Comparison of topical EMLA 5% oral adhesive to benzocaine 20% on the pain experienced during palatal anesthetic infiltration in children

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Abstract

Purpose: The purpose of this investigation was to compare the pain responses of children during local anesthetic infiltration at bilateral palatal sites prepared with the topical application of benzocaine 20% oral adhesive (Orabase-B®) versus benzocaine 20% gel (Hurricaine®) or EMLA 5% oral adhesive (EMLA 5% cream in Orabase Plain®).

Methods: Forty subjects, aged 7-15 years old, received bilateral palatal injections following topical application of anesthetic agents applied in a randomized, crossover design. Pain responses were compared based upon subject self-report using a visual analogue scale (VAS), changes in the subject's heart rate, and operator assessment using a modified Children's Hospital of Eastern Ontario Pain Scale (CPS) that rated behavioral changes in children. Following the injections, the subjects were asked to choose which agent was preferred based on comfort and taste acceptance.

Results: All the agents tested were equivalent in injection pain response comparisons, but Hurricaine® had a slight advantage in expressed subject preference and taste acceptance over the other topical anesthetic agents tested.

Conclusions: The selection of EMLA 5% oral adhesive over other commercially available products containing benzocaine 20% is not recommended for palatal site preparation in children. The lack of demonstrated superiority in efficacy and subject preference, the necessity to custom mix the cream into an oral adhesive paste, the extended duration of time required for onset of action, the greater potential for complications associated with systemic absorption, and product cost preclude the use of EMLA 5% oral adhesive as an intraoral topical anesthetic agent. (Pediatr Dent 23:11-14, 2001)

It is well recognized by the dental profession that avoidance of routine care by some patients occurs because of the negative connotations associated with intraoral local anesthetic injections.[1] The prior application of topical anesthesia helps to alleviate, but does not eliminate, pain associated with needle insertion and anesthetic agent injection.[2] The most popular topical anesthetic preparation is benzocaine 20% gel[3] due to its rapid onset of action (30 seconds), acceptable taste, and lack of systemic absorption.[4] Lidocaine 5% ointment is less frequently used as it has a slower onset of action (2-5 minutes), less acceptable taste, and greater potential for complications associated with systemic absorption due to its water solubility. The systemic uptake of topical lidocaine is relatively slow and similar to its rate of uptake from peripheral nerve block injections.[5]

In 1993, a new topical anesthetic agent, EMLA 5% cream, became available for use in the United States. EMLA is an acronym for "eutectic mixture of local anesthetics" and contains both lidocaine 2.5% and prilocaine 2.5%.[6] EMLA 5% cream has been shown effective in alleviating the pain induced with gingival probing,[7,8] periodontal scaling,[9] and arch bar removal.[10] A 5-minute topical application of EMLA 5% cream significantly reduced pain reported by adults during needle insertion of a dental anesthetic.[11-13] When compared to lidocaine 5% ointment, EMLA 5% cream was also effective in reducing injection pain from the delivery of a dental anesthetic solution.[14,15] EMLA 5% cream has even been reported to provide sufficient but not profound pulpal anesthesia for minor restorative dental procedures.[16,17]

Although preliminary trials were promising for the effectiveness of EMLA 5% cream on palatal mucosa of adults,[11,13,15] this site has not been tested in children. The palatal site is notorious for its inability to acquire adequate topical anesthesia.[2,3] Topical anesthesia is less effective in reducing injection pain at the palatal site due to poor drug penetration through the highly keratinized tissue, the potential for the injection needle to contact the periosteum, the firmly attached keratinized tissue inhibiting tissue distention created by the pressure of the injected solution (volume dependent), and the decreased tissue buffering capacity.[18] Another omission in the literature was that benzocaine 20% gel, the most popular topical anesthetic agent used in dentistry,[3] has never been compared to EMLA 5% cream prior to the initiation of this study.

The eutectic mixture found in EMLA cream allows it to be in liquid form at oral temperature and thus facilitates more rapid absorption into mucosa tissue. Because of the prolonged application time recommended (5 minutes) and the difficulty in maintaining the creamy liquid at the application site, several studies have incorporated EMLA 5% cream directly into an adhesive bandage or patch.[13,15,16] The purpose of this investigation was to compare the efficacy of the intraoral topical application of EMLA 5% oral adhesive to benzocaine 20% on the pain experienced during local anesthesia infiltration at the palatal site in children aged 7-15 years old.

