

# Local anaesthesia using Articaine and Lidocaine in oral and dental surgery: A comparative meta-analysis

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## ABSTRACT

**Background:** Articaine is an amide local anaesthetic, which is gaining popularity for use in dental and oral surgical anaesthesia in the United Kingdom. Hitherto there has been insufficient evidence to recommend articaine above the more commonly used lidocaine for dental procedures. The aim of this study is to compare the efficacy of 4% articaine with 1:100,000 adrenaline (4AA) with that of 2% lidocaine with 1:100,000 adrenaline (2LA) administered as buccal infiltrations for anaesthesia in mandibular permanent first molar teeth. Any significant advantage noted may obviate the need for regional blockage of the inferior dental nerve in dental or minor oral surgical procedure under local anaesthesia. **Objectives:** To review the published literature comparing the efficacies of 4AA and 2LA for achieving pulpal anaesthesia in human mandibular permanent first molar teeth. **Null Hypothesis:** 4AA and 2LA are of equal efficacy when used to anaesthetize mandibular permanent first molar teeth by buccal infiltration. **Method:** An electronic search encompassing Ovid MEDLINE®, PubMed (National Center for Biotechnology Information, US National Library of Medicine), SCOPUS®, SCIRUS®, EMBASE® databases and the Cochrane Library was performed to identify trials relating to the efficacy of 4AA and 2LA local anaesthetic solutions on mandibular first molars in adult participants. Study characteristics and outcome data were extracted as a basis for meta-analysis. **Results:** Three randomised controlled trials were identified for this meta-analysis. The relative efficacy of 4AA over 2LA in anesthetizing permanent first mandibular molars was calculated at 1.57 (95% CI = 1.27 to 1.95). **Conclusion:**

Despite the promising results shown in the meta-analysis it is difficult to say from the evidence presented that 4AA should be used clinically in preference over 2LA.

## KEYWORDS

Lidocaine; Articaine; Meta-Analysis

## 1. INTRODUCTION

Anaesthesia is a key component in the practice of dentistry. A range of local anaesthetic agents is widely available for use. Lidocaine is usually the anaesthetic of choice for most oral surgical procedures in the UK [1]; however, articaine has become increasingly available [2].

First introduced in 1976, 4% articaine solutions have shown high levels of anaesthetic potency and low systemic toxicity in clinical situations, due to its pharmacological profile and physicochemical characteristics [3]. Regional nerves blocks and local infiltration are the most commonly used anaesthetic administration techniques for mandibular teeth; however, buccal infiltration anaesthesia of the mandibular first molar would be beneficial to both clinicians and patients in terms of the ease and comfort [4].

The preference of a local infiltration over that of regional block has previously been described. For the clinician, the ease and speed of administration would be beneficial to the anxious patient. It has also been suggested that there might be fewer risks in patients taking anticoagulant therapies. If a local infiltration of Articaine could provide more effective analgesia than Lidocaine then it might be a preferable analgesic for use in most routine dental procedures.

The authors undertook this study to explore the possibility of using of Articaine (4AA) as a buccal infiltration alone to anaesthetise mandibular first molar teeth, allowing dental, and some minor oral surgery procedures where surgical access is via the buccal cortex.

## 2. OBJECTIVES

To determine how effective buccal infiltration of 4AA is in producing mandibular permanent first molar pulpal anaesthesia when compared to 2LA.

## 3. MATERIALS AND METHODS

### 3.1. Literature Searching

The electronic databases of Ovid MEDLINE®, EM-BASE®, PubMed®, Scopus®, Scirus® and Cochrane Central Register of Controlled Trials were interrogated to identify relevant citations of published trials. In order to identify relevant unpublished or on-going trials further searches of the metaRegister of controlled trials register was also investigated. **Table A1** gives the details of the databases searched along with the search strategies used. Attempts were made to contact the leading manufacturer of articaine within the UK (Septodont®) with regard to any information concerning on-going trials.

### 3.2. Selection of Studies

Randomised controlled trials (RCTs) fulfilling certain specified criteria were selected (**Table 1**). Cohort studies, case series and case reports are excluded from the review owing to the high potential for bias in these study designs. Case-control studies (except where nested as part of a cohort study) and economic evaluations are also excluded. Trials investigating the efficacy of buccal infiltrations of 4AA and 2LA administered to mandibular first molar teeth were included. A detailed list of the exclusion criteria is located in **Table A2**. The search process detailing the number of studies excluded at each point of the data collection is shown in **Figure 1** and is detailed in **Table A1**.

