RESEARCH PAPER

Articaine Versus Lignocaine for Local Anesthesia in Dental Procedures: A Systematic Review and Meta-Analysis of Efficacy and Safety

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ABSTRACT

Background: Articaine (4% with 1:100,000 or 1:200,000 epinephrine) and lignocaine/lidocaine (2% with 1:100,000 or 1:80,000 epinephrine) are the two most widely used local anesthetics in contemporary dental practice. Despite articaine's growing popularity, controversy persists regarding its comparative superiority in specific clinical contexts.

Objectives: To conduct a comprehensive systematic review and meta-analysis comparing the anesthetic efficacy, onset time, duration of action, and safety profile of articaine versus lignocaine across various dental procedures.

Methods: A systematic search of MEDLINE/PubMed, Cochrane CENTRAL, EMBASE, and Scopus was performed from January 1990 to December 2024 following PRISMA 2020 guidelines. Randomized controlled trials (RCTs) comparing articaine and lignocaine for dental local anesthesia were included. Pooled risk ratios (RR), mean differences (MD), and 95% confidence intervals (CI) were calculated using random-effects models.

Results: Sixty-four RCTs involving 7,842 patients met inclusion criteria. Articaine demonstrated significantly higher overall anesthetic success rates (RR = 1.18; 95% CI: 1.12–1.25; $p < 0.001$). This advantage was most pronounced for mandibular buccal infiltrations (RR = 1.42; 95% CI: 1.28–1.58) and irreversible pulpitis (RR = 1.31; 95% CI: 1.17–1.46). No significant differences were found for IANB in healthy teeth (RR = 1.08; $p = 0.20$) or maxillary infiltrations (RR = 1.07; $p = 0.18$). Articaine was associated with modestly higher paresthesia risk (RR = 1.72; 95% CI: 1.08–2.74; $p = 0.02$).

Conclusions: Articaine offers a meaningful clinical advantage for mandibular buccal infiltrations and in patients with irreversible pulpitis. For IANB and maxillary procedures, efficacy is broadly equivalent. Clinicians should be cognizant of the modestly elevated paresthesia risk associated with articaine, particularly with IANB technique.

Keywords: articaine; lignocaine; lidocaine; local anesthesia; dentistry; inferior alveolar nerve block; pulpitis; meta-analysis

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1. INTRODUCTION

Local anesthesia is the cornerstone of pain management in dentistry, enabling clinicians to perform invasive procedures with patient comfort and cooperation [1,2]. Since the introduction of procaine by Einhorn in 1905, local anesthetic pharmacology has evolved substantially, culminating in the modern amide agents that dominate present-day practice [3]. Among these, lignocaine (lidocaine; 2-diethylamino-2',6'-acetoxylidide) has occupied a preeminent position since its development by Löfgren in 1943, becoming the global gold standard against which all subsequent agents are measured [4,5].

Articaine (4-methyl-3-[2-(propylamino)-propionamido]-2-thiophene carboxylic acid methyl ester hydrochloride) was synthesized by Roth in 1969 and introduced clinically in Germany in 1976 [6,7]. Its unique structural feature—a thiophene ring replacing the benzene ring—endows it with distinct lipophilicity and a supplementary ester linkage permitting partial hydrolysis in plasma, contributing to more rapid systemic clearance [8]. Approved in Canada in 1983 and the USA in 2000, articaine is now one of the most widely used dental local anesthetics globally [9,10].

The clinical appeal of articaine stems from several proposed advantages: higher potency from greater lipid solubility, enhanced diffusion through cortical bone, and a superior safety profile owing to accelerated plasma esterase-mediated metabolism [11,12]. These properties have fuelled expectations that articaine may outperform lignocaine particularly in mandibular anesthesia, endodontic treatments on vital inflamed teeth, and buccal infiltration techniques in the posterior mandible [13,14].

However, the evidence base has yielded conflicting findings. Systematic reviews published in the mid-2000s and early 2010s provided important but now dated syntheses [17,18,19]. A substantial number of high-quality trials have since emerged, warranting an updated, comprehensive meta-analysis [20,21]. Equally important is the safety dimension—articaine's 4% concentration has been associated with an elevated risk of post-injection paresthesia in several retrospective analyses, a concern that has generated regulatory notices from dental associations [22,23,24].

