Chiang Mai Dental Journal

Review Article

Is It Possible to Achieve Profound Pulpal Anesthesia in Deep Carious Young Permanent Molars? A Review of the Literature

Yanisa Vetchapitak[1], Papimon Chompu-inwai[1], Natthamet Wongsirichat[2], Jungyi Alexis Liu[3], Chanika Manmontri[1]
[1]Department of Orthodontics and Pediatric Dentistry, Faculty of Dentistry, Chiang Mai University, Thailand
[2]International College of Dentistry, Walailak University, Thailand
[3]Department of Developmental Dentistry, School of Dentistry, University of Texas Health San Antonio, USA

Received: April 9, 2021 • Revised: May 5, 2021 • Accepted: May 18, 2021

Corresponding Author: ***Chanika Manmontri*** *Assistant Professor, Department of Orthodontics and Pediatric Dentistry, Faculty of Dentistry, Chiang Mai University, Chiang Mai 50200, Thailand. (E-mail:* ***chanika.m@cmu.ac.th****)*

Abstract

Creating favorable local anesthesia is an important step for enhancing patient's satisfaction and completion of the dental treatment. Anesthetizing teeth by solely using inferior alveolar nerve block is not effective enough to acquire adequate pulpal anesthesia in young permanent mandibular molars with deep caries, especially in teeth diagnosed with irreversible pulpitis. Promising supplemental injections are therefore essential to increase the success of pulpal anesthesia in these teeth. The aims of this literature review are 1) to provide useful information that dental practitioners should know regarding characteristics of young permanent teeth that can compromise success of pulpal anesthesia, 2) to present current literatures related to pulpal anesthesia in young permanent mandibular molars, and 3) to discuss practical practice in achieving pulpal anesthesia that clinicians may implement in their daily practice.

Keywords: inferior alveolar nerve block, local anesthesia, pediatric patients, pulpal anesthesia, supplement injection

Introduction

Delivering effective pain control by local anesthesia during operative and pulpal treatment in pediatric dentistry is essential for completion of the required procedures and enhancing patient's positive dental experience and attitude. The most commonly used local anesthetic technique in both primary and permanent mandibular teeth is inferior alveolar nerve block (IANB).(1) Despite this technique's popularity among dental practitioners, several studies have reported fluctuating success rates of pulpal anesthesia by IANB in mandibular teeth of adult patients, ranging between 25% to 93% for teeth with normal pulp(2-5), and between 19% to 70% for irreversible pulpitis.(3,6-8) Consequently, various approaches have been proposed and studied to increase the success of IANB, for example, use of different local anesthetic agents, pre-emptive premedication, supplemental injection techniques and pharmacological management.(9) These approaches were reported to successfully improve the success of IANB in adult patients up to 98%.(10-15) However, in the young permanent mandibular molars with deep caries, these methods were not as successful as those in the adult patients.

The aims of this review are to 1) explain unique characteristic of deep carious young permanent mandibular molars that can jeopardize their profound pulpal anesthesia 2) discuss different studied options for increasing the pulpal anesthetic success of IANB in young patients and 3) highlight important clinical steps for clinicians to provide adequate pulpal anesthesia in pediatric patients with deep carious young permanent mandibular molars.

The unique deep carious young permanent teeth – why are they more difficult to anesthetize?

To gain pulpal anesthesia, local anesthetics should be capable of functionally inhibiting sodium influx into the peripheral neural fibers in the pulp tissue, thus blocking the excitation or conduction to the nerve endings and disrupting the pain sensory pathway.[3,16] Sensory nerve fibers of the dental pulp are afferent endings of the trigeminal nerve. These fibers reach the root canal through the apical foramen, enter into the root pulp, and finally form the neuro-vascular bundle.[17] Innervation, vascularization and composition of dental pulp in young and aged permanent teeth are dissimilar and could probably be accounted for difference in anesthetic success between them.[17-19] Young pulps consist of an extensive network of vascular and neural structures scattering throughout the pulp. When the pulpal vessels and nerves entered the coronal part, vascular branches flowed toward the lateral and occlusal surfaces of the pulp and reached the cuspal horns, then a rich subodontoblastic plexus of nerves and blood vessels was formed.[19]

In a physiologic aging process, continuous secretion of secondary dentinal matrix by odontoblasts and a progressive calcification originates and progresses from the radicular to the coronal pulp, resulting in a reduction in size of pulp chambers and root canals.[19] This phenomenon eventually leads to a decrease of the number of blood vessels and nerves supply.[19] Histologically, over 90% of the aged pulp had calcification and nerve degeneration, whereas young pulps had no evidence of pulpal calcification in either coronal or radicular pulp tissues.[18] Furthermore, higher expression of growth factors, like bone morphogenetic protein, transforming growth factor alpha, vascular endothelial growth factor A, and fibroblast growth factors family were presented in the young dental pulp. In contrast, a high expression of genes involving in apoptotic processes were evident in the aged pulp.[20]