**Table 1.** Criteria for selection of studies included in meta-analysis.

Criteria	Definition
<b>Study characteristic</b>	Randomised controlled trials, and controlled trials investigating the efficacy of buccal infiltrations of 4% articaine 1:100,000 adrenaline and 2% lidocaine 1:100,000 adrenaline.
<b>Participant characteristics</b>	Studies of participants aged of 18 or older.
<b>Intervention characteristics</b>	Studies with only infiltrations to mandibular permanent first molar teeth delivered by manual buccal infiltration.
<b>Outcome characteristics</b>	Any clinical outcome, including anaesthetic efficacy by measuring sensory threshold to Electronic Pulp Testing (EPT) measuring no response to maximal stimulation (80 $\mu$ A). Studies providing raw numbers of the effect measures or prevalence. <ul style="list-style-type: none"> <li>• Providing information of the sample size and age group, outcome variables and mean values.</li> </ul>

### 3.3. Data Abstracts and Study Characteristics

The titles and abstracts obtained from the search were independently screened as suggested in the PRISMA protocol [5]. All obtained citations were checked to ensure that they fulfilled the inclusion criteria (**Table 1**). Those satisfying the criteria were then retrieved for analysis.

The data retrieved was extracted to Microsoft Excel® and included the authors, year of publication, study design, sample size, age range, intervention details with regards to the type of anaesthetic used and the measures of effectiveness were recorded (**Table 2**). The data detailing the time of onset and duration of onset of the anaesthetic were recorded; the data recorded for anaesthetic success was extracted. The data was analysed using StatsDirect®.

The assessment criteria according to COHORT [6] and individual study rating can be located in **Table A3**. All of the studies stated that appropriate approval and consent of participants was taken.

## 4. RESULTS

Studies published between 1946 and the present were included within the meta-analysis. The author and a review team screened 177 citations. Data from three randomised controlled trials were included within the statistical analysis (**Tables 2** and **3**).

The relative efficacy of articaine when compared to lidocaine was calculated for each of studies included (**Table 3**) and used to obtain the synthesis value (**Table 4**). This is best illustrated by the forest plot (**Figure 2**). Therefore, the relative efficacy of 4AA over 2LA in anesthetizing permanent first mandibular molars was calculated at 1.57 (95% CI = 1.27 to 1.95).

Cochrane's Q and I<sup>2</sup> values were calculated from the raw data. Although though no significant heterogeneity was seen in the forest plot a random effects model was employed for the analysis due to the small number of relatively small studies included (as shown in **Figure 2**).

