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# Anesthetic efficacy of primary and supplemental buccal/lingual infiltration in patients with irreversible pulpitis in human mandibular molars: a systematic review and meta-analysis

Alpa Gupta[1], Aarushi Sahai[1], Vivek Aggarwal[2], Namrata Mehta[1], Dax Abraham[1], Sucheta Jala[1], Arundeep Singh[1]

[1]Department of Conservative Dentistry and Endodontics, Manav Racha Dental College, Faridabad, India
[2]Department of Conservative Dentistry and Endodontics, Faculty of Dentistry, Jamia Milia Islamia, New Delhi, India

Achieving profound anesthesia in mandibular molars with irreversible pulpitis is a tedious task. This review aimed at evaluating the success of buccal/lingual infiltrations administered with a primary inferior alveolar nerve block (IANB) injection or as a supplemental injection after the failure of the primary injection in symptomatic and asymptomatic patients with irreversible pulpitis in human mandibular molars. The review question was "What will be the success of primary and supplemental infiltration injection in the endodontic treatment of patients with irreversible pulpitis in human mandibular molars?" We searched electronic databases, including Pubmed, Scopus, and Ebsco host and we did a comprehensive manual search. The review protocol was framed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist. We included clinical studies that evaluated and compared the anesthetic outcomes of primary IANB with primary and/or supplementary infiltration injections. Standard evaluation of the included studies was performed and suitable data and inferences were assessed. Twenty-six studies were included, of which 13 were selected for the meta-analysis. In the forest plot representation of the studies evaluating infiltrations, the combined risk ratio (RR) was 1.88 (95% CI: 1.49, 2.37), in favor of the secondary infiltrations with a statistical heterogeneity of 77%. The forest plot analysis for studies comparing primary IANB + infiltration versus primary IANB alone showed a low heterogeneity (0%). The included studies had similar RRs and the combined RR was 1.84 (95% CI: 1.44, 2.34). These findings suggest that supplemental infiltrations given along with a primary IANB provide a better success rate. L'Abbe plots were generated to measure the statistical heterogeneity among the studies. Trial sequential analysis suggested that the number of patients included in the analysis was adequate. Based on the qualitative and quantitative analyses, we concluded that the infiltration technique, either as a primary injection or as a supplementary injection, given after the failure of primary IANB, increases the overall anesthetic efficacy.

**Keywords:** Irreversible Pulpitis; Local Anesthesia; Mandibular Molars.



## INTRODUCTION

Pain-free dental treatment, a myth or a reality? Amidst all the technological advances in achieving predictable success in endodontic therapy, the search for profound anesthesia in patients with irreversible pulpitis continues to be the Achilles heel for many clinicians today. Complete or near-complete control of pulpal pain reduces the patient's fear of endodontic therapy [1-3]. The

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Corresponding Author: Vivek Aggarwal, Department of Conservative Dentistry and Endodontics, Faculty of Dentistry, Jamia Milia Islamia, New Delhi, India
E-mail: drvivekaggarwal@gmail.com

primary objective of a clinician is to calm the patient suffering from acute pain, which may be attributed to either pulpal or periapical pain. Crystal-clear knowledge of various local anesthetic techniques is needed to battle the ongoing situation. Attaining profound anesthesia in teeth with irreversible pulpitis is a tedious task compared to achieving anesthesia in healthy mandibular molars [4]. Further studies have shown that block anesthesia is less successful in achieving anesthesia in mandibular molars [5,6]. Local anesthetic failure can be attributed to numerous mechanisms, including anatomic variations [7-10], decreased local pH [10,11], rapid desensitization of local anesthetic [10], and activation of nociceptors and associated central mechanisms [10,12,13]. Hence, it is imperative to assess an alternate method for achieving profound anesthesia in mandibular molars with irreversible pulpitis [14,15].

Many studies have suggested alternative methods to control the inconvenience and pain experienced by subjects during endodontic treatment, including the use of supplementary injections, such as buccal infiltrations (BI), intraligamentary (IL), intraosseous (IO), and intra-pulpal injections [16,17]. Both IL and IO techniques provide anesthesia to the cancellous bone adjacent to the apex of the injected teeth [18,19].

The IL injection technique is a misleading term for an anesthetic solution that fans out through the outer surface of the cribriform plate, which ultimately diffuses inside the crestal marrow spaces and does not diffuse along the periodontal space [20,21]. It provides anesthesia for almost 20 minutes and may cause postoperative pain [22]. Many clinical studies have reported that the IO route increases pulpal anesthesia after the IANB injection in patients suffering from endodontic pain [10]. The IO route delivers higher doses but entails cortical perforation and requires specialized instruments [10]. Additionally, postoperative hyperocclusion and infection at the site of perforation, and cardiovascular problems may ensue [23-25]. Another problem with this technique is the friction that is generated during osseous perforation by the detachment of perforation drills off the plastic base. In addition, necrosis of the bone and perforation of the roots would occur if the drills were rotated at a persistent motion in the bone, leading to an increase in heat generation [26]. Intrapulpal injection is used as the last choice because it involves restricted access cavity opening, which allows local anesthetic solution to backflow [10].

Although infiltration alone suffices the purpose in the maxillary quadrants, the same is not possible for the mandibular region because of the thick cortical plates [27]. However, it can serve as a supplemental mode of anesthesia in IANB [28-32]. The anesthetic success of endodontic treatment for mandibular molars in patients with irreversible pulpitis has been reviewed. A recent systematic review (Seema Yadav 2015 - add in reference) evaluated the anesthetic success rates of IANB alone or along with supplemental infiltration and found that the success rates of infiltration techniques were clinically evident. However, no meta-analysis has been conducted to confirm the results. Another systematic review (Zanjir 2019) used a network meta-analysis to study several pulpal anesthesia strategies, including different anesthetic solutions and injection techniques along with premedications. This systematic review and meta-analysis focuses on the success of primary and supplementary infiltration injection techniques (both buccal and lingual) in patients with irreversible pulpitis in human mandibular molars.

## METHODS

The protocol of the systematic review was framed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [33]. The prepared protocol was registered with the International Prospective Register of Ongoing Systematic Reviews (PROSPERO) with the number CRD42020210896.

### 1. Eligibility criteria

The review question was formulated using the PICO

Table 1. Lists of a combination of keywords for electronic database search strategy

| Database | Search strategy (2019) | n |
|---|---|---|
| Pubmed | ("buccal infiltration" AND "symptomatic irreversible pulpitis" [All fields] OR "buccal infiltration" AND "asymptomatic irreversible pulpitis" [All fields] OR "buccal infiltration" AND "irreversible pulpitis" [All fields] OR "buccal infiltration" AND "symptomatic irreversible pulpitis" AND "human mandibular molars" [All fields] OR "buccal infiltration" AND "asymptomatic irreversible pulpitis" AND "human mandibular molars" [All fields] OR "buccal infiltration" AND "irreversible pulpitis" AND "human mandibular molars" [All fields] OR "lingual infiltration" AND "symptomatic irreversible pulpitis" [All fields] OR "lingual infiltration" AND "asymptomatic irreversible pulpitis" OR "lingual infiltration" AND "irreversible pulpitis" OR "lingual infiltration" AND "symptomatic irreversible pulpitis" AND "human mandibular molars" OR "lingual infiltration" AND "asymptomatic irreversible pulpitis" AND "human mandibular molars" OR "lingual infiltration" AND "irreversible pulpitis" AND "human mandibular molars" OR "buccal infiltration" AND "irreversible pulpitis" AND "systematic review" OR "lingual infiltration" AND "irreversible pulpitis" AND "systematic review" | 80 |
| EbscoHost | ("buccal infiltration" AND "symptomatic irreversible pulpitis" [All fields] OR "buccal infiltration" AND " asymptomatic irreversible pulpitis" [All fields] OR "buccal infiltration" AND "irreversible pulpitis" [All fields] OR "buccal infiltration" AND "symptomatic irreversible pulpitis" AND "human mandibular molars" [All fields] OR "buccal infiltration" AND "asymptomatic irreversible pulpitis" AND "human mandibular molars" [All fields] OR "buccal infiltration" AND "irreversible pulpitis" AND "human mandibular molars" [All fields] OR "lingual infiltration" AND "symptomatic irreversible pulpitis" [All fields] OR "lingual infiltration" AND "asymptomatic irreversible pulpitis" OR "lingual infiltration" AND "irreversible pulpitis" OR "lingual infiltration" AND "symptomatic irreversible pulpitis" AND "human mandibular molars" OR "lingual infiltration" AND "asymptomatic irreversible pulpitis" AND "human mandibular molars" OR "lingual infiltration" AND "irreversible pulpitis" AND "human mandibular molars" OR "buccal infiltration" AND "irreversible pulpitis" AND "systematic review" OR "lingual infiltration" AND "irreversible pulpitis" AND "systematic review" | 58 |
| Scopus | ("buccal infiltration" AND "symptomatic irreversible pulpitis" [All fields] OR "buccal infiltration" AND "asymptomatic irreversible pulpitis" [All fields] OR "buccal infiltration" AND "irreversible pulpitis" [All fields] OR "buccal infiltration" AND "symptomatic irreversible pulpitis" AND "human mandibular molars" [All fields] OR "buccal infiltration" AND "asymptomatic irreversible pulpitis" AND "human mandibular molars" [All fields] OR "buccal infiltration" AND "irreversible pulpitis" AND "human mandibular molars" [All fields] OR "lingual infiltration" AND "symptomatic irreversible pulpitis" [All fields] OR "lingual infiltration" AND "asymptomatic irreversible pulpitis" OR "lingual infiltration" AND "irreversible pulpitis" OR "lingual infiltration" AND "symptomatic irreversible pulpitis" AND "human mandibular molars" OR "lingual infiltration" AND "asymptomatic irreversible pulpitis" AND "human mandibular molars" OR "lingual infiltration" AND "irreversible pulpitis" AND "human mandibular molars" OR "buccal infiltration" AND "irreversible pulpitis" AND "systematic review" OR "lingual infiltration" AND "irreversible pulpitis" AND "systematic review" | 57 |

framework of systematic review, defining the population, intervention, comparison, and outcome. The formulated PICO was "What will be the success of primary and supplemental infiltration injection technique during endodontic treatment in patients with irreversible pulpitis in human mandibular molars?"

## 2. Information sources and literature search strategy

A comprehensive literature search was performed using the following databases: Medline/Pubmed, Scopus, and Ebsco host, along with an extensive manual search. We used a combination of the following keywords: The systematic search was performed separately by three examiners (AS, NM, and VA) for relevant studies published up to November 2019. Boolean operators "AND" and "OR" were used to build a search string of keywords displayed in Table 1. The collected data were manually searched to identify and exclude duplicates.

## 3. Inclusion criteria

Three investigators (AS, NM, VA) evaluated the articles with their titles and abstracts that were discovered during the electronic and manual searches. Articles meeting the inclusion criteria were extracted. All the remaining articles were obtained and fully screened independently by the three reviewers to reach a consensus. We included studies published from 1960 to November 2019, clinical studies that were published in English with adult human patients undergoing non-surgical root canal treatment, and studies including patients with irreversible pulpitis in human mandibular molars and utilizing infiltration injection as part of the primary IANB injection or as a supplemental injection given after the failure of primary IANB. The included studies reported on the success of primary and supplemental infiltration injection, either in the form of percentages or numbers.

