Review Article
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Effect of warming local anesthesia solutions before intraoral administration in dentistry: a systematic review

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Background: The aim of the present systematic review was to evaluate and compare the efficacy of warmed and unwarmed local anesthesia solutions in reduction of pain during intraoral injection administration.
Methods: PubMed, Ovid SP, and Cochrane Central Register of Controlled Trials were searched from publication years 1990 to 2020 with relevant MeSH terms. Studies were screened by titles and abstracts, followed by full-texts evaluation of the included studies.
Results: A total of four studies were included in the systematic review. Outcomes evaluated were subjective and objective pain during administration of the warmed local anesthesia solution in comparison with the unwarmed local anesthesia solution. Among the four studies that evaluated the self-reported pain score, three studies showed significantly lower pain scores associated with warmed local anesthesia. Only two studies evaluated the observed pain score, and both of them reported a significantly lower pain reaction with the warmed local anesthesia solution.
Conclusion: Within the limits of this systematic review, warming the local anesthesia solution to body temperature (37°C) before administration seemed to reduce the discomfort during intraoral local anaesthesia administration, and more high-quality studies should be carried out to validate the same.

Keywords: Dental Anesthesia; Local Anesthesia; Pain; Warming.

INTRODUCTION

Local anesthesia administration is the first and foremost pre-requisite for most procedures in dentistry [1]. However, the administration of local anesthesia is painful [2]. Among many methods evaluated to reduce the discomfort during local anesthesia administration, warming of the local anesthesia solution is seldom used.

The number of studies in the field of medicine reporting the benefits of warming the local anesthesia solution before administration has gradually increased [3-6]. Some authors reported that the possible explanation behind the improved success of warmed local anesthesia can be attributed to stimulation of the capsaicin receptor, which is a heat-activated ion channel in the pathway of pain [7]. In the meta-analysis by Hogan et al. conducted in 2011, significant pain reduction was observed with the warmed local anesthesia solution for dermal and subcutaneous injections [8].

To the best of our knowledge, there has been no systematic review evaluating the efficacy of warmed local anesthesia for use in dentistry. The aim of the present systematic review was to evaluate and compare the efficacy of intraorally administered warmed and unwarmed

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Table 1. Excluded studies with reasons

No.	Excluded articles	Reasons for exclusion
1.	Courtney, 1999	Survey
2.	Rowshen and Preshaw, 1999	Survey
3.	Davouidi, 2016	Review article

local anesthesia solutions.

METHODS

Protocol: PRISMA guidelines were followed for reporting. Eligibility criteria: The search strategy was selected using the population, intervention, comparison, and outcome (PICO) framework, based on the following question: ***"Does warming of the local anesthesia solution before administration influence pain characteristics?"*** The PICO search strategy for the systematic review was: [P] patient, healthy individual (child or adult); [I] intervention, warming the local anesthesia solution before administration (infiltration or block in the maxilla or mandible); [C] comparison, unwarmed local anesthesia solution; and [O] outcome of interest, pain characteristics (subjective and objective).

An electronic search was performed in three databases: PubMed, Ovid SP, and Cochrane. The search was conducted from publication years 1990 to 2020. The last search was performed on April 30, 2020. Articles published in English only were included. The search was based on the pre-specified question using relevant MeSH terms: "warming" AND "local anesthesia" AND "dental".

Eligibility criteria: Randomized controlled clinical trials comparing warmed local anesthesia to unwarmed local anesthesia for dental injections in subjects were included. Non-randomized studies or non-controlled clinical trials, comparative studies, technical notes, case reports, narrative reviews, and systematic reviews and articles that could not be translated to English were excluded. Initially, studies retrieved after the comprehensive MeSH terms search were imported to Zotero (www.zotero.org) from all databases, and duplicates were excluded. Subsequently, titles and abstracts were screened. Potential articles were then included for a full text review.

Two independent reviewers analyzed the data and recorded them on Excel. The data form contained the information regarding author names and year of publication, study design, number of participants, age, intervention, control, and outcome. The outcome sought for was "pain during administration (subjective and objective)". Only the qualitative data analysis was performed, as only a few studies were available for quantitative data pooling.

