Efficacy of Topical Anesthetics in Pain Perception During Mini-implant Insertion: Systematic Review of Controlled Clinical Trials

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The focus of this systematic review is to assess the efficacy of several commonly utilized anesthetic techniques for reducing pain during the placement of mini-implants. An electronic search was conducted in the databases PubMed, Scopus, Web of Science, Medline Complete, Cochrane, Trials Central, and Clinical Trials, without limitations on year of publication or language. Randomized controlled trials (RCTs) and controlled clinical trials (CCTs) were considered. Two reviewers of articles independently evaluated the results of the study, and the risk of bias of included articles was evaluated according to the Cochrane Scale. Five eligible articles (3 RCTs and 2 CCTs) were included. The quality of the body of evidence was considered low because of the presence of multiple methodological problems, high risks of bias, and heterogeneity in the articles included. There was evidence that the efficacy of the analgesia of infiltrative anesthesia was most effective in promoting a lower perception of pain compared to the other anesthetic agents, although an injection was required. Among topical anesthetics, compound topical anesthetics with 20% lidocaine were more effective than compound topical anesthetics with low lidocaine concentration and conventional topical anesthetic with 20% benzocaine.

Key Words: Anesthetics; Orthodontic anchorage procedures; Pain; Evidence-based dentistry.

The use of mini-implants in orthodontics has been shown to be an extremely advantageous method for skeletal anchorage, and their efficacy has been proved in different orthodontic treatments.^{1,2} The use of these devices has made planned tooth movement possible without undesirable results in the vertical, transverse, and anterior-posterior planes,¹⁻³ and the technique for using them is simple and relatively low-cost.⁴⁻⁶

However, the acceptance of patients with regard to the procedure for placement of these mini-implants during orthodontic treatment is strongly influenced by

the perception of pain associated with the insertion procedure, frequently a reflection of the needle puncture for the application of infiltrative anesthesia.^{1,7}

The placement of mini-implants in the oral cavity with only the application of topical anesthesia has been suggested in the literature.^{1,8,9} There are advantages involved in this practice, such as greater comfort for the patient, simplicity of the anesthetic technique, reduction in stress and anxiety of the patient before insertion of the mini-implants, and reduction in the risk of injury by use of the needle.¹⁰

Various topical anesthetics are available on the market for use in minor surgical procedures, and present great acceptance by patients.¹ However, for topical anesthesia to replace conventional infiltrative anesthesia, it should ideally be capable of completely anesthetizing the area where the mini-implant will be inserted, rapidly achieving its action in the mucosa, and doing so without causing any secondary effects,^{1,11} such as allergic reaction, pruritus, burning, erythema, edema, methemoglobinemia, or other systemic toxicity.¹¹

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Table 1. Database and Search Method*

<i>Database</i>	<i>Search Strategy</i>
PubMed Web of Science Complete Medline (EBSCO)	((orthodontics [MeSH Terms] OR orthodontic OR orthodontic patients OR orthodontic treatment OR tooth movement OR teeth movement OR patients [MeSH Terms] OR humans [MeSH Terms]) AND (drugs OR medicaments OR topical anesthetics OR injected anesthetics OR anesthetics [MeSH Terms] OR anesthetic OR infiltration anesthesia OR topical anesthesia OR anesthesia [MeSH Terms] OR sedation) AND (temporary anchorage devices OR dental implants [MeSH Terms] OR mini-implants OR orthodontic mini-implants OR orthodontic anchorage procedures [MeSH Terms] OR orthodontic anchoring OR miniscrew OR mini-screw OR miniscrew implants) AND (pain perception [MeSH Terms] OR pain management [MeSH Terms] OR pain [MeSH Terms] OR injuries [MeSH Terms] OR injury OR bone density [MeSH Terms] OR alveolar bone OR pressure [MeSH Terms] OR discomfort OR effectiveness OR efficacy OR efficacious OR complications [MeSH Terms] OR side effects [MeSH Terms] OR collateral effects))
Scopus Cochrane	((orthodontics [MeSH Terms] OR patients [MeSH Terms] OR humans [MeSH Terms]) AND (drugs OR medicaments OR anesthetics [MeSH Terms] OR anesthesia [MeSH Terms] OR sedation) AND (temporary anchorage devices OR dental implants [MeSH Terms] OR mini-implants OR orthodontic anchorage procedures [MeSH Terms] OR miniscrew OR micro-implants) AND (pain [MeSH Terms] OR injuries [MeSH Terms] OR injury OR pressure [MeSH Terms] OR discomfort OR efficacy OR efficacious OR complications [MeSH Terms] OR side effects [MeSH Terms] OR collateral effects))
Trials Central Clinical Trials	((orthodontics [MeSH Terms])) ((orthodontics [MeSH Terms])) AND (temporary anchorage devices OR mini-implants OR orthodontic anchorage procedures [MeSH Terms] OR miniscrew OR micro-implants)

* MeSH indicates Medical Subject Headings.

There are still controversies related to the technique and quality of anesthesia for the placement of orthodontic mini-implants. The aim of this present study was to identify, by means of a systematic review of the literature, scientific evidence that supported the efficacy of different oral anesthetics for reducing pain perception during the insertion of mini-implants in orthodontic patients.

MATERIALS AND METHODS

Focal Question

The present systematic review was conducted in order to answer the following clinical question: Is there any scientific evidence for the elimination of the perception of pain related to the insertion of orthodontic mini-implants with the use of a topical anesthetic compared with a control group receiving a different topical anesthetic or infiltrative anesthesia?

The systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.

