Original Article

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Effectiveness of pre-injection use of cryoanesthesia as compared to topical anesthetic gel in reducing pain perception during palatal injections: a randomized controlled trial

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Background: Palatal injections are often painful. We aimed to compare topical ice and 20% benzocaine gel for pre-injection anesthesia before greater palatine nerve block (GPNB) injections.
Methods: A randomized split-mouth clinical trial was conducted among patients aged 15-60-years needing bilateral GPNB injections. A total of 120 palatal sites from 60 patients were randomly allocated to Group A (topical ice) or Group B (20% benzocaine gel). Pain was evaluated using sound, eye, motor (SEM), and the visual analog scale (VAS) in both groups. Inferential analysis was performed using the Mann-Whitney U test.
Results: The mean age of the participants was 20.5 ± 3.9 years. The median VAS score for group A was 11 (Q1 - Q3: 5.25 - 21.75), which was slightly higher than the 10 (Q1 - Q3: 4.0 – 26.75) reported in group B. However, the difference was not statistically significant (P = 0.955). The median SEM score for group A and group B was 3.5 (Q1 - Q3: 3.0 – 4.0) and 4.0 (Q1 - Q3: 3.0 - 4.0), respectively, which was statistically insignificant (P = 0.869).
Conclusion: Using ice as a form of topical anesthetic for achieving pre-injection anesthesia before GPNB was as effective as 20% benzocaine gel.

Keywords: Benzocaine; Cryoanesthesia; Ice; Pain Perception; Palate; Topical Anesthetics.

INTRODUCTION

The International Association for the Study of Pain (IASP) 2020 emphasized that the personal perception of pain depends on psychosocial and biological factors [1]. Despite continuous advances in the techniques for administering local anesthetics, absolute pain control remains difficult to achieve [2]. In addition to fear and anxiety, penetration of the needle through the oral mucosa is often sensed by patients, which can be overwhelming. Generally, patients are mentally prepared to expect some degree of pain and/or discomfort during palatal injections. However, patients may not accept such forms of assurance and become more anxious [3].

Despite advances in injection techniques and buffered local anesthetics, the pain associated with needle insertion has not been completely addressed. Although the degree of anesthesia achieved with topical anesthesia is lower than that achieved with injection anesthesia, it is relatively safe and non-invasive. Topical anesthetics produce local anesthesia by reversibly blocking nerve

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conduction near the site of administration by targeting free nerve endings in the oral mucosa [4].

Topical anesthetic gels are commonly used before oral injections. However, relying only on topical anesthetics does not adequately negate pain. Other factors, such as injection rate and needle size, also affect pain sensation during injection [5]. Multiple studies have shown the effectiveness of different forms and concentrations of intraoral topical anesthetics in reducing pain associated with dental needle injections [6–8]. Topical anesthetics in gel form (benzocaine or lidocaine) are commonly used before an injection. Variable application times, bitter taste, and difficulty in limiting the agent to a confined area within the oral cavity are commonly problems [9]. Although rare, serious systemic complications have been reported in case reports [10].

The use of ice and refrigerant sprays to reduce pain during palatal injections has been described in the literature [2,11-13]. Cryoanesthesia refers to the localized application of coldness to block nerve conduction through the inhibitory pain pathway as part of the gate control system at the level of the spinal cord [14]. Cold-induced neuropraxia also decreases the activation threshold of nociceptors and the conduction velocity of pain signals through the nerves [15].

Palatal tissues are tightly bound to the hard palate. Injection into this tight compartment requires pressure that builds up within the palatal tissues, resulting in pain. Studies have shown that anxious patients have lower pain thresholds than those who are not as anxious and are at an increased risk of vasovagal syncope [16]. Therefore, it is beneficial to use pre-injection anesthetics to achieve less traumatic palatal injections [17,18]. Benzocaine and lignocaine gels have the advantage of being more localized to the intended needle puncture site inside the oral cavity than dispersive aerosol sprays [19,20].

This study compared the effect of ice with 20% benzocaine gel as pre-injection topical anesthesia for reducing pain perception associated with GPNBs, using the visual analog scale (VAS) and sound, eye, motor (SEM) scales.

METHODS

The study was approved by the Institutional Review Committee (IRC) of the B.P. Koirala Institute of Health Sciences, Dharan (Ref no. 556/077/078) and registered in ClinicalTrials. gov (identifier: NCT06165432). The Department of Oral and Maxillofacial Surgery conducted this parallel-arm experimental randomized trial. Considering an alpha error of 5% and a study power of 80% (based on the study by Kosaraju et al. [9]), the estimated sample size was 60 patients for each group (A vs B).

