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**Title: Anaesthetic efficacy of Articaine versus Lidocaine in children's dentistry: a systematic review and meta-analysis.**

## **Abstract**

**Background:** Over the last few years, numerous reviews and studies have awarded articaine hydrochloride local anaesthetic (LA) a superior reputation, with outcomes of different studies demonstrating a general tendency for articaine hydrochloride to outperform lidocaine hydrochloride for dental treatment. Nevertheless, there seems to be no clear agreement on which LA solution is more efficacious in dental treatment for children. There is no previous publication systematically reviewing and summarising the current best evidence with respect to the success rates of LA solutions in children.

**Objectives:** To evaluate the available evidence on the efficacy of two local anaesthetic solutions, lidocaine and articaine, used for dental treatment in children.

**Methods:** A systematic search was conducted on Cochrane CENTRAL Register of Controlled Trials, MEDLINE (OVID; 1950 to June 2017), Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCOhost; 1982 to June 2017), EMBASE (OVID; 1980 to June 2017), SCI-EXPANDED (ISI Web of Knowledge; 1900 to June 2017), key journals, and previous review bibliographies through June 2017. Original research studies that compared articaine with lidocaine for dental treatment in children were included. Methodological quality assessment and assessment of risk of bias was carried out for each of the included studies.

**Results:** Electronic searching identified 525 publications. Following the primary and secondary assessment process, 6 randomized controlled trials (RCT) were included in the final analysis.

There was no difference between patient self-reported pain between articaine and lidocaine during treatment procedures, and no difference in the occurrence of adverse events between articaine and lidocaine injections following treatment in paediatric patients. However substantial heterogeneity was noted in the reporting of outcomes among studies, with the quality of majority of studies being at high risk of bias.

**Conclusion:** Both articaine as infiltration and lidocaine inferior alveolar nerve blocks presented the same efficacy when used for routine dental treatments in paediatric patients. Articaine is similar in terms of safety when compared with lidocaine.

**Key-words:** Systematic review; articaine; lidocaine; local anaesthesia; children

## **Introduction**

Local anaesthetic (LA) solutions have been utilised in clinical dentistry to alleviate or eliminate pain associated with invasive procedures as early as the 19th Century (Malamed 2013). Since then, a broad spectrum of LA has been progressively developing (McDonald 2011). Upon its clinical availability in 1948, lidocaine hydrochloride became the first marketed amide LA, and has maintained its status as the most widely used LA in dentistry since its introduction (Vreeland et al. 1989; McDonald 2011). Proven efficacy, low allergies, and minimal toxicity through clinical use and research have confirmed the value and safety of this LA drug. Thus, it is the “gold standard” to which all new LA is compared (Malamed 2013). Over the last few years, numerous reviews and studies have awarded articaine hydrochloride a superior reputation, primarily based on the notion that it possesses enhanced anaesthetic efficacy (5-29). The results of different studies demonstrated a common trend for articaine hydrochloride to out-perform the lidocaine hydrochloride in dental applications (Dudkiewicz et al. 1987; Donaldson et al. 1987; Wright et al. 1989; Vahatalo et al. 1993; Malamed et al. 2000a; Malamed et al. 2000b; Malamed et al. 2001; Tofoli et al. 2003; Oliveira et al. 2004; Costa et al. 2005; Mikesell et al. 2005; Moore et al. 2006; Ram and Amir 2006; Robertson et al. 2007; Sierra-Rebolledo et al. 2007; Adewumi et al. 2008; Abdulwahab et al. 2009; Matthews et al. 2009; Pabst et al. 2009; Paxton et al. 2009; Tortamano et al. 2009; Katyal 2010; Nuzum et al. 2010; McEntire et al. 2011; Brandt et al. 2011; Martin et al. 2011; Yapp et al. 2011; Yilmaz et al. 2011; Arrow 2012; Odabas et al. 2012; 5-29). However, there seems to be no clear agreement on which LA solution is more efficacious in dental treatment for children.

A search of the literature revealed no previous publication systematically reviewing and summarizing the current best evidence with respect to the success rates of LA solutions in children. The present systematic review was carried out to address this gap in the literature. The aims of the review was to assess the efficacy of of 2% lidocaine hydrochloride and 4% articaine hydrochloride (both with epinephrine as vasoconstrictor), and to compare the outcomes, benefits, and harms of their use in the provision of pulpal and soft tissue analgesia in clinical paediatric dentistry.

