

Pain and Anxiety Levels Using Conventional versus Computer-Controlled Local Anesthetic Systems in Pediatric Patients: A Meta-Analysis

Amaury Pozos-Guillén* / Edith Loredo-Cruz** / Vicente Esparza-Villalpando*** / Ricardo Martínez-Rider**** / Miguel Noyola-Frías***** / Arturo Garrocho-Rangel*****

The objective of this systematic review and meta-analysis was to compare the pain/anxiety levels associated with the anesthetic process by conventional and computer-controlled delivery systems (CCDS) in children. Four electronic databases (PubMed, EMBASE, Scopus, Google Scholar, and Dentistry & Oral Science Source/EBSCO) were comprehensively explored for eligible studies, in English or Spanish, published from January 1995 to December 2019. A systematic literature review and meta-analysis were conducted according to the PRISMA statement, including only randomized controlled clinical trials. An exhaustive search was performed in different electronic databases under a specific PICO-posed question. Relevant studies were selected based on titles and abstracts, and the full texts were retrieved. From these articles, important information was extracted. Wand demonstrated significantly lower pain than the conventional injection did. In the subgroup by pain scale analysis, the Facial Image Scale and Wong-Baker Faces Pain Scale showed a significant difference in favor of the CCDS. In general, the reviewed evidence shows that less perceived pain and anxiety occur when the local anesthetic technique is performed with a CCDS than with the traditional technique.

Keywords: Local Anesthesia, Injection Syringe, Wand, Computerized Methods, Pediatric Dentistry, Systematic Review, Meta-analysis.

From the Faculty of Dentistry, San Luis Potosí University, San Luis Potosí, SLP, México.

* Amaury Pozos-Guillén, DDS, PhD Associate Professor, Pediatric Dentistry Postgraduate Program.

** Edith Loredo-Cruz, DDS, Resident, Pediatric Dentistry Postgraduate Program.

*** Vicente Esparza-Villalpando, DDS, PhD, Associate Professor, Pediatric Dentistry Postgraduate Program.

**** Ricardo Martínez-Rider, DDS, Associate Professor, Department of Oral and Maxillofacial Surgery.

***** Miguel Noyola-Frías, DDS, Associate Professor, Department of Oral and Maxillofacial Surgery.

***** Arturo Garrocho-Rangel, DDS, PhD, Associate Professor, Pediatric Dentistry Postgraduate Program.

Send all Correspondence to:

Arturo Garrocho-Rangel, Faculty of Dentistry, San Luis Potosí University, Av. Dr. Manuel Nava # 2, Zona Universitaria, C.P. 78290; San Luis Potosí, SLP, México.

Phone: 52 (444) 8262357.

E-mail: agarrocho@hotmail.com

INTRODUCTION

The control of dental pain in pediatric patients is the most important issue when providing oral treatments and invasive interventions. An injection of local anesthesia is usually an anxiety-producing procedure that can trigger behavioral problems in patients, especially young patients, and these behavioral problems can affect the performance of the operator.¹ These negative experiences may influence the future oral care of the patient.² With the purpose of addressing the pain and discomfort caused during needle insertion and anesthetic solution deposition, diverse strategies have been traditionally employed, such as adjustments to the room temperature and the use of topical anesthetic ointments, narrow needles, slow injection techniques, vibration during the injection, and occasionally relaxing drugs, as well as an appropriate psychological preparation of the patient.³ However, control of the pressure and vibration of the syringe and needle can be technically difficult to achieve when performed manually.⁴

In 1997, alternative electronic devices for automatic anesthesia delivery were introduced in the dental market for pediatric and adult patients to allow a more comfortable and precise puncture of the needle in soft tissues.¹ These computer-controlled delivery systems (CCDS) have received considerable attention by clinicians because

the exerted pressure, vibration, volume, and rate of the anesthetic flow are automatically fixed and constantly maintained by the system's computer, regardless of the mucosa resistance and density variations;⁵ under these controlled conditions, the injection procedure is potentially less painful even in resilient tissues, such as the palate and periodontal ligament.⁶

Clinical studies have been carried out worldwide in different pediatric populations, comparing the traditional delivery technique and a CCDS regarding the efficacy of reducing pain levels during local anesthesia.⁷ Some researchers favor computerized anesthesia; however, other studies present confusing and contradictory results or do not show any significant differences between both techniques.⁸ In part, this inconsistency can be explained by different methodological limitations that may affect the results. For example, in some studies, dissimilar measurement methods, objective and subjective methods, have been used with children to assess the physiological variations related to pain/anxiety;⁸ in other studies, the duration of the injection procedure was not adequately controlled, and there were failures by the researchers in targeting injection sites according to the manufacturer's recommendations.^{4,9} In this context, the present systematic review/meta-analysis aimed to globally compare the clinical performance, in terms of pain/anxiety caused by the local anesthetic insertion, of the two previously mentioned techniques. This comparison was based on related pain/anxiety data, collected during the injection process, from original randomized controlled trials conducted in pediatric populations. The following was the null hypothesis: there are no significant differences between the conventional (CONV) injection and a CCDS regarding a reduction in pain/anxiety levels during a local anesthetic procedure in children.

METHODS

Data sources

The present systematic review and meta-analysis were carried out according to the guidelines recommended by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement,^{10,11} and Cochrane group recommendations.¹² A focused search question was structured, according to the PICO format, as follows: In pediatric patients undergoing dental anesthesia, are there differences between the conventional injection and a CCDS regarding the resulting perceived pain and/or anxiety?

Literature search

The search was performed by two previously trained and calibrated reviewers (SELC and MANF; Cohen's kappa = 0.89). The selection criteria were randomized controlled clinical trials (RCCT) that were performed in pediatric populations (under 18 years old) and compared the pain and/or anxiety produced by both dental anesthesia techniques CCDS vs. CONV. The exclusion criteria were: papers written in a language different from English, with a comparison of different anesthetic systems or techniques, or studies performed on adult samples. Four electronic databases (PubMed, EMBASE, Scopus, Google Scholar, and Dentistry & Oral Science Source/EBSCO) were comprehensively explored for eligible studies, in English or Spanish, published from January 1995 to December 2019. The main MeSH terms and pertinent keywords were "pediatric (or pediatric) dentistry", "dental anesthesia (anesthesia or analgesia)",

"computerized anesthesia (anesthesia or analgesia) systems", and "Wand", alone or in combination with other synonyms and Boolean operators. Additionally, the reference list of each selected article was screened to identify additional relevant publications. The identified titles and abstracts were carefully assessed. Each potentially relevant article was cross-checked for duplications and retrieved in a full-text version for critical evaluation. Any discrepancy was resolved by discussion and consensus between both reviewers, and if necessary, with a third reviewer (RMR).

Resources selection

Data collection

This stage was performed by two authors (VEV and APG) in an independent manner (kappa=0.93). From the selected full-text articles, crucial information was extracted using a pre-piloted standardized form; the information included the principal author, year of publication, methodological design, type of treatment, sample size, participant characteristics, anesthetic techniques compared (CCDS=computerized; CONV=conventional), characteristics of the anesthetic procedure, adjuvant methods for behavior control, anatomical site of injection, outcome variables (pain and/or anxiety), and relative time of the outcome measurements (during or after the puncture). If any important data were missing in the article, the study's corresponding author was contacted.

Methodological quality appraisal

Included studies were individually and critically evaluated by three independent reviewers (VEV, APG, and AGR) for risk of bias (content validity), employing the methods from two scales specific for RCCTs: OCEMB¹³ and the method by Pozos-Guillén et al.¹⁴ Nine quality domains were assessed: (i) the type of the RCCT (parallel groups or split-mouth/crossover design), (ii) sample size calculation, (iii) randomization characteristics (method and concealment), (iv) evaluator blinding, (v) follow-up issues and drop-out analysis, (vi) measured response variables, (vii) concordance of measuring methods, (viii) assumptions of statistical tests, and (ix) reported results. Each domain was assigned between 0 (worst score) and 2 (best score) points; after summing all the domain points, a total result was obtained (range=1 to 16 points). According to this result, the level of quality of the individual studies was rated as "poor" (1-6), "moderate" (7-11), and "good" (12-16). Again, any disagreement was resolved by discussion and consensus among the reviewers, and the quality appraisal of the 30 included articles was registered.^{1,3-6,9,15-38} See supplementary data Table S1.