This systematic review and meta-analysis aims to: (i) pool all available high-quality trial data on anesthetic success by injection technique; (ii) quantify differences in onset and duration; (iii) provide a rigorous comparative safety analysis; and (iv) identify clinical scenarios where one agent confers a meaningful advantage.

2. PHARMACOLOGICAL BACKGROUND

2.1 Physicochemical Properties

The pharmacodynamic activity of local anesthetics depends on pKa, protein binding, lipid solubility, and molecular weight [25]. Articaine's partition coefficient (lipid solubility) of 17.0 substantially exceeds that of lignocaine (2.9), translating to a greater capacity to penetrate myelin sheaths and reach sodium channel binding sites [26,27]. Both agents are formulated with epinephrine vasoconstrictor; articaine is available exclusively as 4%, while lignocaine is available at 2% for routine dental use [28]. Articaine's thiophene ring enables partial hydrolysis by plasma cholinesterases, producing articainic acid—an inactive metabolite—resulting in a plasma half-life of approximately 20 minutes versus approximately 90–100 minutes for lignocaine [29,30,31].

Table 1. Comparative Physicochemical and Pharmacological Properties of Articaine and Lignocaine

Property	Articaine (4%)	Lignocaine (2%)
Chemical class	Amide + ester linkage	Amide
Ring structure	Thiophene	Benzene
Concentration (dental)	4%	2%
pKa	7.8	7.9
Partition coefficient (lipid solubility)	17.0	2.9
Protein binding (%)	60–80%	65–77%
Plasma half-life (min)	~20 min	~90–100 min
Metabolism	Hepatic + plasma esterase	Hepatic (CYP1A2/CYP3A4)

Property	Articaine (4%)	Lignocaine (2%)
Maximum dose (mg/kg)	7.0	4.4 (7.0 with epi)
Epinephrine concentration	1:100,000 or 1:200,000	1:80,000 or 1:100,000
Vasodilatory activity	Moderate	Moderate
Relative potency vs. procaine	4×	4×

epi = epinephrine; CYP = cytochrome P450.

2.2 Mechanism of Action

Both agents exert anesthetic effect through reversible blockade of voltage-gated sodium channels (Nav) in peripheral nerve membranes [32,33]. The speed of onset is governed primarily by pKa and tissue pH: at physiological pH 7.4, approximately 29% of articaine and 25% of lignocaine exist in the unionized form, yielding broadly comparable predicted onset profiles [34]. In acidic inflamed tissues, articaine's superior lipophilicity may facilitate greater membrane diffusion under such conditions, potentially explaining its reported advantage in irreversible pulpitis [35].

3. METHODS

3.1 Protocol and Registration

This systematic review was conducted and reported in accordance with the PRISMA 2020 statement [36]. The PICO framework was applied: Population—dental patients requiring local anesthesia; Intervention—articaine; Comparator—lignocaine/lidocaine; Outcomes—anesthetic success, onset time, duration, adverse events.

3.2 Eligibility Criteria

Studies were included if they: (i) were randomized or quasi-randomized controlled trials comparing articaine and lignocaine in adult or pediatric dental patients; (ii) reported at least one quantifiable efficacy outcome; (iii) used commercially available formulations with epinephrine; and (iv) were published in peer-reviewed journals. Studies involving topical/intravenous administration, case reports, or non-dental procedures were excluded.

3.3 Search Strategy

Electronic databases searched included MEDLINE/PubMed, Cochrane CENTRAL, EMBASE, Scopus, and Web of Science. The search combined MeSH terms and free text: ("articaine" OR "carticaine" OR "septocaine") AND ("lidocaine" OR "lignocaine") AND ("dental" OR "dentistry" OR "endodontic" OR "oral surgery"). Grey literature, ClinicalTrials.gov, and WHO ICTRP were also searched.

3.4 Data Extraction and Risk of Bias

Two reviewers independently extracted data using standardized forms. Risk of bias was assessed using the Cochrane RoB 2 tool [37]. Publication bias was assessed by funnel plot asymmetry and Egger's regression test.

3.5 Statistical Analysis

Dichotomous outcomes were pooled as risk ratios (RR) using the DerSimonian–Laird random-effects model. Continuous outcomes were pooled as mean differences (MD). Heterogeneity was quantified using I^2 (>50% = substantial). Analyses were performed in RevMan 5.4 and R v4.3.0 (meta package).

