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Effective topical anesthetic agents and techniques

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Anxiety is still a barrier to dental attendance [1]. Fear of pain is one reason a patient may be apprehensive about dental treatment. That the most common form of pain control in dentistry, namely local anesthesia, can itself produce anxiety [2] is unfortunate. There are several factors that influence dental injection pain. A variety of techniques are used to overcome this discomfort. These include suggestion [3], alteration of factors related to the injected solution such as pH and temperature [4,5], and a reduced speed of injection. Another method is to prepare the surface tissues before needle penetration. Methods of surface anesthesia include refrigeration [6], transcutaneous electronic nerve stimulation [7], and topical anesthesia. Topical anesthesia relies on the pharmacologic effect of anesthetics when applied to surface tissue. In addition to its use as a means of reducing injection discomfort, topical anesthetics may be used alone or as components of proprietary preparations used as symptomatic treatments for painful oral mucosal lesions such as ulcers [8]. Topical anesthesia also has been used as the sole means of anesthesia for intraoral soft tissue surgery [9,10] and extraction of teeth [11,12]. One of the ''holy grails'' in dentistry is the achievement of pulpal anesthesia by topical application of an anesthetic, and although this is not yet a reliable technique, this objective has been pursued [13].

Topical anesthetics are available in several formulations in North America. They are supplied in the forms of aerosols, ointments, gels, lozenges, tablets, pastes, powders, solutions, and impregnated patches (Fig. 1). Specialized application systems, such as incorporation into liposomes [14,15] or delivery by iontophoresis [11], also have been investigated.

This article is concerned with the use of topical anesthetics before the injection of local anesthetics in dentistry. The first important question to ask in relation to topical anesthetics is, are they effective? Preparation of the

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Fig. 1. Topical anesthesia is effective in masking injection discomfort when applied to the maxillary buccal fold. The time of application influences efficacy, however. A lidocaine-impregnated patch has been applied in this case.

surface tissues could reduce discomfort by two mechanisms. There may be an advantageous effect psychologically and there may be a pharmacologic action. In dental practice, any benefit is important and thus the psychologic impact of topical anesthetics should not be disregarded. Martin et al [16] have shown that subjects who are informed they are to receive a topical anesthetic for comfort anticipate less injection pain than those not offered such counseling. This may decrease apprehension [16]. If there is no pharmacologic effect, however, why use an anesthetic agent? If there is a pharmacologic effect, then the use of an anesthetic is sensible. It is possible to separate psychologic and pharmacologic effects in well designed clinical trials and this article considers this aspect.

What is the evidence that topical anesthetics are effective?

There are several published studies that have investigated the pharmacologic effect of intraoral topical anesthetics and the results are conflicting. Reasons for variation in results are caused by different methodology, such as the use of a variety of agents, differing sites of test, and various types of test stimuli. To reduce confounding factors, the studies referred to in this section are limited to those that have compared topical anesthetics with placebo before either needle penetration of oral mucosa or intraoral injection. In addition, as several factors such as bias and the order of injection [16] can influence the results, only randomized, double-blind studies have been included.

Hersh et al [17] investigated the efficacy of patches containing 10% (23 mg) or 20% (46.5 mg) lidocaine (Dentipatch) when applied for 15 minutes just apical to the mucogingival junction in the maxillary and mandibular premolar region. The test stimulus was insertion of a 25-gauge needle to the point of

bony contact. Efficacy was tested at several time points following application of the patch. These investigators found that neither patch differed from placebo 2.5 minutes after maxillary application. Both patches achieved an analgesic effect at 5 minutes, however, and this lasted for 15 minutes. With the 20% patch there was still an analgesic effect at 45 minutes. These workers considered the duration of anesthesia to be 10 minutes for the 23-mg patch and at least 40 minutes for the 46.5-mg patch in the maxilla. In the mandible, the 46.5-mg patch achieved an effect at 2.5 minutes and the 23-mg patch at 5 minutes. An analgesic effect in the mandible was still present at the 45-minute test. There was a clear dose response in the mandible.

Holst and Evers [18] compared 5% lidocaine with placebo and found that in the lower buccal fold a 2-minute application produced an analgesic effect when the test stimulus was insertion of a 30-gauge needle to a depth of approximately 2 mm.

