Original Article

pISSN 2383-9309 ▮ eISSN 2383-9317
J Dent Anesth Pain Med 2024;24(1):37-45 ▮ https://doi.org/10.17245/jdapm.2024.24.1.37

Effect of cryoanesthesia and sweet tasting solution in reducing injection pain in pediatric patients aged 7–10 years: a randomized controlled trial

Shital Kiran Davangere Padmanabh, Vishakha Bhausaheb Gangurde, Vikram Jhamb, Nasrin Gori

Department of Pediatric and Preventive Dentistry, College of Dental Sciences, At. Amargadh, Tal. Sihor, Dist. Bhavnagar, Gujarat, India

Background: The delivery of profound local anesthetics helps children receive successful treatment by reducing fear, anxiety, and discomfort during dental procedures. Local anesthetic injections are the most anticipated stimuli in dental surgery. Children's perceptions of pain can be altered by applying cryotherapy to precool the oral mucosa or by diverting their minds through taste distractions before administering local anesthetic injections. This study aimed to evaluate the efficacy of cryoanesthesia and xylitol sweet-tasting solution at the injection site in 7–10-year-old children.

Methods: A total of 42 participants, aged 7–10 years, who underwent dental treatment requiring local anesthesia, were enrolled in the study. The children were randomly divided into three groups. In group I, sterile water was held in the mouth for 2 minutes before anesthetic administration, similar to group II, and in group III, a xylitol sweet-tasting solution was used for 2 minutes before needle insertion. The analysis of pain perception was carried out based on the Visual Analog Scale (VAS) and the Sound, Eyes, and Motor (SEM) scale. For VAS analysis, a one-way analysis of variance (ANOVA) was performed for intergroup comparison, and a post hoc Tukey test was performed for subgroup analysis. For the categorical SEM scale, the Kruskal–Wallis test followed by the post hoc test was performed for intergroup comparison. Where a P value of <0.05 was considered statistically significant at 95% confidence intervals.

Results: Cryoanesthesia significantly reduced pain scores on VAS (4.21 ± 1.42) when compared to those on VAS with xylitol sweet-tasting solution (5.50 ± 1.40) and that with sterile water (6.14 ± 2.47). Intergroup comparison of the VAS scores among the three groups was performed using one-way ANOVA, which demonstrated statistically significant differences (P value <0.026) on the VAS scale. Intergroup comparison of the SEM scale was performed using the Kruskal–Wallis test, followed by post hoc comparison, which exhibited statistically significant differences (P < 0.007) among the three groups for the SEM scale.

Conclusion: Cryoanesthesia demonstrated higher efficacy in reducing injection pain than that exhibited by the xylitol sweet-tasting solution.

Keywords: Cryotherapy; Pain Perception; Visual Analog Scale; Xylitol.

INTRODUCTION

Pain is believed to be the driving force behind seeking dental care; however, pain is also the main reason why treatment is ignored [1]. Pain is an unfavorable emotional and sensory experience linked to or defined in terms of tissue damage, whether present or not. Pain, an

Received: December 15, 2023 • Revised: January 17, 2024 • Accepted: January 22, 2024
Corresponding Author: Shital Kiran Davangere Padmanabh, Professor and Head, Department of Pediatric and Preventive Dentistry, College of Dental Sciences, At. Amargadh, Tal. Sihor Dist. Bhavnagar, Gujarat -364210, India
Phone: +919586116160 E-mail: drskiran@gmail.com

unavoidable component of many dental operations, is also one of the main causes of such dental operations [2]. Many treatments, particularly in pediatric dentistry, require local anesthesia to manage pain [3]. The paradox of this scenario is that local anesthetics, which are the best medications for alleviating and avoiding pain, are also associated with pain [4]. This pain is worsened by needle phobia, also known as blenophobia, which is triggered by the sight of the needle [5].

The rapid development of pain associated with avoidance behaviors may influence future treatment procedures [6,7]. The cornerstone of pediatric behavioral management is the ability to effectively regulate discomfort during dental treatment [4].