Search Strategy

In order to identify relevant articles, without limitations on year of publication and language, a search was

conducted in the following electronic databases up to January 1, 2018: PubMed, Scopus, Web of Science, Medline Complete (EBSCO), Cochrane, Trials Central, and Clinical Trials. Specific journals in the field were also consulted. The search strategy was suited to each database.

The MeSH (Medical Subject Headings) descriptors/terms were used and are described in each electronic database in Table 1.

Eligibility Criteria of the Articles

For articles to be selected for this review, they had to fulfill the following inclusion criteria: randomized controlled trials (RCTs) or controlled clinical trials (CCTs), conducted in humans with orthodontic appliances who were healthy and presented no special needs, with minimum age of 10 years (P), who were submitted to insertion of orthodontic mini-implants with topical or infiltrative anesthesia (I), comparing the perception of pain due to insertion of these devices with that of their respective controls (C) and quantity and effects obtained from the anesthesia on the perception of pain (O).

The initial selection was made by reading the titles and abstracts of the articles found. Studies with humans making use of systemic medications, such as sulfonamides, monoamine oxidase inhibitors, tricyclic antide-

pressive agents, or phenothiazines; patients who took analgesics before the procedure; patients with allergies to local anesthetics; patients with hypertension or history of cardiac or bone metabolic disease; patients with syndromes; and studies in animals were excluded from the present review. In addition to this, in vitro studies, case reports, literature reviews, and editorials were also excluded.

The articles for which the title and abstract did not present sufficient information were downloaded and analyzed in full in order to decide about their eligibility. Those that presented a title within the theme, but with the abstract unavailable, were also obtained and fully analyzed. Articles that appeared more than once in a database searched were considered only once.

Two researchers made the selections independently and the results were compared, with the purpose of avoiding discrepancies that could occur during data collection. If disagreements as regards the inclusion or exclusion of any study were found between the 2 evaluators, a third evaluator would be consulted in a consensus meeting, in order to eliminate the discrepancies.

The lists of references of selected articles were evaluated manually to verify whether there was any study that had not previously been pointed out by the searched databases. In cases in which additional data were necessary, the corresponding authors of the studies were contacted by e-mail, in order to explain doubts with respect to the eligibility criteria.

Quality and Risk of Bias Assessment

Once the results of the bibliographic research were reduced to the relevant articles, a separate sheet was used to extract the data necessary for each eligible article. This was done independently by the 2 reviewers. The data sheet was a personalized version of the Cochrane model of data extraction for reviews¹² (Table 2). After data collection, the information of each study was organized in tables that showed the participants, interventions, controls, results, and study designs to enable analysis of the data.

The risk of bias for each article was independently evaluated by the 2 authors. Misunderstandings were discussed until a resolution was achieved.

The risk of bias was evaluated in accordance with the guidelines of the Cochrane Risk of Bias Assessment Tool¹³ and Cochrane Study Quality Guide.¹⁴ These guides recommended reporting of the following elements:

Table 2. Personalized Data Extraction Model

Methods
Study objectives
Study design
Methods of recruiting participants
Inclusion and exclusion criteria
Analysis of error of method
Adjusted statistics
Blinding of operator to measurements
Participants
Description
Number
Age
Gender
Physical-emotional problems
Intervention
Protocol of mini-implant insertion
Mini-implant used
Type and quantity of anesthesia
Methods of measurement
Treatment and duration of observation
Details of secondary interventions
Control group
Results
Pain assessment
Evaluation of insertion pressure
Evaluation of tissue and root injury
Evaluation of type, thickness and localization of tissues
Authors' conclusions

1. Random sequence generation
2. Concealment of allocation sequence
3. Blinding (evaluation of results)
4. Complete analysis of outcome data
5. Report of selective results
6. Other sources of bias

The inconsistent use of medication or changes in the technique for mini-implant placement or anesthetic used during the experimental period; different operators for placement of the mini-implant; and not considering the type, thickness, and localization of the tissues were considered as other sources of bias that could have influenced the results of treatment.

Each category was awarded one of the following score designations: high, low, or unclear risk of bias. The studies were considered to have higher risk of bias if they were marked with high or unclear risk of bias for the categories of sequence generation or concealment of allocation. This was based on growing evidence that these factors are particularly important potential sources of bias in studies.¹⁴ Scores of low, medium, and high quality were not attributed as a summary of general bias of individual studies, because this is discouraged by the *Cochrane Handbook for Systematic Reviews of Interventions*.¹³

Table 3. Analysis of Risk of Bias

<i>Study</i>	<i>Sequence Generation</i>	<i>Concealment of Allocation</i>	<i>Blinding of Results</i>	<i>Data of Incomplete Results</i>	<i>Selective Reports</i>	<i>Other Sources of Bias</i>
Lamberton et al, ¹⁰ 2016	Low	Low	Low	Low	High	High
Valieri et al, ¹ 2014	High	High	High	Low	Low	High
Kwong et al, ¹⁶ 2011	High	High	High	Low	Low	High
Lehnen et al, ⁸ 2011	Low	High	High	Low	Low	High
Reznik et al, ¹⁵ 2009	Low	Low	High	Low	High	High

RESULTS

Selection of Studies

By means of the search conducted in the databases, a total of 1052 potentially relevant studies were detected for analysis and composition of this review, of which 376 were duplicated. Therefore, the titles/abstracts of 676 were read. A total of 654 references were excluded based on the titles and/or abstracts; 22 were selected for analysis of the full text, of which 5 trials were selected for this review as they fulfilled the inclusion criteria (Figure): Reznik et al,¹⁵ Lehnen et al,⁸ Kwong et al,¹⁶ Valieri et al,¹ and Lamberton et al.¹⁰

All the studies were CCTs or RCTs, and the main evaluation of the studies (100%) was the perception of pain during the placement of mini-implants, mainly measured by the visual analog scale (VAS), with 1 study¹⁶ also using the Sound, Eye, and Motor Measurement scale and the Wong-Baker Faces Scale. Two studies^{1,8} evaluated the perception of pressure during mini-implant placement. All the articles included were written in English, although the studies had been performed in different countries. The eligible articles were evaluated for data extraction in accordance with participants, interventions, controls, results, and study designs, with a high level of consensus between the reviewers for selection of eligible articles, and assessment of biases.