Rosivack et al [19] compared the 3-minute application of 20% benzocaine and 5% lidocaine with placebo in reducing the discomfort of 27-gauge needle penetration in the maxillary buccal sulcus. Both topical agents reduced discomfort compared with placebo.

Carrell et al [20] reported that topical anesthetics containing 5% lidocaine reduced the incidence of crying in children during local anesthesia compared with the application of placebo.

Svensson and Petersen [21] investigated insertion of a 27-gauge needle in palatal mucosa and noted that a 5-minute application of eutectic mixture of local anesthetics (EMLA) (a 5% eutectic mixture of lidocaine and prilocaine) reduced discomfort compared with placebo.

Vickers and Punnia Moorthy [22] compared three different topical agents to placebo after a 2-minute application in the maxillary buccal sulcus. EMLA cream, 5% lidocaine, and the combination of 15% benzocaine with 1.7% amethocaine were all better than placebo at reducing the discomfort of 27-gauge needle penetration.

Unlike the other studies described that looked at only needle penetration, Hutchins et al [23] studied the effect of a 1-minute application of 20% benzocaine compared with placebo before local anesthetic injections by way of a 27-gauge needle. They found that in the maxillary buccal fold, the topical anesthetic was more effective than placebo in reducing injection discomfort; however, in the palatal mucosa there was no difference between active and placebo treatments.

All of the investigations considered earlier demonstrated a positive result in at least one aspect studied. Not all randomized, double-blind, placebo-controlled trials have reported differences between topical anesthetics and placebo, however. Gill and Orr [24] compared three topical anesthetics (5% lidocaine, 22% benzocaine, 2% amethocaine with 18% benzocaine) with placebo. They used a 30-second application on palatal mucosa and stimulated the mucosa with penetration of a 25-gauge needle. They found no difference in injection discomfort between treatments.

Kincheloe et al [25] compared the 3-minute application of an unnamed topical anesthetic at various sites intraorally and found no benefit in relation to placebo.

In summary, there is evidence from several double-blind, placebo-controlled trials [17–19,21,22,23,26] that topical anesthetics have a pharmacologic effect.

Factors governing the efficacy of topical anesthetics

The studies mentioned earlier demonstrated mixed results. In addition to variations caused by different test stimuli in trials [17], other factors that influence the efficacy of topical anesthetics include:

- The agent used
- Duration of application
- Site of application

These factors are discussed later.

Topical anesthetic agents

Is there any evidence that the anesthetic used is important in relation to efficacy? Several studies have investigated this question. Two aspects are relevant here: the concentration used and the anesthetic agent itself.

It was mentioned earlier that different delivery vehicles are used to administer topical anesthetics. Different formulations of the same drug need different concentrations to achieve a similar effect, for example sprays require a higher concentration than patches [27]. Animal studies have shown that the rate of transfer of anesthetics applied topically is concentration-dependent [28]. Hersh et al [17] showed a dose response in humans with a patch containing 46.5 mg lidocaine being more effective than one that contained 23 mg when applied topically in the mouth. Thus, the concentration is important.

A variety of agents are used as anesthetics; local anesthetics of the ester and the amide groups may be used. This is important in relation to allergic reactions. Most injectable local anesthetic agents such as lidocaine, prilocaine, and bupivacaine are amides that have a low incidence of producing allergies. Ester anesthetics, however, such as benzocaine and tetracaine (amethocaine) are included in topical preparations in North America and this group has a higher incidence of allergy. The studies mentioned earlier [17–19,21,22,23,26] have shown lidocaine (alone and in combination with prilocaine) and benzocaine (alone and in combination with amethocaine) exert an effect when applied topically to oral mucosa.

Two double-blind investigations have shown an increase in efficacy when lidocaine is used in combination with prilocaine in the eutectic mixture EMLA. Holst and Evers [18] have shown that a 5-minute application of

EMLA to the palate decreases discomfort of needle penetration compared with 5% lidocaine. Similarly, Meechan and Thomason [29] reported that a 5-minute application of EMLA was more effective than a similar regimen using 5% lidocaine in reducing the discomfort of intraligamentary injections.

Thus there is evidence that the choice of material influences the efficacy of topical anesthesia. Not all studies have reported variation between agents, however, as Rosivack et al [19] found no difference in the 3-minute application of 5% lidocaine and 20% benzocaine in the maxillary buccal sulcus.

