Review Article

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The efficacy of sweet solutions on dental injection related pain: a systematic review of randomized controlled trials

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Oral flavored solutions are effective for pain management. The intraoral application of sweet solutions at the injection site or on the tongue before local anesthetic administration leads to lower self-perceived pain than any other intervention. This systematic review aimed to evaluate the effect of sweet taste on injection pain in patients undergoing dental procedures. This systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42024571962 and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). An initial electronic search without a time limit up to September 2024 revealed 1,087 studies from indexed databases (PubMed, Scopus, Embase, Cochrane, and Web of Science). The Cochrane Bias Assessment Tool was used to evaluate the risk of bias. After eliminating duplicate and automated records, 103 studies were screened for inclusion. After reviewing the titles and abstracts and assessing the eligibility of the studies, three were excluded and eight RCTs were considered appropriate for inclusion and analysis. This review highlights that all the included studies reported significantly reduced pain perception after sweet solutions, regardless of the specific type or concentration.

Keywords: Injections, Intraoral; Pain; Sucrose; Sweetening Agents.

INTRODUCTION

Dental injections cause significant pain, discomfort, and anxiety. Anxiety in patients is associated with increased duration and intensity of pain [1]. Needle-related pain is an essential issue in dental practice, especially in the pediatric population. This can lead to a negative attitude toward oral health and resistance to subsequent dental visits. Previous studies have demonstrated a bidirectional relationship between pain and anxiety [2]. Pain related to dental injections is associated with several factors, including the type of anesthetic, location of injection, technique of administration of anesthesia, use of surface anesthesia, and psychological factors [1]. The application of topical anesthetics as a desensitization method has remained consistent over the years. Topical anesthetics target free nerve endings in the mucosa and reversibly block impulses in that area, leading to a temporary loss of sensation. Nerve conduction is regulated by the decreased permeability of sodium ions, resulting in reduced depolarization and hence loss of action potential [3]. Previous studies have proposed alternative methods to reduce injection pain, such as cryotherapy, manipulation of the injection rate, and use of warm anesthetic solutions and vibrations, among other innovative solutions.

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Non-pharmacological pain management methods are critical in dental settings because of the anxiety and fear related to injections, particularly in the pediatric population.

Oral sucrose and other sweet-tasting or flavored solutions have been demonstrated to be practical means of pain management. Sweet-tasting analgesia before injection is adequate for tongue contact and does not necessarily require ingestion [4]. Several studies have explained the mechanism of action of sweet solutions that contribute to pain management. Sweet-tasting solutions increase beta-endorphin levels, which mediate the release of endogenous opioids, resulting in the subsequent reduction of pain. Endogenous opioids are neuro-modulators that alter the electrical properties of the target neurons and reduce their excitability [5]. A previous review has indicated the effectiveness of sweet tastes in relieving needle-related pain in children. The interventions encompassed various medical procedures, such as heel pricks, venous blood draws, finger pricks, and injections administered subcutaneously or intramuscularly [6]. An extensive literature review suggested that pain alleviation through sweet solutions is possible. The intraoral application of sweet solutions at the injection site or on the tongue before local anesthetic delivery leads to lower self-perceived pain than other interventions [7-9]. However, whether they can be implemented in clinical practice and are more effective for pain alleviation during dental injections remains debatable. This systematic review aimed to assess the effects of sweet solutions on dental injection-related pain in patients undergoing dental procedures.

METHODS

1. Reporting format

This systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42024571962 and compiled according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. A meta-analysis was not performed because of the significant hetero-geneity among the included studies.

2. Focused question

"Are preemptive sweet solutions effective in alleviating pain associated with dental injections?"

3. Patients, interventions, control, outcome (PICO)

(P) Patients undergoing any dental procedure under local anesthesia (injections); (I) Sweet solutions; (C) Topical anesthetic or any other intervention; (O) Perceived Pain; (S) Randomized control trials (RCTs).

4. Eligibility criteria

The inclusion criteria were adopted based on the employed PICO for the study: (i) Population: Children or adults receiving dental injections; (b) Intervention: Utilization of sweet solutions irrespective of concentration and volume, including non-sucrose sweeteners; (c) Control: Use of topical anesthetic or any other intervention; and (d) Outcome: Studies that compared pain perception in experimental and control groups using different measurement scales. Only RCTs were included in this review. Research formats such as case reports, editorials, retrospective studies, and those lacking randomization were deemed ineligible for inclusion.