Many strategies, from localized approaches to distraction strategies, have been studied to reduce the discomfort and pain related to dental injections. Localized techniques include the use of topical medications [8], adjusting the injection pace, buffering by raising the pH of local anesthetics [9], and laser pretreatment [10]. Vibraject (Vibraject, GoldenDent, Roseville, Michigan, USA), DentalVibe (DentalVibe, BING Innovations, Boca Raton, USA), and WAND System (Wand Dental, Inc., Livingston, New Jersey, USA) are examples of vibrotactile instruments that counterstimulate dental injections to provide a pleasant experience.

Another recommended method for reducing patients' perceptions of pain that is successful, efficient, and economical is cryotherapy. The use of ice or refrigerant spray on the anesthetic site to prevent pain from being transmitted to the nerves is known as cryoanesthesia [11]. Patients achieve physiological and psychological benefits from the use of ice as it may divert their attention from discomfort [12]. This approach has been used to treat sprains, cuts, fractures, bruises, insect stings, and other physical injuries [13,14].

A physiological analgesic phenomenon known as "sweet taste-induced analgesia" may also have pain-relieving effects. A well-known notion is that sugar solutions, including sucrose and glucose, raise the threshold for pain during venipuncture, heel lance, and cold pressure tests [15]. Consumption of sweet substances alters the positive emotional state and endogenous opioid activity in the brain. Pain perception may be diminished by increased opioid activity and an improved emotional state [16,17]. According to a review of the medical literature, no studies have compared the effectiveness of sweet-tasting solutions and cryoanesthesia in minimizing injection pain in pediatric patients between the ages of 7 and 10.

METHODS

This randomized controlled three-arm parallel-design clinical trial was designed according to the CONSORT statement to improve the quality of reports of randomized controlled trials 2010 guidelines (http://www.consort-statement.org/).

1. Ethical approval and protocol registration

The Institutional Review Board and Ethics Committee approved all aspects of the research proposal (Ref. CODS/IEC/183/2023). This research was registered in the Clinical Trials Registry of India under ID CTRI/2023/03/050960.

2. Study design, setting and duration

This randomized three-arm parallel study with an equal number of participants was conducted in the outpatient department of pediatric and preventive dentistry for approximately 4 months between April 2023 and July 2023.

3. Sample size

The sample size (n) was derived by using the “comparing two means” formula, using Epi info software v. 3.0. Atlanta, Georgia (US) with an alpha error of 0.05 and power of 80%. Considering the three study groups, a total sample size of 42 participants/patients was derived, with the allocation ratio maintained at 1:1:1 and 14 participants per group.

4. Study materials

Groups	Materials used
Group I (Control Group)	• Sterile water- Fresh sterile water for each participant for the control group.
Group II (Experimental 1)	• Ice pack- The ice pack was prepared by filling sterile water in the small finger of the extra small-size latex gloves. The water-filled part of the gloves was looped and stored in the freezer. The temperature of the ice pack was set between -4°C to 0°C to prevent any risk of frostbite (Fig. 1).
Group III (Experimental 2)	• Xylitol sweet-tasting solution- the solution was prepared by dissolving 30 g of pre-weight xylitol powder (So Sweet Xylitol, Kanha Biogenetic, Jharmajri Baddi, Dist Solan, India) in 100 mL of water in a measuring jar. The xylitol sweet-tasting solution was freshly prepared for each participant (Fig. 2).

- Local anesthesia (2% lignocaine with 1:2,00,000 adrenaline [LOX 2 %, Neon Laboratories Ltd, Mumbai, India]) and a 26-gauge needle (UNOLOK, Hindustan Syringes and Medical Devices Ltd, Faridabad, India) were used for local anesthetic administration in all study participants.
- Assessment tool: Pain perception was analyzed based on the Visual Analog Scale (VAS) and the Sound, Eyes, and Motor (SEM) scale. The subjective pain perception assessment was recorded by having the participant point to the scale, and the objective pain perception was assessed using the SEM scale by the co-investigator who was blinded to all groups.