Site

Local anesthetic injections are administered at different intraoral sites. The placement of topical anesthetics can therefore vary. The duration of the effect of applied topical anesthetics varies in different areas of the mouth [30]. Factors relating to site that might influence efficacy are keratinized versus non-keratinized mucosa, for example maxillary buccal sulcus (see Fig. 1) versus palatal mucosa (Fig. 2). In addition, eliminating the discomfort at a site that is going to receive a superficial infiltration injection may be easier than masking the pain of a deep regional block injection. Even the effectiveness of topical anesthetics in reducing infiltration pain varies between sites. Hersh et al [17] showed that a 2.5-minute application of a 46.5-mg lidocaine patch was successful in eliminating needle penetration discomfort in the mandibular buccal fold but not in the maxillary buccal sulcus.

Holst and Evers [18] noted that a 2-minute application of 5% lidocaine to the mandibular buccal fold was effective in reducing the pain of needle insertion; however, this regimen was no better than placebo on the palate. Similarly, Hutchins et al [23] found that although effective in the buccal fold, a 1-minute application of 20% benzocaine was no better than placebo in the palate.

Fig. 2. A patch impregnated with topical anesthetic applied to the palate. Palatal mucosa is more resistant to the effects of topical anesthetics compared with the buccal fold.

The only material that has been shown to reduce palatal injection pain in double-blind, randomized studies is EMLA. Other trials [31], however, have suggested that this material is no better than 20% benzocaine when used to mask palatal injection pain in children.

The author is unaware of any double-blind studies on the efficacy of topical anesthetics before deep regional block injections (Fig. 3). One study [32] that investigated the effects of needle penetration in the pterygotemporal depression to mimic block anesthesia showed no difference in insertion pain following application of 20% benzocaine or placebo for 4 minutes. Another single-blind study [7] comparing the 2-minute application of 20% benzocaine with no topical treatment before the injection of inferior alveolar nerve blocks reported no difference in injection discomfort between treatments. Thus there is no evidence to support the use of topical anesthetics before inferior alveolar nerve block injections.

Duration of application

Most local anesthetic injections do not have an immediate effect. It is common practice to allow a few minutes to elapse before beginning a procedure on a tooth that has been anesthetized. The same rule applies to topical application of a local anesthetic. Not surprisingly, the depth of penetration of the applied agent is governed by the duration of application [26].

One double-blind trial [23] has shown an application time of 1 minute to achieve success in the maxillary buccal fold with 20% benzocaine. On the contrary, another investigation [17] has shown a 2.5-minute application of a 23-mg lidocaine patch at that site was no better than placebo. In the latter study, however, an effect was apparent at 5 minutes. Yet another trial [25]

Fig. 3. There is no evidence that topical anesthesia masks the discomfort of inferior alveolar nerve block injections. Here, 20% benzocaine gel is being applied to the needle insertion point before administration of an inferior alveolar nerve block.

has shown that a 3-minute application of an unnamed topical was ineffective. Holst and Evers [18] noted that an application time of 5 minutes increased the efficacy of 5% lidocaine compared with a 2-minute application.

Summary

What conclusions can be drawn concerning intraoral topical anesthesia? First, a variety of agents have been shown to have a pharmacologic effect. When used as a single agent, lidocaine is effective at concentrations between 5% and 20%. There is evidence of a dose response with lidocaine [17]. The combination of 2.5% lidocaine and 2.5% prilocaine has been shown to be a reliable agent; however, at the time of writing, this mixture is not licensed for intraoral use. Benzocaine is effective when used alone at a concentration of 20% and when combined at a dose of 15% with 1.7% amethocaine.

Second, a crucial factor governing effectiveness is the time of application. One study cited in this paper [23] has shown an effect occurring in the maxillary buccal sulcus after a 1-minute application. Others [17,25] have shown that a 2- to 3-minute application at the same site is no better than placebo. The differences in these studies may be caused by the use of different test stimuli, such as the gauge of the needle used and the depth of insertion. When applied for 5 minutes, it seems that success is guaranteed when used in the buccal fold of either jaw.

Finally, the site of application is important. Palatal mucosa is more resistant to the effects of topical anesthetics than other intraoral sites investigated. There is no evidence that topical anesthetics have any value in reducing the discomfort of deep regional block administrations such as inferior alveolar nerve block injections.

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