Risk-of-bias assessment: Two reviewers independently assessed the quality of the included articles using the Cochrane criteria. Parameters, such as sequence generation, allocation concealment, participants, personnel and outcome assessment blinding, outcome data completeness, selective outcome reporting, and other miscellaneous sources, were evaluated under the risk-of-bias assessment. Studies presenting a low bias risk in all seven domains were classified as having an overall low risk of bias. Studies presenting a high bias risk in any one domain were considered as having an overall high risk of bias.

RESULTS

In all databases, 82 records were found, three of which were duplicates. Removing the duplicate articles, 79 records were screened by the title and abstract. The full text of the seven potentially relevant papers were evaluated [9-15]. Among them, three papers were excluded [12,14,15]. Reasons for exclusion are presented in table 1. As a result, four studies were included in this final systematic review [9-11,13] (Fig. 1).

Characteristics of included studies: The characteristics of the included studies are presented in table 2. Among

Table 2. Characteristics of included studies

No.	Author-year	Study design	Sample characteristics	Type of injection administered	Reason for injection administration	Local and topical anaesthesia used	Needle gauge	Intervention characteristic and comparison groups	Warming method	Pain perception (self-reported pain by the child) Mean ± SD	Pain reaction (observer-reported pain reaction) Mean ± SD
1.	Gumus, 2019 [9]	Split-mouth randomized clinical study Crossover design.	100 children aged 5–8 years divided into two groups A power analysis was performed while calculating the number of patients (n) considering an error margin of 0.05, a test power of 0.90, and a dropout rate of 0.25.	Bilateral infiltrations in the maxillary molar region	Not mentioned	Articaine 4% and 1:200,000 epinephrine	Not mentioned	G1: Warmed LA solution (37°C) G2: Unwarmed LA solution (21°C)	CALSET (AdDent Inc., USA)	Wong baker faces pain scale, measured separately for boys and girls Child-reported pain scores were significantly lower with the warm local anaesthesia solution (boys, 2.65 ± 1.33; girls, 2.48 ± 1.50) than those with the unwarmed local anaesthesia solution (boys, 6.03 ± 1.39; girls, 6.13 ± 1.42) P-value < 0.001	Pain reaction was evaluated on the FLACC scale. In this study, all variables were measured separately. All measured variables were significantly lower with the warm local anaesthesia solution than those with the unwarmed local anaesthesia solution.
2	Aravena, 2018 [11]	Double-blind, split-mouth randomized clinical trial	72 adults with an age range of 18 to 35 years. Power analysis considering a 5% level of significance, a study power of 90% and including 25% of the sample to account for loss.	Buccal infiltration near the lateral incisor region	Not mentioned.	0.9 mL of lidocaine HCl 2% with epinephrine 1:100,000	30 G	G1: Warmed LA solution (42°C) G2: Unwarmed LA solution (21°C)	Baby bottle warmer (Phillips Avent®)	100 mm visual analogue scale The VAS score was significantly lower with the warm local anaesthesia solution (15 ± 14.67) than with the unwarmed local anaesthesia solution (35.3 ± 16.71). P-value = 0.001	Not measured
3	Kurien, 2018 [10]	Randomized, split-mouth clinical trial	60 children aged 6–12 years Sample size was estimated using the formula: N = Z2 [2SP2]/d2	IANB Injections	Pulp therapy.	2% lignocaine hydrochloride with 1:200,000 epinephrine	27 G	G1: Warmed LA solution (37°C) G2: Unwarmed LA solution G3: Buffered LA solution	Thermostatic water bath.	Wong baker faces pain scale Warmed LA solution resulted in significantly less pain on administration compared to the conventional unwarmed LA solution (P < 0.001).	Pain reaction was evaluated on the SEM scale. The warmed LA solution resulted in significantly lower sound (0.12 ± 0.33), eye (0.24 ± 0.44), and motor (0.16 ± 0.37) scores on administration compared to the conventional unwarmed LA solution (sound, 0.52 ± 0.65; eye, 0.92 ± 0.64; motor, 0.64 ± 0.81). P-value = (0.035, 0.001, and 0.008, respectively)
4.	Ram, 2002 [13]	Randomized, split-mouth clinical trial Single blind	44 children aged 6–11 years The sample size was not calculated.	Block and infiltrations	Operative procedures	2% lidocaine 1:100,000 epinephrine	Not mentioned	G1: Warmed LA solution (42°C) G2: Unwarmed LA solution (21°C)	Thermostatic water bath	VAS scores No significant difference was found in the mean VAS score between the room-temperature solution group and the warmed solution group (23 ± 22 and 21 ± 19, respectively).	Not evaluated