5. Search strategy and data extraction

An electronic database search was performed. A search across different scientific engines, including PubMed, Scopus, Embase, Web of Science, and the Cochrane Library, was performed with no time limitations until September 2024. The keywords used for the search were as follows: 1) sweet solutions, 2) sweetening agents, 3) dental injection, 4) local anesthesia, 5) injection pain, 6) children, 7) adults, and (8) analgesic properties of sweet. All identified keywords were merged using Boolean operators (OR and AND) to broaden the results (Table 1). After an initial search, the authors (MA and TK)

Table 1. Search strategy for electronic databases

Database	Results
PUBMED (("pain"[All Fields] OR "pain reduction"[All Fields]) AND ("dental injection"[All Fields] OR ("dental health services"[MeSH Terms] OR ("dental"[All Fields] AND "health"[All Fields] AND "services"[All Fields]) OR "dental health services"[All Fields] OR "dental"[All Fields] OR "dentally"[All Fields] OR "dentals"[All Fields] OR "intraloral"[All Fields]) OR "local anaesthesia"[All Fields] OR "dental anaesthesia"[All Fields]) AND ("sweetening agents"[All Fields] OR "flavoring agents"[All Fields] OR "nutritive sweeteners"[All Fields] OR "non-nutritive sweeteners"[All Fields] OR ("xylitol"[MeSH Terms] OR "xylitol"[All Fields] OR "xylitols"[All Fields]) OR ("sucrose"[MeSH Terms] OR "sucrose"[All Fields] OR "sucroses"[All Fields]) OR ("sweet"[All Fields] OR "sweetness"[All Fields] OR "sweets"[All Fields]) OR ("flavorant"[All Fields] OR "flavorants"[All Fields] OR "flavorful"[All Fields] OR "flavoring agents"[Pharmacological Action] OR "flavoring agents"[MeSH Terms] OR ("flavoring"[All Fields] AND "agents"[All Fields]) OR "flavoring agents"[All Fields] OR "flavor"[All Fields] OR "flavored"[All Fields] OR "flavoring"[All Fields] OR "flavorings"[All Fields] OR "flavors"[All Fields] OR "flavour"[All Fields] OR "flavoured"[All Fields] OR "flavouring"[All Fields] OR "flavourings"[All Fields] OR "flavours"[All Fields] OR "flavourant"[All Fields] OR "flavourants"[All Fields]))	176
EMBASE ('pain'/exp OR 'pain' OR 'pain reduction'/exp OR 'pain reduction' OR 'pain level') AND ('dental injection' OR 'anesthesia'/exp OR 'anesthesia' OR 'dental anesthesia'/exp OR 'dental anesthesia' OR 'lidocaine'/exp OR 'lidocaine') AND ('sweetening agent'/exp OR 'sweetening agent' OR 'fructose'/exp OR 'fructose' OR 'xylitol'/exp OR 'xylitol' OR 'flavoring agent'/exp OR 'flavoring agent' OR 'flavor'/exp OR 'flavor' OR 'sweet'/exp OR 'sweet')	671
WEB OF SCIENCE (('pain' OR 'pain reduction') AND ('dental injection' OR 'local anesthesia' OR 'anesthesia') AND ('sweetening agent' OR 'xylitol' OR 'sucrose' OR 'flavor'))	148
COCHRANE ('pain' OR 'pain reduction') AND ('dental injection' OR 'local anesthesia' OR 'anesthesia') AND ('sweetening agent' OR 'xylitol' OR 'sucrose' OR 'flavor')	66
SCOPUS (pain) AND (dental anesthesia OR lidocaine OR injection) AND (sweet* OR flavor* OR sucrose OR xylitol OR honey)	24

critically assessed the titles and abstracts of the identified studies, and a review of pertinent studies was performed independently. A comprehensive cross-referencing approach was used, followed by an in-depth manual examination of the selected review articles to identify studies that may have been overlooked during the initial review process. Any discrepancies regarding the potential inclusion of articles were discussed with a third author (JK). Two independent authors (MA and TK) retrieved data from full-text manuscripts according to the inclusion criteria and compiled them in an Excel sheet. This facilitated a preliminary understanding of the patient's profile and identification of potential confounding factors. Heterogeneity analysis confirmed that the meta-analysis was not feasible. The data were organized into distinct tables emphasizing the general characteristics of the included studies, injection techniques, sweet solutions, anesthetics, and outcome variables.

RESULTS

1. Study selection and general characteristics of included studies

An initial search revealed 1,090 studies from multiple databases (PubMed, Embase, Scopus, Web of Sciences, and Cochrane). After eliminating duplicate and automated records, 105 studies were screened for inclusion. Four studies were excluded after reviewing the titles and abstracts and assessing the eligibility of the studies, and eight RCTs were considered appropriate for inclusion and analysis. This flowchart was based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) (Fig. 1). A list of excluded studies with reasons for exclusion is reported (Table 2). All the included studies were RCTs with parallel-group, crossover, or split-mouth designs [7-14]. The intervention arm used sweet solutions at or near the injection site, whereas the control arm received either any other type of intervention or no intervention. Five studies used sucrose [7, 9-12], two used xylitol [7, 8], and two reported the use of honey [13,14]. Simultaneously, the control arm included different materials such as distilled and sterile