5. Methodology

Inclusion criteria-

- Healthy children aged between 7 to 10 years (The American Society of Anesthesiologists/ ASA I)
- Children of both genders
- Children exhibiting a score of III and IV on the Frankl's Behavior Rating scale
- Children requiring local anesthesia for any type of dental treatment following diagnosis and treatment planning

Exclusion criteria-

- Children with any known allergy to local anesthesia
- Children with active pathology at the site of injection

Fig. 1. Sterile water frozen in gloves and used as an ice pack

Fig. 2. Xylitol powder used to prepare the sweet tasting solution

The present study included 42 children aged 7–10 years who reported to the Department of Pediatric and Preventive Dentistry for any type of dental treatment requiring local anesthesia. All the participants were enrolled after obtaining written informed consent from their parents or guardians. To ensure an equal number of participants in each group, enrolment was performed using the block randomization method and an allocation list was formed using computer-generated random numbers. Allocation concealment was achieved by using sealed envelopes containing patient information for group assignment. Allocation generation, enrolment of participants, and assignment of participants to study groups were performed by an assistant (an intern). The principal investigator and study participants were not blinded to the nature of the intervention. However, the

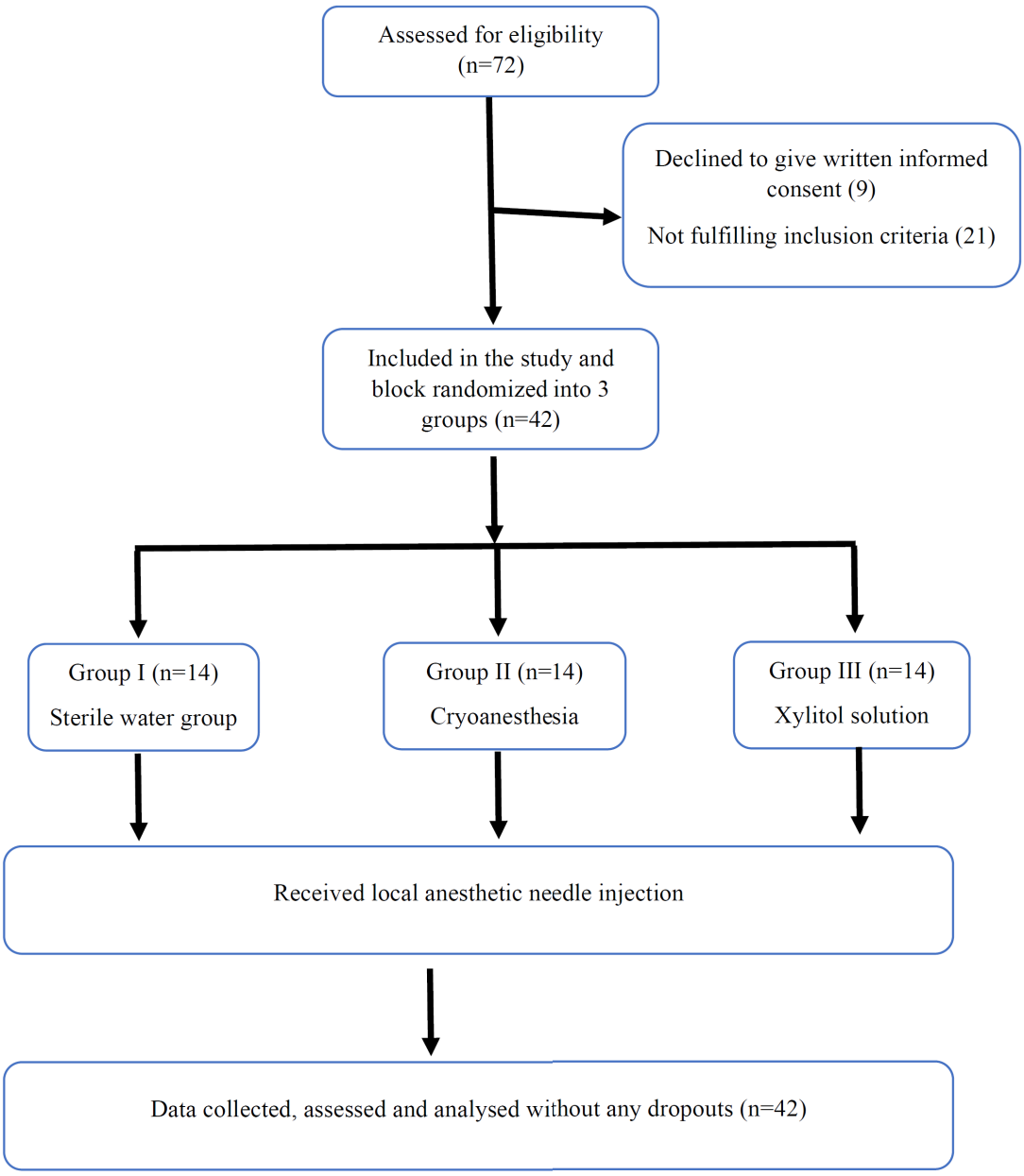

Fig. 3. Consolidated Standards of Reporting Trials (CONSORT) flow chart illustrating the allocation of participants and the research protocol

statistician and co-investigator were blinded until the data were recorded, collected, and analyzed.

In this study, all 42 participants were allocated randomly into three groups: group I, the sterile water group; group II, the cryoanesthesia group; and group III, the xylitol sweet-tasting solution group (Fig. 3). In group I, all the participants were provided 5 mL of fresh sterile water to hold inside the mouth for approximately 2 min and were asked to spit it out before local anesthetic administration, whereas in group II, an ice pack prepared in the small finger of the latex gloves was applied for 2 min on the injection site before local anesthetic administration (Fig. 4). Similarly, in group III, all the participants were provided 5 mL of freshly prepared 30% xylitol sweet-tasting solution to hold inside the mouth for 2 min and were asked to spit it out before local anesthetic administration.