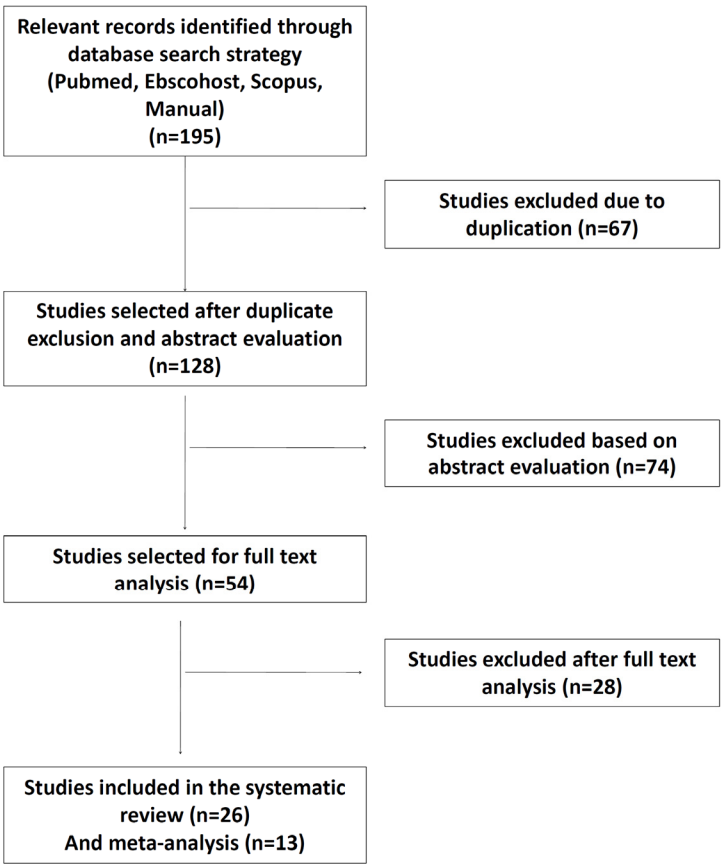


Fig. 1. PRISMA Flow Diagram of the included studies in systematic review and meta-analysis. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

### 4. Exclusion criteria

Studies that evaluated the success of anesthesia utilizing other supplemental techniques, such as IL and IO, and any study reporting the presence of any systemic disease or any effect of medication on anesthetic success, were excluded.

### 5. Data extraction

From the total database search, the relevant articles were manually searched by three authors (AS, AG, VA). The bibliographies of relevant papers and review articles were also screened to calculate the relevant data. Finally, the data were framed in the form of a PRISMA flowchart, as presented in Figure 1.

Two examiners (AG and VA) extracted the data and analyzed each study using the following parameters: author (year)/country, journal, language, age group, total patient size, sex, tooth type, sample size, injection type, case/study type, pain evaluation scale, and success rate with the statistical result. Any disagreements between the two authors (AG and VA) were resolved by the third author (AS).

## RESULTS

Using the search strategy, both through electronic and manual searches, we identified 195 relevant articles. After excluding duplicates, 128 articles were screened for abstract evaluation, out of which 54 were selected for full-text analysis. Considering the strict inclusion and exclusion criteria, after full-text analysis, only 26 articles were included in the systematic review. Of these, 13 studies were included in the meta-analysis and 28 articles were excluded after full-text reading.

**Table 2.** Summary of included studies

| Author | Year and Journal of publication (language) | Tooth type, No. of subjects and Group wise division | Primary or supplemental injection type | Case / Study type | Pain evaluation | Success rate with statistical result |
|---|---|---|---|---|---|---|
| Dianat O, et al. [34] | 2020, Clin Oral Invest | Mandibular molars<br><br>Total patients = 90<br>Age group = 18-65 years<br><br>Group 1 –<br>Males = 16<br>Females = 14<br>1st molars - 20<br>2nd molars - 10<br><br>Group 2 –<br>Males = 14<br>Females = 16<br>1st molars - 18<br>2nd molars - 12<br><br>Group 3 –<br>Males = 17<br>Females = 13<br>1st molars - 21<br>2nd molars - 9 | **Group 1** - IANB - 1.7 ml of 2% lidocaine with 1:100,000 epinephrine<br>**Group 2** IANB + BI - 1.7 ml of 4% articaine with 1:100,000 epinephrine<br>**Group 3** IANB + IS + BI - 0.85 ml of 4% articaine with 1:100,000 epinephrine in mesial and distal aspect of dental papilla. | Symptomatic irreversible pulpitis<br><br>Randomised clinical study | HP VAS<br><br>EPT | **Group 1** = 0.3%<br><br>**Group 2** = 66.6%<br><br>**Group 3** = 80%<br><br>Group 3 results in significantly higher success rate than group 2 and group 1 |
| Shapiro MR, et al. [35] | 2018, J Endod | Total patients = 75<br>Age group –<br>39 ± 15 years<br>Mandibular 1st molars = 36<br>Males = 51<br>Females = 47<br>Mandibular 2nd molars = 39<br>Males = 46<br>Females = 55 | **1°** = IANB (1.7 ml of 4% articaine with 1: 100,000 epinephrine)<br>**2°**<br>**Group 1** =<br>BI (first molars) -<br>1) Articaine - 1.7 ml 4% articaine<br>2) Lidocaine- 1.7 ml 2% lidocaine<br>**Group 2** =<br>BI - (second molars)<br>1) Articaine-1.7 ml 4% articaine<br>2) Lidocaine-1.7 ml 2% lidocaine. | Irreversible pulpitis<br><br>Randomised double-blind clinical trial | HP VAS | **Group 1 -**<br>Articaine = 61%<br>Lidocaine = 66%<br>**Group 2 -**<br>Articaine = 63%<br>Lidocaine = 32%<br><br>No significant difference among Group 1 but articaine was significantly more successful for second molars. |
| Kanaa MD, et al. [28] | 2012, J Endod | Mandibular molars, premolars and anteriors<br>Total patients = 182<br>Age group - 18-66 years<br>Males = 133, Females = 49<br>Molars = 162, Premolars = 18, Anteriors = 2 | **1°** - IANB (2 ml of 2% lidocaine with 1: 80000 epinephrine)<br>Failure of 1°<br>**2° -**<br>**Group 1** = PDL injection<br>**Group 2** = repeat IANB<br>**Group 3** = BI (2ml of 2% articaine HCl with epinephrine 1:100,000)<br>**Group 4** = IO | Irreversible pulpitis<br><br>Randomised clinical trial | EPT | **Group 1** = 48%<br><br>**Group 2** = 32%<br><br>**Group 3** = 84%<br><br>**Group 4** = 68%<br><br>Significant difference among group 1& 2 and group 3 & 4 |
| Dou L, et al. [36] | 2013, Int Endod J | Mandibular molars<br>Total patients = 80<br>Age group - 27-49 years<br><br>Group 1 - 30<br>Males = 13, Females= 17<br><br>Group 2- 30<br>Males = 18<br>Females = 12 | **Group 1**<br>IANB + BI – 4 ml of 2% lidocaine with 1: 100,000 epinephrine+ 0.9 ml of 4% articaine with 1: 100,000 epinephrine<br>**Group 2**<br>IANB + BLI-<br>4 ml of 2% lidocaine with 1: 100,000 epinephrine + 0.9 ml of 4% articaine with 1:100,000 epinephrine | Symptomatic irreversible pulpitis<br><br>Randomised double-blind clinical study | HP VAS | **Group 1** - 70%<br><br>**Group 2** - 62.5%<br><br>No significant difference among groups. |

(continued)

| Author | Year and Journal of publication (language) | Tooth type, No. of subjects and Group wise division | Primary or supplemental injection type | Case / Study type | Pain evaluation | Success rate with statistical result |
|---|---|---|---|---|---|---|
| Poorni S, et al. [5] | 2011, J Endod | Mandibular molars<br>Total patients = 156<br>Age group - 18-30 years<br>Males = 90, Females = 66 | **Group 1** = IANB – 1.8 ml with 4% articaine with 1:100,000 adrenaline<br>**Group 2** = BI – 1.8 ml with 4% articaine with 1:100,000 adrenaline<br>**Group 3** = IANB (control) - 1.8 ml with 2% lidocaine with 1:100,000 adrenaline | Irreversible pulpitis<br>Randomized double-blind clinical trial | HP VAS | Access preparation<br>**Group 1** = 75%<br>**Group 2** = 69.2%<br>**Group 3** = 69.2%<br>Pulp extirpation<br>**Group 1** = 69.2%<br>**Group 2** = 65.4%<br>**Group 3** = 65.4%<br>No statistical significant difference among the study groups. |
| Matthews R, et al. [32] | 2009, J Endod | Mandibular molars or premolars<br>Total patients = 55<br>Age group - 18-71 years Males = 29<br>Females = 26<br>1st molars - 26<br>2nd molars - 23<br>1st premolar - 3<br>2nd premolar - 3 | **1°** - IANB - 2% lidocaine with 1:100,000 epinephrine<br>Failure of **1**<br>**2°** - BI - 1 cartridge of 4% articaine with 1:100,000 epinephrine | Irreversible pulpitis<br>Prospective study | HP VAS | 1st molars = 58% success<br>2nd molars = 48%<br>2nd premolar = 100%<br>1st premolar = 100%<br>Total anesthetic success with BI - 58% |
| Parirokh M, et al. [37] | 2014, Int Endod J | Mandibular 1st molars<br>Total patients = 69<br>Age group- 18-52 years<br>Control group - 36<br>Females = 21, Males = 15<br>Test group - 36<br>Females = 17, Males = 16 | **Group 1** - IANB (control) 3.6 ml of 2% lidocaine with 1: 80000 epinephrine<br>**Group 2** - IANB + BI + IL 1.8 ml of 2% lidocaine with 1/80,000 epinephrine + 1.8 ml lidocaine with 1/80,000 epinephrine + IL | Asymptomatic irreversible pulpitis<br>Randomised controlled trial | HP VAS | **Group 1** - IANB = 22%<br>**Group 2** - IANB + BI + IL = 58%<br>Statistical significant difference among the groups. |
| Shahi S, et al. [38] | 2018, J Endod | Mandibular 1st molars<br>Total patients = 96<br>Age group – 18-65 years<br>Males = 42 Females = 54 | **Group 1** = IANB 1.8 ml 4% articaine with 1:100,000 epinephrine<br>**Group 2** = IANB + BI 0.5 ml 4% articaine with 1:100,000 epinephrine<br>**Group 3** = IANB + BI + PDL | Symptomatic irreversible pulpitis<br>Consort randomised double-blind clinical study | VAS | **Group 1** = 28.1%<br>**Group 2** = 65.6%<br>**Group 3** = 75%<br>No significant difference |
| Aggarwal V, et al. [39] | 2011, J Endod | Mandibular molars (1st and 2nd molars)<br>Total patients = 94<br>Group 1 - Age group - 24-34 years<br>Males = 12<br>Females =11<br>Group 2 - | **Group 1** = IANB (control) 1.8 ml of 2% lidocaine with 1:200,000 epinephrine<br>**Group 2** - IANB + BI - 1.8 ml of 2% lidocaine with 1:200,000 epinephrine + 4% articaine with 100,000 epinephrine<br>**Group 3** - IANB + BI – 1.8 ml of 2% lidocaine with 1:200,000 | Irreversible pulpitis<br>Randomised double-blind study | HP VAS | **Group 1** = 39%<br>**Group 2** = 54%<br>**Group 3** = 62%<br>**Group 4** = 45%<br>No significant difference |