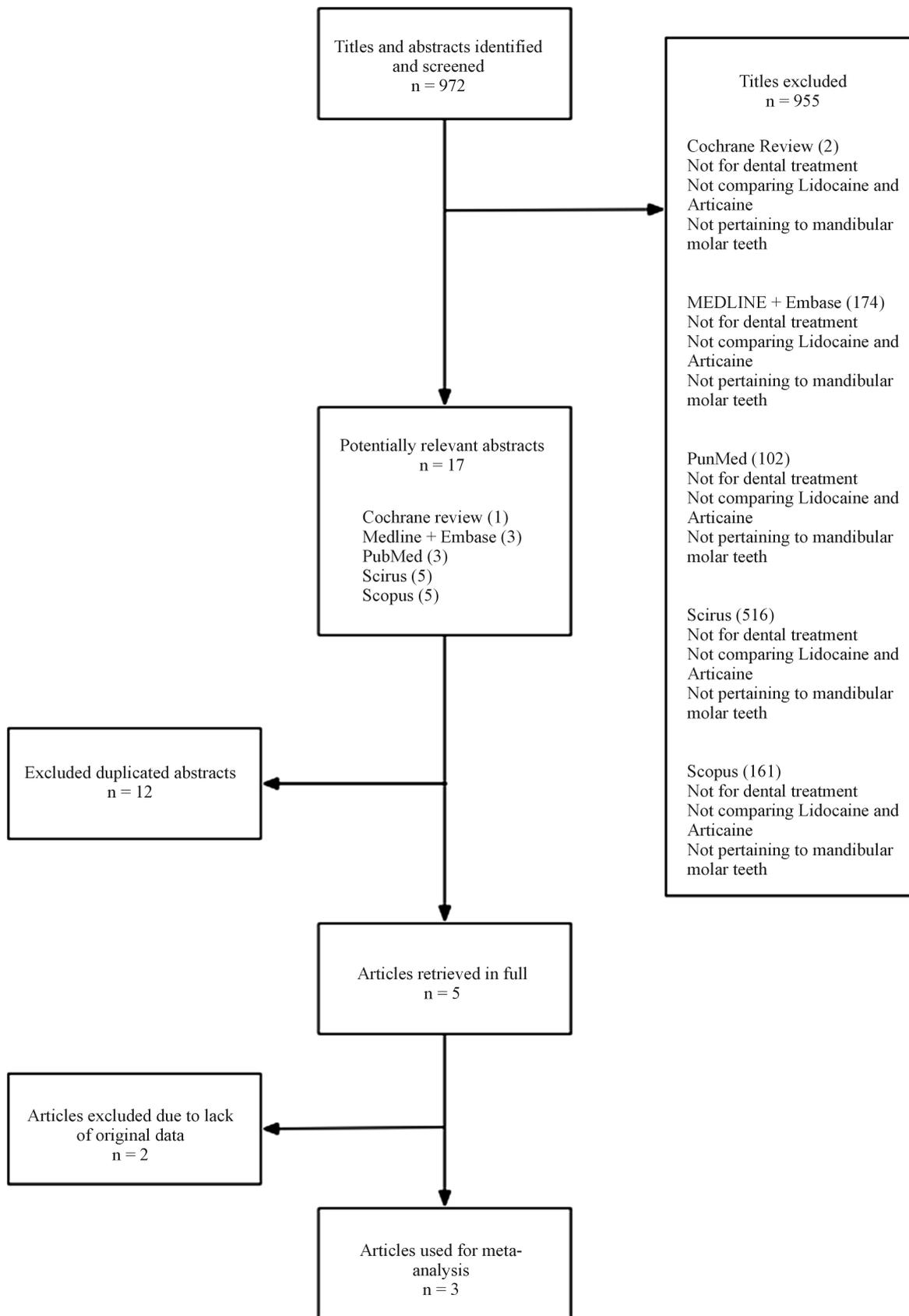


Figure 1. Search process flow diagram.

**Table 2.** Summary of trial characteristics.

Author	Abdulwahab <i>et al.</i> [7]	Robertson <i>et al.</i> [8]	Kanaa <i>et al.</i> [9]
Year	2009	2007	2006
Age group	18 - 53	19 - 51	20 - 30
Mean age	24.9	27	22.8
Prospective (Y/N)	Y	Y	Y
Randomised (Y/N)	Y	Y	Y
Blinded (Y/N)	Y	Y	Y
Cross-over (Y/N)	Y	Y	Y
Sample size	18	60	31
Anaesthetic dose	0.9 ml	1.76 ml	1.8 ml
Outcome variable	No response EPT (80 $\mu$ A)	No response EPT (80 $\mu$ A)	No response EPT (80 $\mu$ A)
Agent used	Lidocaine 2% 1:100,000 adrenaline	Lidocaine 2% 1:100,000 adrenaline	Lidocaine 2% 1:100,000 adrenaline
Mean value	3 (16.7%)	34 (57%)	12 (38.7%)
Agent used 2	Articaine 4% 1:100,000 adrenaline	Articaine 4% 1:100,000 adrenaline	Articaine 4% 1:100,000 adrenaline
Mean value	7 (38.9%)	52 (87%)	20 (64.5%)
p value	0.001	0.0001	0.008
Induction	Injected over 30 seconds	Injected over 25 seconds	0.9 ml/15seconds
EPT testing	Testing every minute for 20 mins	Testing every 3 mins for 60 mins	Testing every 2 mins for 30 mins

**Table 3.** Extracted data for meta-analysis.

Author	Year	Lidocaine success (event)	Sample size (lidocaine group)	Articaine success (event)	Sample size (articaine group)
Abdulwahab <i>et al.</i> [7]	2009	3	18	7	18
Robertson <i>et al.</i> [8]	2007	34	60	52	60
Kanaa <i>et al.</i> [9]	2006	12	31	20	31

## 5. DISCUSSION

### 5.1. Key Findings

This meta-analysis suggests that the anaesthetic efficacy of 4AA when used as a mandibular buccal infiltration is greater than that of 2LA.