## **Methods**

This review was planned, conducted, and reported in adherence to PRISMA standards of quality for reporting systematic reviews and meta-analyses. The PICO methodology was utilized to formulate the research question (Table 1). The research question was: “Does using articaine LA provide superior pulpal and soft tissue anaesthetic efficacy in child patients receiving operative or extraction treatments when compared with lidocaine LA?”

## **Inclusion and Exclusion Criteria**

An article was selected for inclusion in the review if it met the following criteria:

- Clinical trials involving human subjects who fall within the paediatric population (age < 16 years), who were medically healthy and requiring routine dental treatment.
- Studies which provided original data generated by means of a comparative randomized controlled clinical trial design.

- Studies evaluating the anaesthetic effect of local anaesthetic solutions of articaine compared with lidocaine, using volumes of at least 1.0 ml per administration and in combination with a vasoconstrictor, as initial application.
- Studies evaluating interactions comparing local anaesthetic solutions of articaine with lidocaine, using volumes of at least 1.0 ml per administration, and in combination with a vasoconstrictor, for maxillary or mandibular infiltration or inferior dental nerve block.
- Studies that had a clearly defined the method for evaluating anaesthetic success, as well as detailed description of the techniques for administering the anaesthetic solution. The definition of anaesthetic success was that the patient would have described their pain levels as “none” or “mild” as measured using a standard Visual Analogue Scale (VAS), Wong-Baker Facial Pain Scale (W-B FPS) or any equivalent pain scale validated to be used in children during clinical procedures. Letters to the editor, case reports, case-control or cohort studies, review articles and in vitro studies were excluded. Studies on computerised delivery routes and trials evaluating the less commonly used supplemental anaesthetic techniques after the routine infiltration or block anaesthesia were also excluded.

### ***Search Strategy***

A structured electronic search, and reference list screening was undertaken. The following electronic databases were searched: the Cochrane CENTRAL Register of Controlled Trials, MEDLINE (OVID, 1950 to June 2013), Cumulative Index to Nursing and Allied Health Literature

(CINAHL; EBSCOhost, 1982 to June 2013), EMBASE (OVID, 1980 to June 2013), SCI-EXPANDED (ISI Web of Knowledge, 1900 to June 2013). Computerized databases were originally searched in April 2013 for the Cochrane review and the last update was carried out in June 2017. The electronic searches were complemented with a search of clinical trial registers of the reference lists of included studies and relevant systematic reviews, as well as Clinical.gov.com. Furthermore, forward citation tracking of included studies was also used to search for additional studies using the ISI Web of Knowledge. In addition to publications located by this electronic search strategy, attempts to enhance the available references were made. Hand searches were made by reviewing the reference lists of relevant articles, clinical trials, and the tables of content of the journals containing most of the included studies for the last two years. Efforts were also made to locate unpublished, yet inclusion-worthy research. However no unpublished studies were located.

The Subject index terms and MeSH terms used for the search were as follows:

- Local anaesthesia, amid local anaesthetic.
- Dental, dentistry, dental anaesthesia.
- Articaine, carticaine, septocaine, septanest, ultracaine, thiophine, artikent, bartinest, isonest.
- Primary dentition/teeth/tooth, deciduous dentition/teeth/tooth, baby tooth, baby teeth.
- Child, children, adolescent, young people, young person/s, young patient/s, preschool child/ren.

- Lignocaine, lidocaine, lignospan, lignospan special, xylocaine.
- Randomized control trial, control trial, control clinical trial

A detailed systematic review protocol was developed and is available online on the international Prospective Register of Systematic Reviews (PROSPERO), which was approved and registered in the NHS Centre for Reviews and Dissemination (CRD) at the University of York (ref: CRD42013004620).

### **Data extraction and Qualitative Assessment**

A standardized data extraction proforma was utilized to capture relevant data from included studies. This was carried out by two reviewers (FA and HJT). Risk of bias assessment was applied to both study methodology and outcome measures of all included studies. The quality assessment was analyzed based on guidance suggested in Chapter 9 of the Cochrane Handbook of Systematic Reviews of Interventions 5.0.2. for assessing risk of bias of randomized controlled trials (RCTs). Two reviewers (HJT and MSD) independently evaluated the included studies. Additional input from a biostatistician (YFS) was also taken into consideration in the analysis. The risk bias evaluation was conducted based on the following domains: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) other bias or potential threats to validity. Each domain was judged as 'high risk', 'unknown risk' or 'low risk'. A single trial was considered as low risk of bias if all

the seven domains were judged as 'low risk', as 'moderate risk of bias' if any domain was judged as 'unknown risk', or as 'high risk of bias' if any domain was judged as 'high risk of bias'. The information was collected using a standardized data collection proforma. In cases of disagreements, the overall risk of bias was resolved by consensus following discussions between the two reviewers.