As the study employed a split-mouth design, 60 individuals were enrolled. Healthy participants, who (ASA I) met the criteria of the American Society of Anesthesiology (ASA), had intact palatal mucosa on both right and left sides of the mouth, and needed procedures that required bilateral GPNB at different appointments, were selected for this study. The exclusion criteria were pregnancy, smoking, nursing mother, local anesthetic allergy, and history of chronic pain in the face/oral cavity.

Verbal and written informed consent were obtained from the parents/guardians (for minors) and each participant enrolled in the study. Strict confidentiality was maintained. Individuals received one or the other intervention according to their group allocation before the trial (Fig. 1).

1. The first appointment

At the first appointment, the right or left palate was selected randomly using a lottery and allocated to one of two groups: Group A (topical ice) or Group B (20% benzocaine gel). Lottery involved randomly selecting a folded piece of paper for each individual. The lottery paper provided the unique code numbers for each half of the palate and each intervention. The principal investigator was responsible for enrollment and randomization.

2. Ice application

The ice for topical application was prepared by

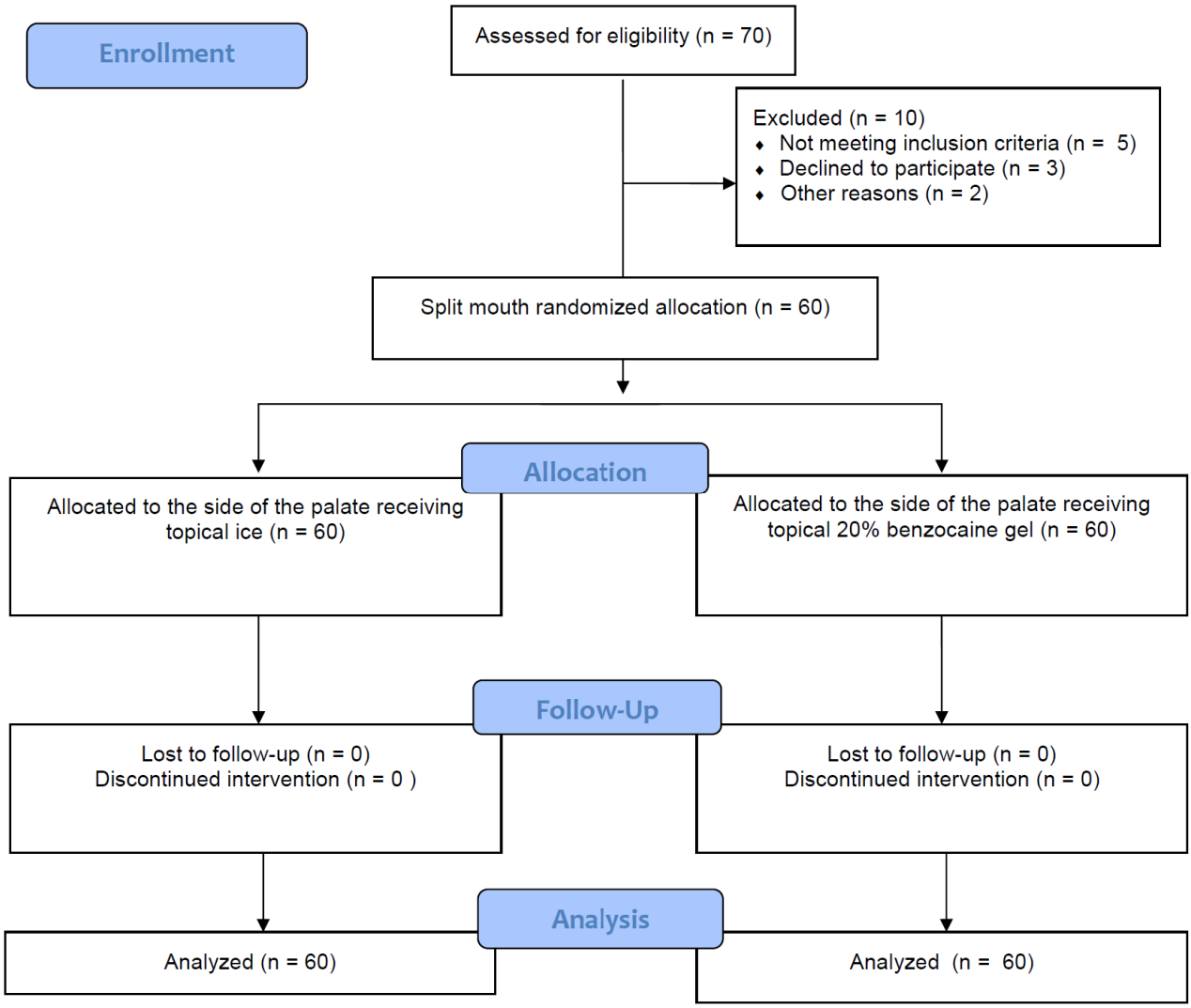

Fig. 1. Consolidated standards of reporting trials (CONSORT) flow chart. n, number.