### 5.2. Biological and Clinical Interpretation

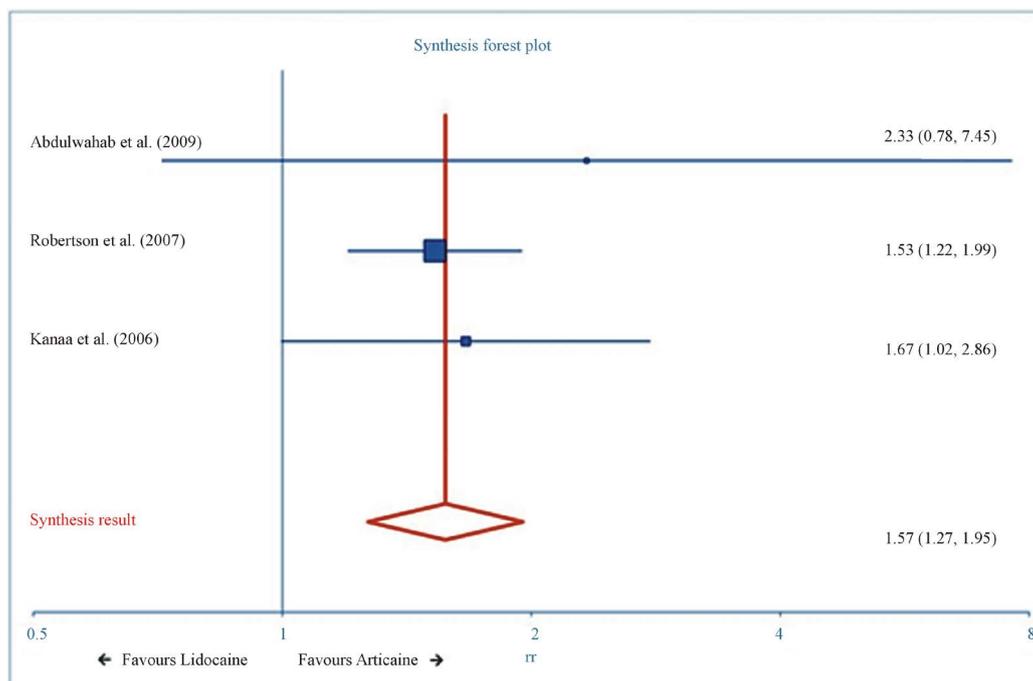
Though the mechanism for the increased efficacy of articaine is not fully understood, Skjevik *et al.* [10] have suggested that Articaine exhibits an exceptional effectiveness in bone tissue penetration along with an additional unique lipophilicity switch in its ability to form an intra-molecular hydrogen bond.

Many studies have investigated articaine buccal infiltration anaesthesia and its application with regards to maxillary and incisor teeth [11,12]. While some have re-

ported no significant difference between the use of articaine or lidocaine [13] many maintain that 4AA is more effective than 2LA in achieving pulpal anaesthesia. Additionally, the onset of pulpal anaesthesia with articaine has been shown to be significantly faster than Lidocaine via buccal infiltration ( $P = 0.03$ ), with a significantly longer duration of soft tissue anaesthesia (3.8 h vs. 2.5 h;  $P < 0.0001$ ) [14,15].

### 5.3. Limitations

The included studies are based upon the use of 2% lidocaine with 1:100,000, adrenaline (epinephrine) whereas the most commonly used formulation for dental and oral surgical procedures in the UK employs adrenaline at the slightly higher concentration of 1:80,000. The concentration difference in vasoconstrictor may well account for a difference in clinical soft-tissue anaesthesia time mean-



**Figure 2.** Relative risk meta-analysis forest plot (random effects).

**Table 4.** Comparison of relative efficacy between studies.

Authors	Relative risk	95% CI (Koopman)	
		Min	Max
<b>Abdulwahab <i>et al.</i>, 2009 [7]</b>	2.33	0.78	7.44
<b>Robertson <i>et al.</i>, 2007 [8]</b>	1.53	1.212	1.99
<b>Kanaa <i>et al.</i>, 2006 [9]</b>	1.67	1.02	2.86
<b>Synthesis result*</b>	1.57	1.27	1.95

\*Random effects model. Non-combinability of studies: Cochran  $Q = 0.57$  ( $df = 2$ )  $P = 0.7512$ ,  $I^2$  (inconsistency) = 0% (95% CI = 0% to 72.9%).

ing that the use of 4AA may make little difference in this aspect.

The trials included in the meta-analysis all considered pulpal anaesthesia to have been achieved following the absence of response to the maximal stimulation (80  $\mu$ A) with the electronic pulp tester on two or more episodes of testing. These results may not be directly transferable to oral surgical procedures such as the extraction of teeth which require anaesthesia of the structures surrounding the tooth.

As only a limited number of trails were available for inclusion within this meta-analysis it is premature to suggest that buccal infiltrations of 4AA in the mandibular region should be the anaesthetic agent and technique of choice.