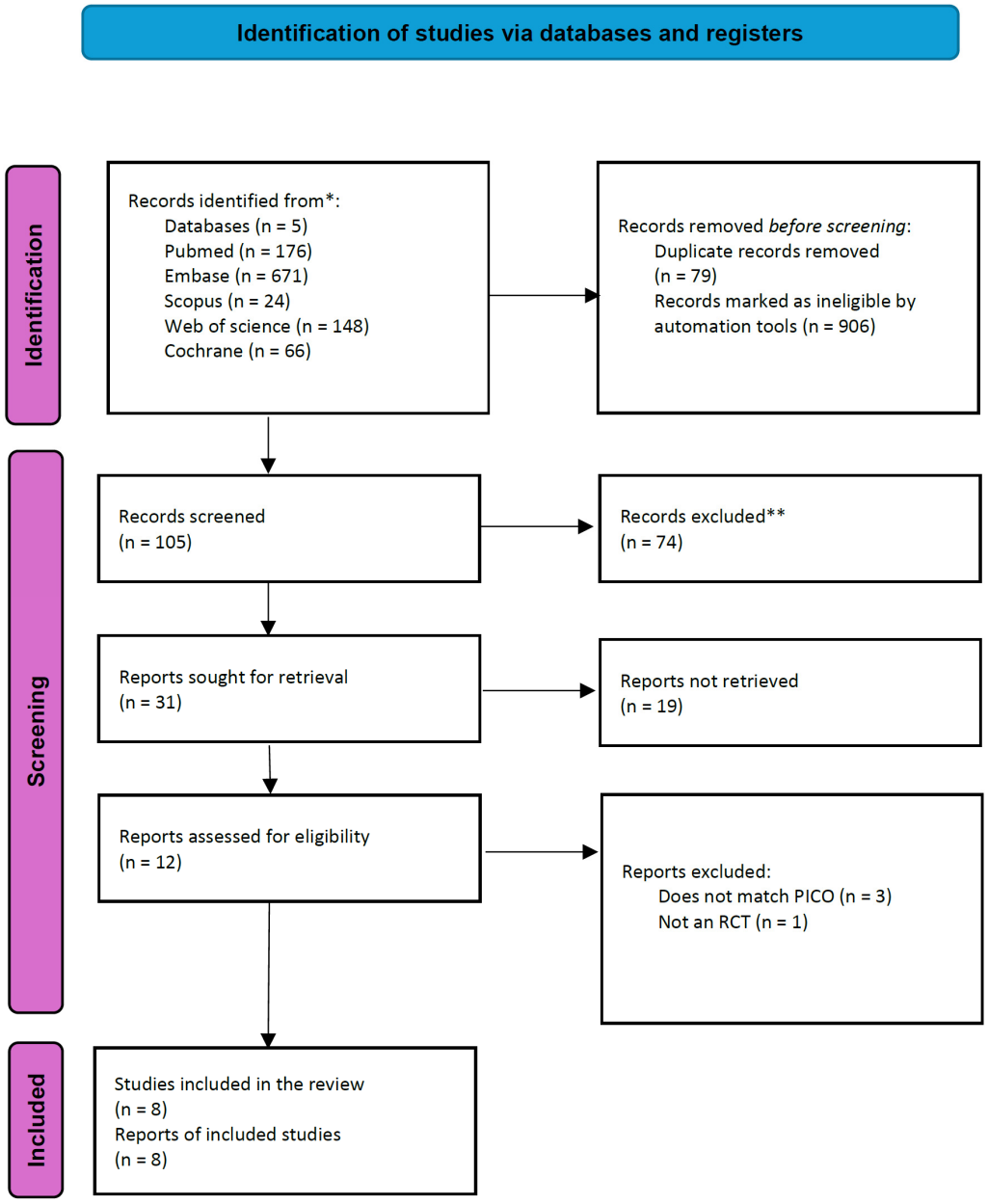

Fig. 1. Study flowchart based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.
*Consider, if feasable to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If autamation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.
n, number; PICO, patients, interventions, control, outcome; RCT, randomized controlled trial.

Table 2. List of excluded studies at full-text review with reasons for exclusion

References	Reasons for exclusion
Shun-ji Shiiba et al. 2011	Focus question not addressed
Deepika A et al. 2012	Focus question not addressed
Ola B. Al Batayneh et al. 2024	Focus question not addressed
Kamalapuram Nirmala et al. 2021	Not an RCT

water [7,8,10,12,13]. Few studies have compared the results of cryotherapy, a combination of sweet solutions, and ethyl chloride spray [8,11,14]. However, a study by Dhingra et al. [11] used cryotherapy, cryotherapy with sucrose, and topical anesthetics as the control arm. The total number of study participants ranged from 30 to 130, with a mean age of 5.80 ± 1.84 years old. Male and