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Fig 1. Behavioral definitions and scoring of the Children's Hospital of Eastern Ontario Pain Scale (CPS)[19]

Item	Behavior	Score	Definition
Cry	No cry	1	Child is not crying
	Moaning	2	Child is moaning or quietly vocalizing
	Crying	2	Child is crying, but the cry is gentle or whimpering
	Scream	3	Child is in a full-lunged cry; sobbing
Facial	Composed	1	Neutral facial expression
	Grimaced	2	Score only if definite negative facial expression
Torso	Neutral	1	Body (not limbs) is at rest; torso is inactive
	Shifting	2	Body is in motion in a shifting or serpentine fashion
	Tense	2	Body is arched or rigid
	Shivering	2	Body is shuddering or shaking involuntarily
	Restrained	2	Body is restrained
Touch	Not touching	1	Child is not touching or grabbing
	Reach	2	Child is reaching for but not touching
	Touch	2	Child is gently touching
	Grab	2	Child is grabbing vigorously
	Restrained	2	Child's arms are restrained
Legs	Neutral	1	Legs may be in any position but are relaxed;
	Squirming	2	Definitive uneasy or restless movements
	Tensed	2	Legs tensed and/or pulled up tightly to body
	Restrained	2	Child's legs are being held down
Verbal	None	1	Child not talking
	Pain complaints	2	Child complains about pain
	Both complaints	2	Child complains about pain and about other things

Final score is calculated as the summation of the behavioral scores for the six items as judged by the observer.

Methods

In the first phase, subjects compared the injection pain experienced at bilateral palatal sites anesthetized topically with Hurricaine® (benzocaine 20% gel, Beutlich Pharmaceuticals, Waukegan, IL) versus Orabase-B® (sodium carboxymethylcellulose oral adhesive with benzocaine 20%, Colgate Oral Pharmaceuticals, Canton, MA) in a randomized, split-mouth, crossover design. The second phase was conducted with a similar design, but Orabase-B® was compared to EMLA 5% cream (lidocaine 2.5% and prilocaine 2.5%, Astra USA, Westborough, MA) manually mixed in Orabase Plain" (sodium carboxymethylcellulose oral adhesive, Colgate Oral Pharmaceuticals, Canton, MA). The first phase was completed on 20 subjects to identify if a difference in pain perception was noted between the gel and adhesive forms of benzocaine 20%. If there was no pain difference identified, then the second phase with a different group of subjects would be performed to compare the two adhesive forms directly.

Individual, calibrated 1.0 mL tuberculin syringes were backloaded with the test agents. Equal amounts of EMLA 5% cream and Orabase Plain® were mixed together into a custom-made preparation, dispensed from the syringe and 0.1 mL of the topical anesthetic agent (equivalent to 1 g) was applied directly to the palatal site with a cotton tip applicator. The order of agent application was performed in a randomized fashion. The left test site was completed first before initiating the trial on the right side. The duration of application for the topical agents was standardized for benzocaine 20% (2 minutes) and EMLA 5% oral adhesive (5 minutes). A sterile, standard 27 gauge short needle in a conventional aspirating dental syringe was used to deliver the local anesthetic solution at a controlled, slow rate of injection. The needle was inserted to the depth of 1-2 mm, attempting to avoid contact with the periosteum. All procedures were performed by the same operator in a standardized manner throughout the duration of the study.

Subjects were recruited for the study if they met the following selection criteria: 1) bilateral restorative procedures on maxillary molars requiring palatal anesthesia during the same appointment; 2) aged 7-15 years; 3) cooperative behavior noted during previous restorative treatment (Frankl scale 3 or 4); and 4) demonstrated competency in using VAS in three trial sessions.