### **Outcome measures and synthesis of results**

The outcomes were recorded for definition of LA success, and the goal of anaesthesia was identified, being either an evaluation of pulpal anaesthetic effect or soft tissue anaesthetic effect . The extracted data was compared according to the timing of when the pain scale was administered, namely during procedure and after procedure. If a study reported pain score after injection, the result was categorized as pain score during procedure. If a study reported pain score on separate occasions, only pain scores reported during procedure and after procedure were extracted. Any validated pain scale used was acceptable for inclusion of a trial into this review.

In studies where the standard deviation (SD) was not reported directly, it was estimated from the standard error (SE). Both SD and SE were estimated according to the methods recommended in Cochrane Handbook of Systematic Reviews for Interventions (Higgins & Green, 2011) if the outcome measure was dichotomized and frequency was reported in the article. For cross-over trials, all measurements from intervention periods and controlled periods were analysed as if the

trial were in a parallel group trial, which is a more conservative approach (Higgins & Green 2011).

As a variety of self-reported pain scale was reported in the selected studies, all self-reported outcomes were summarized by calculating the Hedge's *g* standardized difference in means and corresponding 95% confidence interval. Hedge's *g* standardized difference in means transformed the study results to a common scale that facilitates pooling and it incorporates a small sample bias correction factor (Bradburn et al, 1998).

Random-effects model was used in the meta-analysis. Statistical heterogeneity was assessed across the studies using both I<sup>2</sup> statistics and Chi-square test; I<sup>2</sup> statistics with values of 50% or greater was considered as showing substantial heterogeneity while threshold p-value < 0.1 for chi-square (Higgins & Green, 2011). All included studies were used in the primary analysis regardless of their risk of bias. In a sensitivity analysis, studies with high overall risk of bias were excluded to explore if the quality of included studies had any effect on the combined results.

## **Results**

### ***Search Results***

A total of 525 articles were identified in the initial search, and a repeated search in June 2017 identified a further 5 studies. Based on the present study inclusion/exclusion criteria, 22 articles were retrieved for full text appraisal, following which 16 studies were excluded. **Table 2** shows the reasons for exclusion of these studies. A total of 6 articles met the selection criteria and were

included into the systematic review. The studies Malamad et al in 2000 and 2001, which were published in both the *Journal of the American Dental Association* and *Pediatric Dentistry* was found to be related to the same study population and therefore analysed as a single study. The search and screening process are detailed in the PRISMA flowchart (**Figure 1**).

***Study characteristics (Table 3).***

***Design of included studies:*** Two of the 6 included studies were multi-centre studies (Malamad et al 2000, Ram and Amir 2006), with the rest being conducted as single centres studies. A cross-over design was utilized for 3 out of 6 studies (Ram and Amir 2006, Arrow 2012, Arali and Mytri 2015). Only 2 studies compared LA given as infiltration anaesthesia against each other, whereas 4 studies compared Inferior Dental Nerve (IDN) block and infiltration anaesthesia in the same study.

***Age range:*** The age range of subjects was wide across studies (range: 5 to 16 years), with all subjects being 16 years of age and younger. The reported mean ages were variable, of which 3 studies did not report the mean ages of subjects. (Malamad et al, 2000b, Arali and Mytri 2015, Mittal et al 2015).

***Drug volumes:*** The dosage and amounts of the two LA agents used were not uniform across studies. Only 2 studies compared equivalent concentrations of articaine and lidocaine (Arali and

Mytri 2015; Kolli et al 2017), while the others had variable amounts administered to the child in which the maximum dose was calculated per body weight.

**Treatment complexity:** Simple treatment was defined as single extraction, routine operative treatment; and complex dental treatment being multiple extractions, multiple crowns and surgical procedures. Based on this definition, only 2 studies reported rendering complex treatment (Malamad et al 2000; Ram and Amir 2006).