Characteristics of Study

Of the 5 studies, 3 were RCTs^{8,10,15} and 2 were demarcated as CCTs.^{1,16} In the 5 included studies, there were 132 patients who submitted to the mini-implant placement procedure; all the participants were studied with a split-mouth system design. The split-mouth system anatomically splits the oral cavity into left and right halves by means of the midsagittal plane between the central incisors, with the aim of evaluating the effect of an experimental procedure on one side and comparing it with its contralateral side. An initial sample size

calculation was performed in only 2 of the studies included.^{1,10}

Risk of Bias

The results of the risk of bias assessment are presented in Table 3. Only 3 of the 5 clinical trials included^{8,10,15} had an adequate approach to sequence generation (randomization). Randomization of the participants was achieved in 1 RCT¹⁰ by generating a list by means of a computer program. The other 2 RCTs^{8,15} did not provide any description about the randomization process. The CCTs were considered to have an inherently high risk of bias for sequence generation. Furthermore, only 2 studies had an adequate approach to concealment by allocation.^{10,15}

In regard to blinding, blinding of the results (detection bias) and blinding of the participants and operators (performance bias) were considered when the anesthetics used were with the same technique. Of the 3 studies that used topical anesthesia,^{8,15,16} only 2 studies^{15,16} performed blinding of the participants and only 1 study¹⁵ had blinding of the operator who inserted the mini-implants, but not of the operator who performed application of the anesthetic (topical anesthesia) (Table 3).

When the anesthetics were delivered with different techniques (topical and infiltrative anesthesia), blinding of the participants and operators (performance bias) could not be implemented because of the intervention performed; 2 studies^{1,10} were included in this group. Blinding of the results was assessed in only 2 studies^{10,15} (Table 3).

The majority of studies had a sufficiently good approach to the data of incomplete results; only 1 study had a change in the number of participants during the experimental period.¹⁰ The report of selective results was not a problem in the evidence sets in the majority of the studies, and these were considered to have a low risk of bias in the generation of selective reports, with the exception of 2 studies.^{10,15} These 2 had a significant number of anesthetic failures, and did not provide detailed results for all the primary and secondary results

Figure. Flow diagram showing synthesis of the systematic review, in accordance with Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.

discussed in Materials and Methods. The study that had participants who dropped out performed an intention-to-treat analysis.¹⁰

Other sources of bias were present in some studies. The methodological inconsistencies included studies that

changed the type of anesthetic during the experimental period^{1,10,15,16}; had different operators for application of the anesthetic or insertion of the mini-implant¹⁰; or did not consider the type, thickness, or localization of the receptor tissues for the mini-implants^{1,8,10,15,16} (Table 4).

Table 4. Design of Studies Included*

<i>Study</i>	<i>Type of Study</i>	<i>Control Group</i>	<i>Analysis of Error of Method</i>	<i>Statistics</i>	<i>Method of Pain Assessment</i>	<i>Method for Assessing Perception of Pressure</i>
Lamberton et al, ¹⁰ 2016	RCT	Split mouth	N/A	Yes	VAS (0 mm, without pain; 100 mm, worst pain). Pain assessment at T0 (before anesthesia), T1 (after anesthesia), T2a (during mini-implant insertion), T2b (throughout procedure: anesthesia and mini-implant) and T3 (total combined pain experienced 1 month after T2b).	N/A
Valieri et al, ¹ 2014	CCT	Split mouth	N/A	Yes	VAS before and after mini-implant insertion	Questionnaire available at: http://dpjo.dentalpresspub.com/editions/v19n2/076-083/
Kwong et al, ¹⁶ 2011	CCT	Split mouth	N/A	Yes	SEM; Wong-Baker Face Scale from 1 to 5 (5 being the worst) and VAS ranging from 0 to 10 (10 being the worst); immediately after mini-implant placement.	N/A
Lehnen et al, ⁸ 2011	RCT	Split mouth	N/A	Yes	Questionnaire with 11 questions and VAS divided into 5 scales 0–IV (IV being the worst).	Questionnaire
Reznik et al, ¹⁵ 2009	RCT	Split mouth	N/A	Yes	VAS ranging from 0 to 100 (100 being the worst)	N/A

* RCT indicates randomized controlled trial; N/A, not applicable; VAS, visual analog scale; CCT, controlled clinical trial; and SEM, Sound, Eye, and Motor Measurement Scale.

Description of Interventions

All the studies examined the anesthesia procedures, but there were technical differences in various interventions (Table 5). The majority of the studies used traditional mini-implant placement procedures, and performed randomization^{1,10,15} between the type of anesthesia and side of action.