Table 3. General characteristics of the included studies

Author	Study design	Country	Subjects (n)	M/F	Mean age or age range	Study group	Control group(s)	Duration of study	Sample size analysis	Statistical analysis
Winnier et al. [7]	RCT pilot study	India	30	Sucrose group- M = 7, F = 3 Xylitol group- M = 5, F = 5 Distilled Water group- M = 4, F = 6	Sucrose - 7.90 ± 0.87 Xylitol- 7.90 ± 0.876 Distilled Water- 8.00 ± 0.816	Sucrose Xylitol	Distilled water	4 months	Two-sample means test	SPSS v23
Padmanabh et al. [8]	RCT three-arm parallel study	India	42	Cryoanesthesia: M = 7 F = 7 Xylitol: M = 7 F = 7 Sterile water: M = 7 F = 7	Cryoanesthesia: 7.5 ± 0.94 Xylitol: 7.71 ± 0.91 Sterile water: 7.79 ± 0.89	Xylitol sweet-tasting solution	Cryoanesthesia Sterile water group	4 months	Two-sample means test	SPSS v.21.0
Ghaderi et al. [9]	RCT Split mouth	Iran	56	Sucrose group M = 14 F = 14 Water group M = 11 F = 17	Water group 9.05 ± 0.4 Sucrose 9.15 ± 0.62	Sucrose	Sterile water	NR	NR	SPSS v18
Thambiredd y et al. [10]	RCT parallel-group	India	42	Sucrose group- M = 8 F = 13 Distilled water group- M = 11 F = 10	Sucrose group: 8.38 ± 1.02 Distilled water group: 8.47 ± 1.21	Sucrose	Distilled water	6 months	G power analysis	SPSS v20
Dhingra et al. [11]	RCT split-mouth study	India	132	NR	NR	Sucrose solution	Cryotherapy: ice cubes Cryotherapy + sucrose Topic anesthetic	NR	NR	NR
Ratnaparkhi et al. [12]	RCT single-blind trial	India	60	Sucrose group: M = 20 F = 10 Distilled Water: M = 14 F = 16	Sucrose group: 5.93 ± 1.70 Distilled water group: 5.80 ± 1.84	Sucrose	Distilled water	NR	Two sample means test	SPSS v23
Abbasi et al. [14]	RCT single-blind trial	Pakistan	90	Ethyl chloride: M = 16, F = 14 Honey: M = 16, F = 14 No intervention: M = 15, F = 15	Ethyl chloride 28.6 ± 5.1 Honey 26.76 ± 7.29 No intervention: 29.60 ± 6.48	Honey	Precooling with ethyl chloride No intervention	2 months	NR	SPSS v25
Janiani et al. [13]	RCT Split mouth	India	72	M = 52 F = 20	9 ± 3.9	Honey	Sterile water	6 months	NR	SPSS v20.0

F, female; M, male; n, number; NR, not reported; RCT, randomized controlled trial

female participants were included, except in the study by Dhingra et al. [11], where sex was not reported. The duration of the included studies varied from 2 to 6 months in five studies [7,8,10,13,14]. The duration was not

Table 4. Characteristics of the intervention

Authors	Intervention timing	Type of intervention solution	Amount of intervention solution	Route	Time	Type of control solution	Amount of control solution	Time	Application	Type of dental anesthesia	Injection technique
Winnier et al. [7]	Before topical anesthetic application at the injection site	Sucrose Xylitol	2ml of 30% sucrose solution 2ml of 30% xylitol solution	Application on tongue	2 min	Distilled water	NR	1 min	Application on tongue	2% lignocaine with 1:80,000 adrenaline	Maxillary buccal infiltration
Padmanabh et al. [8]	NR	Xylitol	Xylitol: 5mL	Hold it in your mouth and spit it.	2 min	Sterile water Ice pack	5mL NR	2 min 2 min	Sterile water group: Hold it in your mouth and spit it Ice pack group: Applied on injection site	2% lignocaine with 1:2,00,000 adrenaline	Any dental procedure
Ghaderi et al. [9]	Before the application of the anesthetic gel	Sucrose	10 mL of 30% sucrose solution	Hold it in your mouth and spit it	2 min	Sterile water	10 mL	2 min	Hold it in your mouth and spit it	2% Lidocaine with 1/80,000 Epinephrine	Buccal infiltration injections
Thambireddy et al. [10]	NR	Sucrose	10mL of 30% sucrose solution	Hold it in your mouth and spit it	2 min	Distilled water	10 mL	2 min	Hold it in your mouth and spit it	2% lidocaine with 1:100,000 epinephrine	IAN and lingual nerve blocks (Pulpectomy, root canal, or extraction procedures for primary and permanent mandibular molars)
Dhingra et al. [11]	NR	Sucrose	10mL of 30% solution	Hold and spit	2 min	Cryotherapy Lidocaine spray Combination (sucrose+ cryotherapy)	Ice cubes 2% Ice-cream popsicle	2 min 2min 2 min	Ice cubes: Placed at the injection site for 2 min Lidocaine spray: Application through cotton swab for 2 min Popsicle: Placed at the injection site for 2 min	2% Lidocaine with 1/100,000 epinephrine	IAN block (bilateral extraction of mandibular primary molars)
Ratnaparkhi et al. [12]	Before topical anesthetic application at the injection site	Sucrose	2mL of 30% solution	Applied on the lateral surface of the tongue	2 min	Distilled water	2mL	NR	Applied on the lateral surface of the tongue	2% lignocaine with 1:80,000 adrenaline	Buccal infiltration injections (Endodontic procedures)
Abbasi et al. [14]	NR	Honey	5mL	Hold and spit	1 min	Ethyl chloride spray	-	0.5min	Placed on site of injection	1:80,000 lidocaine solution with epinephrine	Buccal infiltration injections
Janiani et al. [13]	NR	Honey	5mL	Hold and spit	1 min	Sterile water	5mL	1 min	Hold and spit	2% lignocaine with 1:100,000 adrenaline	IAN and maxillary infiltration

IAN, Inferior alveolar nerve; NR, not reported.

mentioned [9,11,12] (Table 3).