In a pathological condition, teeth with inflamed pulpal tissue have additional difficulties attaining pulpal anesthesia because the low tissue pH in areas of inflammation affects the activity of the local anesthetic agent by reducing the amount of the base form of the anesthetic solution needed to penetrate the nerve sheath and membrane. Therefore, there is less ionized form of the anesthetic within the nerve to produce profound anesthesia. Moreover, neurons and their axons innervating an inflamed tissue could have altered resting membrane potentials and reduced thresholds of excitability. Chemical changes extending throughout the affected nerve fibers may alter their capacity to be anesthetized.[2,21] In young pulp, a more prevalent and greater extent of inflammatory process was observed than in the mature pulps.[22]

Put it all together, the more well-supplied of neural and vascular elements, the absence of pulp calcification, the more gene expression of cellular and tissue development, and higher response to noxious stimuli in the deep carious young permanent teeth may be associated with their higher sensitivity and also may lead to higher pulpal anesthetic failure in the deep carious young permanent teeth than in the aged teeth.[17-19,22]

The inferior alveolar nerve block – the most commonly used technique for anesthetizing mandibular teeth

Mandibular molars are innervated by an inferior alveolar nerve, lingual nerve and buccal nerve which are branches of the mandibular nerve, the third division of the trigeminal nerve.[23] Techniques for anesthetizing mandibular teeth include inferior alveolar nerve block (IANB) and long buccal nerve block.[16] The IANB is the most commonly used injection technique for achieving local anesthesia of mandibular teeth in both primary and permanent dentitions.[1] Moreover, this technique is the most common technique studied regarding efficacy of pulpal anesthesia of permanent mandibular molar in pediatric patients.[24] Techniques for IANB administration in both adult and pediatric patients are thoroughly described elsewhere.[16,24] After administration of IANB, soft tissue anesthesia should occur within 4.5 to 6 minutes and pulpal anesthesia should occur within 5 to 19 minutes.[9] The major advantage of IANB is that one injection provides anesthesia to a wide area, which is useful when providing treatment throughout a quadrant of dental arch. IANB has some drawbacks including difficulty in achieving anesthesia because of anatomic variations, deep and invasive needle penetration, delayed onset of anesthesia, high incidence of positive aspiration, and multiple possible complications, such as trismus, paresthesia, hematoma, and undesired soft and/or hard tissue anesthesia with possible patient-induced injury, particularly in children.[24,25] IANB can also be difficult to perform and has the highest percentage of clinical failures (up to 81%) even when it is administered properly.(16,24)

Previous studies have reported that the anesthetic success of IANB ranged between 25-93% in mandibular teeth with normal pulp(2-5) and between 19-70% in mandibular teeth with irreversible pulpitis.(3,6-8) Most clinical studies were performed in adult patients (age over 18 years old) and had corresponding results that IANB alone could not provide complete efficacy of pulpal anesthesia, especially in patients suffering from irreversible pulpitis.(4,5,8,10,26-30)

Different strategies used for increasing the success of inferior alveolar nerve block in young patients

Factors associated with the local anesthetic failure can be categorized into two major categories: the operator dependent factors, including technique administration and anesthetic solution, and the patient dependent factors, including anatomical, pathological and psychological factors.(31) Consequently, several strategies have been introduced to achieve profound pulpal anesthesia of mandibular teeth, especially in the ones with inflamed pulp tissue, by manipulating those aforementioned factors. These strategies include changing the local anesthetic agents, increasing the volume of the anesthetic solution, preemptive medication, and inhalation sedation. Moreover, several supplemental injection techniques have been introduced, for example, intra-osseous injection, intraligamentary injection, supplemental mandibular buccal infiltration, and intraseptal injection.(16,21,32) It should be noted that most clinical studies about pulpal anesthetic success in permanent teeth were performed in subjects who are older than 18 years of age. There are only few studies focusing on pulpal anesthetic success in young permanent teeth.

Local anesthetic agents and pulpal anesthesia: Does the type of anesthetic agent, volume, or epinephrine concentration matter?