injecting 0.5 ml of clean bottled drinking water into the swab stick packet and freezing it overnight (Fig. 2). After the palatal mucosa anterior to the greater palatine foramen was dried using a sterile gauze, a frozen cotton swab was placed in the same area for 1 min. With the frozen cotton swab stick in place, an injection of 2% lidocaine (0.5 ml) with 1:200,000 epinephrine was administered using a 27-gauge needle which was inserted into the mucosa immediately below the swab stick (Fig. 3).

3. Topical anesthetic application

Approximately 0.2 ml of 20% benzocaine gel (ProGel-B, Septodont) was applied with a swab stick to the anesthetic site for 2 min. The injection of local anesthetics was performed in the same way as above.

4. Evaluation

The SEM score was used to measure objective pain by a blinded observer during the injection, and objective pain was marked by the patient on the VAS scale after the injection. Any evidence of local or systemic adverse effects was recorded, and acceptability was graded on a 5-point Likert scale including two extreme responses and a neutral option (1. Very bad, 2 Bad, 3. Satisfactory 4. Good, and 5. Very Good). Participants were invited to provide additional comments.

Fig. 2. A frozen swab stick used in this study

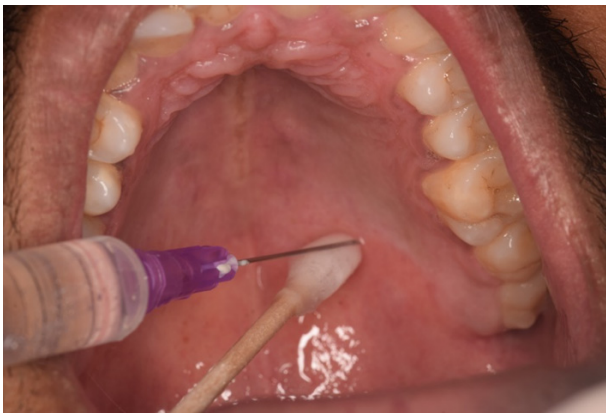

Fig. 3. The administration of greater palatine nerve block injection with the frozen swab stick in place

Table 1. SEM and VAS scores between males and females in the topical ice group (n = 60) and the 20% benzocaine group

Pain scale	Gender	Topical ice Median (Q_1 - Q_3)	P value	20% benzocaine Median (Q_1 - Q_3)	P value
SEM score	M	4 (3.0 – 4.0)	0.903	4 (3.0 – 4.0)	0.761
	F	3 (3.0 – 4.0)		4 (3.0 – 4.0)	
VAS score (mm)	M	13 (6.0 – 22.0)	0.664	10 (4.0 – 28.0)	0.653
	F	10 (5.0 – 22.5)		10 (4.0 – 26.5)	

Mann-Whitney U Test
F, female; M, male; n, number; Q, quartile; SEM, sound, eye, motor; VAS, visual analog scale.
P value < 0.05% is statistically significant

5. The second appointment

The second appointment was scheduled after two weeks to ensure that no confounding pain from the first procedure was present at the second visit. During the second appointment, the contralateral palatal mucosal site and the comparative intervention were used. The same protocol as the first appointment was followed in the second appointment.

6. Statistical methods

The primary outcome was whether topical ice and 20% benzocaine gel had similar effects in reducing subjective and objective pain as measured by the VAS and SEM scales, respectively. A statistical power calculation based on previous results concluded that 60 patients would be needed to achieve 80% power and detect the primary outcome at a significance of 0.05. The Mann-Whitney U test was used to compare groups A and B in terms of the pain scores measured via the VAS and SEM scales.

RESULTS

Data were collected from August 5, 2019, to August 30, 2020. Sixty patients (39 females and 21 males, aged 20.5 ± 3.9 years at enrollment, were included. Informed consent was received from all participants and where indicated, their guardians.