2. General characteristics of a sweet solution, local anesthesia, and injection techniques

Two studies reported the application of the sweet solution on the tongue [7,12], compared to other studies in which participants were instructed to hold and spit out the sweet solution before administration of the dental injection [8-11,13,14]. Two studies used 2 mL of the 30% sweet solution for the intervention group [7,12], whereas

Table 5. Characteristics of the outcome

Authors	Who evaluates the pain	Parameters assessed	Time of pain evaluation	Statistical significance	Outcome
Winnier et al. [7]	Examiners	SEM	After injection and rinsing	P = 0.00	Xylitol may be equally effective as sucrose in minimizing pain during dental injections
		WBFPS		P = 0.00	
Padmanabh et al. [8]	Co-investigator	VAS	After LA injection	P = 0.026	Xylitol solution was better than the control or sterile water group in lowering injection pain but less effective than cryoanesthesia in reducing the impression of pain.
		SEM	During LA injection	P = 0.007	
Ghaderi et al. [9]	Dentist	VAS	NR	P < .001	There was less pain and discomfort when receiving a sweet-tasting sucrose solution before injection
		SEM		P < .001	
Thambireddy et al. [10]	Assistant	AES	During LA injection	P < .001	Intraoral sweet-tasting sucrose solution could lighten the pain when administered before dental injection
Dhingra et al. [11]	Dentist	VAS	NR	P = 0.00	The least amount of pain is associated with a combination of cryotherapy + sucrose (popsicle) when applied before administration of local anesthesia.
		SEM		P = 0.00	
		FLACC		P = 0.599 (Difference between sucrose and popsicle group) P = 0.00 (For all other group differences)	
Ratnaparkhi et al. [12]	Examiner	WBFPS	After LA injection and rinsing	P < 0.001	Prior application of sucrose or sweet solution reduces the pain on injection.
		SEM	After LA injection and rinsing	P < 0.001	
Abbasi et al. [14]	NR	VAS	NR	P < 0.001	Honey can be effectively used as an analgesic agent to decrease the pain associated with the prick of dental local anesthetic injections.
Janiani et al. [13]	NR	WBFPS	After LA injection	P = 0.00	Pain values after the honey solution intake were significantly lower than those of the control group.
		SEM	After LA injection	P = 0.007	

FLACC, face, legs, activity, cry, consolability; LA, local anesthesia; NR, not reported; SEM, sound, eyes and motor; VAS, visual analog scale; WBFPS, Wong-Baker faces pain scale.

three studies used 10 mL of the 30% sweet solution [9-11]. Two studies used 5 mL of honey solution to assess its effectiveness in pain perception [13,14]. Only one study used 5 mL of xylitol solution [8]. In all included studies, the intervention time for sweet solutions ranged from 1 to 2 min [7-14]. In contrast, the intervention time for the control arm in seven studies ranged from 0.5 to 2 min; however, Ratnaparkhi et al. [12] did not report the intervention time for distilled water. Four studies used topical anesthetics before or after administering the intervention [7,9,11,12]. At the same time, the four studies didn't report the application of topical anesthesia [8,10,13,14]. All the included RCTs reported the use of lidocaine with epinephrine [7-14]. Two studies used 2% lignocaine with 1:80,000 adrenaline [7,12]. Padmanabh et al. [8] used 2% lignocaine with 1:2,00,000 adrenaline solution. Janiani et al. [13] used 2% lignocaine with 1:100,000 adrenaline. Two studies used 2% lidocaine and 1/80,000 epinephrine [9,14]. Two studies used 2% lidocaine with 1/100,000 epinephrine [10,11]. Four studies reported that buccal infiltration injections were administered when the pain level was recorded [7,9,12, 4], and one study compared the pain level after inferior alveolar nerve block and maxillary infiltration [13]. In contrast, other studies mentioned inferior alveolar nerve block [10,11] and one study did not mention any specific injection technique [8] (Table 4).

3. General characteristics of outcomes

All RCTs evaluated pain using different scales, noting that multiple scales were used in a single study. Six RCTs used the Sound, Eyes, and Motor (SEM) scale for pain assessment [7-9,11-13]; four studies reported the use of the Visual Analog Scale (VAS) [8,9,11,14], and three studies used the Wong-Baker Faces Pain Scale (WBFPS) for post-injection pain assessment [7,12,13]. Other pain

Table 6. Risk of bias in the included studies

Author	Randomization sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Overall
Winnier et al. [7]	Low	Some concerns	Low	Low	Low	Low	Low	Some concerns
Padmanabh et al. [8]	Low	Low	High	Low	Low	Some concerns	Low	High
Ghaderi et al. [9]	Low	Low	High	Low	Low	Some concerns	Some concerns	High
Thambireddy et al. [10]	Low	High	High	High	Low	Low	Some concerns	High
Dhingra et al. [11]	Some concerns	Some concerns	Some concerns	Low	Low	Low	Some concerns	Some concerns
Ratnaparkhi et al. [12]	Low	High	Low	Some concerns	Low	Low	Low	High
Abbasi et al. [14]	Low	Some concerns	High	High	Low	Low	Some concerns	High
Janiani et al. [13]	Low	Low	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns

scales were also utilized, including physiological parameters such as heart and pulse rate, face, legs, activity, crying, and consolability (FLACC) scale [10, 11]. Three RCTs measured pain only after LA injection [7,12,13]. A study done by Thambireddy et al. [10] assessed pain during LA administration. Only one RCT measured pain during and after dental injection [8]. However, in three studies, the time of pain evaluation was not reported [9,11,14].