Collected data included the subject's gender, chronologic age in months, and heart rate (pre-, intra-, and post-injection measured by pulse oximetry), pain assessments by the subject using a visual analogue scale[19] (VAS) and by the operator using a modification of the Children's Hospital of Eastern Ontario Pain Scale[19] (CPS), and a post-trial questionnaire comparing overall comfort, taste acceptability, and agent preference. The behavioral definitions and scoring criteria for CPS is illustrated in Fig 1. The VAS is a highly utilized pain measurement scale for children. This scale is a 100 mm horizontal line with visual descriptive anchors at each end. The left end of the line is labeled "no pain/no hurting," which is reinforced by a caricature of a smiling/happy face above it. The opposite end of the line (right side) is labeled "worst possible pain/hurting" and is reinforced similarly by a caricature of a crying/distressed face above it. The subject is instructed to mark a vertical line along the 100 mm rule to express his/her level of discomfort from the injection. The pain score is calculated by measuring the millimeter distance of the mark from the left end. For both the VAS and CPS, the higher the score, the higher the subject's pain intensity.

Results

A population of 40 subjects (19 males and 21 females) were selected for the study (20 subjects tested in each of two phases). All child subjects and their parents provided written consent as approved by the University's Institutional Review Board prior to participation in the clinical trial. The mean age of the subjects was 129 ± 34 months with a range of 89 to 191 months. Table 1 illustrates the mean values for the VAS scores, CPS, and the heart rate before, during, and after anesthetic infiltration. Table 2 illustrates the results pertaining to subject's reported comfort, taste, and agent preference.

Table 1. Comparison of Pain Perception Measured by Visual Analogue Scale (VAS), Modified CPS, and Heart Rates (mean ± SEM) Recorded During Anesthetic Injection into Palatal Tissue Prepared with Different Topical Agents

	Phase I			Phase II		
	Benzocaine 20% in Orabase [1]	Benzocaine 20% Gel[2]	Difference*	Benzocaine 20% in Orabase[1]	EMLA 5% cream[3] in Orabase Plain[4]	Difference*
VAS	61 ± 6	67 ± 6	*P*= 0.244	60 ± 7	63 ± 8	*P*= 0.645
CPS	7 ± 0	7 ± 0	*P*= 0.189	7 ± 1	7 ± 0	*P*= 0.162
Pre-injection heart rate	84 ± 3	83 ± 3	*P*= 0.245	84 ± 2	82 ± 2	*P*= 0.052
Injection heart rate	92 ± 3	92 ± 4	*P*= 0.817	92 ± 2	89 ± 4	*P*= 0.272
Post-injection heart rate	86 ± 2	86 ± 2	*P*= 0.697	84 ± 2	83 ± 2	*P*= 0.520

* paired t-test, [1]Orabase-B®, Colgate Oral Pharmaceuticals, Canton, MA, [2] Hurricaine®, Beutlich Pharmaceuticals, Waukegan, IL, [3] Lidocaine 2.5% and Prilocaine 2.5%, Astra USA, Westborough, MA, [4] Orabase Plain®, Colgate Oral Pharmaceuticals, Canton, MA

When Hurricaine was compared to Orabase-B® (Phase I), no significant differences during palatal injection were found for the subject's pain perception (VAS) and operator's assessment of the subject's pain using CPS. There was an increased mean heart rate during the injection when compared with the mean pre- and post-injection heart rate values, but no significant differences in heart rates were shown between the two agents. There were no profound differences in the discomfort reported by the subjects, but Hurricaine was rated slightly better for taste acceptance and agent preference.

When Orabase-B® was compared to EMLA cream in Orabase Plain® (Phase II), no significant differences during palatal injection were found for the subject's pain perception (VAS) and operator's assessment of the subject's pain using CPS. There was an increased mean heart rate during the injection when compared with the mean pre- and post-injection heart rate values, but no significant differences in heart rates were shown between the two agents. No profound differences in discomfort between the two agents was reported by the subjects. However, the subjects expressed greater taste acceptance and agent preference for Orabase-B®.

