, all four quadrants cannot be treated simultaneously with infiltration anesthesia and dentists are required to administer additional anesthetics [30]. Thus, there are ongoing efforts to develop a topical anesthetic that could be used for periodontal procedures [31,32].

1. HurriPAK Periodontal Anesthetic Kit

HurriPak (Beutlich LP Pharmaceuticals, FL, USA) is a 20% benzocaine solution that is sold as a needle-free

periodontal anesthetic kit. The product comprises of a plastic syringe (3 ml) and disposable plastic tips [1], which are inserted deep within the gingival sulcus. The onset of action is 30 seconds and duration of action is approximately 15 minutes. Fifteen minutes is generally not enough time for performing procedures in adults, so re-administration of the solution, infiltration anesthesia, or periodontal ligament anesthesia using needle injections may be needed.

2. Cetacaine Topical Anesthetic

Cetacaine (Cetylite, NJ, USA) contains 14% benzocaine, 2% butamben, and 2% tetracaine-hydrochloric acid and is used for controlling local pain in all mucous membranes, except for the eyes [1]. This product should never be used for injections. The anesthetic kit is comprised of the solution, a syringe, and applicator tip that enables access to the periodontal pocket. The solution may be applied using a cotton swab or microbrush.

3. Oraqix Subgingival Anesthetic

In 2004, the FDA approved Oraqix (Dentsply, Pennsylvania, USA) for dental use. Oraqix contains 2.5% lidocaine and 2.5% prilocaine and is packaged with 20 cartridges and tips [1,14]. It is a non-injectable gel anesthetic that is administered by insertion into the gingival sulcus, where it produces its anesthetic effects to enable deep scaling and root planing [33-37]. It has been reported that Oraqix is also effective for application of orthodontic bands [38]. Combining Oraqix with other local anesthetics must be performed with caution.

SIDE EFFECTS AND PRECAUTIONS

Topical local anesthetics are considered relatively safe and not many adverse reactions have been associated with them. The most common side effect is tissue stimulation (when topical anesthetics are applied for prolonged periods) and a temporary altered sense of taste [39]. However, some types of topical anesthetics that combine

esters and amides to produce potent anesthetic effects have a potential risk for allergic reactions. Ester-based agents, as PABA derivatives, are known allergens and a subset of the population have shown allergic reactions to these drugs. Actual allergic reactions to amide-based local anesthetics are highly rare [40]. If the patient has a history of allergic reactions to local anesthetics, the dose of the anesthetic used at the time and whether the patient received dental treatment after the allergic reaction should be checked. If no decision can be made regarding the patient's allergy to the anesthetic, the patient should be sent to an allergy specialist for testing with a diluted solution as well as a subcutaneous injection of an undiluted solution. If an allergy is present, the patient may show signs and symptoms, such as skin stimulation accompanied by itching, edema, swollen marks in the face and neck, nasal discharge, shortness of breath, wheezing, and headache [41].

In addition, benzocaine is a well-known cause of methemoglobinemia [42]. The FDA continually warns healthcare specialists and patients that benzocaine-associated methemoglobinemia is consistently documented in the literature and can induce severe or even fatal outcomes [1,43,44]. Methemoglobinemia, which has also been associated with EMLA cream and prilocaine [45,46], is a disorder in which a high concentration of methemoglobin (hemoglobin with the iron in the heme group oxidized to the ferric state) accumulates in the blood. It induces cyanosis and is caused either by a genetic metabolic defect in humans or drug intake. Benzocaine is prohibited in patients with a history of methemoglobinemia or pediatric patients younger than two years of age [47]. Methemoglobinemia may result even with a single administration of benzocaine or may result unexpectedly after a few administrations. Signs and symptoms may occur in a few minutes to two hours after using topical benzocaine within the oral cavity or spraying benzocaine into the oropharyngeal isthmus to prevent vomiting.

It has been reported that EMLA cream can sometimes lead to regional pallor, flare, edema, an early burning

sensation, and rare itching [48]. In addition, it may also induce allergic and anaphylactic reactions, including hives, vascular edema, bronchospasms, and shock. Although rare, EMLA may result in methemoglobinemia in children [45,49].

CONCLUSION

Topical anesthetics are highly useful for reducing discomfort, pain, and anxiety during dental procedures. Traditional topical anesthetic agents with benzocaine and lidocaine as active ingredients are available in various forms and products should be selected based on the intended use. In addition, newly developed topical anesthetic products feature heightened anesthetic effects by combining several ingredients or could be used on periodontal tissues. Although rare, topical anesthetics can induce allergic reactions or side effects, such as methemoglobinemia; therefore, practitioners should perform thorough history-taking and be careful not to overdose patients. It is recommended that dentists gain a proper understanding of topical anesthetics in order to improve the quality of care.

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