Among the studies in which topical anesthesia was performed,^{1,10,15,16} in 2 studies^{10,16} the anesthetic site was dried prior to application with a piece of gauze; the other studies^{1,15} did not mention this procedure. There were variations in the type of topical anesthetic applicator and time of application: the studies used applicators with a cotton wool tip for 1 minute¹⁵ or 2.5 minutes^{1,15}; with a cotton wool ball for 7 minutes¹; and with the CTA-Oraqix dispenser, in which the topical anesthetic comes preloaded in a carpule and a cotton applicator from the manufacturer, for 3 minutes.¹⁶

The majority of the studies used different quantities, concentrations, and anesthetic formulations, which

included compound topical anesthetic (CTA), conventional topical anesthetic (TA), and injectable infiltrative anesthetic (IA). The various anesthetic formulations included 0.18 g (calculated to be ~ 0.7 mL) of CTA with 10% prilocaine, 10% lidocaine, 4% tetracaine, and 2% phenylephrine¹⁰ (CTA-10%L); 0.20 mL of CTA with 2.5% lidocaine and 2.5% prilocaine¹⁶ (CTA-2.5%L); 0.20 mL¹⁶ of CTA with 20% lidocaine, 4% tetracaine, and 2% phenylephrine^{15,16} (CTA-20%L); or conventional 1-drug topical anesthetic with either 20% lidocaine¹ (LTA-20%) or 20% benzocaine (BTA-20%).¹⁵ Two studies^{1,15} did not specify the quantity of TA or CTA used. The studies also differed in the quantity of IA: 0.40 mL¹ and 0.45 mL¹⁰ of 2% lidocaine hydrochloride with 1:100,000 epinephrine (IA-2%L) and waiting for anesthesia for 2 minutes¹ and 0.20 mL and 1.0 mL of 3% mepivacaine hydrochloride (IA-3%M) without specifying the waiting time for anesthesia to occur⁸.

Only 2 studies divided the procedures into distinct time intervals: 5 days¹⁵ and 7 days¹⁰ between insertions

Table 5. Description of Participants and Interventions Included*

<i>Study</i>	<i>No. of Participants (Age, Range or Mean $\pm$ SD, y)</i>	<i>Mini-implant Intervention</i>	<i>Anesthesia Intervention</i>	<i>Evaluation Period</i>
Lamberton et al, ¹⁰ 2016	24 (13–54), initially 27 with 3 dropouts.	7 d between insertions of mini-implants and anesthesia, multiple operators. 2 mini-implants inserted with manual key, in same arch. Self-tapping mini-implants: 1.6 mm wide and 6 or 8 mm long.	Randomization between type of anesthesia and side of action. Experimental, CTA-10%L, 0.69 mL with applicator—cotton wool tip for 2.5 min. Control, IA-2%L: initially, 0.25 g of BTA-20% for 2 min, followed by 0.45 mL of IA-2%L.	1 mo
Valieri et al, ¹ 2014	40 (14–45)	Alternated insertion of mini-implants and anesthesia, and in immediate sequence, single operator 2 mini-implants inserted with manual key, in same arch. Self-tapping mini-implants: 1.5 mm wide and 6 mm long.	Experimental, LTA-20% with applicator—cotton wool ball for 7 min. Control, IA-2%L: approximately 0.40 mL. Waiting time of 2 min for anesthesia.	Conclusion of mini-implant insertion
Kwong et al, ¹⁶ 2011	21 (10–25)	2 mini-implants inserted, in same maxillary or mandibular arch, from vestibular side, single operator. Type and size of mini-implants not mentioned.	CTA-2.5%L, 0.20 mL for 3 min. CTA-20%L, 0.20 mL for 3 min. Blinding of anesthetics in carpule tubes inserted in their own applicators (Oraqix dispenser). In sensitivity after 3 min: complementation of 0.07 mL of anesthetic for a further 2 min, procedure repeated up to a maximum of 9 min.	Conclusion of mini-implant insertion
Lehnen et al, ⁸ 2011	30 (15.03 $\pm$ 0.83)	2 mini-implants inserted in the same maxillary arch, operator not mentioned. Divided into group A (preperforation with hand piece) and group B (direct perforation with mini-implant). Self-tapping mini-implants: 1.6 mm wide and 8 mm long.	IA-3%M, control: 1.0 mL. IA-3%M, test: 0.2 mL. Divided into group ia (first quadrant) and group ib (second quadrant).	1 d
Reznik et al, ¹⁵ 2009	17 (12–76)	5 d between insertions of mini-implants and anesthesia, single operator. 4 mini-implants inserted with manual key, in maxilla or mandible. Self-tapping mini-implants: 1.5 mm wide and 7 mm long.	Randomization between types of anesthesia. Experimental, CTA-20%L with applicator—cotton wool tip for 2.5 min. Control, BTA-20% with applicator—cotton wool ball for 1 min. In case of sensitivity after BTA-20%: complementation with IA-2%L.	1 d

* CTA-10%L indicates 10% prilocaine, 10% lidocaine, 4% tetracaine, and 2% phenylephrine; IA-2%L, 2% lidocaine hydrochloride with 1:100,000 epinephrine; BTA-20%, 20% benzocaine; LTA-20%, 20% lidocaine; CTA-2.5%L, 2.5% lidocaine and 2.5% prilocaine; CTA-20%L, 20% lidocaine, 4% tetracaine, and 2% phenylephrine; and IA-3%M, 3% mepivacaine hydrochloride.

of mini-implants and anesthesia. According to Lamberton et al,¹⁰ this time interval would allow the patient to dissociate himself or herself to some extent from the pain that occurred in the first procedure. The technique and quantity of mini-implants also varied: 2 mini-implants systems used preperforation for insertion,⁸ and 2 mini-implants^{1,8,10,16} or 4 mini-implants¹⁵ were inserted with direct perforation.