(continued)

| Author | Year and Journal of publication (language) | Tooth type, No. of subjects and Group wise division | Primary or supplemental injection type | Case / Study type | Pain evaluation | Success rate with statistical result |
|---|---|---|---|---|---|---|
| | | Age group - 26-35 years Males = 11, Females = 13<br>Group 3 - Age group - 24-34 years Males = 11 Females = 13<br>Group 4 - Age group - 25-36 years Males = 11 Females = 12 | epinephrine + 1 ml / 30 mg of ketorolac tromethamine<br>**Group 4** - IANB + BI – 1.8 ml of 2% lidocaine with 1:200,000 epinephrine + 1 ml / 4 mg of dexamethasone | | | |
| Rosenberg PA, et al. [40] | 2007, J Endod | Maxillary and Mandibular teeth Total = 48 Age group - 22-58 years Maxillary - 22 Mandibular - 26 Males = 23, Females = 25 | **Group 1 -** (maxillary)- BI A) lidocaine B) articaine<br>**Group 2** - (mandibular)<br>**1°** IANB of 3.6cc of 2% lidocaine with 1:100,000 epinephrine. Failure<br>**2°** BI-<br>a) 1.8cc of 2% lidocaine with 1: 100,000 epinephrine<br>b) 1.8cc of 4% articaine with 100,000 epinephrine | Irreversible pulpitis<br>Randomised double-blind trial. | VAS | Mean score for - 4% articaine = 70.5% For lidocaine = 62.2%<br>No significant difference |
| Aggarwal V, et al. [30] | 2009, J Endod | Mandibular posterior teeth (1st and 2nd molars) Total patients = 84<br>Group 1 - 24-37 years Males = 14 Females = 10<br>Group 2 - 23-36 years Males = 16 Females = 14<br>Group 3 - 26-37 years Males = 15 Females = 15 | **Group 1** - IANB (control) 2% lidocaine with 1:200,0000 epinephrine<br>**Group 2** - IANB + BI + LI – 2% lidocaine with 1:200,0000 epinephrine + 1.7 ml of 2% articaine with 1:200,000 epinephrine + 1.7 ml of 2% articaine with 1:200,000 epinephrine<br>**Group 3** - IANB + BI + LI – 2% lidocaine with 1:200,0000 | Irreversible pulpitis<br>Randomized double-blind study | HP VAS | **Group 1** - 33% **Group 2** - 67% **Group 3** - 47%<br>No significant difference |
| Fan S, et al. [41] | 2009, Oral Surg Med Oral Pathol Oral Radiol Endod | Mandibular first molars Total = 57 Age group - 18-50 years Males = 34, Females = 23 | **Group 1 -** IANB + PDL<br>**Group 2 –** IANB + BI - 1.7 ml of 4% articaine/hcl with epinephrine 1:100,000 + 0.4 ml of 4% articaine/hcl with epinephrine 1:100,000 | Irreversible pulpitis | HP VAS | **Group 1 -** 83.3% **Group 2** - 81.4%<br>No significant difference |
| Parirokh M, et al. [29] | 2010, Oral Surg Oral Med Oral Pathol Oral Radiol Endod | Mandibular 1st molar teeth Total = 84 Age groups - 18-35 years | **Group 1**- IANB 1.8 ml of 2% lidocaine with 1/80,000 epinephrine<br>**Group 2**- IANB | Symptomatic irreversible pulpitis Randomized double-blind study | HP VAS | Success **Group 1** - 14.8% **Group 2** - 39.3% **Group 3** - 65.4% |

(continued)

| Author | Year and Journal of publication (language) | Tooth type, No. of subjects and Group wise division | Primary or supplemental injection type | Case / Study type | Pain evaluation | Success rate with statistical result |
|---|---|---|---|---|---|---|
| | | | 3.6 ml of 2% lidocaine with 1/80,000 epinephrine<br>**Group 3** - IANB + BI<br>1.8 ml of lidocaine with 1/80,000 epinephrine | | | Group 3 is more significant than group 1 |
| | | Group 1 -<br>Male = 10<br>Females = 17<br><br>Group 2 -<br>Males = 8<br>Females = 20<br><br>Group 3 -<br>Males = 7<br>Females = 20 | | | | |
| Ashraf H, et al. [42] | 2013, J Endod | 1st or 2nd Mandibular molars<br>Age group – above 20 years<br>Total = 102<br>Males = 47<br>Females = 55 | **1°** - IANB<br>1.8 ml of 2% lidocaine with 100,000 epinephrine or 4% articaine with 100,000 epinephrine respectively to the groups<br>Failure<br>**2°**<br>**Group 1 -** BI - 1.8 ml of 2% lignocaine with 100,000 epinephrine<br>**Group 2** - BI - 1.8 ml of 4% articaine with 100,000 epinephrine | Irreversible pulpitis<br>Randomized double- blind Study | HP VAS | Success<br>**Group 1** - 29%<br>**Group 2** - 71%<br><br>No significant difference |
| Ahmad ZH, et al. [43] | 2014, J Contemp Dent Pract | Mandibular molars<br>Age groups - 18-40 years<br>Total = 45<br><br>Group 1 -<br>Without BI - 6<br>With BI - 9<br>Failure with BI - 3<br><br>Group 2 -<br>Without BI - 9<br>With BI - 6<br>Failure with BI - 2<br><br>Group 3 -<br>Without BI - 13<br>With BI - 2<br>Failure with BI - 0 | **1°**- IANB<br>2% lidocaine with 1:100,000 epinephrine<br><br>Failure<br>**2°**<br>**Group 1**<br>(1st molars)<br>BI = 4% articaine with 1:100,000 epinephrine<br>**Group 2**<br>(2nd molars)<br>BI<br>**Group 3** (premolars)<br>BI | Symptomatic irreversible pulpitis | HP VAS | **Group 1** - 42%<br>**Group 2** - 48%<br>**Group 3** - 73%<br><br>No significant difference |
| Fowler S, et al. [44] | 2016, J Endod | Mandibular molars<br>(1st molars, 2nd molars, premolars)<br>Total = 221<br>Age groups - 18-65 years<br>Males - 97<br>Females - 124 | **1°**- IANB<br>2% lidocaine with 1:100,000 epinephrine<br><br>Failure<br>**2°**<br>**Group 1**<br>(1st molars)<br>BI = 4% articaine with 1:100,000 epinephrine<br>**Group 2**<br>(2nd molars) - BI | Symptomatic irreversible pulpitis | HP VAS | **Group 1** - 42%<br>**Group 2** - 48%<br>**Group 3** - 73%<br><br>No significant difference |

(continued)

| Author | Year and Journal of publication (language) | Tooth type, No. of subjects and Group wise division | Primary or supplemental injection type | Case / Study type | Pain evaluation | Success rate with statistical result |
|---|---|---|---|---|---|---|
| | | | **Group 3** (premolars) - BI | | | |
| Singla M, et al. [45] | 2015, Int Endod J | Mandibular 1st and 2nd molars<br>Total = 147 | **1°**- IANB<br>1.8 ml of 4% articaine with 1:100,000 epinephrine<br>Failure<br>**2°**<br>**Group 1** - BI<br>1.8 ml of 4% articaine with 1:100,000 epinephrine<br>**Group 2** - BI<br>3.6 ml of 4% articaine with 100,000 epinephrine | Symptomatic irreversible pulpitis<br>Randomized double-blind trial | HP VAS | **Group 1** - 62%<br>**Group 2** - 64%<br><br>No significant difference |
| Rogers BS, et al. [46] | 2014, J Endod | Mandibular molars<br>Total - 74<br>Group 1<br>1st molars = 18<br>2nd molars = 21<br>3rd molars = -<br>Males = 17<br>Females = 22<br>Group 2<br>1st molars = 17<br>2nd molars = 17<br>3rd molars = 1<br>Males = 12<br>Females = 23 | **1°**- IANB<br>1.7 ml of 4% articaine with 1:100,000 epinephrine.<br><br>Failure<br>**2°**<br>**Group 1** - BI 1.7 ml of 4% articaine<br>**Group 2** - BI<br>1.7 ml of 2% lidocaine | Irreversible pulpitis<br>Randomized, double-blind study | HP VAS | **Group 1** - 62%<br>**Group 2** - 37%<br><br>Group 1 is more effective than group 2 |
| Yadav M, et al. [47] | 2015, J Endod | 1st or 2nd mandibular molars<br>Total = 150<br>Group 1 - 75<br>(each group - 25)<br><br>Group 2 - 75<br>(each group - 25) | **Group 1**-4% articaine with 1:100,000 epinephrine<br>**Group 1** -<br>a) 0.9 ml BI + 0.9 ml LI<br>Group 1 -<br>b) pre-operative oral medication of ketorolac<br>Group 1 -<br>c) pre-operative oral medication of ketorolac (10 mg) + 0.9 ml (BI + LI) with either articaine or lidocaine<br>**Group 2** -<br>2% lidocaine with 1:80,000 epinephrine<br>Group 2 -<br>a) 0.9 ml BI + 0.9 ml LI<br>Group 2 -<br>b) pre-operative oral medication of ketorolac<br>Group 2 -<br>c) pre-operative oral medication of ketorolac (10 mg) + 0.9 ml (BI+LI) with either articaine or lidocaine | Irreversible pulpitis<br>Randomized controlled, double-blind study | HP-VAS | **Group 1** = 64%<br>**Group 2** = 32%<br><br>Group 1c) is more significant with success rate of 76% |
| Saatchi M, et al. [48] | 2016, J Endod | First mandibular molars<br>Total = 100<br>Age group - 18-53 years<br>Group 1<br>Males = 13 | **Group 1**<br>BI- 0.7 ml of 8.4% sodium bicarbonate with 0.3 ml 2% lidocaine containing 1:80,000 epinephrine<br>**Group 2** – BI - | Symptomatic irreversible pulpitis<br>Randomized double-blind study | HP VAS | **Group 1** = 78%<br>**Group 2** = 44%<br><br>Group 1 is significant than group 2 |