The pain (assessed using SEM and VAS scales) experienced by males vs females in topical ice and 20% benzocaine groups were not significantly different (Table 1). The pain experienced during GPNB injections after pre-injection anesthesia using ice versus 20% benzocaine gel was also not statistically significant (Table 2).

Patient acceptance is schematically represented in Fig. 4. No side effects, such as burning/stinging sensation, local hypersensitivity reactions (urticaria, erythema, and

Table 2. SEM and VAS scores between the topical ice group (n = 60) and the 20% benzocaine group (n = 60)

Pain scale	Topical ice Median (Q_1 - Q_3)	20% benzocaine Median (Q_1 - Q_3)	P value
SEM score	3.5 (3.0 – 4.0)	4 (3.0 – 4.0)	0.869
VAS score (mm)	11 (5.3 – 21.8)	10 (4.0 – 26.8)	0.955

Mann-Whitney U Test
n, number; Q, quartile; SEM, sound, eye, motor; VAS, visual analog scale.
P value < 0.05% is statistically significant

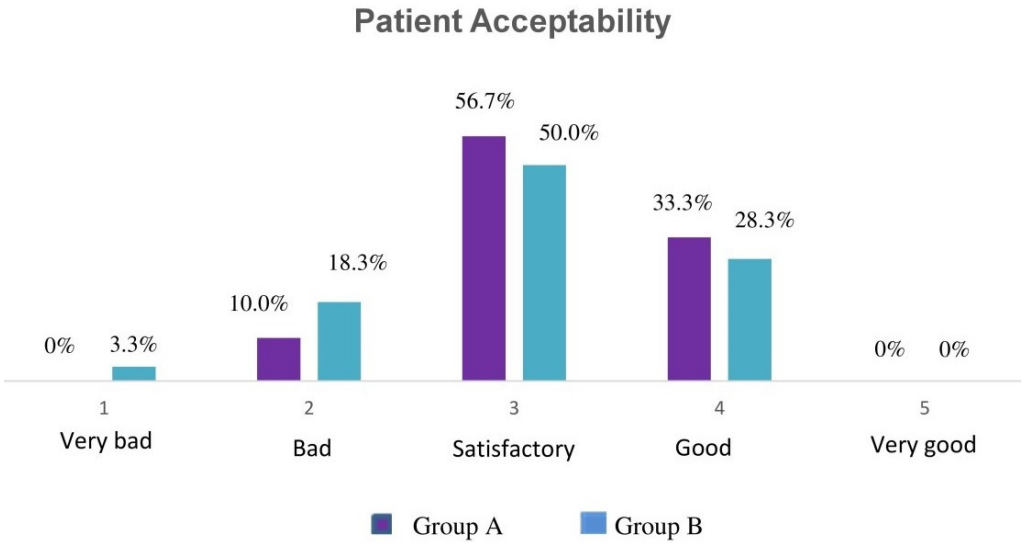

Fig. 4. Patient acceptability distribution between Group A (topical ice) and Group B (20% benzocaine)

itchiness), or systemic reactions (dizziness, drowsiness, and palpitations), were observed in either group.

DISCUSSION

The purpose of using topical anesthetics before dental injections is to minimize pain as effectively and non-invasively as possible. Ironically, local anesthesia, which aims to eliminate pain, is itself a painful process. Moreover, fear and unpleasant experiences associated with painful injections may lead to the avoidance of dental treatment and intraoperative vasovagal syncope [16]. Of the different types of dental injections, the GPNB is considered as more painful.

The VAS is simple and easy to use and it is recognized as a valid and reliable for measuring acute pain [21,22]. It is difficult to evaluate pain perception using a subjective scale (VAS). Thus, an objective scale (SEM) was also used in our study. The SEM is a reliable measure for rating observed pain [23,24].

Pre-cooling as a form of topical anesthesia has been shown to be an effective measure to alleviate pain during intraoral injections [2,9,13,17]. Various pre-cooling techniques have been used, such as refrigerant sprays [9,25] and ice [2,9,13,17] applied in various forms. However, refrigerant spray carries a greater risk to the oral mucosa than ice. For example, ulceration and contact dermatitis have been associated with refrigerant spray [26].

A study by Bose et al. [13] showed that the topical use of ice pre-treatment reduced injection pain compared to that of no ice pretreatment. Furthermore, topical ice application pre-injection has shown promising results, even when compared to other techniques [2,11,17]. However, few studies have demonstrated its effectiveness

with palatal injections [13,17]. Notably, some studies have demonstrated no significant pain reduction during palatal injections after applying topical ice and anesthetics pre-injection [2,27].