Summary measures, data synthesis, and meta-analysis

The two collected primary outcome measures were the related pain and the behavior level exhibited during the anesthetic process by the study participants. These outcomes were expressed as continuous or categorical variables, depending on the results reported by each study; however, only continuous data were used in the analysis because it was not possible to group the categorical variables between the studies. All statistical analysis tests (descriptive and inferential) and the forest plot construction were carried out using R software v. 3.2.0, including the *Meta* and *Metafor* R packages. Data were summarized and considered suitable for pooling only if the studies from which the data were extracted used similar interventions, included control groups, and used similar outcome

measures. The estimator that was used was the standardized mean difference (SMD), its standard deviation, and the corresponding 95% confidence interval (95% CI) to compare the differences between the competing anesthetic techniques in terms of associated pain and the child's anxiety (behavior) level. For all hypothesis testing, the differences in the results were considered significant when the two-tailed p-value was <0.05. The I² index and Cochran's Q test (with their 95% CI) were employed to measure heterogeneity among the selected studies. An I² value of <50% corresponded to low heterogeneity, and a fixed-effects (FE) model was subsequently performed; an I² value of >50% corresponded to high heterogeneity, and a random-effects (RE) model was performed according to the DerSimonian-Laird method. Both models were used to assess whether the differences in effects between the anesthetic techniques were statistically significant. Forest plots were assessed by calculating the tau-squared value and its 95% CI. Publication bias was not evaluated.

Review

The PRISMA flowchart for the selection process is presented in Fig. 1. The initial electronic search identified 9,707 references. After screening the titles and abstracts and removing duplicates, 9,652 articles were excluded. Forty-five studies were considered potentially relevant and the full text was critically evaluated; then, 15 of these studies³⁹⁻⁵⁴ were discarded due to diverse reasons. Finally, 30 RCCT articles were included in the qualitative synthesis; all of them compared the computerized technique to traditional anesthesia; 18 of them used the parallel-group design, and the remaining studies followed the split-mouth method. All these studies were categorized as having moderate or high methodological quality. Fifteen articles were submitted to the meta-analysis (quantitative synthesis)

Fig. 1 describes the whole process of the present systematic review. The general characteristics of the CCDS studies that were included^{1,3-6,9,15-38} are reported in supplementary data Table S2, and the excluded studies³⁹⁻⁵⁴ are reported in supplementary data Table S3.

Systematic review

For the qualitative synthesis, five different comparisons were carried out between CCDS vs. CONV regarding different outcome measures: (i) pain, (ii) anxiety, (iii) child's behavior, (iv) pain according to the anatomical site/technique (infiltrative, intraligamentary (ILA), inferior alveolar nerve blocking (IANB), and palate injection), and (v) diverse physiological parameters. The different comparisons included were made considering the differences in the response between the techniques, injection, and anatomical sites. These considerations have to do with previous reports where the IANB technique is known to have high failure rates and cause greater pain and consequently also anxiety, in addition to other risks associated with the anatomical injection site. On the other hand, ILA is recognized as a technique of immediate action and limited to a specific area. IANB and ILA are included in the conventional (CONV) category and are compared against computerized in the different dimensions selected as outcome measures.

The methodologic quality of individual studies is described in supplementary data Table S2. The three most frequent reasons for diminishing the global quality score were an inadequate method for the randomization process, a lack of evidence supporting the assumptions of the statistical tests, and an inappropriate blinding process for the outcome measurements.

CCDS vs. CONV (pain). A total of 24 studies compared the pain perception level among the child participants using different

Figure 1. PRISMA flow chart for the literature search.

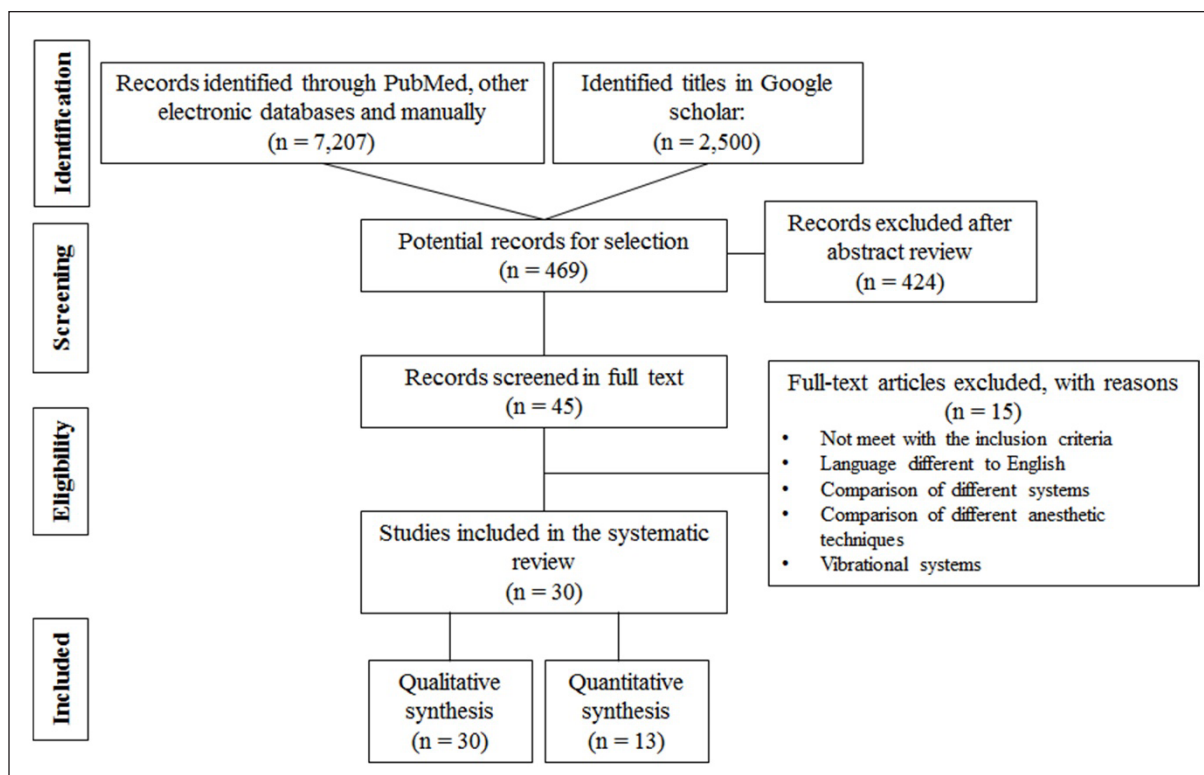


Figure 2. Forest plot of the comparison between CCDS (Wand) and conventional injection (anxiety/behavior).