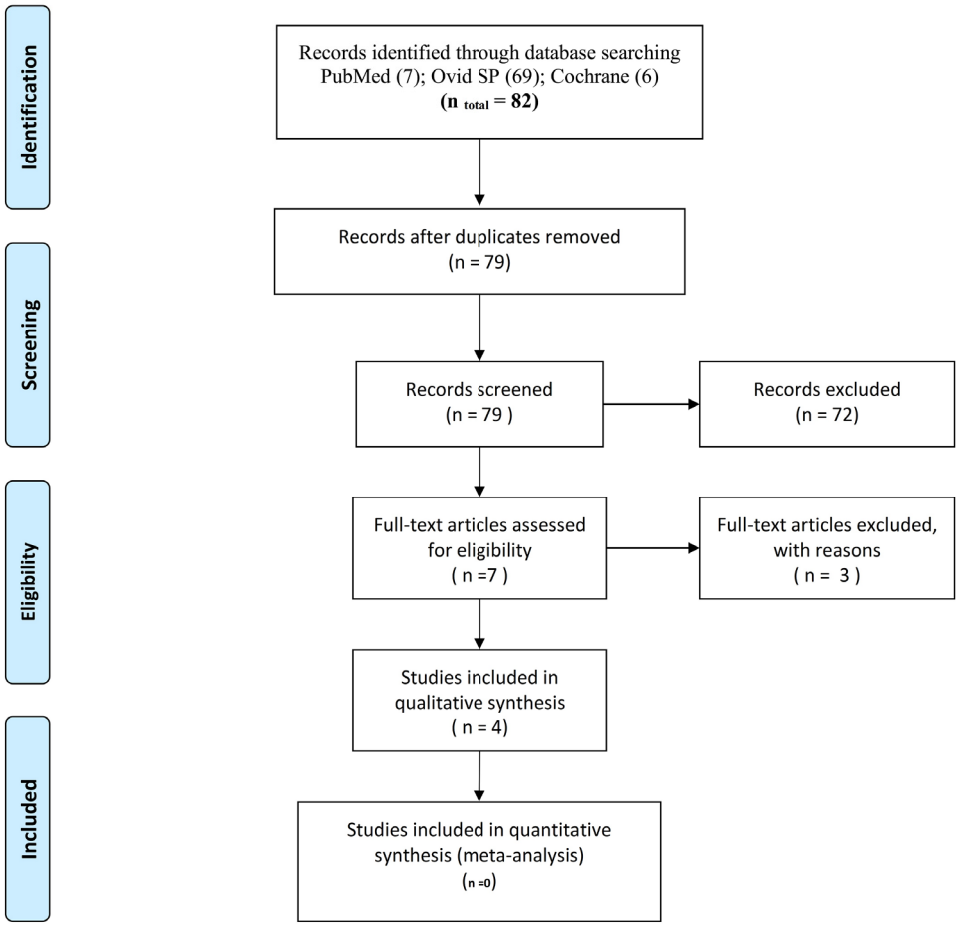

Fig. 1. PRISMA 2009 flow diagram

the four included studies, one was published in 2019, two in 2018, and one in 2002. All studies had the randomized split-mouth design [9-11,13].

Risk of Bias: Cochrane guidelines were followed to evaluate the risk of bias (Fig. 2). For all included studies, randomization was carried out (n = 4). Allocation concealment was not mentioned clearly in any of the included studies. In three studies, both participants and personnel were blinded. In the study by Ram et al., 2002, only participants were blinded, and the operator was not blinded. All four studies were free from attrition bias, selective reporting bias, and any other miscellaneous bias.

DISCUSSION

Local anesthesia is regarded as a severe pain-evoking procedure in dentistry. Researchers have been evaluating different methods to reduce the discomfort associated with intraoral injections. Injection site preparation methods include application of topical anesthesia, precooling the injection site [16-19], and vibratory (physical) stimulation of the injection site [20,21]. Psychological methods include distraction [22-28], technical changes, such as changing the needle diameter [29,30], and warming and buffering the local anesthesia solution. These methods reduce the discomfort associated with intraoral local anesthesia administration [31-33].