### *Analysis of outcome measures*

#### *Onset of anaesthesia*

All included papers compared treatment outcomes at a patient level. Only 3 studies reported evaluating onset time of anaesthesia, in which one study categorized the onset time (Ram and Amir 2006), while 2 other studies reported the mean onset time (Arrow 2012; Arali and Mytri 2015). Methods for evaluation of onset time were mostly subjective evaluations by patients, with 2 studies evaluating the onset by asking the child when the sensation of soft tissue numbness started (Ram and Amir 2006; Arrow 2012), while one paper (Arali and Mytri 2015) did not detail the method used for evaluation of anaesthesia onset. The delay in time for checking of anaesthesia onset varied between studies (from 2 minutes to 5 minutes after LA delivery).

### ***Adverse effects***

Four out of 6 studies evaluated the occurrence of adverse events (Malamad et al 2000; Ram and Amir 2006; Arrow 2012; Kolli et al 2017). Among these, only one study (Kolli et al 2017) reported not having any adverse events. Reports of postoperative complications included lip-biting, cheek-biting, pain at injection site, tooth tenderness, and episodes of aching jaw. These reported adverse effects were elicited largely through post-operative phone calls, and were patient-reported with the help of the parents, or elicited directly from the parents. For the 3 studies that summarized minor adverse events, the following were evaluated and pooled: post-procedural pain, headache, accidental lip/soft tissue injury, need for supplemental injections etc. No significance differences were found in terms of risk of adverse events between lidocaine and articaine (RR=1.59; 95%= 0.68 to 3.73; p-value=0.281). No evidence of heterogeneity was observed (I2=0.0%; p-value = 0.440).

### ***Anaesthetic success and meta-analysis of pain ratings***

Among the studies included in the review, evaluation of anaesthetic efficacy was largely carried out in the treatment phase of the study. Only 2 studies (Ram and Amir 2006; Arali and Mytri 2015) reported on patient's pain during the injection phase.

### Patient self-reported pain during procedure

Based on the data from 3 studies (Arali and Myrti 2015; Arrow 2012; Ram and Amir 2006), the Hedge's g standardized mean difference 0.06 (95%CI= -0.17 to 0.29; p-value=0.614) from the random-effects meta-analysis demonstrated no difference in self-reported pain during procedure between lidocaine and articaine. No evidence of heterogeneity was observed (I<sup>2</sup>=0.0%; p-value = 0.809).

### Patient self-reported pain after procedure

Based on the data from 4 studies (Kolli et al 2017; Malamed et al 2000; Mittal et al 2015; Ram and Amir 2006), the Hedge's g standardized mean difference 0.37 (95% CI= 0.08 to 0.67; p-value=0.013) indicated that articaine was better than lidocaine in reducing pain intensity after procedure. No evidence of heterogeneity was observed (I<sup>2</sup>=44.1%; p-value = 0.147).

### ***Risk Bias and Quality Assessment***

Both visual inspection of funnel plot (**Figure 3**) and Egger's test suggested no publication bias was detected for self-reported pain after procedure and adverse events. However, Egger's test demonstrated likelihood of publication bias in self-reported pain during procedure (p-value=0.015). Among the included studies, only 1 study had low risk of bias, whereas 3 studies had high risk of bias, and 2 studies had moderate/uncertain risk of bias. Therefore, the overall risk of bias across studies was deemed to be high. **Table 4** shows the risk bias summaries of evaluated categories in each included study.

## **Discussion**

Pain control is paramount in reducing fear and anxiety associated with dental procedures. As such, efficacious LA agents couple with good behaviour management skills and operator proficiency remains the backbone of anxiety control and henceforth treatment success in young paediatric patients.

### ***Comparisons of different volumes of LA***

In this review, it was found that a range of LA volumes were administered across studies. However, these volumes were compared similarly as they were considered to be clinically reasonable amounts which would produce adequate anaesthesia for the treatment procedures evaluated. Only 2 studies directly compared equivalent concentrations of articaine hydrochloride and lidocaine hydrochloride (Arali and Myrti 2015; Kolli et al 2017). Furthermore, the need for supplemental injections was evaluated in 2 studies (Ram and Amir 2006; Arali and Myrti 2015). The necessity for top up of LA solutions intra-operatively, which was not always in the same patient, was found to be required for both articaine and lidocaine treatment groups. This therefore suggests equal inability of both anaesthetic agents to achieve profound anaesthesia with the amounts given, and therefore reflecting possible inadequate LA delivered for the clinical requirement of the condition/procedure. In view of this, the volume difference between the LA delivered and the extent of its impact on individual clinical outcomes cannot reliably be determined.