Discussion

Although the actual efficacy of topical anesthesia in reducing pain associated with the intraoral injection of local anesthesia is in dispute,[2,20-24] its routine use is still strongly advocated.[3] Acute pain can be influenced by psychological factors, such as anxiety, fear, trust, and perceived control over the stimulus, which may well account for the equivocal findings of dental topical anesthesia efficacy. Martin and co-workers[25] concluded that the widespread belief among patients that topical anesthetics are effective at reducing injection pain may serve to reduce the anticipatory anxiety associated with an impending dental injection, thus making the injection experience less aversive. Their results supported the contention that the intensity of the injection pain experienced was significantly less than anticipated by the patient. Injection site location also plays a role in pain perception. A recent study reported that the efficacy of topical anesthesia in the mandibular arch varied with the site of administration.[26] Injection rate, solution volume, agent pH, and tissue buffering capacity are additional variables confounding the reported pain experience.[18]

EMLA 5% cream was recently reported to be superior to four other topical agents and a placebo in its ability to increase pain threshold to intraoral pressure in adults.[27] This application to keratinized gingiva holds promise in reducing pain created by rubber dam clamp placement where isolation without local anesthesia is preferred for some clinical procedures such as sealants and preventive resin restorations. In a recent clinical trial, Tulga and Mutlu compared injection pain following the topical application of EMLA 5% cream to benzocaine 20% gel in 20 children, aged 10-15 years, receiving bilateral buccal infiltrations.[28] They concluded, based on VAS measurements, that benzocaine was statistically better than EMLA in reducing injection pain during maxillary infiltration and that benzocaine had better taste acceptance in children.

Contrary to previous studies demonstrating promising results for the topical application of EMLA 5% cream to the palatal injection site in adults,[11,13,15] this study did not reveal superior effectiveness in reducing injection pain for children using EMLA 5% oral adhesive when compared to benzocaine 20% in gel and adhesive forms. Intraoral use of EMLA cream is not recommended by the manufacturer because of the claim that safe dosing amounts are unknown for mucosal applications.[29] The FDA has approved the use of an intraoral lidoacaine patch[30] containing 46 mg and numerous formula-

Table 2. Comparison of Subject's Comfort, Taste, and Preference For Different Topical Anesthetic Agents

	Phase I		Phase II	
Preference	Benzocaine 20% in Orabase[1]	Benzocaine 20% Gel[2]	Benzocaine 20% in Orabase[1]	EMLA 5% cream[3] in Orabase Plain[4]
Comfort	53%	47%	53%	47%
Taste	33%	67%	71%	29%
Agent (Overall)	44%	56%	67%	33%

[1]Orabase-B®, Colgate Oral Pharmaceuticals, Canton, MA, [2] Hurricaine®, Beutlich Pharmaceuticals, Waukegan, IL, [3] Lidocaine 2.5% and Prilocaine 2.5%, Astra USA, Westborough, MA, [4] Orabase Plain®, Colgate Oral Pharmaceuticals, Canton, MA

tions of lidocaine 5% in gel, ointment, and solution and lidocaine 10% in an aerosol are recommended for use[13] and have received the Seal of Acceptance by the ADA.[4] This acknowledgment, in the presence of numerous clinical trials demonstrating the safety of EMLA 5% cream for intraoral use, justifies the off-label application of this product. There are some practical disadvantages to using EMLA 5% cream intraorally including bland taste (a pH of 9 may even create a bitter taste), low viscosity with resultant difficulty in retaining it at the desired site, prolonged time of application (5 minutes vs. 2 minutes for conventional agents applied to the palatal mucosa), and product cost.

Conclusions

When the prior application of topical EMLA 5% oral adhesive (EMLA 5% cream in Orabase Plain®) was compared to benzocaine 20% oral adhesive (Orabase-B®) directly and to benzocaine 20% gel (Hurricaine®) indirectly during local anesthetic infiltration at the palatal site of children, the following conclusions were drawn:

1. EMLA 5% cream in Orabase Plain® was equally effective as Orabase-B®, which displayed a similar efficacy to Hurricaine" based upon injection pain response as measured by subject self-report (VAS, comfort comparison, and heart rate) and operator assessment (CPS).
2. Although all the agents tested were equivalent in injection pain response comparisons, Hurricaine" had a slight advantage in expressed subject preference and taste acceptance over the other topical anesthetic agents tested.
3. The lack of demonstrated superiority in efficacy and subject preference, the necessity to custom mix the cream into an oral adhesive paste, the extended duration of time (5 minutes) required for onset of action, the greater potential for complications associated with systemic absorption, and the product cost preclude the selection of EMLA 5% oral adhesive over other commercially available products containing benzocaine 20%.

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