In the field of medicine, warming the local anesthesia

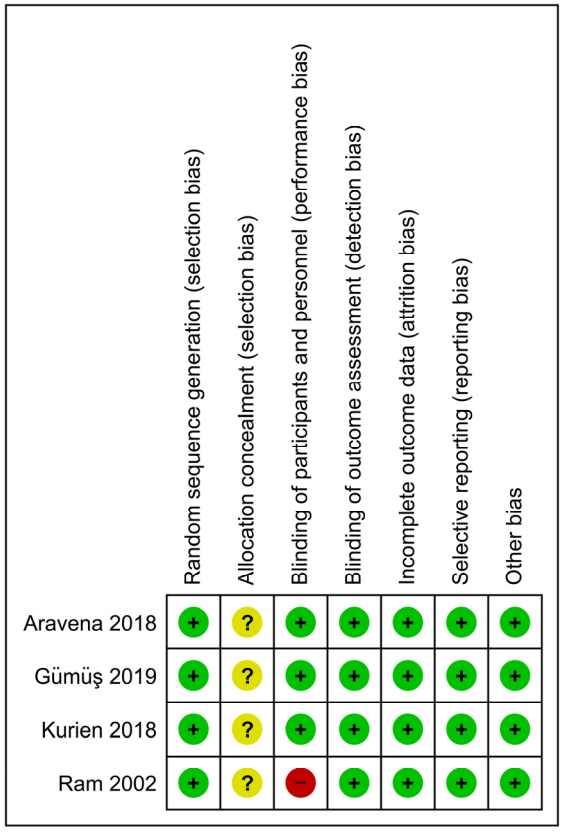

Fig. 2. Risk of bias summary

solution to body temperature (37°C) is considered to be associated with reduced pain intensity during subcutaneous local anesthesia administration for minor oral surgeries [34]. An increasing number of studies in dentistry have been reporting decreased discomfort associated with the administration of the warm local anesthesia solution in lieu of local anesthetic solutions at room temperature. The potential question of efficacy of warming local anesthesia solutions is addressed in this current systematic review.

All the four studies included for the final review were randomized control trials with the split-mouth design [9-11,13]. Three of the studies were double-blinded [9-11], while the study by Ram et al., 2002, followed single-blinding [13]. The age of the subjects reported in included studies ranged from 5 to 35 years.

In our systematic review, only dental injections (infiltration or block) in subjects of any age comparing warmed and unwarmed local anesthetic solutions were assessed. Among the four included studies, three reported injecting the local anesthesia solution at 37°C [9,10,13], while only the study by Aravena et al., 2019, reported a temperature of 42°C [11]. The temperature of unwarmed solution was reported to be 21°C in all studies. Except for the study by Gumus and Aydinbelge, 2019 (which used articaine 4%) [9], the remaining three studies reported the usage of lignocaine [10,11,13]. A high concentration of epinephrine (1:1,00,000) was used in two studies [11,13].

Methods of warming anesthetic solutions: Warming the local anesthetic solution is accomplished with the thermostatic heat bath [10,13], baby bottle warmer [11], or Calset composite warmer [9].

Type of injection: Only the inferior alveolar nerve block was evaluated in the study by Kurien et al., 2018 [10]. Buccal infiltrations in the maxilla were evaluated in the studies by Gumus and Aydinbelge, 2019, and Aravena et al., 2019 [9,11]. Both infiltrations and blocks were evaluated in the study by Ram et al., 2002 [13].

Outcomes evaluated were subjective and objective pain experiences during the administration of the warmed local anesthesia solution in comparison with the unwarmed local anesthesia solution.

Comparison of subjective pain (self-reported pain) in subjects receiving warmed and unwarmed local anesthesia solutions: All four included studies evaluated self-reported pain. Two studies evaluated subjective pain on the visual analog score (VAS) [11,13], and the other two studies used Wong Baker-FACES Pain Scale (WB-FPS) [9,10]. Only the study by Ram et al., 2002, reported no significant difference in the VAS score (mean ± standard deviation) between warmed (21 ± 19) and unwarmed (23 ± 22) local anesthesia solutions ($P > 0.05$). The three other studies reported significantly lower subjective pain with the warmed local anesthesia solution in comparison with the unwarmed local anesthesia solution ([Gumus and Aydinbelge, 2019: warmed local anesthesia solution, WB-FPS score, boys 2.65 ± 1.33 vs. girls 2.48 ± 1.50; unbuffered solution, WB-FPS score, boys 6.03 ± 1.39 vs. girls 6.13 ± 1.42; $P < 0.001$];

[Aravina, 2018: warmed local anesthesia solution, VAS score, 15 ± 14.67, unwarmed local anesthesia solution, VAS score, 35.3 ± 16.71; P = 0.001]; [Kurien, 2018: warm local anesthesia solution to unbuffered solution, WB-FPS score, P < 0.001]) [9-11]. In conclusion, most studies reported lower discomfort associated with the warmed local anesthesia solution compared to the unwarmed local anesthesia solution at room temperature.