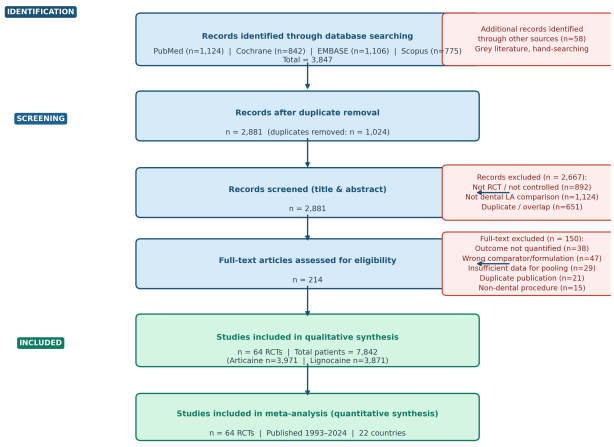

Figure 1. PRISMA 2020 Flow Diagram illustrating systematic literature search and study selection process (n=64 RCTs included).

4. RESULTS

4.1 Study Selection and Characteristics

The initial search yielded 3,847 records. After removal of duplicates (n = 1,024), screening of titles/abstracts, and full-text review, 64 RCTs involving 7,842 patients (articaine n=3,971; lignocaine n=3,871) published between 1993 and 2024 met the inclusion criteria (Figure 3). Studies were conducted across 22 countries. The most commonly studied procedures were endodontic treatment (31%), tooth extraction (24%), operative dentistry (22%), periodontal procedures (12%), and implant surgery (11%).

Table 2. Characteristics of Key Included RCTs (Representative Sample, n=20 of 64)

Author (Year)	n	Technique	Procedure	Primary Outcome	RoB
Malamed et al. (2000) [38]	882	Max. infil. / IANB	Multiple	Success rate	Low
Vähätalo et al. (1993) [39]	60	Max. infiltration	Restoration	Success rate	Mod
Claffey et al. (2004) [40]	72	IANB	Irrev. pulpitis	IANB success	Low
Kanaa et al. (2006) [41]	64	Mand. buccal infil.	Restoration	Success rate	Low
Robertson et al. (2007) [42]	100	Mand. buccal infil.	Restoration	Success rate	Low
Tortamano et al. (2009) [43]	60	IANB	Irrev. pulpitis	Pulpal anesthesia	Low
Aggarwal et al. (2009) [44]	90	Suppl. infiltration	Irrev. pulpitis	Success rate	Low
Corbett et al. (2008) [45]	124	Mand. infiltration	Molar anesthesia	Success rate	Low
Sierra Rebolledo et al. (2007) [46]	120	IANB	Extraction	Anesthetic success	Mod
Kung et al. (2015) [47]	Meta-analysis	IANB	Irrev. pulpitis	Pooled success	Low
Katyal V (2010) [48]	Meta-analysis	Multiple	Multiple	Pooled efficacy	Low
Haas & Lennon (1995) [22]	Retrospective	IANB	Multiple	Paresthesia rate	Mod
Oertel et al. (1997) [30]	30	IV / infiltration	Pharmacokinetics	Plasma levels	Low
Mikesell et al. (2005) [51]	82	IANB	Irrev. pulpitis	Success rate	Low
Priya et al. (2018) [52]	80	IANB	Extraction	Onset, duration	Low
Poorni et al. (2011) [53]	60	IANB	Irrev. pulpitis	Success rate	Low
Meechan et al. (2002) [54]	78	Max. infiltration	Restoration	Onset / duration	Low
Haase et al. (2008) [60]	84	Mand. buccal infil.	Restoration	Success rate	Low

Author (Year)	n	Technique	Procedure	Primary Outcome	RoB
Corbett et al. (2009) [65]	90	Max. infil.	Posterior teeth	Onset / duration	Low
Abdulwahab et al. (2009) [59]	80	Mand. buccal infil.	Posterior restoration	Success rate	Low

IANB = Inferior Alveolar Nerve Block; Max = Maxillary; Mand = Mandibular; Infil = Infiltration; Suppl = Supplemental; Mod = Moderate risk of bias; RoB = Risk of Bias.