### *Anaesthetic routes of administration (IDN block versus infiltration) for delivery of LA*

Apart from comparisons of different concentrations of LAs, this review also included studies which utilized different methods for delivering LA, namely infiltration and IDN block. Additionally, the methodology for tooth selection for anaesthetic evaluation varied greatly among studies, as were the number of teeth evaluated per experimental administration. Both infiltration and block anaesthesia are the two most common methods for delivering local anaesthetic solutions in clinical dentistry (Malamed 2013), and both routes of administration were considered within the scope of this review, in which the efficacy of local anaesthetic solutions were evaluated in scenarios where it was given as a combination of both techniques, i.e. local infiltration as well as IDN block anaesthesia.

Nerve blocks have been shown to be more painful than infiltration technique due to the higher volume, longer duration of injection and penetrance of needle into multiple deeper structures (Sharaf 1997) . On the other hand, infiltration anaesthesia is perceived to be less technique sensitive, and possibly also less painful during administration. It is however interesting to note that 2 studies in this review conversely showed more crying during infiltration than block anaesthesia (Ram and Amir 2006; Arrow 2012). The study by Arrow (2012) reported a 100% clinician judgement of LA success with IDN block and 68% with infiltration, which was attributed to the level of clinical experience of the performing dentists and frequent use of the IDN block technique compared to infiltration in the treatment of mandibular posterior teeth in children. Although it can be argued that some operators will be more skilled than others at delivering IDN block to either side of the jaw, it should be noted that the extent of the effect of intra-operator variability or performance bias remains uncertain and cannot be evaluated within

the scope of this review. Moreover, it should be highlighted that majority of studies did not evaluate patients' pain perception during LA delivery, and only evaluated pain experienced during the procedure, and this would be interesting to evaluate in the design of future studies.

Noteworthy is that all studies in this review utilized infiltration for administration of articaine, with the route of administration for articaine being largely pre-determined by the fact that articaine is not recommended for use as block anaesthesia in children in some countries. Studies have shown that while infiltration anaesthesia may be successful in up to 100% of cases in the maxilla regardless of whether articaine or lignocaine is administered (Vahatalo et al 1993), this was not the same for posterior mandible, where the success rates were variable for articaine used. (ref: Kwon et al 2014). However, these studies were carried out in adults, and the results may not be applicable to children as it is believed that there is enhanced vestibule-palatal diffusion of articaine in children as the maxillary bone has yet to become sclerotic with age.

The ability of articaine to anaesthetise palatal tissues in a single buccal infiltration injection was evaluated in 2 studies (Mittal et al 2015; Kolli et al 2017). Despite delivering similar quantities of LA in both studies, the studies had contradictory outcomes with one study (Kolli et al 2017) reporting successful maxillary primary molar extractions procedures using articaine LA bypassing palatal injections, while none of the groups were found to be able to achieve adequate palatal anaesthesia with buccal infiltration in the other (Mittal et al 2015). Therefore, more future studies on the ability of articaine to achieve profound anaesthesia with buccal infiltration alone is required in order to reach a more definite conclusion on this.

### *Adverse events*

In terms of safety and patient reported outcomes following the procedure, the meta-analysis conducted found no difference between the groups. Adverse events were reported in 4 out of 6 included studies. It should be highlighted that adverse events were not clinically verified but instead commonly self-reported by patients with the help of their parents, or by parents by means of a post-operative phone call, thus predisposing it to some degree of bias. That being said, these reported adverse events were generally minor, with no reports of paraesthesia. Although there were reports of mild allergic type reactions (e.g. rash or pruritis) among studies evaluated, more severe reactions such as oedema, urticaria, erythema and anaphylactic shocks were not reported in any of the included studies. Additionally, it would be likely that those allergic to articaine would also respond similarly to other amide based local anaesthetic agents including lignocaine (Malamad et al 2000). However, it should be noted that the children enrolled in the studies were healthy patients who are at less risk of having complications associated with local anaesthesia. Therefore it is not possible to ascertain the risk of either local anaesthetic agent on child patients with other co-morbidities.