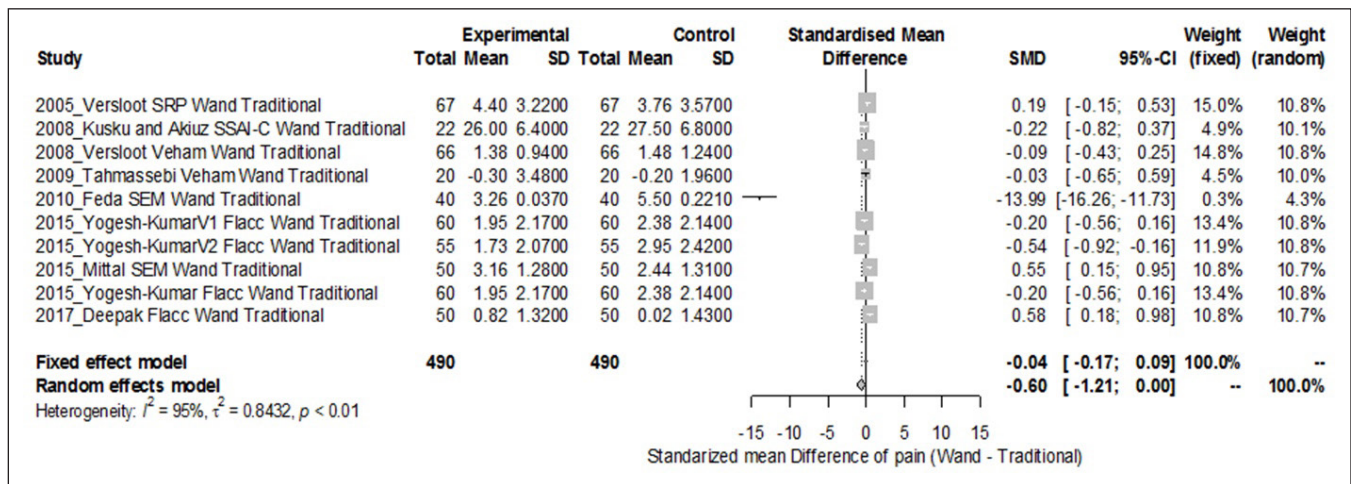
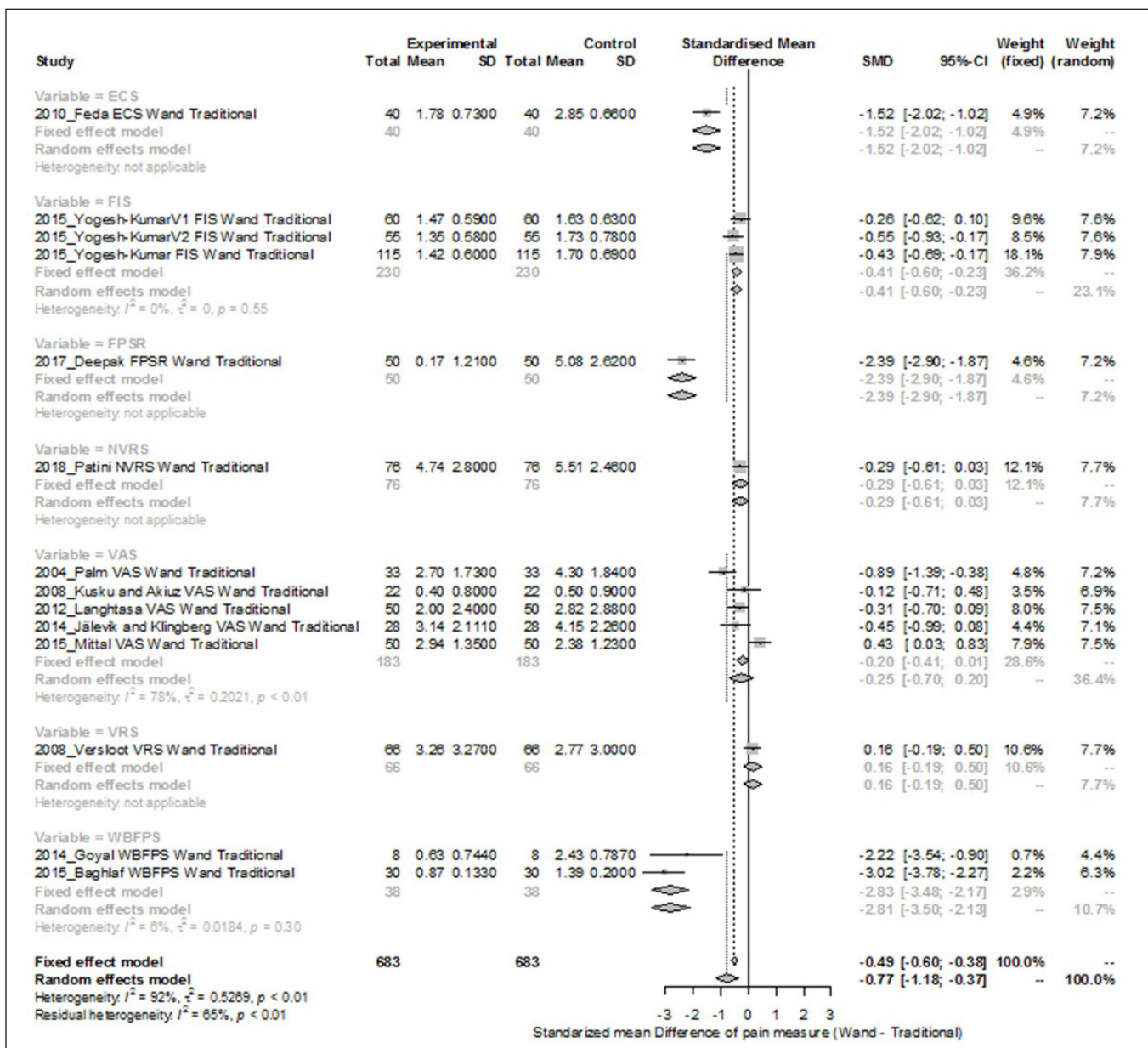


Figure 3. Forest plot of the comparison between CCDS (Wand) and conventional injection (pain perception).



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measurement tools. According to the findings from Palm *et al.*,²⁸ San Martín *et al.*,³³ Feda *et al.*,⁹ Langthasa *et al.*,²⁵ Goyal *et al.*,²¹ Jälevik and Klingberg,³ Baghlah *et al.*,¹⁸ Mittal *et al.*,^{6,27} Yogesh-Kumar *et al.*,^{37,38} Deepak *et al.*,¹⁹ and Garret-Bernardin *et al.*,²⁰ CCDS demonstrated significantly less perceived pain during local anesthesia than CONV did, while other authors, such as Asarch *et al.*,¹⁷ Gibson *et al.*,¹ Versloot *et al.*,^{35,36} Al Amoudi *et al.*,¹⁵ Kusku and Akiuz,²⁴ Tahmassebi *et al.*,³⁴ Kandiah and Tahmassebi,²² Alamoudi *et al.*,¹⁶ Maldonado-Ramírez *et al.*,²⁶ and Pattini *et al.*,²⁹ did not find a significant difference between the two methods.

CCDS vs. CONV (anxiety). Eighteen articles compared the level of anxiety between the two study groups. Asarch *et al.*,¹⁷ Ram and Peretz,³¹ Versloot *et al.*,^{35,36} Koyuturk *et al.*,²³ Goyal *et al.*,²¹ and Maldonado-Ramírez *et al.*,²⁶ determined no difference in anxiety levels; however, Gibson *et al.*,¹ Allen *et al.*,⁴ Klein *et al.*,⁵ Feda *et al.*,⁹ Baghlah *et al.*,¹⁸ Yogesh-Kumar *et al.*,^{37,38} and Deepak *et al.*,¹⁹ favored the CCDS technique compared to the CONV technique.

CCDS vs. CONV (anatomical site/technique). Several researchers investigated the anesthetic efficacy between the two revised infiltrative techniques. These studies did not find any differences in efficacy: Koyuturk *et al.*,²³ Kuscu and Akiuz,²⁴ Kandiah and Tahmassebi,²² Queiroz *et al.*,³⁰ Yogesh-Kumar *et al.*,³⁸ and Maldonado-Ramírez *et al.*,²⁶ Instead, Yogesh-Kumar *et al.*,³⁷ and Deepak *et al.*,¹⁹ showed the superiority of CCDS compared to CONV. Regarding the ILA injection, only three studies were conducted,^{20,27,29} and the findings of these studies favored the CCDS anesthetic method over the CONV method. For IANB, CCDS demonstrated higher efficacy than CONV in two studies (Palm *et al.*,²⁸ and Baghlah *et al.*,¹⁸) Ram and Peretz³¹ and Alamoudi *et al.*,¹⁶ found no significant differences. When palate injection was revised, nine studies reported superiority of CCDS over CONV: Gibson *et al.*,¹ Allen *et al.*,⁴ Klein *et al.*,⁵ San Martín-López *et al.*,³³ Ram and Kassirer,³² Feda *et al.*,⁹ Goyal *et al.*,²¹ Jälevik and Klingberg,³ and Mittal *et al.*,⁶ on the other hand, Asarch *et al.*,¹⁷ Al Amoudi *et al.*,¹⁵ Versloot *et al.*,³⁶ and Tahmassebi *et al.*,³⁴ did not detect any differences.

CCDS vs. CONV (physiological variables). A variety of physiological parameters, such as cardiac frequency and arterial tension, were evaluated in the participants during the anesthetic process. San Martín-López *et al.*,³³ Yogesh-Kumar *et al.*,^{37,38} Garret-Bernardin *et al.*,²⁰ Patini *et al.*,²⁹ and Mittal *et al.*,²⁷ determined that the cardiac frequency was higher when the CONV technique was employed, and Kusku and Akiuz,²⁴ Langthasa *et al.*,²⁵ Mittal *et al.*,⁶ and Deepak *et al.*,¹⁹ did not show any significant differences in the same parameter. Arterial tension, which was used as a physiologic measure, showed no changes with either anesthetic method.

Meta-analysis

For the quantitative analysis, only two separate direct comparisons were conducted: CCDS vs. CONV (anxiety/patient's behavior), and CCDS vs. CONV (pain). The I^2 test and Cochran's test revealed high heterogeneity among the identified studies; thus, a random-effects model was the most suitable tool for calculating a global summary measure in the three meta-analyses. Fig. 2 and 3 summarize the data and results from the different comparisons through forest plots.

CCDS vs. CONV (anxiety/behaviour). Nine studies^{6,9,19,24,34,35-38} including 490 patients compared the resulting anxiety/behavior

between the two anesthetic techniques. Again, the heterogeneity was rated as high ($I^2=94.8\%$, $Q=173.38$). Statistical analyses of the raw data were performed as described in the previous paragraph. The estimated standardized mean difference was -0.6035 (95% CI= -1.2067 to 0.002 ; z stat= -1.96 , $p=0.0499$) (Fig. 2); according to these results, there were no significant differences in anxiety/behavior between the study groups. The average methodological quality of the studies was 10.0 ± 1.32 .