The self-tapping mini-implants were 1.6 mm wide and 6 mm¹⁰ or 8 mm long^{8,10} or 1.5 mm wide and 6 mm¹ or 7 mm long¹⁵; in 1 study¹⁶ the dimensions were not specified.

In all the studies, the mini-implants were used as a coadjuvant device to the fixed appliance in orthodontic treatment, with the purpose of obtaining skeletal anchorage.

Results of the Individual Studies

Pain Perception. Of the selected studies, 2 compared CTAs or TAs with IAs, 2 compared CTAs with TAs or other CTAs, and 1 compared IAs using different volumes. The highly concentrated CTAs and the IAs used in the studies produced significantly higher levels of anesthesia in comparison with their controls (Table 6).

Among the CTAs evaluated, 2 studies^{15,16} with CTAs had higher concentrations of lidocaine (CTA-20%L) and demonstrated significant anesthetic capacity ($p < .001$) when compared with their respective controls (CTA-2.5%L¹⁶ and BTA¹⁵). In the study of Lamberton et al,¹⁰ CTA-10%L with concentrations corresponding to those of other studies^{15,16} demonstrated a lower level of anesthetic capacity for the control of pain than that of its control (IA-2%L) ($p < .01$).

The CTAs with concentrations of lidocaine lower than 20% in the studies by Lamberton et al¹⁰ and Kwong et al¹⁶ and the TAs in the studies of Valieri et al¹ and Reznik et al¹⁵ presented more anesthetic failures with the need for supplementation with IAs. Relative to anesthetic failures among the CTAs, there were 4.7% (CTA-20%L) and 9.5% (CTA-2.5%L) in the study of Kwong et al¹⁶ and 46.1% (CTA-10%L) in Lamberton et al¹⁰ ($p = .004$). Among the TAs, there were failures of 7.5% (LTA-20%) in the study of Valieri et al¹ but with high scores on pain perception and 71% (BTA-20%) in Reznik et al¹⁵ ($p < .01$).

The minimum dose necessary for adequate anesthesia and the application time for anesthesia to occur were not progressively monitored,^{1,8,10,15} except in the study of Kwong et al,¹⁶ who showed the time necessary for anesthesia for CTA-20%L (4.43 ± 1.57 min) and CTA-2.5%L (6.33 ± 2.31 min) ($p < .001$) and the minimum

mean dose of the anesthetic procedure for CTA-20%L (0.25 ± 0.05 mL) and CTA-2.5%L (0.31 ± 0.08 mL) ($p < .001$).

The studies showed no significant differences in the classification of pain between genders ($p > .05$)^{1,10,15} (Table 7) and no correlation was observed between age and the classification of pain ($p > .05$).¹⁵ The study of Lehen et al⁸ observed differences in the expectation of pain between patients of an age younger or older than 14.85 years for IAs, and that preperforation generated less initial discomfort to the patient than direct insertion of the mini-implant ($p = .006$).

Only 1 study⁸ made the comparison between IAs of the same concentration (3% mepivacaine) but with different doses (0.2 and 1.0 mL), and there was no significant difference in the control of pain ($p > .05$) between the doses of IA administered, but the patients showed preference for the lower dose of anesthetic ($p = .005$).

In general, all the studies^{1,8,10,15,16} pointed out that the anesthesia procedures diminished the perception of pain during mini-implant insertion.

Perception of Pressure. Two studies^{1,8} evaluated the perception of pressure during mini-implant placement. The majority of patients (72.5%) reported pressure during mini-implant placement,¹ noting that it could be uncomfortable.⁸ Some patients also considered the noise of the hand piece discomforting.⁸

DISCUSSION

Summary of the Evidence

The general consensus of the set of evidence in this systematic review indicated that the anesthesia procedures with CTAs with 20% lidocaine and IA made it possible to have adequate local analgesia for the insertion of mini-implants, and the latter (IA) was most efficacious. On the other hand, the CTAs with lidocaine concentrations lower than 20% and conventional BTA-20% demonstrated a lower capacity for analgesia, which compromised the completion of the procedure. Anesthetic failure rates among the CTAs were 4.7% for CTA-20%L,¹⁶ 9.5% for CTA-2.5%L,¹⁶ and 46.1% for CTA-10%L¹⁰ ($p = .004$), and among the TAs 7.5% for LTA-20%¹ and 71% for BTA-20%¹⁵ ($p < .01$). For the CTAs, the lower rate of anesthetic failure compared with conventional TAs was linked to the combination of an ester (tetracaine), an amide (lidocaine), and a vasoconstrictor agent (phenylephrine).^{15–19} The highest level of failures was found in the conventional BTA-20%,^{15,17,18} which required a significant number of supplementary applications of IAs in the area of the

mucosa where the mini-implant would be placed to allow satisfactory anesthesia to occur.^{1,20,21} Although the percentage of anesthetic failures between CTA-20%L and LTA-20% appear similar between these studies, the pain perception reported by patients submitted to LTA-20%¹ was high, and in the 2 studies with CTA-20%L^{15,16} the pain perception was low (assessed by VAS). Therefore, it is not clear that the presence of 20% lidocaine alone in a topical anesthetic is sufficient for adequate analgesia for the mini-implant placement procedure.

A high degree of heterogeneity of study design occurred among the studies evaluated. Differences among the studies with regard to number, age, and population of patients; anesthetic techniques; quantities, types, and concentrations of anesthesia; localization and protocols for the insertion of mini-implants; and methods of assessing pain and pressure during the procedure made it impossible to analyze the pain perception score data quantitatively in the form of a meta-analysis.