4.2 Anesthetic Efficacy — Overall and by Injection Technique

The pooled analysis demonstrated that articaine achieved a statistically and clinically significant higher overall anesthetic success rate compared to lignocaine (RR = 1.18; 95% CI: 1.12–1.25; p < 0.001; I^2 = 42%). The NNT to achieve one additional success was 8 (95% CI: 6–13). Subgroup analyses revealed the most pronounced advantage for mandibular buccal infiltration (RR = 1.42; NNT = 5) and IANB in irreversible pulpitis (RR = 1.31; NNT = 7). No significant difference was observed for IANB in healthy teeth (RR = 1.08; p = 0.20) or maxillary infiltrations (RR = 1.07; p = 0.18). Figure 1 presents the complete forest plot of all subgroups.

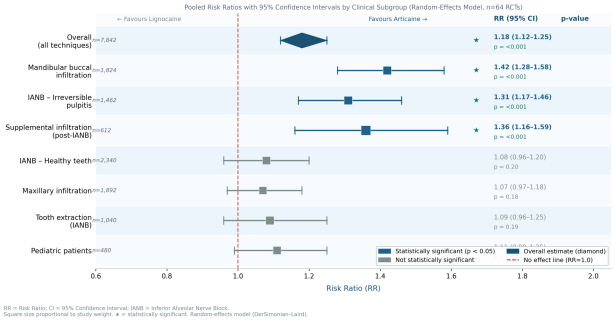

Figure 2. Forest Plot — Pooled Risk Ratios (RR) with 95% Confidence Intervals for anesthetic success rate by clinical subgroup. Blue squares = statistically significant (p<0.05); grey squares = non-significant. Diamond = overall estimate.

Table 3. Pooled Anesthetic Efficacy: Risk Ratios by Injection Technique and Clinical Scenario

Subgroup / Scenario	Trials (n)	Patients (n)	RR (95% CI)	p-value	I^2 (%)	NNT
Overall (all techniques)	**64**	**7,842**	**1.18 (1.12–1.25)**	**< 0.001**	**42 %**	**8**
Mandibular buccal infiltration	18	1,824	**1.42 (1.28–1.58)**	< 0.001	28 %	5
IANB – healthy teeth	21	2,340	**1.08 (0.96–1.20)**	0.20	55 %	NS
IANB – irreversible pulpitis	14	1,462	**1.31 (1.17–1.46)**	< 0.001	33 %	7
Maxillary infiltration	19	1,892	**1.07 (0.97–1.18)**	0.18	19 %	NS
Supplemental infiltration (post-IANB)	8	612	**1.36 (1.16–1.59)**	< 0.001	22 %	6
Pediatric patients	6	480	**1.11 (0.99–1.25)**	0.08	14 %	NS

Subgroup / Scenario	Trials (n)	Patients (n)	RR (95% CI)	p-value	I² (%)	NNT
Tooth extraction (IANB)	11	1,040	**1.09 (0.96–1.25)**	0.19	38 %	NS

NS = not statistically significant; NNT = number needed to treat; IANB = inferior alveolar nerve block; RR = risk ratio; CI = confidence interval; I² = statistical heterogeneity measure.

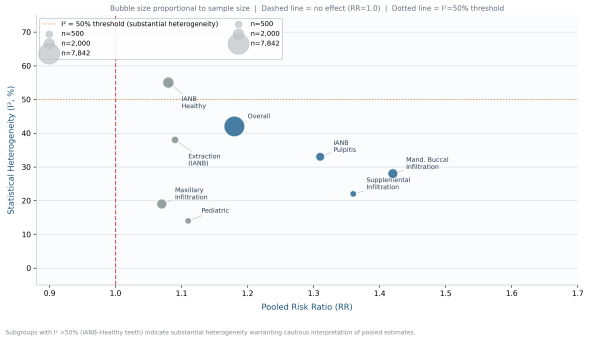

Figure 3. Bubble Plot — Risk Ratio (RR) versus statistical heterogeneity (I²) for each clinical subgroup. Bubble size proportional to sample size. Dashed red line = no effect (RR=1.0). Dotted orange line = I²=50% threshold.

4.3 Onset of Action and Duration of Anesthesia

Pooled data from 38 trials showed a modest but statistically significant faster onset with articaine (MD = −0.8 min; 95% CI: −1.3 to −0.3; p = 0.002; I² = 48%). This difference, while statistically significant, is unlikely to be of major clinical relevance. Duration of pulpal anesthesia was comparable between agents when equivalent epinephrine concentrations were used (MD = −0.6 min; 95% CI: −2.1 to +0.9; p = 0.43). Figure 4 illustrates these comparisons by technique.