CCDS vs. CONV (pain). Thirteen studies^{3,6,9,18,19,21,24,25,28,29,36-38} involving 683 participants compared the pain caused by the two injection techniques, which was measured by different child-specific scales. The summary estimator used was the standardized mean difference. Due to the resulting high heterogeneity ($I^2=91.9\%$, $Q=160.35$), raw values were analyzed using the inverse variance method with a random-effects model; for this statistical procedure, the inter-study variance was determined by tau-squared with the DerSimonian-Laird estimator. Thus, the calculated standardized mean difference among the included studies was -0.7713 (95% CI= -1.1769 to -0.3656 ; z stat= -3.73 , $p=0.002$). Thus, CCDS demonstrated significantly less pain than conventional injection. In the subgroup by pain scale analysis, the Facial Image Scale (FIS) and Wong-Baker Faces Pain Scale (WBFPS) scores show significant differences in favor of CCDS. The Visual Analogue Scale (VAS) does not show differences between groups, and the least scales were analyzed together in the global estimator because only one study used each scale (Fig. 3). The average value for the methodological quality (risk of bias) of the included studies was 9.92 ± 1.8 .

DISCUSSION

In the clinical practice of pediatric dentistry, pain has been considered a subjective sensation encompassing a variety of individual psychological and physiological issues, such as the patient's stress level, trust, personality, and perceived control over a pain stimulus.⁵⁴ When treating pediatric patients, the management of pain associated with local anesthesia is a crucial aspect that may influence a child's behavioral response in the dental chair; a painful injection may inflict fear and anxiety, thus contributing to a child's refusal of dental treatment, depending on the child's maturation level of physical, cognitive and emotional systems.³⁷ For this reason, numerous investigations have focused on seeking adequate tools for children that ensure a painless administration of anesthesia and maximize comfort, cooperation, and compliance.²⁰

The present systematic review and meta-analysis were performed exclusively on RCCT. The obtained data showed variable results in terms of pain/anxiety caused by a CCDS and the conventional injection. In this systematic review, we included 30 studies (a total of 2,202 pediatric patients recruited) that used CCDS. Articles with a sufficient amount of raw data were grouped into two different comparison groups: a) CCDS (only the Wand system) vs. the traditional technique comparing the associated pain level (13 studies including 683 treatments in pediatric patients), and b) CCDS (only the Wand system) vs. the traditional technique comparing the anxiety/behavior level (9 studies including 490 treatments in patients). The global methodological quality of these comparisons was rated as moderate (9.92 to 10.5). In this context, it is important to mention that Libonati *et al.*,⁷ previously performed a similarly focused systematic review/meta-analysis, from which some of their

reported findings agree with ours. However, there are two essential methodological differences between the two studies. Firstly, they limited the eligibility criteria to cross-over and split-mouth designs, while we expanded our search to any type of RCCT. Secondly, half of the studies selected for the qualitative and quantitative assessments by Libonati and colleagues included clinical trials carried out in adult samples (ranging from 18 to 70 years old); in contrast, we deemed eligible only studies performed with pediatric patients (under 18 years old).

In the comparison of CCDS (Wand) vs. the conventional infiltration method, the qualitative synthesis of perceived pain is contradictory, in part due to the different methods employed to measure the intensity of pain and the clinical conditions of the trials. In their review, Sivaramakrishnan and Sridharan⁵⁵ found 6 articles that evaluated pain during the infiltration of local anesthetics. Some of these studies reported a difference in favor of CCDS over the traditional method; however, the effectiveness of CCDS was not conclusive.⁴⁸ In another similar review by Kwak *et al.*,⁵⁶ it was reported that the use of CCDS to reduce perceived pain in children is also inconclusive.⁵⁶ These contradictory results are in line with the findings of the present review; according to the qualitative synthesis, the effectiveness of CCDS varied within each study, and the results did not show a clear benefit of CCDS compared to the traditional method. On the other hand, the quantitative synthesis of CCDS determined a significant reduction in perceived pain, and the degree of heterogeneity of the different evaluation methods employed in the included studies was also apparent in the meta-analysis ($I^2 > 90\%$); thus, a comparison was made by a random-effects model. Additionally, when studies used different measurement scales for the same response (in this case pain and anxiety), the global estimator SMD (and its standard deviation) was useful to compare and group the different types of data; in this context, the SMD is defined as an adimensional variable that, in our study, demonstrated a significant difference in favor of CCDS (Wand) over CONV. These results show that the perception of pain was lower in children who received the infiltration of anesthetic with the CCDS system than in those who received the anesthetic with the traditional method. These results are in concordance with the findings reported by Libonati *et al.*,⁷ in which perceived pain was significantly reduced in the CCDS group than in the CONV group. On the other hand, de Camargo-Smolarek *et al.*,⁸ recently performed another systematic review comparing the same injection techniques (computerized vs. conventional) for children regarding two issues: pain perception and disruptive behavior. For the variable “pain perception”, when the analysis took all studies together, regardless of their methodological quality (risk of bias), there was a significant difference in favor of CCDS systems; for the variable “disruptive behavior” there was no difference between the two anesthetic techniques. However, when only studies with a low risk of bias were included in their statistical comparison for the variable “reduction of pain”, they found no significant differences between the two methods.

The main study hypothesis for the present meta-analysis aimed to test the difference between CCDS and the traditional infiltration method, independently of the scale used to measure pain/anxiety and patient behavior levels. However, one common conclusion reported in most reviews about this clinical issue is the heterogeneity and subjectivity of the reported response variables.^{7,8} This weakness was

also present in this systematic review; therefore, it is an important matter to consider for the clinical interpretation of the use of CCDS in children.

The measurement of pain in the pediatric population represents a true challenge because the results from behavior scales depend on the degree of concordance of the evaluators, and self-reported results depend on the children’s age and their capacity to understand the indications for the scale. Other variables, such as certain physiological variables, have been used to attain an objective measurement of pain in children. However, in many cases, the values of these objective variables are not always related to the intensity of pain perceived by the patient.⁵⁷ This discrepancy may become a source of bias and complicate one’s ability to make a valid conclusion regarding the efficacy of CCDS because, although CCDS can be useful, the employed scale may not be sufficiently accurate to correctly measure the perceived pain. The same issue is present for the quantitative data related to behavior/anxiety levels. When a comparison was performed between the CCDS and CONV methods, the evidence did not show a significant difference in favor of CCDS. Again, the retrieved data do not allow the effectiveness of CCDS to be established, and other concomitant factors may influence the pain perceived by children during local anesthetic infiltration. Another methodological deficiency in the present review was in the comparison of the anatomical sites of the anesthetic punctures; articles that compared different techniques in different anatomical sites we excluded, because the perception of pain during the palatine infiltration techniques is different than that during the inferior alveolar nerve block (IANB), intraligamentary (ILA) or buccal infiltration techniques. In their review, Baghlaif *et al.*,⁵⁸ evaluated the efficacy of a CCDS in the ILA technique and concluded that the system was useful to significantly reduce the pain perceived by children; however, they did not analyze different techniques between the experimental and control groups. Perhaps, the reduction in pain perceived in the ILA technique compared to the IANB was only due to the natural pain caused by these techniques and not specifically associated with the use of the CCDS.

Finally, this systematic review aimed to find all relevant articles in this field and group the largest number of studies quantitatively rather than by the heterogeneity, design, variables, or scales used. Although the global estimator in the meta-analysis indicates a pain reduction with a CCDS, this finding is inconclusive because the subgroup analysis by pain scales indicates a difference in favor of CCDS for some scales and no effect for other scales. Due to the small number of studies that used each scale, the subgroup analysis is not valid; for this reason, we indicate only the global estimator in this comparison. For future clinical studies, we suggest the use of a standardized pain scale by age and both behavioral and self-reported scales; experiments with individual systems and comparisons of the same anesthetic technique between experimental and control groups are necessary to correctly establish the effects of CCDS. Also, more well-controlled clinical trials are necessary to confirm these reported findings, preferably trials that follow the parameters suggested by the CONSORT guidelines.

Globally, the evidence elicited from the present systematic review and meta-analysis determines a marginal decrease in the pain and anxiety perceived by pediatric patients when the local anesthetic technique was performed with a CCDS. However, the

use of different types of pain scales in the different included studies is a potential factor of bias to consider during the interpretation of the results in the child population. Although CCDS are currently deemed as clinically useful and practical devices for dental pediatric patients, it is necessary further high-quality research to confirm the findings reported here.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

SUPPLEMENTARY DATA

Table S1. Methodological quality appraisal of selected studies.