All results indicated that sweet solutions can effectively decrease dental injection pain ($P < 0.05$), except in two cases. The study done by Winnier et al. [7] concluded that xylitol might be as effective as sucrose in minimizing pain during dental injections ($P = 0.00$). Dhingra et al. [11] indicated that least pain was associated with the combination of cryotherapy and sucrose (popsicle) when applied before the administration of local anesthesia. This difference was significant compared with that of sucrose ($P = 0.00$). However, the difference between the sucrose and popsicle groups was not statistically significant ($P = 0.599$) [11]. The study by Padmanabh et al. [8] reported that xylitol solution was better than the control or sterile water group in lowering injection pain, but less effective than cryoanesthesia in reducing the impression of pain. The difference was significant for VAS ($P = 0.026$). Studies by Ghaderi et al. [9], Thambireddy et al. [10], Ratnaparkhi et al. [12], and Abbasi et al. [14] reported that sweet solutions significantly reduced pain upon injection compared to other materials, such as sterile water, distilled water, and ethyl chloride spray ($P < 0.001$). These findings are also consistent with the study conducted by Janiani et al., in which pain levels after honey intake were significantly lower than those in the control group on the WBFPS and SEM pain assessment tools ($P < 0.05$) [13] (Table 5).

4. Risk of bias

Risk of bias analysis for randomized trials was performed using the Revised Cochrane RoB tool 2. Bias was evaluated using criteria, such as random sequence generation, allocation concealment, selective reporting, participant and personnel blinding, outcome assessment, and outcome data integrity. The study bias evaluation grouped risks into high, low, and areas of concern. The randomization sequence generation bias was low in all seven studies, attributable to the computerized randomization sequence, lottery method, and block randomization [7-10,12-14], except in one study that included 132 participants and described it as randomized. However, this does not explain the method used for the random sequence generation [11]. Allocation concealment bias was low in three studies because they