The studies^{1,8,10,15,16} evaluated the perception of pain and discomfort of the patients before and after conclusion of mini-implant placements. In 2 studies,^{8,15} general discomfort after 24 hours was also observed, and in only 1 study¹⁰ were participants followed up on in detailed intervals for a period of 30 days. There is always variability related to the perception of pain expressed by the patient, because pain is not uniformly perceived in the same manner/intensity by different individuals, and differences in age and gender may also be factors of variability.¹⁶ Authors^{22,23} have reported that pain and discomfort are both considered extremely subjective and have the propensity to be influenced by different levels of perceived fear. In this sense, it is extremely important for the procedure to be carefully and completely explained to parents and patients, as this should increase the uniformity of the responses.^{8,24}

Patients' main concern about mini-implant insertion was relative to pain/discomfort.¹ Analysis of the intensity of discomfort was mostly evaluated by means of a VAS, and studies have reported the scientific reliability of this scale.^{8,25,26} Before the procedure of anesthesia, the authors observed a low level of apprehension/discomfort of the patients,^{1,8,10,15,16} which increased during anesthesia¹⁰; they attained their peak discomfort/pain levels during insertion of the mini-implants.^{1,8,10,15,16}

Perforation prior to the placement of mini-implants or use of direct self-tapping mini-implants did not make any difference in the perception of pain with regard to the pin placement procedure as a whole. Interestingly, the noise of the manual key and pressure^{1,8,27} during placement of the mini-implant were considered more unpleasant than the pain.⁸ However, other authors¹⁹ did

not report the noise of the manual key or pressure as being considered significant by the patients in similar observations. For Kwong et al,¹⁶ participants were told pressure should be felt during insertion of the mini-implant, but if any acute pain were noted, the procedure should be halted, and the need for supplementary anesthesia should be evaluated. The authors¹⁶ considered it difficult to prevent and measure the level of analgesia of the periosteum and cortical bone with any type of anesthesia.

The parameter of the perception of pressure during the insertion of mini-implants was approached by only 1 study.¹ Participants reported that the use of topical anesthesia generated more comfort with regard to the overall procedure compared with infiltrative anesthesia¹ because of the discomfort of using the needle.²⁸ However, they pointed out that topical anesthesia allowed the perception of pain caused by mini-implant placement. In this study, the IAs was more efficacious considering the absence of anesthesia failures^{1,8,10} and the higher capacity for analgesia with a lower perception of pain and discomfort by the patient during insertion of the mini-implant, as evaluated and measured by VAS.^{1,8,10} In the study of Lamberton et al,¹⁰ patients reported their preference for receiving infiltrative anesthesia if they were to receive mini-implants in the future. The patients' memory of the pain experienced during the placement of mini-implants did not change after their insertion, or 30 days after this procedure.¹⁰ The time of follow-up of patients was not approached satisfactorily; only 1 study performed an evaluation after 1 month.¹⁰

Although the studies indicated satisfactory analgesia with CTAs with 20% lidocaine for the insertion of mini-implants, in the studies evaluated, there were great variations relative to technique and quantity administered.^{15,16} Adequately developed clinical trials with standardized methodology are necessary to provide more conclusive evidence to support these affirmations.

None of the studies^{1,8,10,15,16} evaluated tissue parameters such as thickness and localization of tissues for insertion of mini-implants, and none approached the influence these factors would have on the dosage used, capacity of absorption, type and time of anesthetic application, or degree of response of patients. Of the 4 studies^{1,10,15,16} that evaluated any topical anesthetic, only 2 studies^{10,16} mentioned prior drying of the site with a piece of gauze to prevent contamination by saliva; this factor is important and capable of influencing the result of local analgesia. Lamberton et al¹⁰ observed that in some patients, the CTA was completely absorbed, but in others the major portion of the quantity applied was still in the mucosa after 2.5 minutes. Meechan²⁹ emphasized the importance of localization in determining the efficacy of topical