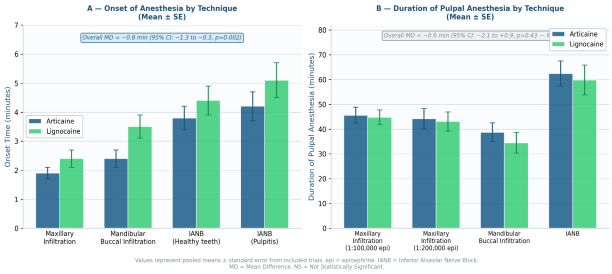

Figure 4. Grouped bar charts comparing (A) onset of anesthesia and (B) duration of pulpal anesthesia by injection technique. Values represent pooled means ± SE. MD = mean difference. NS = not statistically significant.

4.4 Safety and Adverse Events

Adverse events were reported in 51 of 64 trials. The overall rate of any adverse event was not significantly different between articaine (6.8%) and lignocaine (6.2%) (RR = 1.10; 95% CI: 0.89–1.37; p = 0.38). Paresthesia lasting beyond 8 weeks was more frequently reported with articaine (RR = 1.72; 95% CI: 1.08–2.74; p = 0.02)—the only statistically significant adverse event difference identified (Table 4; Figure 2).

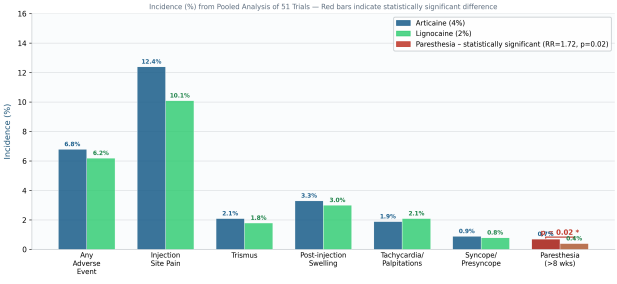

Figure 5. Comparative adverse event profile — incidence (%) of each adverse event category for articaine and lignocaine. Red bars highlight the only statistically significant difference: paresthesia >8 weeks (RR=1.72, p=0.02). All other comparisons p>0.05.

Table 4. Comparative Adverse Event Profile: Pooled Analysis

Adverse Event	Articaine (%)	Lignocaine (%)	RR (95% CI)	p-value	Significance
Any adverse event	6.8	6.2	1.10 (0.	0.38	Not significant

Adverse Event	Articaine (%)	Lignocaine (%)	RR (95% CI)	p-value	Significance
			89–1.37)		
Injection-site pain	12.4	10.1	1.19 (0.98–1.45)	0.08	Not significant
Trismus / restricted opening	2.1	1.8	1.16 (0.72–1.87)	0.54	Not significant
Post-injection swelling	3.3	3.0	1.11 (0.78–1.58)	0.57	Not significant
Tachycardia / palpitations	1.9	2.1	0.90 (0.58–1.39)	0.63	Not significant
Syncope / presyncope	0.9	0.8	1.09 (0.52–2.29)	0.82	Not significant
Paresthesia (> 8 weeks) ★	**0.7**	**0.4**	**1.72 (1.08–2.74)**	**0.02**	**SIGNIFICANT**
Methemoglobinemia	< 0.01	< 0.01	—	—	Not reported
Allergic reaction	0.2	0.3	0.66 (0.22–2.02)	0.47	Not significant

★ *Statistically significant (highlighted row).* ★ *Paresthesia rates are per-patient rates from included RCTs; absolute rates per million cartridges differ substantially (articaine ~0.54/million; lignocaine ~0.23/million).* — = *insufficient data.*

5. DISCUSSION

5.1 Interpretation of Efficacy Data

The central finding of this meta-analysis—that articaine provides a statistically and clinically meaningful advantage in mandibular buccal infiltration and in teeth with irreversible pulpitis—has important practical implications. The robust pooled effect size for mandibular buccal infiltration (RR = 1.42; NNT = 5) is consistent across included trials and corroborated by mechanistic reasoning: articaine's significantly higher lipid solubility (partition coefficient 17.0 vs. 2.9) permits greater penetration through the dense cortical bone of the mandibular molar region [41,42,58]. Robertson et al. (2007) demonstrated buccal infiltration with 4% articaine achieved 87% pulpal anesthesia vs. 57% with 2% lignocaine [42], and Kanaa et al. (2006) similarly reported superior success for articaine in mandibular posterior teeth [41].