First author, Year	RCT design	Sample size calculation 1 = Unspecified / pilot study, 2 = Present.	Randomization 0 = Not present, 1 = Not clear, 2 = Present (homogeneous groups).	Randomization (method) 0 = Unsuitable/not described, 1 = Adequate.	Blinding 0 = Not described, 1 = Not clear/inappropriate, 2 = Present and described.	Follow-up 0 = Incomplete, 1 = Intention to treat / other methods of analysis, 2 = Full	Response variable 0 = Qualitative subjective, 1 = Qualitative objective, 2 = Quantitative	Concordance of measuring method 0 = Not present, 1 = Not clear, 2 = Present/testing laboratory	Assumptions of statistical test 0 = Not present, 1 = Not clear / categorical data, 2 = Present and described	Results 0 = Incomplete, 1 = Complete	Total
<i>Computer-controlled local anesthesia delivery systems</i>											
Asarch, 1999 ¹⁷	P	1	2	0	2	2	1	1	0	1	10
Gibson, 2000 ¹	P	1	2	0	0	2	1	1	1	1	9
Allen, 2003 ⁴	P	1	2	0	0	2	1	2	0	1	9
Ram, 2003 ³¹	P	1	2	0	0	2	1	2	0	1	9
Palm, 2004 ²⁸	SM	1	2	1	2	2	1	1	1	1	12
San Martin, 2005 ³³	SM	1	0	0	2	2	1	1	2	1	10
Klein, 2005 ⁵	P	1	2	0	0	2	1	1	0	1	8
Versloot, 2005 ³⁵	P	2	2	1	0	2	1	2	0	1	11
Ram, 2006 ³²	P	1	2	0	0	2	1	1	0	1	8
Al Almoudi, 2008 ¹⁵	P	1	0	0	0	2	1	1	0	1	6
Kusku, 2008 ²⁴	SM	1	2	0	0	2	1	1	1	1	9
Versloot, 2008 ³⁶	SM	1	2	1	0	2	1	2	1	1	11
Koyuturk, 2009 ²³	P	1	2	0	0	2	1	1	0	1	8
Tahmassebi, 2009 ³⁴	P	2	2	1	0	2	1	1	0	1	10
Feda, 2010 ⁹	SM	1	2	0	0	2	1	1	0	1	8
Langhasa, 2012 ²⁵	SM	1	2	0	0	2	1	1	0	1	8
Kandiah, 2012 ²²	P	2	2	1	2	1	1	1	2	1	13
Goyal, 2014 ²¹	SM	1	2	0	0	2	1	1	0	1	8
Jälevik, 2014 ³	SM	1	2	0	0	2	1	1	0	1	8

First author, Year	RCT design	Sample size calculation 1 = Unspecified / pilot study, 2 = Present.	Randomization 0 = Not present, 1 = Not clear, 2 = Present (homogeneous groups).	Randomization (method) 0 = Unsuitable/not described, 1 = Adequate.	Blinding 0 = Not described, 1 = Not clear/inappropriate, 2 = Present and described.	Follow-up 0 = Incomplete, 1 = Intention to treat / other methods of analysis, 2 = Full	Response variable 0 = Qualitative subjective, 1 = Qualitative objective, 2 = Quantitative	Concordance of measuring method 0 = Not present, 1 = Not clear, 2 = Present/testing laboratory	Assumptions of statistical test 0 = Not present, 1 = Not clear / categorical data, 2 = Present and described	Results 0 = Incomplete, 1 = Complete	Total
Baghlaf, 2015 ¹⁸	P	2	2	1	0	2	1	2	0	1	11
Yogesh-Kumar, 2015 ³⁷	SM	1	2	1	0	2	1	1	0	1	9
Mittal, 2015 ⁶	P	1	2	0	0	2	1	2	2	1	11
Queiroz, 2015 ³⁰	SM	1	2	0	0	2	1	1	0	1	8
Yogesh-Kumar, 2015 ³⁸	SM	1	2	1	0	2	1	1	0	1	9
Alamoudi, 2016 ¹⁶	P	2	2	0	2	2	1	2	0	1	12
Maldonado-Ramirez, 2017 ²⁶	P	1	2	0	0	2	1	1	0	1	8
Deepak, 2017 ¹⁹	P	2	2	1	0	2	1	1	2	1	12
Garret-Bernardin, 2017 ²⁰	SM	1	2	1	0	2	1	2	0	1	10
Patini, 2018 ²⁹	P	2	2	1	2	2	1	1	1	1	13
Mittal, 2019 ²⁷	P	2	2	0	0	2	1	2	0	0	9

P (Parallel design)
SM (Split-mouth design)

Table S2. Characteristics of the included studies (Computer-controlled local anesthesia delivery systems).

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Asarch, 1999 ¹⁷	Parallel	Restorative treatment	57 patients Age: 5-13 yrs	Wand (CCDS)	Topical anesthetic for 30-45 sec. Lidocaine 2%, epinephrine 1:100,000 Needle 30G IANB: 1.8 cc Buccal: 0.90 cc Palatal: 0.23 cc Slow mode	57	IANB Buccal and palatal infiltration	Pain perception: VAS, after the injection Pain behavior: Established pain behavior code: 1) Non-interfering body movements, 2) Crying, 3) Movement disruptive to treatment, and 4) Movement requiring restraint, with intervals of 15 sec during injection Treatment satisfaction: Likert rating scale, At the end of the treatment Duration of injection
Gibson, 2000 ¹	Parallel	Operative dentistry	62 patients Age: 5-13 yrs All patients had a previous dental experience, including local anesthesia	Wand (CCDS)	Topical anesthetic for 60 sec Lidocaine 2%, epinephrine 1:100,000 Needle 30G 1.0 cc Slow injection speed	31	AMSA P-ASA	Pain perception: VAS after the restoration was completed Pain behavior: Established pain behavior code: 1) Body movements; 2) Crying; 3) Movements requiring a restraint; and 4) Movements requiring a temporary halt to treatment, during the treatment, these measures were made after the anesthesia Overall treatment satisfaction: With five questions: 6 points (1) Representing strong disagreement from the patient; (6) Signifying strong agreement to the statement by the patient

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Allen, 2003 ⁴	Parallel	Restorative treatment	40 patients Age: 2-5 yrs ASA I	Wand (CCDS)	Topical anesthetic for 30 sec Lidocaine 2%, epinephrine 1:100,000 Needle 30G 1.0 cc Slow mode	20	AMSA P-ASA	Pain behavior: Established pain behavior code: 1) Body movements, 2) Crying, 3) Restraint, 4) Stoppage of treatment, at intervals of 15 sec during the injection
				Conventional syringe	Topical anesthetic for 30 sec Lidocaine 2%, epinephrine 1:100,000 Needle 30G 1.0 cc	20	Buccal and palatal infiltration	
				Wand (CCDS)	Topical anesthetic gel (5% Lidocaine)	55	IANB Buccal infiltration of the palatal zone, the needle was inserted in the gingival sulcus	
				Group 1: 3-5 yrs	Lidocaine 2%, epinephrine 1:100,000 Needle 30G Slow rate	47		Pain behavior: MBPS: 1) Facial display, 2) Arm/leg movements, 3) Torso movements, and 4) Crying, during the administration of the local anesthetic injection
			102 patients Age: 3-10 yrs ASA I with no prior dental treatment	Group 2: 6-10 yrs				
				Conventional syringe	Topical anaesthetic gel (5% Lidocaine)	55	IANB Buccal infiltration to the palatal zone was performed through the already anesthetized buccal papilla	
				Group 1: 3-5 yrs	Lidocaine 2%, epinephrine 1:100,000 Needle: 30G 1mL/min	47		
				Group 2: 6-10 yrs				
				Wand (CCDS)	Topical anesthetic for 1 min Mepivacaine 20%, adrenaline 1:100,000 Needle 27G Slow mode 1.5 mL 90 sec	33	IANB	Pain perception: VAS, immediately after the injection
								Pain behavior: Crying, moving the head, or other disruptive behaviors were noted during the injection
			33 patients Age: 7-18 yrs	Conventional syringe (Aspject)	Topical anesthetic for 1min Mepivacaine 20%, adrenaline 1:10,000. Needle 27G 1.5 mL Standard technique 60-90 sec	33	IANB	Anaesthetic onset: The children were instructed to inform at the time of the numbness of the lip from the extraction of the needle until the numbness of the lip was reported
Palm, 2004 ²⁸	Split-mouth	Operative dentistry						

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
San Martin, 2005 ³³	Split-mouth	Dental restoration	64 patients Age: 9-12 yrs	Wand (CCDS)	Topical anesthetic for 1 min Lidocaine 2%, epinephrine 1:100,000 Needle 30G Slow mode Buccal: 0.90 mL Palatal 0.45 mL	64	Buccal and palatal infiltration	Pain perception: VAS, after each injection HR: During the injection
Klein, 2005 ⁵	Parallel	Coronal and/or radicular pulp tissue removal with subsequent crown placement and/or extractions	21 patients Age: 3-5 yrs ASA I with a previous dental experience	Compu Med (CCDS)	Topical anesthetic for 30 sec Lidocaine 2%, epinephrine 1:100,000 Needle 30G 1.4 mL	12	P-ASA	Disruptive behavior: ADBC 1. Body movements (B); 2. Crying (C); 3. Movements requiring restraint (R); 4. Movements requiring temporary interruption of treatment for behavior management interventions (D), at 15-sec intervals during the procedure for 20 min
Versloot, 2005 ³⁵	Parallel	Dental treatment	125 patients Age: 4-11 years ASA I Low-anxious children and Highly-anxious children	Wand (CCDS)	Topical anesthetic for 30 sec Lidocaine 2%, epinephrine 1:100,000 Needle 30G 1.8 mL	9	Supraperiosteal buccal and palatal infiltration	Pain perception: VAS modified, after the injection Pain behavior: Pain behavior coded by body movement, Muscle tension, Crying or screaming, Verbal protest, Bodily resistance at 15-sec intervals of the injection phase Distress: Venham's (modified), at 15-sec intervals CFSS-DS: For the parents.
					Topical anesthetic was not used	67	AMSA P-ASA (maxillary) PDL (mandible)	
					Topical anesthetic for 60 sec	58	Buccal and palatal infiltration (maxillary) IANB	