Pain perception was assessed using subjective and

Fig. 4. Application of ice pack prepared by sterile water frozen in gloves

objective scores on two different scales. Subjective pain perception was recorded and assessed based on the VAS after local anesthetic administration by asking the patient to identify the most preferred image on the scale. Objective pain perception was recorded using the SEM scale during local anesthetic administration by a co-investigator who was blinded to the groups. The subsequent treatment for all participants was completed after local anesthetic administration, and no other behavioral management techniques were used before or during local anesthetic administration in all study participants.

6. Statistical analysis

The data obtained was coded and entered into Microsoft Excel 2007/2013. Descriptive and Frequency analysis was done by using Statistical Product and Service Solution (SPSS) (v.21.0) software (Armonk, NY, USA). For VAS analysis, a one-way analysis of variance (ANOVA) was performed for intergroup comparison, and a post hoc Tukey test was performed for subgroup analysis. As the categorical scales were used in our study, median, quartiles (Q), and interquartile range (IQR) were determined, and the Kruskal–Wallis test followed by the post hoc test was performed for intergroup comparison. Where a P value of < 0.05 was considered statistically significant at 95% confidence intervals.

Table 1. Mean and standard deviation of Visual Analog Scale scores among three groups

	N	Mean	Std. Deviation
Group I	14	6.1429	2.47626
Group II	14	4.2143	1.42389
Group III	14	5.5000	1.40055

N, number; Std, standard.

RESULTS

In the present study, 42 participants were allocated to three different groups and assessed for pain perception, as displayed in the CONSORT flow diagram.

This study included children aged 7 to 10 years with the mean age being 7.5 ± 0.94 in group I, 7.71 ± 0.91 in group II, and 7.79 ± 0.89 in group III. Comparison of age among the three groups demonstrated no significant differences, with a test value of 0.369 and a P-value of 0.694, respectively. An equal number of male and female participants were included in the study, with seven males (50%) and seven females (50%) in all three groups.