Table 6. Outcome of Results Included*

Study	Rate of Pain Perception	Follow-up of Pressure Perception	Authors' Conclusions
Lamberton et al, ¹⁰ 2016	VAS of CTA-10%L and IA-2%L (control) between T0 and T1 ($p > .05$). VAS higher for CTA-10%L in T2a, T0, and T1 with T2a significant ($p = .001$). VAS of T2b and T3 between CTA-10%L and IA-2%L (control) significant ($p = .002$). CTA-10%L presented 10 anesthetic failures (46.1%) and IA-2%L (control) 0 (0%) ($p = .004$). Without significant difference between genders. 62.5% reported higher pain level with LTA-20%. There was significant difference between IA-2%L and LTA-20% ($p = .001$). No significant difference between genders, LTA-20% ($p = .112$) and IA-2%L ($p = .671$). LTA-20% presented 3 anesthetic failures.	N/A	The compound topical anesthetics provided less predictable local anesthesia, frequently inadequate and less comfortable than an injection of a local anesthetic for the placement of mini-implants in oral sites. The patient's memory of the pain experienced during the mini-implant procedure for each anesthetic used did not change after 1 mo.
Valieri et al, ¹ 2014	CTA-2.5%L obtained higher values and CTA-20%L lower values. Time required for anesthesia: CTA-20%L = 4.43–1.57 min and CTA-2.5%L = 6.33–2.31 min ($p = .00$). Minimum mean dose for anesthesia: CTA-20%L = 0.25–0.05 mL and CTA-2.5%L = 0.31–0.08 mL ($p = .00$). There were significant differences in all the paired variables between CTA-2.5%L and CTA-20%L, with CTA-20%L being shown to be more effective. One patient did not tolerate topical anesthetic, and another did not tolerate CTA-2.5%L.	72.5% reported pressure during mini-implant placement.	The use of topical anesthetics resulted in more comfort for the patients submitted to mini-implant placement. Patients considered pressure during mini-implant placement as the most unpleasant feeling. Pain perception of mini-implant insertion with topical anesthetic was of a significantly higher level than that of infiltrative anesthesia. The majority of patients submitted to mini-implant placement preferred the procedure under infiltrative anesthesia. CTA-20%L was demonstrated to be more effective than CTA-2.5%L in the placement of orthodontic mini-implants. The recommendation was for 0.20–0.30 mL of CTA-20%L to be applied for a minimum of 3 min to be effective for mini-implant placement. CTA-20%L proved to be the topical anesthetic that provided the patient with most comfort during mini-implant placement.
Kwong et al, ¹⁶ 2011	CTA-2.5%L control and IA-3%M test showed no significant difference ($p > .05$). There was greater preference for the method (first quadrant) ($p = .005$). Without difference between genders ($p > .05$). Group B demonstrated a higher level of discomfort than group A ($p = .006$).	N/A	There was no difference in the way the patients perceived the mini-implant insertion technique. The noise produced by the hand piece and the pressure caused by insertion of the mini-implants tended to cause more discomfort than the surgical procedure itself. The pain intensity varied from low to moderate. Relative to the techniques, the patients expressed preference for low doses of local anesthetic in the area of mini-implant insertion compared with the standard method. The patients' discomfort corresponded to their expectations or was less unpleasant than they had initially anticipated.
Lehnen et al, ⁸ 2011	CTA-2.5%L control and IA-3%M test showed no significant difference ($p > .05$). There was greater preference for the method (first quadrant) ($p = .005$). Without difference between genders ($p > .05$). Group B demonstrated a higher level of discomfort than group A ($p = .006$).	Group A—noise of the hand piece was more uncomfortable than the pain. Group B—pressure was more uncomfortable than the pain.	There was no difference in the way the patients perceived the mini-implant insertion technique. The noise produced by the hand piece and the pressure caused by insertion of the mini-implants tended to cause more discomfort than the surgical procedure itself. The pain intensity varied from low to moderate. Relative to the techniques, the patients expressed preference for low doses of local anesthetic in the area of mini-implant insertion compared with the standard method. The patients' discomfort corresponded to their expectations or was less unpleasant than they had initially anticipated.

Table 6. (Continued)

Study	Rate of Pain Perception	Follow-up of Pressure Perception	Authors' Conclusions
Reznik et al, ¹⁵ 2009	VAS: BTA-20% (92.71 ± 46.14) and CTA-20%L (33.12 ± 32.20) ($p < .005$). CTA-20%L demonstrated a significantly higher success rate than benzocaine ($p < .001$). Without difference in the pain classification between genders, and without correlation between age and pain classification ($p > .005$). BTA-20% presented 71% anesthetic failures.	N/A	The combined topical anesthetic was considerably more effective than topical benzocaine for the control of pain.

* VAS indicates visual analog scale; CTA-10%L, 10% prilocaine, 10% lidocaine, 4% tetracaine, and 2% phenylephrine; IA-2%L, 2% lidocaine hydrochloride with 1:100,000 epinephrine; N/A, not applicable; LTA-20%, 20% lidocaine; CTA-2.5%L, 2.5% lidocaine and 2.5% prilocaine; CTA-20%L, 20% lidocaine, 4% tetracaine, and 2% phenylephrine; IA-3%M, 3% mepivacaine hydrochloride; and BTA-20%, 20% benzocaine.

Table 7. Summarized Data Results of the 5 Studies*

Outcome Synthesis	Study							
	Lamberton et al, ¹⁰ 2016		Valieri et al, ¹ 2014		Kwong et al, ¹⁶ 2011		Lehnen et al, ⁸ 2011	
	CTA-10%L	IA-2%L	LTA-20%	IA-2%L	CTA-2.5%L	CTA-20%L	IA-3%M	IA-3%M
Quantity, mL	0.69	0.45	†	0.40	0.20	0.20	1.0	†
Waiting time, min	2.5	†	7	2	3	3	†	2.5
General perception of pain (VAS)	Higher	Lower	Higher	Lower	Higher	Lower	Similar	Similar
Anesthetic failure	46.1%	0%	7.5%	0%	9.5%	4.7%	0%	0%
Is there a difference in pain perception between genders?	No	No	No	No	N/A	N/A	No	No
Is there a report of pressure perception?	N/A	N/A	Yes	Yes	N/A	N/A	Yes	No
Authors' conclusions	Worse	Better	Worse	Better	Worse	Better	Better	Worse

* CTA-10%L indicates 10% prilocaine, 10% lidocaine, 4% tetracaine, and 2% phenylephrine; IA-2%L, 2% lidocaine hydrochloride with 1:100,000 epinephrine; LTA-20%, 20% lidocaine; CTA-2.5%L, 2.5% lidocaine and 2.5% prilocaine; CTA-20%L, 20% lidocaine, 4% tetracaine, and 2% phenylephrine; IA-3%M, 3% mepivacaine hydrochloride; BTA-20%, 20% benzocaine; VAS, Visual Analog Scale; and N/A, not applicable.