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Ram, 2006 ³²	Parallel	Extractions, pulpotomy, pulpectomy, strip crowns	138 patients Age: 24-48 months ASA I	Wand (CCDS)	Lidocaine 2%, epinephrine 1: 100,000 Needle 30G, ultra-short Group A PDL injection Slow rate 0.6 mL Group B: P-ASA injection Slow rate 1 mL Lidocaine 2%, epinephrine 1: 100,000 Needle 30G, ultra-short The injection rate was slow: 1 mL/min The amount of local anesthetic solution 0.9 mL	45 40	PDL P-ASA	Pain behavior: MBPS suggested by Taddio: 1) Facial display, 2) Arm/leg movements, 3) Torso movements and 4) Crying, registered by a trained dental assistant during the injection
Al Almoudi, 2008 ¹⁵	Parallel	Pulpotomy or extractions (maxillary primary molars)	80 patients Age: 5-8 yrs Frankl 3 y 4 ASA I	Wand (CCDS) Conventional syringe	Local anesthetic Lidocaine 2%, epinephrine 1: 100,000 Needle 30G, ultra-short Slow rate (0.5mL/min) 1.0 mL Group I: The pulpotomy group 40 teeth (4 groups) Group IB: 10 maxillaries 1st molars Group ID: 10 maxillaries 2nd molars Group IIB: 10 maxillaries 1st molars Group IID: 10 maxillaries 2nd molars Topical anesthetic for 1 min Local anesthetic Lidocaine 2%, epinephrine 1: 100,000 Needle 30G, ultra-short Slow rate (0.5mL/min) 1.0 mL Group II: The Extraction group 40 tooth (4 groups) Group IA: 10 maxillaries 1st molars Group IC: 10 maxillaries 2nd molars Group IIA: 10 maxillaries 1st molars Group IIC: 10 maxillaries 2nd molars Topical anesthetic for 1 min Local anesthetic Lidocaine 2%, epinephrine 1: 100,000 Needle 30G, ultra-short Slow rate (0.5mL/min) 1.0 mL	40 40	AMSA and P-ASA Buccal and palatal infiltration	Pain reaction and behavior: SEM, the reactions are classified on a scale from 1-4 categories: 1) Comfort, 2) Mild discomfort, 3) Moderately painful, and 4) Painful for each of the S, E, and M codes, during placement of the clamp drilling the tooth, entering the pulp, pulp extirpation, and rubber dam removal Anesthetic effectiveness: Evaluated the effectiveness of the different injection techniques: SEM

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Kusku, 2008 ²⁴	Split-mouth	Two carious teeth, one on each side of the maxilla	41 patients Age: 9-13 yrs ASA I Anxious children Non-anxious children CFSS-DS	Not anxious	Topical anaesthesia spray (lidocaine, 10 mg/dose) Articaine 4%, 1:100,000 epinephrine Needle 30G	22 2 ^a session	Buccal infiltration	Pain perception: VAS, immediately after the treatment
				Wand (CCDS)	1.5 mL anesthetic solution Slow rate mode and fast injection mode	20 3 ^a session		Dental anxiety: CFSS-DS, FIS, and SSAI-C
				Anxious	Set inject traditional plastic injector Topical anesthesia spray (lidocaine, 10 mg/dose) Articaine 4%, 1: 100,000 epinephrine	19 2 ^a session		HR: Pulse oximeter
Versloot, 2008 ³⁶	Parallel	Dental treatments	147 patients Age: 4-11 yrs	Conventional syringe	Articaine 4%, 1: 100,000 epinephrine Needle 30G and 12 mm 1.5 mL anesthetic solution Injected very slowly	21 3 ^a session	Buccal infiltration	
				Wand (CCDS)	Topical anesthetic benzocaine The local anesthetic used was not reported	71	AMSA P-ASA PDL for maxillary teeth or the mandible	Pain perception: VRS (a modified version of the visual rating scale), after the injection Pain-related behavior: Body movement, Muscle tension, Crying or screaming, Verbal protest, Bodily resistance, for 15-sec intervals of the entire injection period
		Conventional syringe		Topical anesthetic benzocaine The local anesthetic used was not reported		76	Maxillary teeth, buccal or palatal IANB	Distress: Venham's (modified), 15-sec interval of the entire injection period Dental anxiety: CFSS-DS, by the parent, while the child was treated

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Koyuturk, 2009 ²³	Parallel	Operative dentistry	104 patients Age: 6-12 yrs ASA I	Wand (CCDS)	Topical anesthetic spray (10% lidocaine)	49	Infiltrative anesthesia in the mandible and maxilla	Pain Behavior: MBPS suggested by Taddio: 1) Crying; 2) Facial display; 3) Hand movement; 4) Torso movement; 5) Leg movement, during the injection
				First dentist	The local anesthetic used was not reported	55		
				Second dentist	Short needle Slow rate: (100 sec)			
				Conventional syringe	Topical anesthetic spray (10% lidocaine).	49	Infiltrative anesthesia in the mandible and maxilla	
Tahmassebi, 2009 ³⁴	Parallel	Restoration on either side of the maxilla	38 patients Age: 3- 10 yrs ASA I No previous dental experience	Wand (CCDS)	Topical benzocaine gel 20% for 2 min Lidocaine 2%, adrenaline 1:80,000	20	Buccal infiltration and direct palatal injection	Pain perception: Modified VAS scale, after the injection
				Conventional syringe	Topical benzocaine gel 20% for 2 min 2% with adrenaline 1:80,000	18	Buccal and intra-papillary infiltration followed by palatal injection	Anxiety: Venham scale, before and after the dental injection

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Feda, 2010 ⁹	Split-mouth	Dental treatments	40 patients Age: 7-10 years ASA I Frankl: 3 and 4	Wand (CCDS)	Topical anesthetic: benzocaine 20% for 1 min Lidocaine 2%, epinephrine 1:100,000 Short Needle 30G Slow mode: (0.5 mL/min Volume: 1.0 mL Topical anesthetic: benzocaine 20% for 1 min Lidocaine 2%, epinephrine 1:100,000 Short Needle 30G Buccal: 0.8 mL Palatal: 0.2 mL Speed: 1mL/min	40	AMSA	Pain perception: ECS, after each injection Pain behavior: SEM, during the injection, intervals 15 sec
Langthasa, 2012 ²⁵	Split-mouth	Various dental procedures	50 patients Age: 6-14 years ASA I Cooperative children	Comfort control syringe (CCDS)	2% Lidocaine 1:80,000 adrenaline Needle of 30G	50	Infiltration	Pain perception: VAS and FRS, after the injection HR: Pulse oximeter before, during, and after the procedure Temperature: Digital thermometer, before, during, and after the procedure Temperature: before and after the procedure
Kandiah, 2012 ²²	Parallel	Operative dentistry	30 patients Age: 8-16 years ASA I	Wand (CCDS)	Topical anesthetic: benzocaine 20% for 2 min Lidocaine 2%, adrenaline 1:80,000 1.8 mL Topical anesthetic benzocaine 20% for 2 min Lidocaine 2%, adrenaline 1:80,000 1.8 mL	15	Buccal infiltration	Pain perception: Modified VAS, after the injection Time for administration: Chronometer Anaesthetic onset: Two consecutive readings by the Electric pulp tester of 80

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Goyal, 2014 ²¹	Split-mouth	Extraction	15 patients Age: 8-10 years ASA I No previous dental treatment	Wand (CCDS)	Topical anesthetic, 2% lidocaine, for 60 sec Lidocaine 2%, epinephrine 1:80,000 Buccal infiltration: 0.9 mL Palatal or lingual infiltration: 0.4 mL Needle 27G Slow speed	15	Buccal infiltration followed by lingual or palatal infiltration	Pain perception: WBFPS, after the injection Pain behavior: FBRs, during and after the procedure Anxiety: MCDAS and HR, pre-operative phase, during and after the procedure
Jälevik, 2014 ³	Split-mouth	Extractions and exposures of impacted teeth (canines)	28 patients Age: 12-18 yrs Not fearful: 24 Fearful: 4 Had no or very limited experiences of dental injections and oral surgery.	Wand (CCDS) Conventional syringe	Topical anesthetic (5% lidocaine ointment) for 2 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G Volume of the injected analgesic solution: 2.4 cc 7 patients required additional anesthesia during the suturing Topical anesthetic (5% lidocaine ointment) for 2 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G Injection speed did not exceed 1.8 cc per 2 min Volume of the injected analgesic solution: 3.6	28	P-AMSA AMSA Buccal and palatal infiltration	Pain perception: VAS, immediately after each of the injections and after the surgical procedures were finished Dental fear and anxiety: CFSS-DS, before the procedure