The mean ± standard deviation VAS scores for all three group are as follows: group I (6.14 ± 2.47), group II (4.21 ± 1.42) and group III (5.50 ± 1.40) (Table 1). The intergroup comparison of VAS scores among the three groups was performed using a one-way ANOVA. This comparison demonstrated statistically significant differences among all three groups on the VAS scale ($P = 0.026$) (Table 2). Post hoc pairwise comparisons of VAS scores among the three groups were performed using Tukey's post hoc test. This comparison revealed statistically significant differences ($P < 0.05$) only between groups I and II ($P = 0.022$) (Table 3).

As SEM is a categorical scale, the median, Q, and IQR were determined in our study. For the SEM scale, the medians for groups I and III were similar, and that of group II was lower than that of the other two groups. Similarly, Q1, Q2, and Q3 were also determined for all three groups, which demonstrated that the IQR for groups I, II, and III were 1.37, 0.7, and 1.0, respectively, with

Table 2. Intergroup comparison of Visual Analog Scale scale among the three groups

	Sum of Squares	df	Mean Square	F	P value
Between Groups	27.000	2	13.500	4.002	0.026*
Within Groups	131.571	39	3.374		
Total	158.571	41			

df, degree of freedom. *P value < 0.05 statistically significant

Table 3. Post hoc pairwise comparison of Visual Analog Scale scale among the three groups

(I) Groups	(J) Groups	Mean Difference (I-J)	Std. Error	P value	95% Confidence Interval	
					Lower Bound	Upper Bound
Group I	Group II	1.92857*	0.69422	0.022*	0.2372	3.6199
	Group III	0.64286	0.69422	0.627	-1.0485	2.3342
Group II	Group I	-1.92857*	0.69422	0.022*	-3.6199	-0.2372
	Group III	-1.28571	0.69422	0.166	-2.9771	0.4056
Group III	Group I	-0.64286	0.69422	0.627	-2.3342	1.0485
	Group II	1.28571	0.69422	0.166	-0.4056	2.9771

Std, standard. *P value < 0.05 statistically significant

Table 4. Median, quartiles and interquartile range of Sound, Eyes, and Motor scale across three groups

		Group I	Group II	Group III
Median		2.4500	1.6000	2.3000
Quartiles	Q1	2.0000	1.3000	1.9000
	Q2	2.4500	1.6000	2.3000
	Q3	3.3750	2.0000	2.6000
IQR		1.37	0.7	1.0

IQR, interquartile range.

the lowest IQR noted in group II (Table 4). The Intergroup comparison of the SEM scale was performed using the Kruskal–Wallis test, followed by post hoc comparison. This comparison displayed statistically significant differences among the three groups for the SEM scale, with a P value of 0.007.

DISCUSSION

Treatments involving needles, ranging from standard pediatric vaccinations to dental work, can be confusing for children of all ages. Although necessary, these operations are considered painful, potentially leading to long-term anxiety of needle pain and generating anxiety and discomfort in both parents and children [18]. To reduce discomfort and anxiety, efficient pain-relief strategies must be implemented regularly in all settings where procedures involving needles are performed. Thus, the purpose of this study was to assess the effects of cryoanesthesia and a sweet-tasting solution containing xylitol on pain associated with needle injection in children aged between 7 and 10 years. Children who received cryoanesthesia and sweet-tasting fluid containing xylitol reported reduced pain and discomfort after injections.

Pain management is crucial in pediatric dentistry, particularly when administering injections. Cooling, commonly referred to as cryoanesthesia, is one such approach that involves cooling a specific location to prevent the local neuronal transmission of painful stimuli. Cooling can also be applied as a spray of refrigerants or using ice. One of the first methods of local anesthesia and analgesia, the application of ice before or after painful treatment, has been practiced for thousands of years [13, 19].

The main advantage of cryoanesthesia is that, unlike

other topical anesthetics and analgesics, it operates on all cells, rather than just nerve cells, resulting in instantaneous anesthesia [20]. Although the anesthesia created by cryoanesthesia only lasts for 2–5 seconds, it is effective in reducing pain associated with needle insertion [21].