(continued)

| Author | Year and Journal of publication (language) | Tooth type, No. of subjects and Group wise division | Primary or supplemental injection type | Case / Study type | Pain evaluation | Success rate with statistical result |
|---|---|---|---|---|---|---|
| | | Females = 37<br>Group 2<br>Males = 14<br>Females = 36 | 0.7 ml sterile distilled water with 0.3 ml of 2% lidocaine with 1:80,000 epinephrine.<br>- After 15 minutes, all the patients received conventional IANB injection using 3.6 ml 2% lidocaine with 1:80,000 epinephrine | | | |
| Monteiro MR, et al. [49] | 2015, Int Endod J | Mandibular molars ($1^{st}$ and $2^{nd}$ molars)<br>Total = 50<br>Age group - above 18 years<br>Group 1 -<br>$1^{st}$ molars - 17<br>$2^{nd}$ molars - 13<br>Males = 5<br>Females = 25<br>Group 2<br>$1^{st}$ molars - 13<br>$2^{nd}$ molars - 7<br>Male = 4<br>Female = 16 | **Group 1** - BI<br>1.8 ml of 4% articaine with 1:100,000 epinephrine + LI of 0.6 ml of articaine solution.<br>**Group 2** - IANB<br>1.8 ml of 2% lidocaine with 1:100,000 epinephrine | Irreversible pulpitis<br>Randomized clinical study | HP-VAS | **Group 1** = 40%<br>**Group 2** = 10%<br><br>No significant difference |
| Ghoddusi J, et al. [50] | 2018, Iran Endod J | Mandibular molars<br>Age group – 18-50 years<br>Total = 45<br>IANB + BLI - 24<br>GG + BLI- 21 | **Group 1** - IANB<br>3.6 ml 2% lidocaine with 100,000 epinephrine<br>Failure<br>**2°**<br>1) BI<br>2) LI<br>1.8 ml of 2% lidocaine with 100,000 epinephrine<br>**Group 2 -**<br>Gow-Gates<br>3.6 ml 2% lidocaine with 100,000 epinephrine<br>Failure<br>**2°**<br>1) BI<br>2) LI<br>1.8 ml of 2% lidocaine with 100,000 epinephrine | Symptomatic irreversible pulpitis<br>Randomized double-blind clinical trial | VAS | **Group 1** - 42.5%<br>**Group 2** - 50%<br><br>No significant difference |
| Zain M, et al. [51] | 2016, J Coll Physicians Surg Pak | $1^{st}$ mandibular molars<br>Age group - 18-60 years<br>Total: 156<br>Group 1<br>Males - 46<br>Females - 32<br>Group 2<br>Males = 46<br>Females = 32 | **Group 1**<br>IANB<br>1.8 ml of 2% lidocaine with 1:100,000 epinephrine<br>**Group 2**<br>BI<br>4% articaine with 1:100,000 epinephrine | Symptomatic irreversible pulpitis<br>Randomized control trial | HP VAS | **Group 1** - 62.8%<br>**Group 2** - 76.9%<br><br>No significant difference |
| Saberi EA, et al. [52] | 2014, Zahedan J Res Med Sci | Mandibular molars<br>Total = 75<br>Age group - 20-50 years<br>Males = 39 | **Group 1** - BI<br>1.8 ml of 4% articaine with 1:100,000 epinephrine<br>**Group 2** - BI | Symptomatic irreversible pulpitis<br>Randomized double-blind clinical trial | VAS | Success<br>**Group 1** = 68%<br>**Group 2** = 52%<br>**Group 3** = 64% |

(continued)

| Author | Year and Journal of publication (language) | Tooth type, No. of subjects and Group wise division | Primary or supplemental injection type | Case / Study type | Pain evaluation | Success rate with statistical result |
|---|---|---|---|---|---|---|
| | | Females = 36 | 1.8 ml of 4% articaine + 0.1 ml of morphine with 1:100,000 epinephrine<br>**Group 3** - IANB (control)<br>1.8 ml of 2% lidocaine with 1:100,000 epinephrine | | | No statistically difference |
| Akhlaghi NM, et al. [53] | 2016, J Endod | Mandibular molars<br>Total = 40<br>Age group = 18-65 years<br><br>Group 1 -<br>Males = 9<br>Females = 11<br><br>Group 2 -<br>Males = 7<br>Females = 13 | 1°<br>IANB+BI<br>1.8 ml of 4% artcaine with 1:100,000 epinephrine + 0.9 ml articaine<br>**Group 1** – BI<br>30 mg/ml ketorolac tromethamine<br>**Group 2** – BI<br>(control)<br>Normal saline | Acute irreversible pulpitis double-blind randomized clinical trial | HP VAS | **Group 1** = 40%<br>**Group 2** = 15%<br><br>Significant difference. |
| Rajput F, et al. [54] | 2015, Pak Oral Dental J | Mandibular first molar<br>Total = 60<br>Age group = 18-65 years | **Group 1** – BI<br>1.7 ml of 4% articaine with 1:100,000 epinephrine<br>**Group 2** – IANB<br>1.2 ml of 2% lidocaine with 1:200,000 epinephrine. | Symptomatic irreversible pulpitis<br>Randomized clinical trial | HP VAS | **Group 1** = 52.4%<br>**Group 2** = 47.6%<br><br>Statistically not significant |

BI, buccal infiltrations; EPT, electric pulp tester; HP VAS,Heft Parker Visual Analog Scale; IANB, inferior alveolar nerve block; IL, intraligamentary; IO, intraosseous.

A thorough qualitative and quantitative analysis was carried out for the included studies.

## 1. Qualitative analysis

### 1) Study characteristics

In the final interpretation, twenty-six studies [5,28-30, 32,34-54] were involved, which were related to the success of infiltration injection as a primary or supplemental technique in patients with irreversible pulpitis in mandibular molars.

The individual characteristics of each included study are described in Table 2.

## 2. Outcomes

Based on the individual study criteria, the evaluated results showed successful anesthesia. Either the Heft Parker Visual Analog Scale (HP VAS) or Visual analog scale (VAS) was used to define success in studies when patients reported no pain, mild/bearable pain, or discomfort during access cavity preparation, except in one study conducted by Kanaa et al. [28], who defined profound anesthesia as 'no' response to the electric pulp tester (EPT).

Dianat et al. [34] used both HP VAS scores and EPT to define successful anesthesia.

## 3. Risk of bias assessment

The Cochrane Collaboration ''Risk of Bias'' tool was used to evaluate the methodological quality of the studies involved [55]. The risk of bias was assessed using RevMan 5.3 software. The risks of bias domains evaluated were selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other potential sources of bias. Risk of

bias was indicated as low, high, or unclear. Thirteen studies [28-30,32,34,37-39,42-46] that were involved in the meta-analysis were part of the risk of bias assessment. The first analysis involved studies comparing a primary IANB versus a secondary infiltration injection given after the failure of the first injection [28,32,42-46]. The other analysis involved studies comparing the infiltration injections given along a primary IANB versus IANB given alone [29,30,34,37-39].

The evaluation criteria in both analyses were success rates. The remaining 13 studies did not meet the analysis criteria [5,35,36,40,41-54]. The evaluation was performed by two reviewers separately, and any disparity among them was resolved by consensus.

### 4. Interpretation of studies

A randomized clinical trial by Dianat et al. (2020) [34] compared the anesthetic success of three types of techniques in patients diagnosed with symptomatic irreversible pulpitis in their mandibular molars. Ninety patients were randomly divided into three groups according to anesthetic techniques. The first group received 2% lidocaine IANB, the second group received 4% articaine IANB plus BI, and the third group received IANB plus BI, along with articaine injected intra-septally in both the proximal papillae. Pain was recorded using HP VAS and EPT before and after the anesthetic injection, as well as during access preparation. No or mild pain (pain score of ≤ 54 mm on the HP VAS) on pulpal access was designated as successful. The success rates for groups I, II, and III were 30.33%, 66.66%, and 80.00%, respectively. The mean VAS score after injection was significantly lower in group II and group III than in group I, whereas the EPT score after injection was significantly higher in groups II and III than in group I ($P = 0.016$).

Shapiro et al. (2018) [35] comparatively evaluated the anesthetic efficiency of 4% articaine with 2% lidocaine for supplemental BI in mandibular first molars and second molars with irreversible pulpitis after the failure of IANB. A total of 199 patients diagnosed with irreversible pulpitis in the mandibular molar were injected with an IANB using 4% articaine. If the patients had a positive response to cold or pain upon initiation of endodontic treatment, the subjects were randomly injected with supplemental 4% articaine or 2% lidocaine. A score of ≤ 54 mm on the HP VAS was considered successful anesthesia. IANB with 4% articaine showed anesthetic success in 25% of the subjects. The success rate for articaine supplemental injection in first molars was 61%, and that for second molars was 63% ($P > 0.05$). Lidocaine resulted in successful anesthesia in 66% of first molars and 32% of second molars ($P = 0.004$). The difference was significant only for the second molars and the results for the first molars were similar for both solutions.

Kanaa et al. (2012) [28], through a randomized clinical study, compared the efficiency of the supplemental repeat inferior alveolar nerve block (rIANB) injected with 2% lidocaine and epinephrine, BI with 4% articaine and epinephrine, and IL or IO injection (both using 2% lidocaine and epinephrine) after the failure of primary IANB to achieve complete analgesia during endodontic treatment of irreversible pulpitis in mandibular teeth. A total of 182 patients were injected with 2 mL of 2% lidocaine with 1:80,000 epinephrine as the primary IANB. One hundred out of 182 patients complained of pain during treatment and were then randomly divided into four groups according to four supplementary injection techniques: rIANB with lidocaine, articaine buccal infi ltration (ABI), lidocaine IL, and orlidocaine IO injection. The treatment was initiated only after receiving a negative response to the maximum reading of the electric pulp tester. No pain was regarded as successful anesthesia. ABI and IO exhibited a higher success rate of painless treatment (84% and 68%, respectively) than rIANB or IL supplementary techniques (32% and 48%, respectively). The difference was statistically significant ($P = 0.001$).

Dou et al. (2013) [36] investigated the effect of supplemental lingual infiltration (LI) in mandibular molars after the failure of primary IANB and subsequent BI injection in patients with irreversible pulpitis. Eighty patients were given the standard IANB injection using

4 mL of 2% lidocaine with 1:100,000 epinephrine, after which, patients with marked lower lip numbness were further randomly divided into two groups. In one group, 40 subjects were given supplemental BI (0.9 mL) of 4% articaine with 1:100,000 epinephrine and in the second group of buccal LI (BLI), 40 patients received supplemental BI (0.9 mL) of 4% articaine with 1:100,000 epinephrine followed by LI using the same dose of the solution. Treatment was initiated 15 min after the injection. HP VAS scoring was used to record pain during treatment. No or mild pain on endodontic access and initial instrumentation were considered successful anesthesia. The success rate for BI was found to be 70%, while that of BLI was 62.5%. There was no statistically significant difference between the two groups (P = 0.478).

Poorni et al. (2011) [5] studied the anesthetic efficiency of 4% articaine with 1:100,000 epinephrine injected as IANB along with infiltration techniques to anesthetize mandibular molars with irreversible pulpitis. The study design included three groups (two tests and one control). The patients in the test groups were injected with either conventional IANB or 4% articaine with 1:100,000 epinephrine, whereas only conventional IANB injection of 2% lidocaine with 1:100,000 epinephrine was administered to subjects in the control group. The HP VAS was used to assess pain after injection during pulpal access and extirpation. The three groups showed signifi cantly different results, although BI and IANB with 4% articaine exhibited equal efficacy.