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Baghlaif, 2015 ¹⁸	Parallel	Molar pulpotomy	91 patients Age: 5-9 years Frankl: 3 and 4	Wand (CCDS) STA	Topical anesthesia was benzocaine Lidocaine 2%, epinephrine 1:100,000 Needle 30G short needle Turbo mode Topical anesthesia was benzocaine Lidocaine 2%, epinephrine 1:100,000 Needle 30G short needle Mode: Low rate 1.2 mL of lidocaine (0.6 mL mesiolingually and 0.6 mL distolingually)	30	IANB	Pain perception: WBFFS, during and after completion of the injection Pain behavior: Body movements, crying, restraint, and stoppage of treatment, during the insertion of the anesthesia and recorded every 15-sec intervals
				Wand (CCDS) STA	Topical anesthesia was benzocaine Lidocaine 2%, epinephrine 1:100,000 Needle 27G Standard technique 1.8 mL	31	IANB	
				Wand (CCDS) STA	Lidocaine 2%, epinephrine 1:100,000 Needle 30G Modo STA: (1 cc per 207 sec)	Visit 1: 60	Maxillary or mandibular block	Pain perception: FIS, after the injection procedure
Yogesh-Kumar, 2015 ³⁷	Split-mouth	Operative dentistry	120 patients Age: 7-11 years ASA I No history of dental treatment	Conventional syringe	Lidocaine 2%, epinephrine 1:100,000 Needle 30G 1mL/min	Visit 2: 55 Visit 1: 60 Visit 2: 55	Maxillary or mandibular block	HR: Pulse oximeter, 10 min before and during the procedure Disruptive behavior: FLACC, during the injection

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Mittal, 2015 ⁶	Parallel	Extractions	100 patients Age: 8-13 yrs ASA I Frankl: 3 and 4	Wand (CCDS) STA	Topical anesthetic for 1 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G 0.72 mL buccal infiltration 0.36 mL palatal infiltration Slow speed mode Topical anesthetic for 1 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G 0.72 mL buccal infiltration 0.36 mL palatal infiltration Standard technique	50	Buccal and palatal infiltration	Pain perception: VAS, after the injection. SEM, during the injection HR: Pulse oximeter, before and during buccal and palatal local anesthesia
Queiroz, 2015 ³⁰	Split-mouth	Operative dentistry	20 patients Age: 7-12 yrs ASA I	Wand (CCDS)	Topical anesthetic: Benzocaine for 3min Articaine 4%, epinephrine 1:100,000 1.8 mL Slow flow Topical anesthetic: Benzocaine for 3 min Articaine 4%, epinephrine 1:100,000 1.8 mL Slow flow	20	Infiltrative maxillary anesthesia	Transitory stress levels: Measurement of salivary cortisol (Radioimmunoassay technique), before and after was done after 15 min each anesthetic technique
Yogesh-Kumar, 2015 ³⁸	Split-mouth	Not reported	120 patients Age: 7-11 yrs ASA I	Conventional syringe Wand (CCDS) STA	Topical anesthetic for 30 sec Lidocaine 2%, epinephrine 1:100,000 Needle 30G, Mode STA ¼ slow mode Topical anesthetic for 30 sec Lidocaine 2%, epinephrine 1:100,000 Needle 30G, 1 mL/min	115	Infiltrative maxillary anesthesia STA	Anxiety state: STAIC before and after anesthesia Pain perception: FIS modified, after the injection Pain behavior: FLACC, during the injection HR: Pulse oximeter, before and during the injection procedure

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Alamoudi, 2016 ¹⁶	Parallel	Primary mandibular molar pulpotomy	91 patients Age: 5-9 yrs ASA I Frankl: 3 and 4	Wand (CCDS) STA	Topical anesthetic was benzocaine Lidocaine 2%, epinephrine 1:100,000 Needle 27G Turbo mode	30	IANB	Effectiveness of the anesthesia: SEM, during the placement of the clamp, the drilling of the tooth, on entering the pulp, on pulp extirpation, and at rubber dam removal
				Wand (CCDS) STA	Topical anesthetic was benzocaine Lidocaine 2%, epinephrine 1:100,000 Needle 30G Mode: Low rate 1.2 mL of lidocaine (0.6 mL mesiolingually and 0.6 mL distolingually)	30	PDL	Postoperative pain: The parent was contacted by phone the day after the child received the anesthesia
Maldonado-Ramirez, 2017 ²⁶	Parallel	Sealant for pits and fissures, pulpotomy, steel crowns, and extractions	120 patients Age: 4- 10 yrs	Wand (CCDS)	Topical anesthetic was benzocaine Lidocaine 2%, epinephrine 1:100,000 Needle 27G Standard technique	31	IANB (80-90 sec)	Postoperative lip biting: The parent was contacted by phone the day after the child received the anesthesia
				Conventional syringe	Topical anesthetic was applied for 3 min The local anesthetic used was not reported	60	Infiltration	Pain perception: VAS and Frankl, at the time of the puncture and anesthetic infiltration
				Conventional syringe	The local anesthetic used was not reported	60	Infiltration	

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Deepak, 2017 ¹⁹	Parallel	Extractions	100 patients Age: 6-10 yrs ASA I	EJOA (CCDS)	Topical anesthetic for 1 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G Volume: 1mL	50	Maxillary buccal infiltration and mandibular	Pain perception: FPS-R, before, during, and after the injection Pain behavior: FLACC during the injection and FBRs, during the oral examination, radiography, topical anesthesia, extraction, and exit to the clinic HR: Pulse oximeter, before, during, and after the injection Anxiety: MCDAS, before, during, and after completing the procedure Pain perception: VAS, immediately after the injection Level of collaboration: Venham modified, during the injection HR: Pulse oximeter, before and after the injection Level of satisfaction of the patient: Scale from 1 to 10, at the end of the procedure
Garret-Bernardin, 2017 ²⁰	Split-mouth	Operative dentistry or extraction	67 patients Age: 7-15 yrs ASA: I Without previous dental local anesthetic experience	Conventional syringe Wand (CCDS) STA	Topical anesthetic for 1 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G Spray with lidocaine 10% Mepivacaine 20mg/mL, adrenaline 1:100,000 Needle 30G IIL STA: Speed mode 0.005 mL/sec	50 67	Maxillary buccal infiltration and mandibular Intralinguamary (IL)	
Patini, 2018 ²⁰	Split-mouth	Extraction	76 patients Age: 5-12 yrs ASA I	Conventional syringe Wand (CCDS)	Spray with lidocaine 10% Mepivacaine 20mg/mL, adrenaline 1:100,000 Needle 30G, extra short Mepivacaine 2%, epinephrine 1:100,000 Needle 30G 1.8 mL Mode STA (0.005 mL/sec) Mepivacaine 2%, epinephrine 1:100,000 Needle 30G, extra short 1.8 mL	67 76	Intralinguamary (IL) IL Palatal injection	

First author, Year	Design	Dental treatment	Patients characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique	Response variables described in the study
Mittal, 2019 ²⁷	Parallel	Extraction	82 patients Age: 6-13 yrs	Wand (CCDS) Conventional syringe	Spray with lidocaine for 1 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G 0.36 mL Spray with lidocaine for 1 min Lidocaine 2%, epinephrine 1:80,000 Needle 30G, extra short 0.36 mL	51 51	IL IL	Pain perception: SEM and FPS before, during, and after injection HR: Pulse oximeter

ADBC: Anxious and Disruptive Behavior Code
AMSA: Anterior Middle Superior Alveolar
ASA: American Society of Anesthesiologists
CCDS: Computer Controlled Local Anaesthesia Delivery Systems
CFSS-DS: Children's Fear Survey Schedule-Dental Subscale
ECS: Eland Color Scale
FBRS: Frenkel's Behavior Rating Scale
FIS: Facial Image Scale
FLACC: Face, Legs, Activity, Cry, Consolability
MCDAS: Modified Child Dental Anxiety Scale
FPS-R: Faces Pain Scale-Revised
FRS: Face Rating Scale
HR: Heart Rate
IANB: Inferior Alveolar Nerve Block
IL: Intraalveolar
MBPS: Modified Behavioral Pain Scale
NVRS: Numerical Visual Rating Scale
P-ASA: Palatal Alveolar Superior Alveolar
PDL: Periodontal Ligament
SEM: Sounds, Eyes and Motor
STA: Single Tooth Anaesthesia
STAIC: State-Trait Anxiety Inventory for Children
SSAI-C: Spielberg's State Anxiety Inventory for Children
VAS: Visual Analogue Scale
VRS: Visual Rating Scale
WBFPS: Wong-Baker Faces Pain Scale

Table S3. Characteristics of the not included trials.