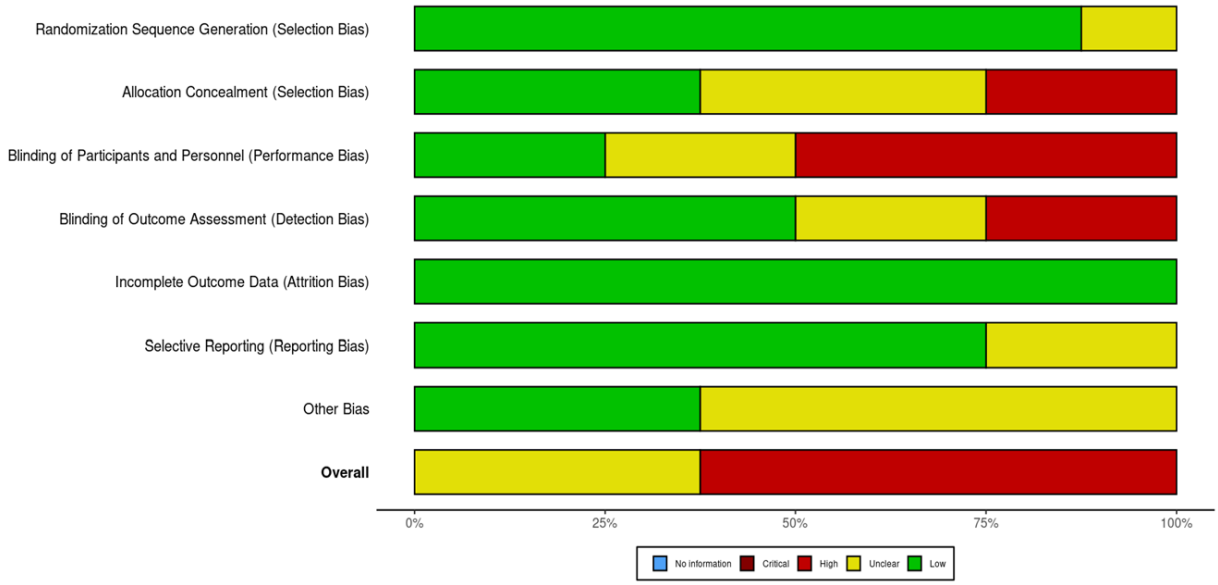

Fig. 2. Overall risk of bias of included studies

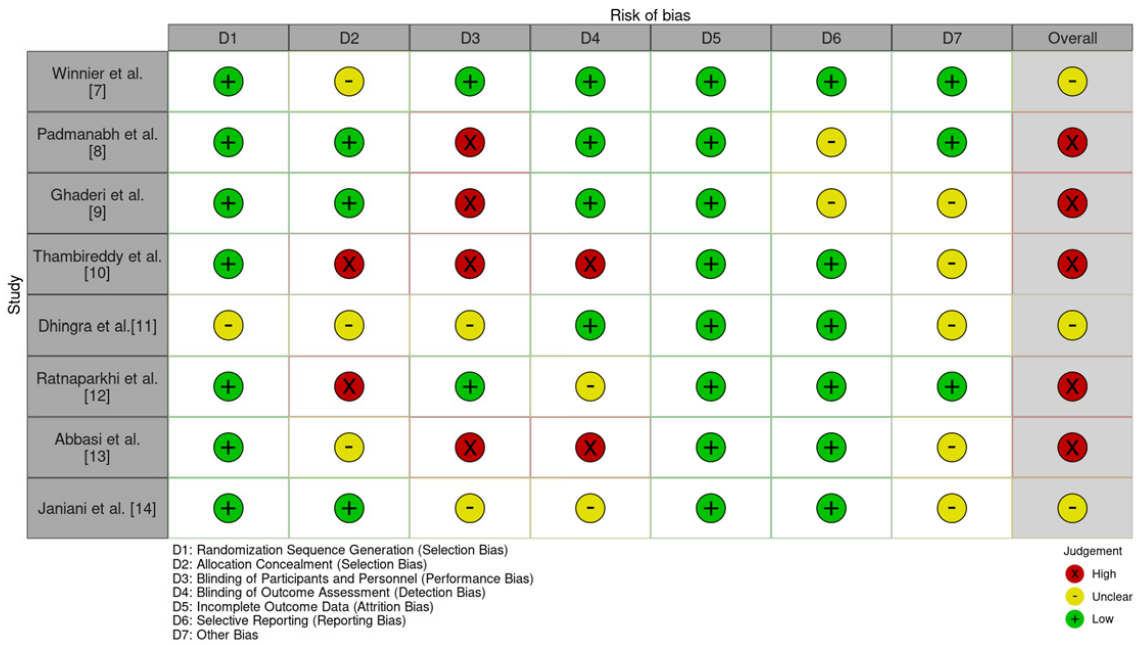

Fig. 3. Traffic light plot

used sealed envelopes with patient information or a person unaware of the research methodology for allocation to different groups [8,9,13], whereas it was high in two studies. Bias was high because the person allocating the treatment was aware of the treatment allocation sequence [10,12]. Some concern arose about allocation concealment in three studies, as the methodology did not clarify whether investigators or research personnel subverted the treatment allocated to the randomized group [7,11,14]. Additionally, various studies lacked blinding between participants and research personnel. Therefore, the performance bias was high in four studies [8-10,14] Poorly reported outcome assessors were identified in four studies, categorizing them under "high" bias and "some concerns" categories [10,12-14]. All studies explained the outcomes addressed in the

methodology. Other potential reasons leading to bias were that not all outcomes were reported in alignment with the aim of the study, and a few participants declined to participate, thereby resulting in insufficient representation of the population within the sampled group. Thus, five RCTs had a high risk of bias [8-10,12,14], whereas the risk of bias in three RCTs was unclear [7,11,13] (Table 6, Figs. 2 and 3).

DISCUSSION

Intra-oral administration of local anesthesia is essential for dental care delivery and it is a painful experience for patients [15]. Many techniques complementary to local anesthetic injections have been tested to reduce pain associated with different underlying mechanisms [16]. Research on photobiomodulation therapy has demonstrated increased beta-endorphin and nitric oxide levels coupled with reduced C-fiber activity, ultimately resulting in diminished injection-associated pain [17-19]. Other measures include cryotherapy, which reduces cellular metabolism, nerve conduction velocities, and local blood flow, thus reducing pain at the injection site [20,21]. The effects of pre-cooling the injection site and utilizing a warm anesthetic solution to relieve pain have also been reported [22,23]. Studies on the pre-emptive use of sweet solutions to minimize injection pain show that they are highly effective [6,8,9,14]. One accepted theory of pain reduction is that sweet solutions activate the endogenous opioid system, which modulates the pain response. Opioid-mediated pain suppression modulates the descending pain pathway by inhibiting the release of GABA, thereby inhibiting pain perception [5]. Theories on the mechanism of action of sucrose diverge, with some suggesting sedative properties (not analgesic) and others attributing its effects to distraction rather than direct analgesia [24].

This review explored the effect of sweet solutions on reducing injection pain before dental treatment. All RCTs in this review included participants with a mean age of under 18, except Abbasi et al., who evaluated the effect of honey on participants with an average age of 26.76 ± 7.29 years. This study reports that honey may be an effective analgesic agent for reducing preprocedural injection pain. Three studies reported an association between demographic variables and pain [9,10,14]. Two studies found no relationship between age, sex, height, weight, and pain perception. Alternatively, the findings presented by Ghaderi et al. suggested that a higher BMI was correlated with a reduced analgesic effect of sweet solutions. This finding is consistent with another report that reported a significant effect of sucrose in children with average weight compared to those who were overweight [25].