Matthews et al. (2009) [32] determined the anesthetic success of secondary BI injection with 4% articaine, with 1:100,000 epinephrine in mandibular posteriors diagnosed with irreversible pulpitis after failed IANB. Fifty-five patients with irreversible pulpitis in a mandibular posterior tooth were injected with an IANB, and the block was considered to have failed if the patient complained of moderate-to-severe pain on pulpal access. Subsequent injections of BI were performed using 4% articaine with 1:100,000 epinephrine. A painless-access biomechanical preparation was designated as successful anesthesia. The resulting anesthetic success was achieved in 58% of the mandibular posterior teeth. The anesthetic success rate for BI of articaine in the first molar was 58%, the second molar was 48%, the second premolar was 100%, and the first premolar was 100%.

Parirokh et al. (2014) [37] studied the anesthetic action of primary IANB injection for mandibular first molar teeth with irreversible pulpitis, with or without supplemental BI and IL injection. 82 patients with symptomatic irreversible pulpitis were injected with either a combined injection of IL + BI + IANB or standard IANB injection in mandibular first molars. HP VAS pain scores were recorded in response to the cold test at three stages: before the treatment began, during access preparation, and at instrumentation. Anesthetic success was defined as no or mild pain in any of the three stages. In the final stage of treatment, only 69 subjects were included in the study. Traditional IANB was successful in 22% of the patients, while the combination of injections was successful in 58% of the patients. The results were statistically significant (P = 0.003).

Shahi et al. (2018) [38] studied the anesthetic efficacy of three types of injection techniques using articaine in mandibular first molars with symptomatic irreversible pulpitis. The three methods were IANB, IANB + IL, and IANB + BI injected before beginning the endodontic treatment. Ninety-six patients were selected and randomly assigned to three groups. Treatment was initiated 20 min after the injection. Each injection used articaine 4% with 1:100,000 epinephrine. Based on the VAS, no or mild pain upon access cavity preparation or initial instrumentation was considered successful. The success rate for IANBs + IL injection was 75%, and that for IANBs + BI was 65.6%. For the standard IANB injected alone, the success rate was only 28.1% (P < 0.05).

Aggarwal et al. (2011) [39] evaluated the effects of ketorolac and dexamethasone infiltration injected with conventional IANB. Ninety-four subjects who were actively experiencing pain were injected with a traditional IANB of 2% lidocaine with 1:200,000 epinephrine. Twenty-four patients were set as controls and were not

given any supplemental injections. Another 24 patients were given supplemental BI of 4% articaine with 1:100,000 epinephrine, and another set of 24 patients was given supplemental BI of 1 mL/4 mg of dexamethasone. Twenty-six patients received supplemental BI of 1 mL/30 mg of ketorolac tromethamine, but because the first 2 patients complained of severe pain after ketorolac infi ltration and were excluded, the rest of the subjects were given an infiltration of 0.9 mL of 4% articaine before ketorolac. Pulpal access was started 15 minutes after the primary IANB. HP VAS scoring was performed to record the pain. Anesthesia was considered successful if the patient had no pain or mild pain; 39% of the patients in the control group showed successful anesthesia. BI of articaine and articaine plus ketorolac showed significantly high success rates of 54% and 62%, respectively ($P < 0.05$). Supplemental dexamethasone infiltration showed 45% success, which was not significant when compared with the results in the control group.

Rosenberg et al. (2007) [40] studied the anesthetic success of 4% articaine with 1:100,000 epinephrine compared with 2% lidocaine with 1:100,000 epinephrine as a solution for supplemental injections on maxillary and mandibular teeth with irreversible pulpitis. Forty-eight patients required supplemental BI for root canal treatment and were administered either 4% articaine or 2% lidocaine (both with 1:100,000 epinephrine as a vasoconstrictor). VAS scores were evaluated to record pain severity after the injection, and the mean scores were 15.28 for articaine and 19.70 for lidocaine. The mean percentage change in the VAS score was 70.5% and 62.2% for articaine and lidocaine, respectively. However, these differences were not significant in the statistical analyses.

Aggarwal et al. (2009) [30] studied the anesthetic efficiency of the supplemental infiltration technique in 84 subjects with active pain, receiving a standard IANB of 2% lidocaine with 1:200,000 epinephrine. Twenty-four patients were included in the control group and were not injected with supplemental infiltration. Thirty patients received supplemental BI + LI of 2% articaine with 1:200,000 epinephrine and another 30 patients received BI + LI of 2% lidocaine with 1:200,000 epinephrine. After 15 minutes of initial IANB, pulpal access was initiated, and the pain scores were recorded on the HP VAS. Patients who reported 'none' or 'mild' pain were considered to have achieved successful anesthesia. Supplemental BI + LI with lidocaine or articaine improved the success rate from 33% (of the primary IANB alone) to 47% and 67%, respectively. Additionally, the success rate with 4% articaine was significantly higher than that with 2% lidocaine ($P < 0.05$).

Fan et al. (2009) [41] evaluated the anesthetic efficiency of IANB + BI and IANB + PDL articaine injections in patients with irreversible pulpitis in the mandibular first molars. Fifty-seven subjects randomly received traditional IANB injections of 1.7 mL 4% articaine/HCl with 1:100,000 epinephrine with either BI or PDL injections containing 0.4 mL articaine/HCl with 1:100,000 epinephrine. The patients reported the severity of the pain experienced during injections and access cavity preparation on the HP VAS. Anesthetic success was seen in 81.48% of IANB + BI cases compared with 83.33% for IANB + PDL. The observed differences between the two groups was significant ($P < 0.05$).

Parirokh et al. (2010) [29] evaluated the success of IANB combined with BI for mandibular molars with irreversible pulpitis. Eighty-four patients were randomly divided into three groups ($n = 28$ in each group). Lidocaine 2% with 1:80,000 epinephrine was used as the solution of choice. Patients received 1.8 mL of anesthesia as IANB in first group, 3.6 mL as IANB in the second group, and 1.8 mL of IANB and 1.8 mL of BI in the third group. VAS was used to record pain intensity before anesthesia and discomfort experienced before and during root canal access. Groups I, II, and III showed success rates of 14.8%, 39.3%, and 65.4%, respectively, with the third group showing significantly better anesthetic success ($P < 0.05$).

Ashraf et al. (2013) [42] conducted a comparative analysis of the anesthetic efficacy of BI as a supplemental injection using articaine or lidocaine with an IANB. A

total of 125 mandibular molars with irreversible pulpitis were injected with an IANB using either 2% lidocaine or 4% articaine (both with 1:100,000 epinephrine). A total of 102 patients complained of moderate-to-severe pain on pulpal access and were given supplemental BI injections using the same anesthetic solution as that of primary IANB. No pain or minimal pain during instrumentation was deemed successful. Lidocaine was successful in only 29% of the teeth, whereas articaine was successful in 71% ($P < 0.001$), and this difference was significant in the statistical analysis.

Ahmad et al. (2014) [43] investigated the effect of IANB using 4% articaine and 2% lidocaine (with different concentrations of vasoconstrictor). Supplemental BI was provided if the IANB failed. Forty-five patients with irreversible pulpitis of a mandibular posterior tooth were divided into three groups according to the anesthetic injection: Group I received 2% lidocaine with 1:200,000 epinephrine, Group II received 2% lidocaine with 1:80,000 epinephrine, and group III was injected with 4% articaine with 1:100,000 epinephrine. Supplemental BI was administered to patients who complained of pain during root canal therapy. The percentage of successful anesthesia and failed anesthesia were calculated and tabulated using the VAS. Most subjects (87%) injected with articaine reported satisfactory anesthesia with IANB alone. Only 2 (13%) subjects were given an additional infiltration injection, and none of the patients failed to obtain complete anesthesia with articaine. On the other hand, 40% of the subjects receiving lidocaine injections obtained satisfactory results with 1:200,000 epinephrine and 60% were satisfied with 1:80,000 epinephrine.

Fowler et al. (2016) [44] investigated the anesthetic effect of primary IANB and supplemental articaine BI injected after the failure of primary injection in the posterior teeth of patients presenting with symptomatic irreversible pulpitis. A total of 375 subjects were selected and injected with 2% lidocaine with 1:100,000 epinephrine as IANB. After confirming lip numbness, treatment was initiated. A total of 204 patients complained of moderate-to-severe pain, following which, a supplementary BI injection was administered using 4% articaine with 1:100,000 epinephrine. Successful anesthesia was confirmed on no or mild pain on access preparation and instrumentation (VAS rating of 0 or $\leq$ 54). Twenty five percent of first and second molars and 39% of premolars achieved successful anesthesia. For the supplemental articaine infiltration, 42% of first molars, 48% of second molars, and 73% of premolars were successfully anesthetized. No significant differences were found between the molars ($P = 0.3450$), but there was a significant difference between the percentages of premolars and molars, that is, second molars with premolars ($P = 0.0411$) and first molars with premolars ($P = 0.0132$).

Singla et al. (2015) [45] comparatively studied the anesthetic success of two volumes (1.8 mL versus 3.6 mL) of 4% articaine with 1:100,000 epinephrine solution injected as a supplemental BI after the failure of primary IANB in teeth with symptomatic irreversible pulpitis. A total of 234 subjects received IANB with 1.8 mL of 4% articaine with 1:100,000 epinephrine. Pain scoring was performed using the HP VAS, and no or weak/mild pain during the root canal procedures was deemed satisfactory (HP VAS score < 55 mm). Total 147 patients experienced 'moderate-to-severe' pain (HP VAS score $\geq$ 55 mm), so they were further randomized into 2 groups and received BI with either 1.8mL or 3.6mL of the same anaesthetic solution. Primary articaine IANB was successful in 37% of the cases and supplementary BI with 1.8 mL and 3.6 mL volumes succeeded in 62% and 64% cases, respectively. However, these differences were not statistically significant.

Rogers et al. (2014) [46] evaluated and compared 4% articaine with 2% lidocaine for their anesthetic effect when injected as supplemental BI injections after failed IANB in mandibular molars with irreversible pulpitis. One hundred emergency subjects were selected and injected with 1.7 mL of 4% articaine with 1:100,000 epinephrine as an IANB. Seventy-four patients were randomly injected with 4% articaine or 2% lidocaine as supplemental BI after failed IANB. No pain or mild pain

according to the VAS score during the procedure was considered successful. IANB was successful in 26% of the cases. The success rate of articaine BI (62%) was significantly higher than that of lidocaine BI (37%).

Yadav et al. (2015) [47] conducted a randomized study on 150 emergency patients with mandibular first and/or second molars diagnosed with irreversible pulpitis. The patients were divided into two groups: Group 1 was injected with 4% articaine and 1:100,000 epinephrine and group II with 2% lidocaine and 1:80,000 epinephrine. Furthermore, the two groups had three sub-groups each, with 25 patients in each sub-group: BI and LI with articaine and lidocaine, respectively; preoperative oral medication of ketorolac and preoperative oral medication of ketorolac followed by BI and LI with articaine and lidocaine, respectively. All patients with profound lip numbness were considered to have successful anesthesia. No pain or mild pain during root canal procedures was deemed successful analgesia. Articaine IANB with infi ltration and oral ketorolac premedication had a signifi cantly high success rate of 76%. Articaine and lidocaine IANB plus infiltration injection without premedication showed success rates of 64% and 32%, respectively ($P < 0.05$).