First author, Year	Design (type)	Exclusion reason	Patient characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique
Ran, 2003 ⁴⁹	Parallel	Different anesthetic technique	88 patients Age: 24-48 months ASA I	Wand (CCDS)	Lidocaine 2%, epinephrine 1:100,000 Needle 30G Slow mode 0.6 mL Lidocaine 2%, epinephrine 1:100,000	43	PDL
Oztaş, 2005 ⁴⁸	Split-mouth	Different anesthetic technique	25 patients Age: 6-10 yrs ASA I	Wand (CCDS)	Each tooth was 0.9 mL Lidocaine 2%, epinephrine 1:100,000 Needle 30G Slow mode Lidocaine 2%, epinephrine 1:100,000	25	PDL
van Dinter, 2006 ⁵²	NR	Article in Dutch	125 patients Age: 4-11 yrs	Wand (CCDS) Conventional syringe	Needle 30G Slow (2 min) Low anxiety level High anxiety level Low anxiety level High anxiety level Tetracaine topical 2%, for 2 min	67 58	Buccal, palatal and mandibular infiltration
Zaho, 2011 ⁵³	NR	Article in Chinese	30 patients Age: 4-9 yrs	CCDS Conventional syringe	Articaine 4%, epinephrine 1:100,000 0.3 mL Tetracaine topical 2%, for 2 min Articaine 4%, epinephrine 1:100,000	15 15	Buccal infiltration PDL mandibular
				Conventional syringe	Articaine 4%, epinephrine 1:100,000	15	Buccal infiltration

First author, Year	Design (type)	Exclusion reason	Patient characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique
Roeber, 2011 ⁴²	Parallel	Vibrational system	90 patients Age: 4-8 yrs	Conventional syringe with Vibraject Conventional syringe without Vibraject	Topical anesthetic Topical anesthetic	44 46	Not described
Nieuwenhuizen, 2013 ⁴⁷	Parallel	Different system comparison	112 patients Age: 4-6 yrs Low and high anxiety children	SleeperOne Wand (CCDS)	Topical anesthetic Articaine 0.6 mL Topical anesthetic Articaine 0.6 mL Lidocaine 2%, epinephrine 1:200,000	52 60	Infiltration intraosseous in maxillary and mandibular
Bansal, 2014 ⁴⁵	NR	Different system comparison	90 patients Age: 6-10 yrs ASA I With no previous dental experience	Conventional syringe TENS and conventional syringe	Buccal (0.90 mL) and Palatal infiltrations (0.45 mL) 1 mL/min Lidocaine 2%, epinephrine 1:200,000 For maxillary primary molars, electrode pads were placed over the apices of the primary molars just below the zygoma Buccal (0.90 mL) and Palatal infiltrations (0.45 mL).	30 30	Buccal and palatal infiltrations
				CCS	Comfort Control TM Syringe Buccal (0.90 mL) and Palatal infiltrations (0.45 mL) 1 mL/min	30	

First author, Year	Design (type)	Exclusion reason	Patient characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique
Ching, 2014 ³⁹	Split-mouth	Vibrational system	36 patients Age: 10-17 yrs	DentalVibe and conventional syringe	Topical anesthetic Benzocaine 20% for 2 min Lidocaine 2%, epinephrine 1:100,000 Needle 30G Volume: 0.85 mL Speed: 30 a 40 sec	17	Buccal infiltration
				Conventional syringe without DentalVibe	Topical anesthetic Benzocaine 20% for 2 min Lidocaine 2%, epinephrine 1:100,000 Needle 30G Volume: 0.85 mL Speed: 30 a 40 sec	19	
Elbay, 2015 ⁴⁰	Split-mouth	Vibrational system	60 patients Age: 6-12 years ASA I	Traditional syringe+ DentalVibe group	1 mL of Articaine Hydrochloride, epinephrine 1:100,000 Topical anesthetic spray for 60 sec	60	IANB
				Traditional syringe group	1 mL of Articaine Hydrochloride, epinephrine 1:100,000 Needle 27G Topical anesthetic spray for 60 sec.	60	
Şermet Elbay, 2015 ⁵⁰	Split-mouth	Vibrational system	60 patients Age: 6-12 yrs Frankl 3 and 4	Traditional syringe+ DentalVibe	0.2-0.3 mL of Articaine Hydrochloride, epinephrine 1:100,000 Topical anesthetic spray for 60 sec	60	Palatal infiltration
				Traditional syringe	0.2-0.3 mL of Articaine Hydrochloride, epinephrine 1:100,000 Needle 27G Topical anesthetic spray for 60 sec	60	

First author, Year	Design (type)	Exclusion reason	Patient characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique
Şermet Elbay, 2016 ⁴³	Split-mouth	Vibrational system	59 patients Age: 6-12 yrs ASA I	DentalVibe with conventional syringe	Topical anesthetic spray for 60 sec 1 mL of Articaine Hydrochloride, epinephrine 1:100,000	59	Supraperiosteal infiltration
				Conventional syringe without DentalVibe	Needle 27G Topical anesthetic spray for 60 sec		
				Conventional syringe with out DentalVibe	1 mL of Articaine Hydrochloride, epinephrine 1:100,000 Needle 27G		
Choudhari, 2017 ⁴⁶	Parallel	Different system comparison	100 patients: Age: 8-12 yrs	Application of 20% benzocaine gel at the injection site for 2 min	Topical Benzocaine 20% for 2 min Lidocaine 2%, epinephrine 1:200,000	50	AINB
				Application of TENS electrodes extraorally	Lidocaine 2%, epinephrine 1:200,000		
Raslan, 2018 ⁴¹	Split-mouth	Vibrational system	40 patients Age: 6-12 years ASA I Frankl 3 and 4 Children lacked the previous dental experience	DentalVibe with a conventional syringe	Articaine 4%, epinephrine 1:100,000 Needle 27G	40	Buccal infiltration maxillary
				Conventional syringe with out DentalVibe	1 mL/min Articaine 4%, epinephrine 1:100,000		
					Needle 27G 1 mL/min		
							Palatal infiltration maxillary IANB

First author, Year	Design (type)	Exclusion reason	Patient characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique
Tung, 2018 ⁴⁴	Parallel	Vibrational system	150 patients Age: 7-14 yrs Frankl 3 and 4	Injection with no vibration	Lidocaine 2%, epinephrine 1:100,000.	50	Maxillary infiltration or IANB and long buccal injection
					20% benzocaine topical anesthetic gel		
					Needle 30G		
					27 mg of lidocaine and 0.0135 mg epinephrine		
					AINB: 36 mg of lidocaine and 0.018 mg of epinephrine Manual vibration for five sec		
					Lidocaine 2%, epinephrine 1:100,000		
					20% benzocaine topical anesthetic gel		
					Needle 30G		
					27 mg of lidocaine and 0.0135 mg epinephrine		
					AINB: 36 mg of lidocaine and 0.018 mg of epinephrine Vibrate for 10 seconds before needle placement		
Lidocaine 2%, epinephrine 1:100,000	injection with DentalVibe	50					
20% benzocaine topical anesthetic gel							
Needle 30G							
27 mg of lidocaine and 0.0135 mg epinephrine							
AINB: 36 mg of lidocaine and 0.018 mg of epinephrine							
Lidocaine 2%, epinephrine 1:100,000							
20% benzocaine topical anesthetic gel							
Needle 30G							
27 mg of lidocaine and 0.0135 mg epinephrine							
AINB: 36 mg of lidocaine and 0.018 mg of epinephrine							

First author, Year	Design (type)	Exclusion reason	Patient characteristics	Type infiltration	Injection parameters	N of treatments	Blocking technique
Small-Faugeron, 2019 ⁵¹	Parallel and Split-mouth	Different anesthetic technique	158 patients Age: 7-15 yrs ASA I Venham 0-2	CCDS "Quick sleeper"	Topical lidocaine 2% for 1-2 min Articaine 4%, adrenalin 1:200,000 Needle 30G	Parallel: 63 Split mouth: 30	Intraosseous anesthesia
				Conventional syringe	Topical lidocaine 2% for 1-2 min Articaine 4%, adrenalin 1:200,000 Needle 30G	Parallel: 65 Split mouth: 30	

ASA: American Society of Anesthesiologists

IANB: Inferior Alveolar Nerve Block

PDL: Periodontal Ligament

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