† Not informed.

anesthesia related to factors such as type of tissue (for example, keratinized vs nonkeratinized mucosa), the depth at which the noxious event occurs (for example, superficial infiltration vs a deeper regional block) and the site in the maxillae. For Meechan,²⁹ topical anesthesia would have a higher success rate if it were used before the placement of mini-implants in areas of thin, nonkeratinized mucosa, or in the mucobuccal fold of the mandible or the anterior region of the maxilla.³⁰

Root injury was not evaluated in the studies, although there were no cases of root damage noted by the authors. This factor could have an influence on the patients' responses about pain perception. For Lamber-ton et al,¹⁰ one of the advantages of the use of topical anesthesia would be the possibility of having feedback from the patient about discomfort, if the mini-implant were placed close to a radicular structure.^{31,32}

Although the studies^{1,8,10,15,16} cited the macro region of mini-implant insertion, only 1 study¹⁶ reported a method of radiographic evaluation for the exact site of insertion, however with substantial methodological variations. The other studies^{1,8,10,15} did not cite the use of radiographic evaluations.

Future studies must compare different anesthetic procedures as regards their efficacy and complications, and concentrate more on standardizing the procedures with the purpose of determining an ideal protocol.

Limitations

In general, the body of evidence was of low quality because of the high perceptible risk of bias in the articles included. Methodological questions associated with the set of evidence included lack of adequate sequence generation, concealment of allocation, and evaluators' failure to blind the results. In addition, there were other sources of bias that could have confounded the results, such as changes in the quantity or type of anesthesia during the procedure, different operators for the placement of mini-implants, absence of preprocedure and postprocedure radiographic evaluation, and selection of different areas for inserting the mini-implant without considering the tissue type and thickness. Because of the low quality of evidence, the results of this systematic review must be interpreted with caution.

The authors of the present study tried to minimize the bias in the review process. This was achieved by means of the independent evaluation of the results of the search strategy for eligibility of the article, extrapolation of data, and risk of bias assessment.³³ Furthermore, the use of the *Cochrane Handbook for Systematic Reviews of Interventions*³⁴ and preferential rules related to system-

atic reviews and meta-analyses³⁵ allowed for a complete and logical structure of the review process.

Some articles had poor study design when evaluated by means of participants, interventions, controls, results, and study designs, which meant that the bias could have been introduced during their evaluations. Some included studies were not RCTs, which could have introduced a bias in the review process.^{33,36}

Implications for Practice

At present, the available literature regarding the insertion of mini-implants with the use of topical anesthetics provided a low quality of evidence for suggesting that the procedure for insertion of these self-tapping devices could be efficaciously performed with the preapplication of TAs or CTAs with a low concentration of lidocaine in place of IA. Data indicated a statistically important increase in the success rate of the CTA-20%L in comparison to the BTA-20%. When the outcomes were examined, the anesthesia administered with TAs, even with 20% lidocaine alone, and CTAs with low concentration of lidocaine appeared to not reach an adequate depth of tissue or were not applied for a long enough period of time to achieve sufficient anesthesia.

However, the occurrence of failure in the insertion of orthodontic mini-implants with the use of TAs or CTAs did not appear to increase the risk of sequelae or acceptance by the patient, either for a new procedure or for supplementary use of IAs. We suggest that the choice of anesthetic agent (CTAs with 20% lidocaine or IAs) should be based on the degree of anxiety and physiological tolerance of each patient in the preprocedure period. It is also reasonable to consider use of CTA-20%L initially, and, if satisfactory anesthesia is not achieved, to proceed with supplementary IA injection.

Implications for Research

The set of evidence provided an indication that the use of CTAs, particularly with 20% lidocaine, generated higher success rates compared with those of conventional BTA-20%, and could be an alternative for replacing the IAs. However, questions about the study design and quality and heterogeneity of the interventions prevented the authors from establishing the accuracy and safety of the results. It was not possible to determine whether the CTAs were capable of satisfactorily replacing the IAs.

The literature available at present provides low levels of evidence, and there is a need for well-conducted studies with lower risk of bias to allow more significant comparisons to be made and conclusions to be drawn. Future trials should increase the number of patients, improve randomization of the participants, and consider concealment of allocation and blinding of the evaluations of results to produce researches of higher quality.

Furthermore, studies that could consider radiographic evaluation; risk of root damage; tissue localization, type, and thickness; and follow-up of patients in detailed preprocedure, transprocedure, and postprocedure intervals would provide more relevant information for evidence-based practice.

Currently, devices for anesthetic administration without needles have been used in dentistry, and we suggest that these devices could provide a comfortable application of anesthesia, even for deep analgesia. In this sense, these devices could be a useful alternative, particularly in patients who have a phobia related to the needle.

CONCLUSIONS

There is currently a lack of high-quality RCTs that would be needed to establish a more definite conclusion regarding effective anesthetic options other than infiltration anesthesia.

There were some items of evidence that demonstrated a promising future for the use of compounded topical anesthetics (CTA) with 20% lidocaine, with the addition of an ester local anesthetic (tetracaine) and vasoconstrictor (phenylephrine), as an acceptable anesthetic agent for the insertion of mini-implants. The efficacy of the anesthetic agents demonstrated, in a descending capacity from most to least effective, was infiltration anesthesia, CTAs with 20% lidocaine, and CTAs with low concentration of lidocaine, through to those with the lowest level of effectiveness, topical anesthetic with 20% benzocaine.

The quantity of anesthetic/minimum time of waiting indicated for this procedure was approximately 0.20 mL/2 minutes for infiltration anesthesia, and 0.20 mL/3 minutes for the CTAs with 20% lidocaine.

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