A broad diversity of methods exists for preparing topical ice [2,11,28]. Moreover, custom-made ice cones are also available [11]. Refrigerant sprays are typically applied using special applicator tips [9]. Clinically, ice is difficult to handle. In our study, we used sterile cotton swab sticks for the topical application of 20% benzocaine gel and frozen cotton swab sticks for topical pre-cooling. Frozen cotton buds are easy to prepare and safe to apply. It minimizes the risk of slippage from the operator's hand compared with a block of ice [12].

In some studies, the pre-cooling time ranged from 2 to 5 min [2,14]. Studies by Lathwal et al. [11] and Ghaderi et. al. [29] support an application time of one minute only, which was the duration used in this present study. The short application time prevents adverse effects and minimizes discomfort [2].

Benzocaine is an FDA-approved drug. A concentration of 20% is the most for topical anesthetics in dentistry [19]. The topical application of benzocaine is relatively safe. Rarely, drug-induced sensitization, such as urticaria, erythema, itchiness, and edema, have been reported. However, one of its most life-threatening side effects is methemoglobinemia [4].

Reports of local or systemic adverse effects of topical anesthetic drugs are uncommon [30]. In this study, no local or systemic adverse effects were observed. We used a low dose (0.2 g, i.e, 0.2 ml) of 20% benzocaine as per studies by Moshin et al. [31] and Nusstein et al. [32]. The topical use of low-dose benzocaine and a short application time, as in our study, appears to be relatively safe. Other studies have also reported no adverse effects with the use of 20% topical benzocaine gel as a topical anesthetic before dental injections [6,20].

In the studies by Kumari et al. [17] and Kosaraju et al. [9], two palatal injections, one on either side of the palate, were administered at the same appointment. However, to minimize the risk of bias from benzocaine on one side of the palate, the injections were administered at different appointments in our study. We maintained a minimum time interval of two weeks between the first and second appointments, as in the study conducted by Hindocha et al. [2]. As mentioned, in our study, subjective and objective pain scores between patients receiving topical ice versus those receiving 20% benzocaine topical gel were not statistically significant ($P > 0.005$). Similarly, the findings of Amruthavarsini et al. [24], Wiswall et al. [27], and Anantharaj et al. [33] demonstrated that pre-cooling was equally as effective as 20% benzocaine in reducing injection pain. In contrast, Ghaderi et al. [29], Vafaei et al. [34], and Kosaraju et al. [9] showed that pre-cooling was superior to topical anesthetic gels in their studies.

The VAS scores in our study were lower in both groups than that in other similar studies [24,34]. The variation in pain scores observed in our study compared with other studies may be attributed to age differences. Most studies have been conducted in pediatric populations, as children are known to be more sensitive to pain [35]. Using a smaller gauge (27- or 30-gauge) needle seems logical to result in less injection pain. However, Flanagant et al. (2007) [36] found no differences in injection pain among 25-, 27- and 30-gauge needles. Hence, although many studies have used 30-gauge needles [2,9,17], it would not have significantly reduced injection pain as compared to 27-gauge needles used in our study.

Our findings showed that a higher proportion of participants reported a bad or very bad taste following 20% benzocaine gel in comparison to ice. Hence, the patient's experience with topical anesthesia can be improved if a different substance is used. Previous studies have also emphasized the bad taste associated with anesthetic gels [2,9]. Importantly, our study did not show a significant difference in subjective and objective pain during GPNB injection following topical ice for 1 min and 20% benzocaine gel for 2 min as pre-injection anesthesia.

This study has some limitations. A potential risk of bias due to the temperature of ice was possible, as it was

obvious to patients which method was used. Moreover, It is always a challenge to study pain, as individual psychosocial states and behaviors are subjective and may increase the risk of confounding, during objective pain comparisons of different individuals. To overcome these, we used a split-mouth study design.

Although both agents appeared to be clinically safe in our study, the use of topical ice resulted in no adverse effects. The method described for applying topical ice to the palatal mucosa is easy to perform. The application time was shorter and did not cause a bad taste experience. Within the limitations of this study, topical ice demonstrated the same effectiveness as 20% benzocaine gel. Hence, ice should be considered as an alternative for pre-injection anesthesia, especially when topical anesthesia gels are not available, or for patients with a history of allergy to topical anesthesia.

Further studies should be conducted with a larger sample size to compare a variety of topical anesthetic agents, injection techniques, or application times. Moreover, in future studies, a control group treated with a placebo should be considered to further assess the effectiveness of topical ice.

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Ashok Dongol: Writing - original draft, Writing - review & editing
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