#### 5.4. Comparison to Previous Work

A meta-analysis conducted by Katyal, [16] investigating

the efficacy and safety of articaine versus lidocaine in dental treatments supports the argument that articaine is more effective than lidocaine in providing anaesthetic success in the first molar region. Although higher pain scores for delivery were recorded, articaine has still been suggested as superior for use as an anaesthetic agent in dental treatment.

## 6. CONCLUSION

In this study 4AA has been shown to have greater efficacy in achieving pulpal anaesthesia in mandibular permanent first molar teeth than 2LA when administered via buccal infiltration on analysis of three studies. The increase in efficacy may be as high as 1.57. The small numbers of available studies in this analysis indicate that more work is required before the results can be directly translated into clinical practice.

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**APPENDIX**

**Table A1.** A table outlining search strategies and number of hits per database.

Electronic databases and search strategy	No. hits per database
Cochrane Central Register of Controlled Trials Search Strategy: articaine and dental and trial.	3
Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>, Ovid OLDMEDLINE(R) <1946 to 1965>, Embase Classic + Embase <1947 to 2013 March 29> Search Strategy: (articaine and dental and trial).mp. [mp = ti, ab, ot, nm, hw, kf, ps, rs, ui, an, sh, tn, dm, mf, dv, kw] (189) remove duplicates (177)	177
Database: PubMed Search Strategy: (articaine and dental and trial) Query Translation: ("carticaine" [MeSH Terms] OR "carticaine" [All Fields] OR "articaine"[All Fields]) AND ("dental clinics" [MeSH Terms] OR "dental" [All Fields] AND "clinics" [All Fields]) OR "dental clinics" [All Fields] OR "dental" [All Fields] AND ("clinical trials as topic" [MeSH Terms] OR "clinical" [All Fields] AND "trials" [All Fields] AND "topic" [All Fields]) OR "clinical trials as topic" [All Fields] OR "trial" [All Fields])	105
Scirus Search Strategy: (articaine and dental and trial).	521
Scopus Search Strategy: (articaine and dental and trial).	166
<b>Total</b>	<b>972</b>

Databases last accessed 15<sup>th</sup> June 2013.

**Table A2.** Data search exclusion criteria.

Design	Narratives with no original data Book chapters not reporting the original data source Studies not providing the raw data of the effect measures Studies not relating to anaesthesia of lower first molar teeth Studies not including the use of 2% lidocaine 1:100,000 adrenaline and 4% articaine 1:100,000 adrenaline Studies exclusively relating to children <16 years of age
Data	Studies not reporting sample size

**Table A3.** Criteria for quality and the quality assessment of the included trials.

	Criteria for assessing the quality of the included trials
<b>1) Random Sequence Generation</b>	Adequate—Details on random generation satisfying CONSORT criteria. Unclear—No details as to the process of randomization. Inadequate—Assignment.
<b>2) Randomisation: Allocation Concealment Mechanism</b>	Adequate—Details on the Allocation Concealment Mechanism satisfying CONSORT criteria. Unclear—No details as to the process of concealment mechanism. Inadequate—no concealment mechanism used.
<b>3) Blinding of Operator</b>	Adequate—Specified operator adequately blinded. Unclear—Blinding not specified. Inadequate—the operator was aware of which groups the participants had been randomized.
<b>4) Handling of Losses</b>	Adequate—information provided with regards to those participants who violated the protocol of the study, dropped out or were withdrawn. Unclear—No details within text. Inadequate—numbers of participants lost with no information. Not applicable.
<b>5) Analysis for Losses</b>	Adequate—Information suggesting intention to treat analysis to include participant within trial regardless of what had occurred. Unclear—No details within text. Inadequate—the approach as suggested by CONSORT was not utilised. Not applicable.

**Table showing the quality assessment of included trials**

Author	Quality Rating					Explanation
	1	2	3	4	5	
<b>Abdulwahab <i>et al.</i></b>	A	A	A	N	A	Randomly assigned participants to one of six treatment allocations— $6 \times 6$ Latin Square Design Manufacture labels removed from dental cartridges, cartridges placed in coded envelopes.
<b>Robertson <i>et al.</i></b>	A	A	A	A	N	The anaesthetics were randomly assigned a six-digit number from a random number table each subject was assigned to one of the formulations to determine the anaesthetic being delivered; only the numbers were recorded on the data collection sheet. Masked cartridges and blinded participants.
<b>Kanaa <i>et al.</i></b>	A	A	A	A	N	The Randomization was determined using a computer-generated sequence of random numbers, by an author not involved in the anaesthetic delivery. The investigator enrolling the participants was blinded and both the participant and the operator were blinded to the drug being delivered. All 31 participants received all of the interventions.