Comparison of objective pain (observer-rated pain/pain reaction) in subjects receiving warmed and unwarmed local anesthesia solutions: Pain reaction was evaluated only in two studies [9,10]. Gumus and Aydinbelge, 2019, evaluated pain reaction on the Faces, Legs, Activity, Cry, Consolability scale. Kurien, 2018, evaluated pain reaction on the Sound, Eye, Motor scale. Both studies reported significantly lower objective pain with the warmed local anesthesia solution in comparison with the unwarmed local anesthesia solution ([Gumus and Aydinbelge, 2019: warmed local anesthesia solution, face score, boys 0.40 ± 0.29 vs. girls 0.43 ± 0.34; leg score, girls, 0.34 ± 0.25 vs. boys, 0.35 ± 0.21; activity score, girls, 0.31 ± 0.27 vs. boys, 0.26 ± 0.20; cry score, girls, 0.54 ± 0.39 vs. boys, 0.57 ± 0.48; consolability score, girls, 0.34 ± 0.21 vs. boys, 0.39 ± 0.35; unwarmed local anesthesia solution, face score, girls, 1.10 ± 0.31 vs. boys, 1.16 ± 0.35; leg score, girls, 0.50 ± 0.27 vs. boys, 0.48 ± 0.36; activity score, girls, 0.52 ± 0.31 vs. boys, 0.33 ± 0.26; cry score, girls, 0.60 ± 0.38 vs. boys, 0.59 ± 0.41; consolability score, girls, 0.43 ± 0.25 vs. boys, 0.41 ± 0.27; P < 0.05]; [Kurien, 2018, warmed local anesthesia solution, sound, 0.12 ± 0.33; eye, 0.24 ± 0.44; motor, 0.16 ± 0.37; unwarmed local anesthesia solution, sound, 0.52 ± 0.65; eye, 0.92 ± 0.64; motor, 0.64 ± 0.81; p-value: sound, 0.035; eye, 0.001; motor, 0.008]) [9,10]. In conclusion, lower pain reaction was observed with the warmed local anesthesia solution in comparison with the unwarmed or room-temperature local anesthesia solution.

Summary of evidence: This systematic review compared subjective pain reported and objective pain evaluated when warmed and unwarmed local anesthesia solutions were used for intraoral injections. Most studies favored warmed local anesthesia solutions.

Limitations of this review: The number of available studies was low for qualitative and quantitative analyses. All studies did not use the same gauge needle for the injection. The injection site differed across studies. Among the four included studies, three involved children with the age ranging from 5 to 12 years, while one involved subjects aged from 18 to 35 years. Moreover, the scales of measurement of subjective pain differed across included studies (VAS and WB-FPS). The objective pain score was not measured in two studies. Owing to the limited number of studies available and diversity among the available studies, the meta-analysis was not performed.

Recommendations for future research: Studies available on this topic are extremely limited. We recommend the following future research topics:

1. Warmed versus unwarmed local anesthesia solutions should be evaluated for pain-related outcomes separately in adults and children, the maxilla and mandible, block injections and infiltrations, and inflamed and uninflamed tissues.
2. Combination of buffering and warming local anesthesia for pain-related outcomes.
3. Comparing warming alone, buffering alone, and a combination of both warming and buffering of local anesthesia solutions for pain-related outcomes.

Conclusions: Based on the aforementioned discussion, the following conclusions can be drawn:

- Warming the local anesthesia solution might benefit in reducing discomfort during the administration of intraoral injections, but the available evidence is limited.
- More well-planned and well-executed randomized control trials with an adequate sample size should be carried out.

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Sunnypriyatham Tirupathi: Conceptualization, Data curation, Formal analysis, Methodology, Resources, Software, Visualization, Writing - original draft, Writing - review & editing
Srinitya Rajasekhar: Writing - review & editing

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