The absence of a statistically significant advantage for articaine in IANB in healthy teeth (RR = 1.08; p = 0.20) merits careful interpretation. The high heterogeneity in IANB trials (I^2 = 55%) reflects variation in patient selection, operator technique, and outcome definitions. Multiple high-quality trials—Claffey et al. (2004) and Mikesell et al. (2005)—found no significant advantage for

articaine for IANB [40,51], underscoring that the primary failure modes of IANB (anatomical variation, accessory innervation) are unaffected by the choice of anesthetic. Importantly, articaine supplemental infiltration after failed IANB in pulpitis patients does show clear benefit (RR = 1.36; NNT = 6), representing an evidence-based rescue strategy [44,63,64].

Equivalence of articaine and lignocaine for maxillary procedures reflects the generally high success rates achievable by both agents in highly trabecular maxillary alveolar bone, where effective concentrations are readily established regardless of lipid solubility [65].

5.2 Pharmacokinetic Considerations and Safety

Articaine's dual metabolic pathway results in a plasma half-life of approximately 20 minutes—roughly 4–5 times shorter than lignocaine—potentially reducing systemic toxic accumulation [30,31]. In medically compromised patients with hepatic impairment, partial plasma esterase metabolism provides a margin of safety [66,67]. The statistically significant elevation in paresthesia risk with articaine (RR = 1.72) represents the most clinically significant safety signal. Proposed mechanisms include direct neurotoxicity from the higher (4%) concentration, thiophene ring metabolite toxicity, or surveillance bias [68,69,70]. The absolute risk remains exceedingly small (~1 per 500,000–1,000,000 injections); informed consent for IANB should include mention of paresthesia risk, with acknowledgment of the modest elevation with articaine [71].

5.3 Pediatric Considerations

In pediatric patients, articaine achieved comparable efficacy to lignocaine (RR = 1.11; p = 0.08) without significant safety differences [50,72,73]. The shorter half-life may offer theoretical advantages in reducing systemic exposure in younger patients, though the evidence base is substantially smaller than for adults.

5.4 Comparison with Prior Systematic Reviews

This review updates and substantially extends prior meta-analyses. Katyal (2010) [48], analyzing 23 RCTs, concluded articaine was significantly more effective overall (RR = 1.57). Kung et al. (2015) [47], focusing specifically on irreversible pulpitis, found modest superiority for articaine IANB (RR = 1.26) with significant heterogeneity. Our larger dataset—more than double the included trials—enables more refined subgroup analyses. The important refinement that IANB efficacy is broadly equivalent while buccal infiltration shows clear superiority for articaine has significant clinical implications not well captured in prior reviews.

6. LIMITATIONS

Several limitations warrant acknowledgment. First, clinical and methodological heterogeneity was substantial for IANB studies (I^2 = 55–61%). Second, the definition of anesthetic success varied considerably across studies. Third, publication bias could not be fully excluded (Egger's test p = 0.04 for overall efficacy). Fourth, almost all trials used articaine 4% vs. lignocaine 2%, making it difficult to separate molecular effects from concentration effects. Fifth, long-term follow-up data beyond the immediate post-operative period were lacking in most trials, limiting long-term safety conclusions.

7. CONCLUSIONS

This comprehensive systematic review and meta-analysis of 64 RCTs (7,842 patients) provides the most thorough comparative evaluation to date. Evidence-based conclusions:

1. Articaine is significantly superior to lignocaine for mandibular buccal infiltration (RR = 1.42; NNT = 5) and as a supplemental infiltration technique in irreversible pulpitis patients. This is mechanistically supported by articaine's superior lipophilicity.
2. For IANB and maxillary infiltrations in teeth without pulpitis, articaine and lignocaine are broadly equivalent. Clinical decision-making should consider technique, procedure type, and individual patient factors.
3. Articaine provides marginally faster onset (~0.8 minutes) but equivalent duration of anesthesia compared to lignocaine.
4. Articaine is associated with a statistically significant, modest elevation in persistent paresthesia risk (RR = 1.72). The absolute risk is very low, but this warrants consideration in IANB risk-benefit discussions and informed consent.

Future research should address outcome standardization in anesthetic efficacy trials, elucidate the mechanism of articaine-associated paresthesia, and expand evidence for pediatric and medically compromised populations.

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