Saatchi et al. (2016) [48] evaluated the anesthetic effect of BI using sodium bicarbonate for mandibular first molars in patients with symptomatic irreversible pulpitis. A total of 100 patients were randomly administered a BI injection. In group 1, 0.7 mL of 8.4% sodium bicarbonate with 0.3 mL of 2% lidocaine containing 1:80,000 epinephrine was injected, and in group 2, 0.7 mL sterile distilled water was injected with the same dose of lidocaine as in the other group. Following the BI injection, all patients were administered standard IANB using 3.6 mL of the same lidocaine solution. Anesthetic success was determined only when lip numbness was present. HP VAS scores of no or mild pain during access cavity preparation or initial instrumentation were deemed to have a satisfactory anesthetic effect. The BI of sodium bicarbonate was successful in 78% of the cases, whereas for BI without bicarbonate, only 44% of the cases were considered successful ($P < 0.001$).

Monteiro et al. (2015) [49] investigated the anesthesia achieved by IANB of 1.8 mL 2% lidocaine compared to a BI of 1.8 mL 4% articaine, both with 1:100,000 epinephrine, in patients with symptomatic irreversible pulpits. Fifty subjects were randomly divided into 30 patients receiving articaine injections and 20 receiving lidocaine injections. No pain after a single injection (IANB or BI) or one supplemental injection needed for emergency root canal treatment was considered successful anesthesia. Articaine showed a higher success rate of 40% compared to only 10% with lidocaine. No significant differences were observed between the groups. Ghoddusi et al. (2018) [50] compared the anesthetic effect of IANB and the Gow-Gates technique in mandibular molars with symptomatic irreversible pulpitis. Eighty patients randomly received either IANB or Gow-Gates injection using 2% lidocaine with 1:100,000 epinephrine. Afterward, pain during caries removal and pulpal access were recorded, following which patients were randomly injected with either BI or LI. A total of 45 patients reported pain in both groups. The VAS was used to evaluate pain. The success rates of the Gow-Gates and IANB techniques were 50% and 42.5%, respectively, with no significant difference ($P = 0.562$). There was a significant reduction in pain severity in all subgroups, including supplementary infiltrations ($P < 0.05$). A significantly greater reduction in pain severity was observed with LI given after IANB, as compared to LI after Gow-Gates injection ($P < 0.05$).

Zain et al. (2016) [51] conducted a randomized control trial to study the pulpal anesthetic effect in mandibular first molars by injecting either 4% articaine BI or 2% lidocaine IANB. A total of 156 patients diagnosed with irreversible pulpitis in the first molar were randomly divided into two groups. Group 1 patients were injected with 4% articaine BI and group 2 patients were administered IANB of 2% lidocaine. HP VAS scoring was performed to report pain during the root canal treatment procedures. In 76.9% of the cases, 4% ArticaineBI was successful, whereas lidocaine IANB was

successful in 62.8%. The differences were not statistically significant.

Saberi et al. (2014) [52] conducted a randomized double-blind clinical trial to identify and compare the anesthetic effects of articaine and articaine plus morphine for BI in mandibular posterior teeth diagnosed with irreversible pulpitis. Seventy-five patients were divided into 3 groups and randomly injected with either a BI of 4% articaine or articaine morphine (both with 1:100,000 epinephrine) or traditional IANB of 2% lidocaine with 1:800,000 epinephrine. Pain scoring on the VAS was performed before and after the anesthetic injection and during endodontic access. The success rates of articaine, articaine-morphine, and lidocaine were 68%, 52%, and 64%, respectively. No statistically significant difference was found among the groups.

Akhlaghi et al. (2016) [53] investigated the effect of ketorolac BI on the success of IANB injection in patients with acute irreversible pulpitis. The HP VAS was used to evaluate pain. Forty subjects were injected with a standard IANB injection and a BI of 4% articaine with 1:100,000 epinephrine. The patients were then divided into two groups, with the first test group receiving BI of 30 mg/mL ketorolac, and the second control group receiving BI of normal saline. After observing a negative response to the EPT twice, treatment was initiated. HP VAS scoring of pain was performed. Successful anesthesia was defined as no or minimal pain during the procedure, without any need for supplemental injections. Adding BI significantly increased the success rate from 15% in the control group to 40% in the test group ($P < 0.05$).

Rajput et al. (2015) [54] comparatively studied the anesthetic efficacy of 4% articaine with 1:100,000 epinephrine for BI and 2% lidocaine with 1:200,000 epinephrine for IANB in patients with irreversible pulpitis in mandibular first molars. Sixty patients were randomly divided into two groups. Group 1 received a BI of 1.7 ml of 4% articaine with 1:100,000 epinephrine and group 2 patients were given standard IANB with 1.8 ml of 2% lidocaine with 1:200,000 epinephrine. Anesthetic success was defined as no or minimal pain on endodontic access, according to the VAS score. Twenty two patients (52.4%) achieved successful anesthesia with 4% articaine, while 20 patients (47.6%) had pain reduction in the 2% lignocaine group. However, the observed results were not statistically significant ($P = 0.220$).

## 5. Quality assessment

Figures 2 and 3 show the assessment for risk of bias categories. The categories analyzed included biases such as selection bias, performance bias, detection bias, attrition bias, reporting bias, and assessment of randomization and blinding followed in each individual study. Of all the included studies, six depicted a low risk of bias in almost every domain [29,30,39,42-46]. One study reported a high risk of bias in the selection [34]. Another study showed a high risk of performance and detection bias and a low risk in every bias domain [28]. Two studies were in the low risk of bias category, except for a few domains that were under unclear risk, as randomization and blinding was not possible in these two studies [32,44]. Two other studies had a low risk of bias, except that the performance bias of both studies is unclear [37,38]. All individual studies were assessed qualitatively for each category.

## 6. Quantitative analysis

### 1) Meta-analysis

### 2) Forest plot calculations

The meta-analysis was performed using RevMan 5.3, and two different meta-analyses were conducted for the included studies. The first analysis involved studies comparing a primary IANB versus a secondary infiltration injection (given after the failure of the first injection) [28,34,42-46].

The other analyses involved studies comparing the infiltration injections given along a primary IANB versus IANB given alone [29,30,34,37-39]. The effect size in both analyses was the success rate. The remaining studies were excluded from meta-analysis. Figure 2 shows the

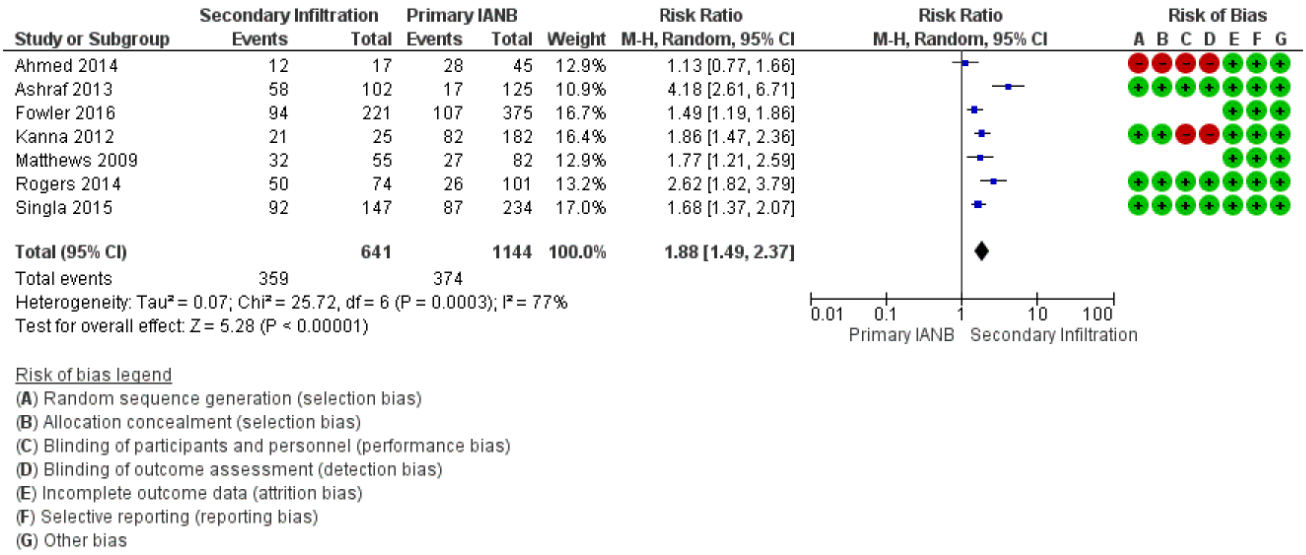


Fig. 2. Forest plot representation of meta-analysis performed on the studies evaluating the secondary infiltration injections.

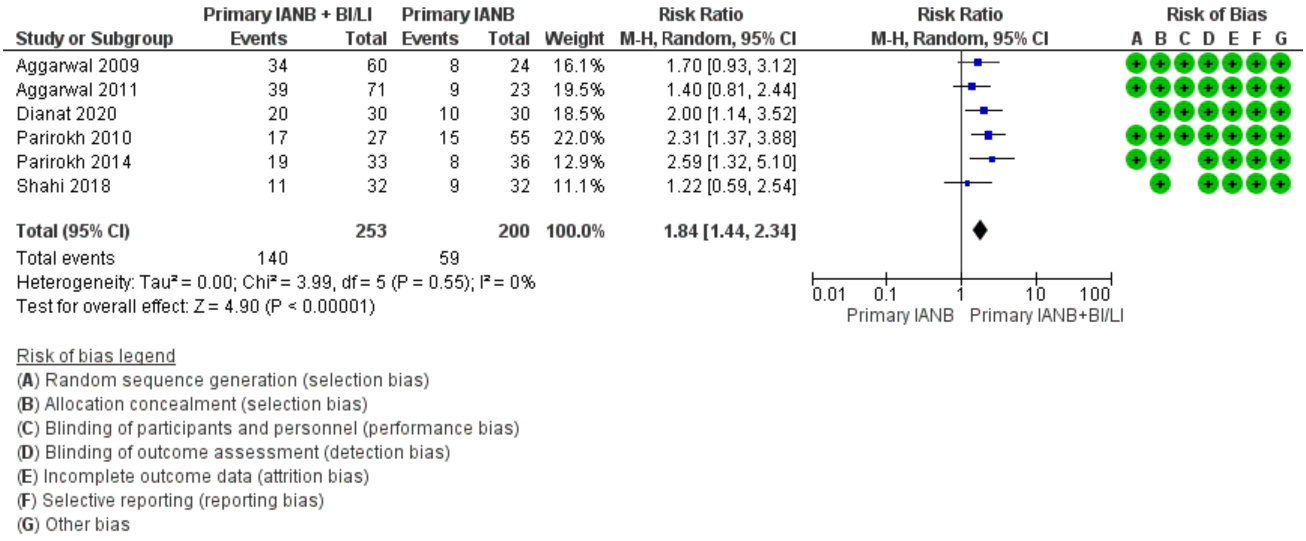


Fig. 3. Forest plot representation of meta-analysis performed on the studies evaluating primary IANB + infiltration versus primary IANB. IANB, inferior alveolar nerve block.

forest plot representation of the random-effect meta-analysis performed on studies evaluating secondary infiltration injections. The combined risk ratio (RR) was 1.88 (95% CI: 1.49, 2.37) in favor of the secondary infiltration injections. The statistical heterogeneity among the studies was 77%. The high statistical heterogeneity can be attributed to the varying confidence intervals (CIs) of different studies. In contrast, the forest plot analysis (Fig. 3) of studies comparing primary IANB + infiltration versus primary IANB alone had a low heterogeneity (0%). The included studies had similar RRs and the combined RR was 1.84 (95% CI: 1.44, 2.34). The results of both forest plots suggest that supplemental infiltration injections, given along with a primary IANB, provide better success rates. Moreover, when the primary IANB fails, supplementary infiltration injections improve success rates.