All studies reported reduced pain perception following intraoral application or administration of sweet solutions. Winnier et al. concluded that the type of sweet solution used did not affect pain perception; no significant difference was observed between the effects of sucrose and xylitol in alleviating pain [7]. However, a study by Padmanabh et al. showed that the use of xylitol is more effective than sterile water in reducing injection pain but less effective than cryotherapy [8]. Another study evaluated the effectiveness of cryotherapy and sucrose and reported that the least pain was associated with its combined use compared to sucrose alone and other interventions [11]. The evidence presented in this review supports the effectiveness of sweet solutions for pain management. However, comparative studies evaluating their efficacy against cryotherapy and other nonpharmacological approaches remain limited. None of the RCTs included in this study explored the sustained effects of sucrose on future dental appointments. However, evidence suggests the sustained effectiveness of sucrose over time. A study of the pain profiles of preterm infants for skin-breaking procedures using sucrose revealed that the analgesic efficacy of sucrose is sustained over future appointments [26]. All included studies used variable amounts of solutions to explore their effect on dental injection pain. Two studies used 2 mL of 30% sweet solution [7,12], and three RCTs tested the impact of 10

mL of 30% sweet solutions [9-11]. Two studies reported using 5 mL sweet solutions to evaluate their effectiveness in reducing injection-associated pain [8,14]. Irrespective of the solution utilized, all studies reported significant differences, that is, decreased pain perception was associated with sweet solutions. These findings are consistent with those of another RCT that tested the optimal sucrose dose for alleviating procedural pain in neonates during a skin-breaking heel-lance procedure. The administration of a minimal dose of sucrose (0.1 mL) was as effective as the other doses. Pain intensity did not vary significantly with changes in the concentration or dose of the sweet solution [27].

Several studies have used combined strategies to hinder the isolation of the effects of sweet solutions. Three RCTs used the intervention before applying topical anesthetic gel [7,9,12]. Four studies did not report whether topical gel or other strategy was utilized [8,10,11,14]. Therefore, interpreting these results requires careful consideration, because the combined use of sweet solutions with other strategies introduces potential confounding factors, making it challenging to determine the independent effect of sweet solutions.

The strength of this review is the inclusion of only RCTs. However, owing to the heterogeneity of the included RCTs, a meta-analysis was not feasible. The included RCTs exhibited variability in study design, including differences in doses of sweet solutions, concentrations, participant characteristics, types of dental procedures, and scales used for pain assessment, thus limiting the ability to conduct a quantitative review. The limitations of this study include measuring pain based on the child's expressions or understanding. Self-reporting of pain or discomfort by a child is not always a reliable indicator because various developmental, environmental, and personal issues can influence it. Thus, the use of physiological scales in some studies can be a valid explanation for reduced pain perception after using a sweet solution as an intervention. Another limitation of this review is that none of the included RCTs studied behavioral outcomes, such as crying duration or bodily movements, to compare groups that utilized sweet solutions with those that did not. No evidence supports the claim that reducing injection pain using sweet solutions improves overall patient attendance or oral health. Limited evidence exists regarding the long-term safety of sucrose administration for procedural pain. A systematic review suggested a potential link between repeated sucrose doses and poor neurological development in preterm infants. However, the findings showed no significant adverse effects on long-term neurobehavioral development [28]. This concern is minimal in dentistry, because sweet solutions are applied topically rather than orally. Previous studies have reported hyperalgesia in infants exposed to sucrose during procedural pain management. However, the evidence indicates that the prevalence of hyperalgesia in these infants is comparable to that in healthy infants [29]. A paucity of studies focuses on the side effects and long-term behavioral outcomes of using sweet solutions along with intra-oral injections. The current evidence highlights several barriers and facilitators that influence the use of sweet solutions for pain management in medical settings. Major facilitators include the absence of specialized training, ease of availability, and robust evidence supporting its efficacy, all of which encourage its adoption in clinical practice. However, a significant barrier is the absence of institutional or hospital-level policies outlining protocols, dosage, frequency, and potential side effects. Another notable barrier is the perception that implementing this technique may require additional time per patient, potentially increasing the workload in busy clinical settings. Additionally, a lack of awareness of this pain management technique often leads to limited confidence in communicating its use to patients. The contraindications and side effects of the oral administration of sweet solutions, including sucrose intolerance/glucose malabsorption and vomiting/choking, have been studied in infants and children undergoing medical procedures. However, their applicability in dental settings, diverse demographics, and population groups is limited. Thus, extensive research is needed to evaluate

the efficacy and tolerability of sweet solutions in diverse demographic groups, including adults, and to assess the applicability of those findings to participants with complex medical conditions or special needs [30,31].

CONCLUSION

This review highlights that all the included studies reported significantly reduced pain perception after the application of sweet solutions, regardless of the specific type or concentration. This review also underscores the necessity for the careful evaluation of demographic variables, as the findings indicate a potential relationship between analgesic efficacy and other characteristics. However, evidence suggests that sucrose, xylitol, and honey can mitigate injection pain. Variability in methodologies, including the combination of interventions and measurement approaches, and the need for a detailed clinical protocol make implementing this in dental practice challenging.

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