Oral sucrose and other sweet therapies have been utilized for over a century to relieve children's discomfort, and even earlier. Infants were advised to be given dates and sugar solutions laced with cocaine, opium, or alcohol for the same purpose between the 1840s and the early 1900s [22]. Numerous studies indicate that the hedonic response to sweetness, such as sucrose, increases the release of endogenous opioids [23–26]. This is further supported by the finding that opioid antagonists reduce hedonic responses and eliminate the analgesic effects of sweet-tasting solutions [27]. Our study used a 30% xylitol sweet-tasting solution as a sweetening agent, even though the use of sucrose solution has been well investigated [11,28]. The main advantage of xylitol over sucrose is that it acts as a cariostatic agent [29].

The VAS scale was used in our study to record the subjective sense of anxiety, and the results indicated a high overall reduction in anxiety in group II (cryoanesthesia), followed by group III (xylitol sweet tasting solution), and group I (sterile water). Subjective measurements are typically regarded as the gold standard [30]. As the VAS is universally applicable, simple, and reproducible with few errors, we utilized it for our subjective evaluation [31]. The SEM scale, which considers vocal emotions, bodily movements, and eyes, has been used to objectively quantify pain [32].

The outcomes of our investigation corroborate the effectiveness of cryoanesthesia and a sweet-tasting solution in mitigating injection discomfort during the delivery of a local anesthetic solution for dental procedures. In the SEM scale, the group receiving cryoanesthesia demonstrated the lowest IQR, followed by the sweet-tasting solution, and sterile water. These findings were consistent with those of Farahani and Aminabadi [4] and Harbert [33]. Duncan et al [34] and Hameed et al. [35], who used a refrigerant spray as a cooling agent in contact with the tissue before administering an intraoral injection, obtained similar results. The findings of the current study are corroborated by Kosaraju and Vanderwalle [5], as well as by Kuwahara and Skinner, who reported in various studies on a reduction in pain caused by applying cryotherapy to the anesthetic site [36]. Compared with topical anesthetic gels, precooling before infiltration anesthesia decreased the impression of pain in pediatric patients, according to the findings of Mohiuddin et al. [37].

In our trial, we employed a 30% xylitol solution, which was better than the control or sterile water group in lowering injection pain but less effective than cryoanesthesia in reducing children's impression of pain. Several authors have claimed that sweet tastes help reduce the perception of pain. For example, Ghaderi discovered that administering a sweet-tasting sucrose solution to children before dental injections decreased their level of pain and discomfort [38]. A sweet-tasting honey solution was identified to be useful by Janiani and Gurunathan D [39] for reducing pain during inferior alveolar nerve block and infiltration anesthesia. Using a CPT/C neurometer, Shiiba et al. [40] investigated the impact of sweet taste stimulation on the oral mucosa pain tolerance threshold and discovered that, in children, but not in adults, stimulation increased the pain threshold.

The current trial's results supported the theory that, when a local anesthetic is being administered, precooling the injection site and administering a sweet solution before the needle is inserted increases injection tolerance and aids in controlling pediatric patients' behavior during dental procedures. However, the study's limitations include the injection rate and needle depth, which, owing to the varied anatomy encountered, were constant but not similar. Due to the nature of the interventions and the varying application and taste techniques, blinding the participants and the principal investigator was impossible. Cryoanesthesia using ice was effective in alleviating injection pain as a non-pharmacological method among children when compared to the pain control achieved by

xylitol sweet-tasting solution in children aged 7–10 years.

Clinical significance

One of the main stimuli in dental operations that causes anxiety or fear is the injection of local anesthetics. An easy and affordable technique to alleviate the pain and anxiety associated with local anesthesia injections is cryotherapy and xylitol sweet-tasting solution, which minimizes the dread of pain associated with the procedure involving children with Frankel's Behaviors III and IV.