Additionally, articaine was found to be more superior in terms of reducing pain intensity post-procedure, which remained unchanged even following sensitivity analysis in which studies with high overall risk of bias were excluded. Articaine was also found to have longer lasting effect on soft tissue numbness in some studies. Alongside this comes the concern of prolonged numbness following articaine use (Adewumi et al 2008), which can lead to other undesirable outcomes such as lip and cheek biting in children. This, while reported in some children, was neither found to be of a high number nor was it raised as a substantial concern among the included studies.

## *Study Limitations and Recommendations*

### *Objectivity in assessing anaesthesia onset and efficacy in paediatric patients*

The main approaches for all reviewed studies in determining anaesthetic efficacy was through patient reported pain experienced during the procedure, with the patient rating pain using a pain scale instrument during dental treatments. As a variety of self-reported pain scale was reported in the selected studies, all self-reported outcomes were summarized by calculating the Hedge's  $g$  standardized difference in means and corresponding 95% confidence interval. Hedge's  $g$  standardized difference in means transformed the study results to a common scale that facilitates pooling and it incorporates a small sample bias correction factor (Bradburn et al, 1998).

Having said that, the overall reporting for local anaesthetic onset was found to be inadequately addressed in the studies included in the review. The authors were not able to analyse onset time of articaine compared with lidocaine, as only 2 studies reported onset time while 1 of the them categorized the onset time instead of reporting the mean and SD. Additionally, it was noted that onset of anaesthesia was often reported as the child's subjective report of soft tissue symptoms, and symptomatic testing of soft tissue analgesia was undertaken at a certain time point after completion of anaesthetic administration. Some studies also reported success of local analgesia being determined by clinicians using clinic-based methods, e.g. patient response and report to tactile testing for soft tissue analgesia, as well as patient report of pain following commencement of treatment. These subjective methods may not be completely reliable as presence of soft tissue anaesthesia may not be accurately reflective of having achieved profound pulpal anaesthesia, and more objective measurements methods are recommended to be undertaken instead (Palm et al 2004 ). Suggested methods in the literature for confirmation of anaesthesia include the use of

Electric Pulp Tester (EPT) at 60 sec periodicities or thermal tests using cold stimuli (Hsiao-Wu et al 2007), which has been reported for use in several local anaesthesia studies but has been criticized for not being able to guarantee pulpal anaesthesia in clinical scenarios such as irreversible pulpitis (Cooley et al, 1984). Future studies should therefore look into more objective methods for assessment of anaesthesia onset in their study designs.

### ***Overall validity of results***

The main aim of this systematic review was to provide a comprehensive and current overview of the available evidence on the efficacy of local anaesthetic solutions (lidocaine /articaine) used for local anaesthesia in children's clinical dentistry. The internal validity of an RCT is strongly related to reporting of adequate methodology for random allocation, blinding, allocation concealment and patient follow-up. It has been shown that trials with poor or inadequately reported methodology tend to exaggerate treatment effects (Schultz et al. 1995). Extensive efforts were made to identify all relevant and comparable clinical studies in order to completely investigate, compare and draw conclusions on these two anaesthetic agents. Despite this, inconsistencies in methodology and outcome measures with potentially high sources of bias were observed among majority of the 6 included studies.

Although it was noted that 3 out of 6 studies had attempted to reduce inter-operator variability by having a single operator administer the local anaesthesia for all patients enrolled in the study (Arali and Myrti 2015, Mittal et al 2015, Kolli et al 2017), the possibility of potential effects of clinical heterogeneity within and between studies cannot be fully excluded, nor avoided in a review of this nature. Finally, the authors found substantial heterogeneity in the reporting of outcomes among studies, which has made comparison and synthesis of outcomes difficult. This

review calls for more rigorous methodologies to be employed in the design and execution of future clinical trials and better standardization of reporting outcomes and in order to achieve better-quality comparability between studies.

### **Conclusions:**

1. Considering the present findings, the quality of RCTs which were included in this review was generally inadequate with high risk of bias.
2. Both articaine as infiltration and lidocaine IAD nerve blocks presented the same efficacy when used for routine dental treatments.
3. There was no difference between patient self-reported pain between articaine and lidocaine during treatment procedures. However, patients reported less pain post-procedure following articaine injections, but the difference was not statistically significant.
4. There was no difference in the occurrence of adverse events between articaine and lidocaine injections following treatment in paediatric patients.

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