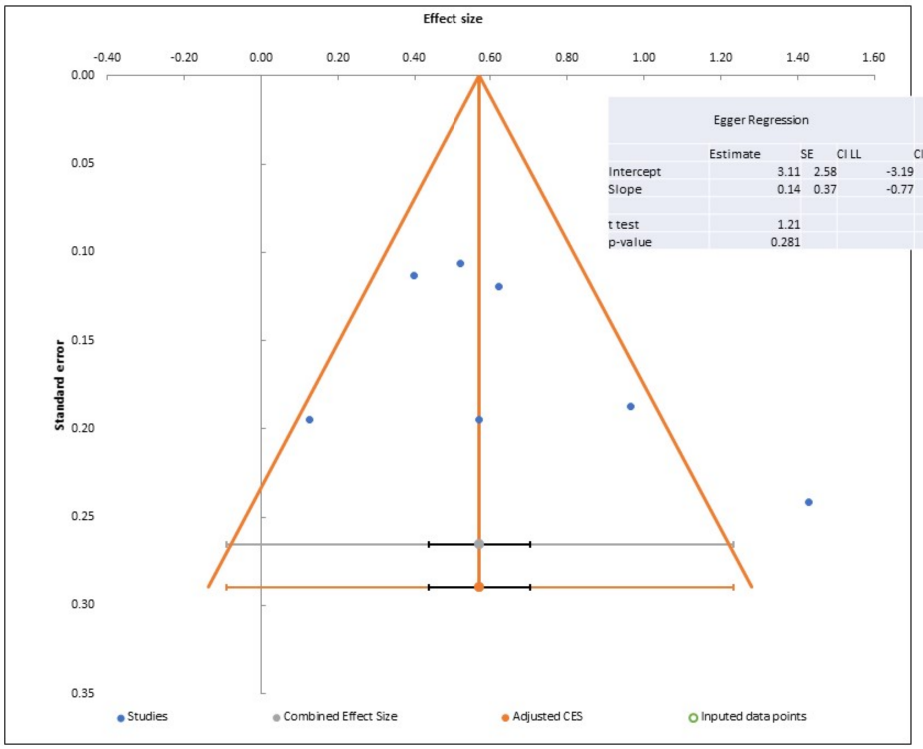


Fig. 4. Publication bias quantified using Egger regression test for studies evaluating the secondary infiltration injections.

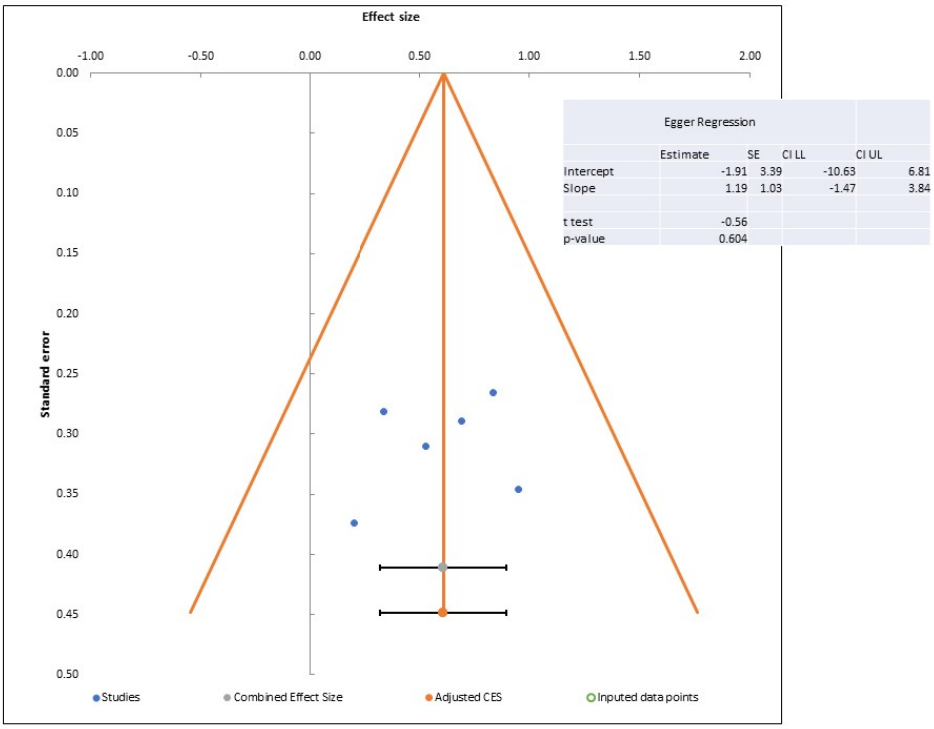


Fig. 5. Publication bias quantified using Egger regression test for studies evaluating primary IANB + infiltration versus primary IANB. IANB, inferior alveolar nerve block.

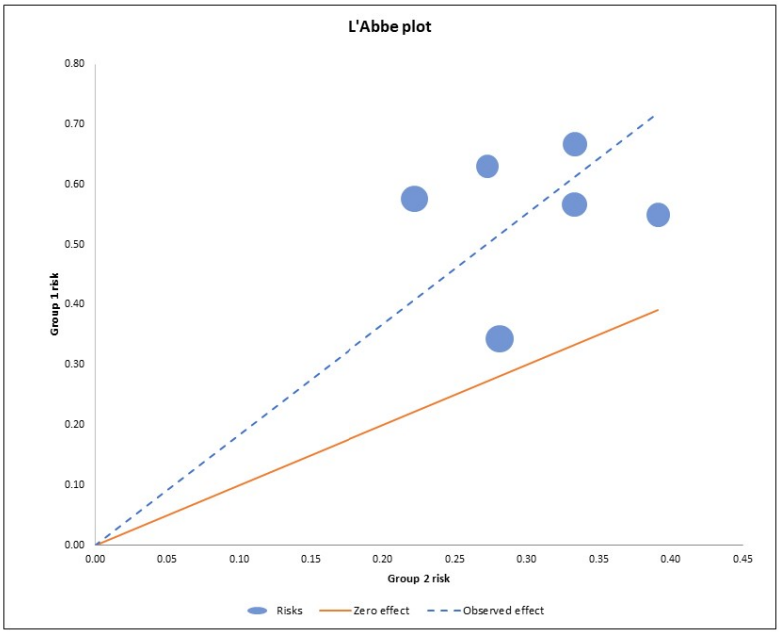


Fig. 6. L'Abbe plots for studies comparing secondary infiltrations after failed IANB. IANB, inferior alveolar nerve block.

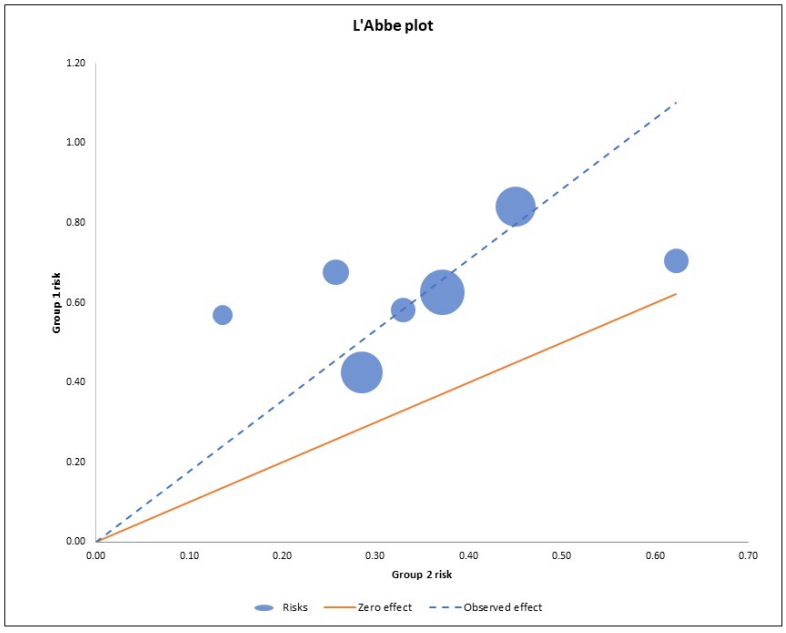


Fig. 7. L'Abbe plots for studies comparing primary IANB + infiltration versus primary IANB. IANB, inferior alveolar nerve block.

## 7. Funnel plots

To assess publication bias, funnel plots were created. The extent of publication bias was based on visual examination of funnel plot symmetry. The funnel plot of studies evaluating secondary infiltration injections had a low publication bias. The extent of publication bias was quantified using the Egger regression test (Fig. 4), which showed a low publication bias (P = 0.281). Studies comparing primary IANB + infiltration with primary IANB alone also had low publication bias. The eager regression test (Fig. 5) showed a low extent of publication bias (P = 0.6044).

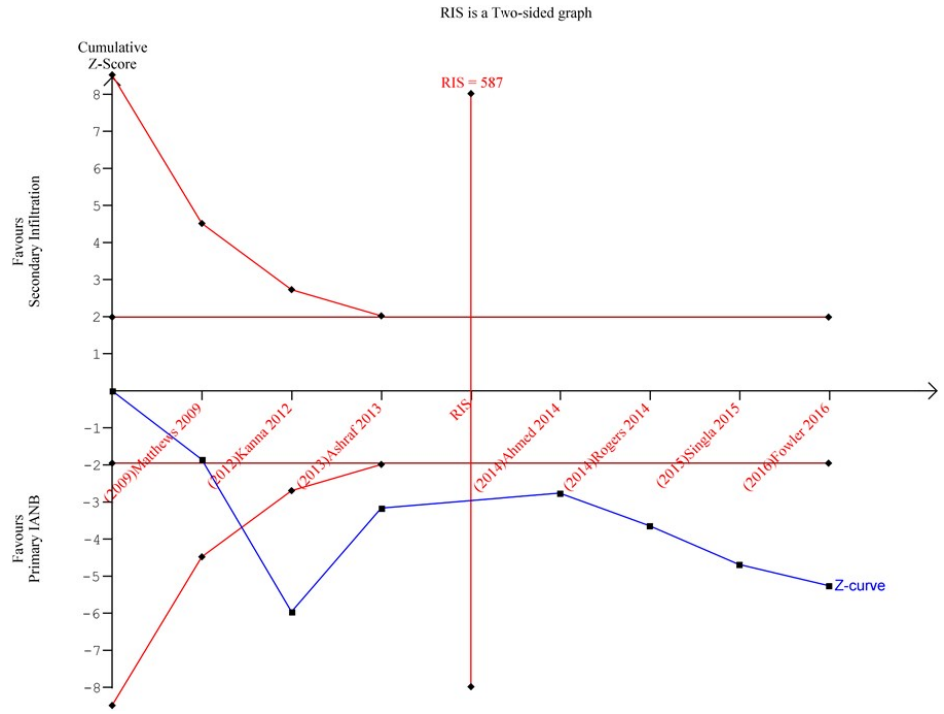


Fig. 8. Required information size and the combined information size of the included studies evaluating secondary infiltration.