AUTHOR ORCIDs

Shital Kiran Davangere Padmanabh: https://orcid.org/0000-0003-2896-8446
Vishakha Bhausaheb Gangurde: https://orcid.org/0000-0002-1626-2924
Vikram Jhamb: https://orcid.org/0000-0003-4607-215X
Nasrin Gori: https://orcid.org/0009-0004-0370-7965

AUTHOR CONTRIBUTIONS

Shital Kiran Davangere Padmanabh: Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing
Vishakha Bhausaheb Gangurde: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Supervision, Validation, Writing - original draft, Writing - review & editing
Vikram Jhamb: Conceptualization, Project administration, Writing - original draft, Writing - review & editing
Nasrin Gori: Conceptualization, Project administration, Writing - original draft, Writing - review & editing

CONFLICT OF INTEREST: The authors declare no conflicts of interest.
FUNDING: There is no financial support and sponsorship to declare.

REFERENCES

1. Lakshmanan L, Ravindran V. Efficacy of cryotherapy application on the pain perception during intraoral injection: a randomized controlled trial. Int J Clin Pediatr Dent 2021; 14: 616-20.
2. Thambireddy S, Svsg N, Nuvvula S. Sucrose solution for alleviating needle pain during inferior alveolar nerve block in children aged 7–10 years: a randomized clinical trial. J Dent Anesth Pain Med 2023; 23: 273-80.
3. M M A, Khatri A, Kalra N, Tyagi R, Khandelwal D. Pain perception and efficacy of local analgesia using 2% lignocaine, buffered lignocaine, and 4% articaine in pediatric dental procedures. J Dent Anesth Pain Med 2019; 19: 101-9.
4. Aminabadi NA, Farahani RM. The effect of pre-cooling the injection site on pediatric pain perception during the administration of local anesthesia. J Contemp Dent Pract 2009; 10: 43-50.
5. Kosaraju A, Vandewalle KS. A Comparison of a refrigerant and a topical anesthetic gel as preinjection anesthetics. J Am Dent Assoc 2009; 140: 68-72.
6. Marks I. Blood-injury phobia: a review. Am J Psychiatry 1988; 145: 1207-13.
7. Grassick P. The fear behind the fear: a case study of apparent simple injection phobia. J Behav Ther Exp Psychiatry 1990; 21: 281-7.
8. O'Brien L, Taddio A, Lyszkiewicz DA, Koren G. A critical review of the topical local anesthetic amethocaine (Ametop) for pediatric pain. Paediatr Drugs 2005; 7: 41-54.
9. Younis I, Bhutiani RP. Taking the 'ouch' out–effect of buffering commercial xylocaine on infiltration and procedure pain – a prospective, randomised, double-blind, controlled trial. Ann R Coll Surg Engl 2004; 86: 213-7.
10. Ghaderi F, Ghaderi R, Davarmanesh M, Bayani M. Pain management during needle insertion with low level laser. Eur J Paediatr Dent 2016; 17: 151-4.
11. Priyantham S, Nuvvula S. Intraoral topical anaesthesia in paediatric dentistry: review. Int J Pharm Bio Sci 2016; 7: 346-53.
12. Greenstein G. Therapeutic efficacy of cold therapy after intraoral surgical procedures: a literature review. J Periodontol 2007; 78: 790-800.
13. Meeusen R, Lievens P. The use of cryotherapy in sports injuries. Sports Med 1986; 3: 398-414.
14. Brandner B, Munro B, Bromby LM, Hetreed M. Evaluation