## 8. L'Abbe plots

L'Abbe plots were generated for both analyses, and are shown in Figures 6 and 7. The risks of success were plotted against each other. The risk of success for supplementary infiltration was plotted on the y-axis and the risk of success of IANB was plotted on the x-axis. The solid diagonal line represents the studies in which the risk of success did not differ between the groups. Studies above this line have a higher risk of success in the supplementary infiltration group than in the IANB group. The dashed line shows the estimated effects based on the analysis model. Figure 6 shows the L'Abbe plots for studies comparing the secondary infiltrations given after the failure of IANB. All the studies were above the solid line along the dashed line, showing that the risk of success was higher in the infiltration injection group. The scattered studies also represented the level of heterogeneity among the studies. The L'Abbe plots (Fig. 7) of studies comparing primary IANB + infiltration versus primary IANB also showed that the estimated effect was in favor of the IANB + infiltration group. Both studies were near the dashed line, suggesting minimal statistical heterogeneity among them.

## 9. Trial sequential analysis (TSA)

TSA calculations were performed and graphs were plotted with a type I error of 5%. The required information size (RIS) was calculated using a random-effects model to evaluate RRs with a power of 80%. The incidence in the control group was maintained at 30%. The incidence in the intervention arm was maintained at 60% (relative risk reduction of -100%). For the group evaluating secondary infiltrations given after failure of a primary IANB, the RIS was calculated using a heterogeneity correction of 79%, as suggested by the model variance. The high statistical heterogeneity among the included studies increased the RIS to 587. However, the combined information size of the included studies surpassed that of the RIS, with cumulative $Z > 1.96$ (Fig. 8). TSA for the group comparing primary IANB + infiltration versus primary IANB alone has a low heterogeneity and the heterogeneity correction was maintained at 0%, as suggested by the model variance. The RIS was calculated

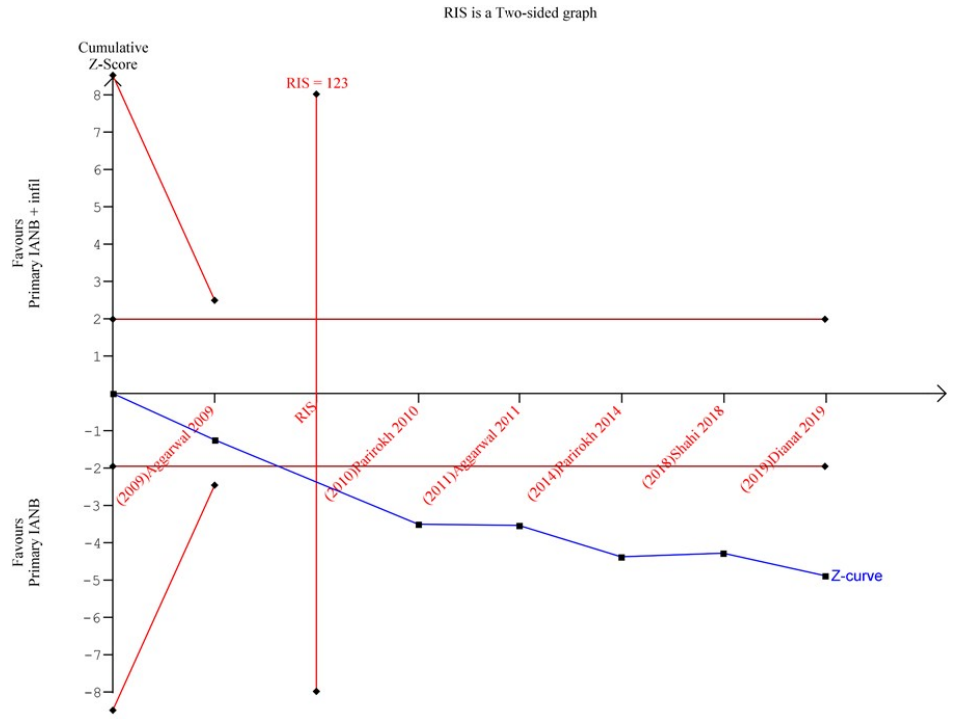


Fig. 9. Required information size and the combined information size of the included studies evaluating primary IANB + infiltration versus primary IANB. IANB, inferior alveolar nerve block.

using a random model with an incidence of 30% and 55% in the control and intervention groups, respectively (relative reduction of − 83.33%). The RIS for this group was estimated to be 123 subjects (Fig. 9). The information size was greater than that of the RIS, with $Z > 1.96$, confirming the beneficial effect of primary IANB + infiltration. It should be noted that an increase in heterogeneity led to an increased RIS in the first analysis.

## DISCUSSION

Complete analgesia in the mandibular posterior region during dental procedures is often regarded as difficult to achieve. IANB is the most standardized and frequently used injection technique for inducing anesthesia in this region. However, the reduced efficacy of IANB can be attributed to factors such as the thickness of the cortical bone, overlying soft tissue, and accessory innervations [28,56,57]. Nerve block success in an un-inflamed pulp was reported to be 70%, as compared to only 30% in patients diagnosed with irreversible pulpitis [11,14, 58-63]. Reports suggest that the failure rate of local anesthesia in patients with irreversible pulpitis is eight times higher than the failure rate in normal patients.

The current review summarizes the anesthetic value of infiltration injection techniques, either applied as a primary or supplemental injection in patients diagnosed with irreversible pulpitis in human mandibular molars.

Other techniques, such as IO and IL, are often applied to raise anesthetic efficacy in difficult situations. However, the infiltration technique is a simple, easy, and comfortable technique for achieving desirable anesthetic levels [42].

Recently, the BI technique has been used in the mandible in various studies. Some of the authors have shown that the use of only BI or BLI can produce profound anesthesia in subjects with 32% to 67% when administered with lidocaine, and 57% to 92% when administered with articaine, even when the IANB is not administered [31,64-66]. A recent meta-analysis (involving studies with healthy and inflamed pulp) revealed that

articaine was 3.8 times more potent in an infiltration injection than lidocaine [67].

In the mandible, a BLI anesthetic injection containing articaine was suggested for sufficient anesthesia in the anterior tooth pulps [68]. This BLI technique showed significant improvement in the anesthetic action in healthy mandibular incisor pulps than when labial infiltration used solo [68]. However, in mandibular molars, a part of the supplementary LI remains debatable. It has been observed that in the first mandibular molars, LI was less efficacious than BI in achieving anesthesia in healthy subjects [69]. Meechan et al. [16] observed no difference in anesthetic efficacy for healthy mandibular molars between BI alone and BLIs. The effectiveness of a supplementary LI in mandibular molars when IANB and BI have already been administered, especially in irreversible pulpitis cases, where it has not been examined. Only a few studies have searched supplemental LI with IANB + BI and have not found any significant results in the success rates of anesthesia [30,36]. More such studies are required to determine an appropriate and reliable outcome of LI as a supplemental injection technique to primary IANB + BI.

Yadav [70] compared and evaluated the anesthetic success rates of the IANB injection technique alone or injected along with supplemental infiltration technique to achieve profound anesthesia in mandibular posteriors with irreversible pulpitis. This review included studies published up to 2014, and no meta-analysis was conducted for the included studies.

Infiltration injection has been tested in the field of endodontics, both as a primary or supplemental technique. Various clinical studies have focused on the success of infiltration techniques (BI/LI), either as a primary or supplemental injection in subjects with mandibular posteriors suffering from irreversible pulpitis. Studies showing the anesthetic success of supplemental infiltration injected after the failure of primary IANB in teeth with irreversible pulpitis exhibited a high success rate of 40% to 73% [34,42,43,45,46], apart from the study conducted by Kanaa et al. [28], which gave an even higher success rate of 84%. This high success rate could be attributed to the injection of a larger volume of anesthetic solution with BI. Lastly, studies in which the IANB plus infiltration technique was given as a primary injection in subjects suffering from irreversible pulpitis showed a success rate of 45% to 67% [29,30,34,37-39].

The current review only focused on the success of pulpal anesthetic injection techniques, regardless of the different anesthetic solutions and concentrations used in the included studies. Therefore, only the success of the infiltration technique on anesthetic efficacy was considered.

Risk of bias assessment was performed for the included studies in the current review, and it was found to be low in every category that was tested. The qualitative results of the review were quantified through two types of meta-analyses based on specific characteristics of the study. The first analysis involved a comparison of the anesthetic success rates of primary IANB versus secondary infiltration injections administered after failure of primary IANB. This meta-analysis, when represented as a forest plot, revealed 87% statistical heterogeneity among the studies that further increased the calculated RIS to 778. However, the calculated RIS was still less than the combined information size, which reaffirmed the reliability of our meta-analysis, which could be considered sufficient to prove that secondary infiltration injection is better than primary IANB administered alone. In contrast, the second meta-analysis involved a comparison of success rates of the infiltration injections given as part of the primary injection alongside IANB versus IANB administered alone. The forest plot revealed a low heterogeneity of 0%, and eventually, the calculation of RIS was performed at 123, which was again less than the combined information size. One limitation of the second meta-analysis quantification is that one of the studies included by Parirokh et al. [37] used a combined success rate of the IL that was injected along with IANB and BI, which could have influenced the final result of the analysis to certain limits. Overall, these results suggest better success rates of infiltration techniques, given along

with a primary IANB.

The qualitative and quantitative results of the current review suggest the incorporation of a simple and easy infiltration injection technique as a primary injection along with IANB in routine clinical practice.

## CONCLUSION

Based on the qualitative and quantitative analyses, we can conclude that the infiltration technique, either as a primary injection or as a supplementary injection, when given after the failure of primary IANB increases the overall anesthetic efficacy.


### AUTHOR ORCIDs

**Alpa Gupta:** https://orcid.org/0000-0003-2834-0608
**Aarushi Sahai:** https://orcid.org/0000-0002-7519-9339
**Vivek Aggarwal:** https://orcid.org/0000-0002-9792-4554
**Namrata Mehta:** https://orcid.org/0000-0002-4836-524X
**Dax Abraham:** https://orcid.org/0000-0002-6870-6689
**Sucheta Jala:** https://orcid.org/0000-0001-9680-3147
**Arundeep Singh:** https://orcid.org/0000-0003-2342-9486


### AUTHOR CONTRIBUTIONS

**Alpa Gupta:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing

**Aarushi Sahai:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing - original draft

**Vivek Aggarwal:** Data curation, Formal analysis, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing - review & editing

**Namrata Mehta:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Validation, Visualization, Writing - original draft, Writing - review & editing

**Dax Abraham:** Conceptualization, Formal analysis, Investigation, Project administration, Resources, Supervision, Validation, Writing - review & editing

**Sucheta Jala:** Data curation, Formal analysis, Software, Supervision, Validation, Writing - review & editing

**Arundeep Singh:** Formal analysis, Project administration, Resources, Supervision, Validation, Visualization

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