of the contribution to postoperative analgesia by local cooling of the wound. Anaesthesia 1996; 51: 1021-5.
15. Leng HY, Zheng XL, Yan L, Zhang XH, He HY, Xiang M. Effects of different types and concentration of oral sweet solution on reducing neonatal pain during heel lance procedures. Zhonghua Er Ke Za Zhi 2013; 51: 654-8.
16. Mysels DJ, Sullivan MA. The relationship between opioid and sugar intake: review of evidence and clinical applications. J Opioid Manag 2010; 6: 445-52.
17. Kakeda T, Ogino Y, Moriya F, Saito S. Sweet taste-induced analgesia: an fMRI study. Neuroreport 2010; 21: 427-31.
18. Diekema DS. Improving childhood vaccination rates. N Engl J Med 2012; 366: 391-3.
19. Russell SC, Doyle E. A risk-benefit assessment of topical percutaneous local anaesthetics in children. Drug Saf 1997; 16: 279-87.
20. Atkinson RS, Rushman GB, Alfred LJ. A synopsis of anaesthesia. In: Textbook of Anaesthesia. 10th ed. Wright Publication. 1987; pp 311-7.
21. Michael JA. Roenigk HH Jr. New developments in local anesthesia. In: Textbook of surgical dermatology: advances in current practice, St Louis Mosby Publication 1993. pp 3-11.
22. Bean WB. The golden age of quackery. Journal of the American Medical Association 1960; 174: 1351-2.
23. Kanarek RB, White ES, Biegen MT, Marks-Kaufman R. Dietary influences on morphine-induced analgesia in rats. Pharmacol Biochem Behav 1991; 38: 681-4.
24. D'Anci KE, Kanarek RB, Marks Kaufman R. Beyond sweet taste: saccharin, sucrose, and polycose differ in their effects upon morphine induced analgesia. Pharmacol Biochem Behav 1997; 56: 341-5.
25. Abdollahi M, Nikfar S, Habibi L. Saccharin effects on morphine induced antinociception in the mouse formalin test. Pharmacol Res 2000; 42: 255-9.
26. Kanarek RB, Homoleski B. Modulation of morphine induced antinociception by palatable solutions in male and female rats. Pharmacol Biochem Behav 2000; 66: 653-9.
27. Anseloni VC, Ren K, DubnerR, Ennis M. A brainstem substrate for analgesia elicited by intraoral sucrose. Neuroscience 2005; 133: 231-43.
28. Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database Syst Rev 2016; 7: CD001069.
29. Riley P, Moore D, Ahmed F, Sharif MO, Worthington HV. Xylitol containing products for preventing dental caries in children and adults. Cochrane Database Syst Rev 2015; 2015: CD010743.
30. Tomlinson D, von Baeyer CL, Stinson JN, Sung L. A systematic review of faces scales for the self-report of pain intensity in children. Paediatrics 2010: 126: 1168-98.
31. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. J Clin Nurs 2005; 14: 798-804.
32. Wright GZ, Weinberger SJ, Marti R, Plotzke O. The effectiveness of infiltration anesthesia in the mandibular primary molar region. Paediatr Dent 1991; 13: 278-83.
33. Harbert H. Topical ice: a precursor to palatal injections. J Endod 1989; 15: 27-8.
34. Duncan JD, Reeves GW, Fitchie JG. Technique to diminish discomfort from the palatal injection. J Prosthet Dent 1992; 67: 901-2.
35. Hameed NN, Sargod SS, Bhat SS, Hegde SK, Bava MM. Effectiveness of precooling the injection site using tetrafluorethane on pain perception in children. J Indian Soc Pedod Prev Dent 2018; 36: 296-300.
36. Kuwahara RT, Skinner RB. EMLA versus ice as a topical anesthetic. Dermatol Surg 2001; 27: 495-6.
37. Mohiuddin I, Setty JV, Srinivasan I, Desai JA. Topical application of local anaesthetic gel vs ice in paediatric patients for infiltration anaesthesia. J Evolut Med Dent Sci 2015; 4: 12934-40.
38. Ghaderi F, Ahmadbeigi M, Vossoughi M, Sardarian A. The efficacy of administrating a sweet-tasting solution for reducing the pain related to dental injections in children: a randomized controlled trial. Int J Paediatr Dent 2021; 31: 184-90.
39. Janiani P, Gurunathan D. Effectiveness of pre-administered natural sweet-tasting solution for decreasing pain associated with dental injections in children: a split-mouth randomized controlled trial. J Contemp Dent Pract 2021; 22: 1434-7.
40. Shiiba SJ, Sakamoto E, Sago T, Furuta H, Yamamoto T, Tada Y, et al. Effect of sweet solutions on pain tolerance threshold in pediatric oral mucosa. Pediatr Dent J 2012; 22: 22-6.