Lidocaine is the most widely used local anesthetic agent in dental treatment because it was the first agent available for dentistry and has been used as the gold standard for comparison of any new types of local anesthetic agents.(33) However, the pulpal anesthetic success of IANB in teeth with irreversible pulpitis of adult patients when using 2% lidocaine with 1:100,000 epinephrine varied between 23% to 70%.(8) To overcome this shortcoming of lidocaine's unreliable anesthetic result, many studies focused on exploring alternative anesthetic solutions that provide higher success. Articaine is an agent that has been widely studied and conveyed promising results. The pulpal anesthetic success rates of 4% articaine with 1:100,000 epinephrine were reported to range between 24% to 88%.(8,33) Most studies reported higher success rates of articaine than those of lidocaine. A recent systematic review and meta-analysis concluded that there is a higher success of articaine than lidocaine when used for supplementary injection via infiltration technique after IANB during endodontic treatment of mandibular teeth with irreversible pulpitis ($p<0.05$).(8,33) This superiority of articaine over lidocaine may relate to its intramolecular hydrogen bonding in thiophene ring which facilitates its bone penetration.(34) Moreover, the presence of the thiophene ring enhances the lipid solubility of articaine, leading to its better diffusion of the solution through the neuronal membrane, when compared to other local anesthetic solutions.(34) Several literatures support the use of articaine in pediatric patients for its safety and efficiency but its use is restricted, based on the manufacturer's instructions, for children above the age of four years.(35) However, many studies have shown that articaine is safe for children under 4 years of age, and that the pharmacokinetic profile of articaine is very similar for children and adults.(35,36) Moreover, there is no conclusive evidence demonstrating its toxicity in children. The findings of Elheeny(35) supported the efficient and safe use of 4% articaine with 1:100,000 epinephrine in children below 4 years old.(37)

Another potential method to increase pulpal anesthesia success is to increase the injection volume of the local anesthetic agent. However, there is no general agreement regarding the influence of the volume of anesthetic solution on the success rate of pulpal anesthesia in mandibular teeth. While several investigations have shown that higher volumes of anesthetic solution may increase the success rate(38-40); conversely, other studies have reported no significant difference of the pulpal anesthetic success with higher volumes.(9,41,42) In addition, vasoconstrictor such as epinephrine may have several potential benefits. It decreases the peak plasma concentration of the local anesthetic agent, increases the duration and the quality of anesthesia, reduces the minimum concentration of anesthetic needed for nerve block, and reduces blood loss during surgical procedures.(43) Interestingly, the concentration of epinephrine seems not to be associated with the anesthetic efficacy of anesthetic solution.(44)

Preemptive medication and inhalation sedation: useful adjuncts for patients with irreversible pulpitis

Several types of medication, including benzodiazepines, nonsteroidal anti-Inflammatory Drugs (NSAIDs), corticosteroids and nitrous oxide/oxygen inhalation have been used to achieve profound pulpal anesthesia of mandibular teeth.(45,46) The concept of using benzodiazepines is based on the fact that the drug can decrease anxiety and that may also increase anesthetic success rate.(45) The reasons for using NSAIDs and corticosteroids are to inhibit inflammation and to induce analgesia by inhibition of cyclooxygenase activity enzymes.(47) The reason behind the use of nitrous oxide/oxygen inhalation is its anxiolytic and analgesic effects. Consequently, nitrous oxide/oxygen has been recommended for patients whom profound local anesthesia cannot be obtained.(48)

In pediatric patients, one clinical study showed that preemptive medication and use of nitrous oxide/ oxygen inhalation sedation may potentially increase success of pulpal anesthesia in mandibular molars diagnosed with symptomatic irreversible pulpitis.(46) All patients in this study received 10 mg/kg (maximum of 600 mg per dose) of ibuprofen syrup immediately after a meal, 1 hour before a treatment procedure. After that, patients received nitrous oxide/ oxygen via nasal hood by the slow titration or rapid induction method, as appropriate for each patient, until the patient reached a good stage of sedation. The range of nitrous oxide concentration administered was between 30% and 50%. After 5 minutes, the treatment began, and the concentration of nitrous oxide/ oxygen was maintained throughout the procedure. Before starting the treatment, all patients then received IANB with long buccal nerve block for a permanent mandibular molar with 1.7 ml of 4% articaine with 1:100,000 epinephrine. In patients premedicated with ibuprofen using nitrous oxide/ oxygen inhalation sedation, the success rate was 71%, whereas patients in the control group who received premedication and 100% oxygen had success rate at only 19%. Although this study exhibited significant favorable effect of nitrous oxide/ oxygen sedation by increasing the difference of success rates up to 52%, the 95% confidence interval of this difference had a very wide range (22.9% to 80.7%). In fact, this may be the result of small sample size in this preliminary (16 and 17 patients in the treatment and control groups, respectively). Therefore, to confirm the beneficial effect of nitrous oxide/ oxygen inhalation sedation in pediatric patients with permanent mandibular molars diagnosed with symptomatic irreversible pulpitis, further well designed randomized controlled trial with a larger sample size is required.

Supplemental injection following inferior alveolar nerve block

Intraosseous injection (IO) is one of the most successful methods among all supplemental anesthesia techniques because the technique allows delivery of local anesthetic solutions directly into the cancellous bone surrounding the affected tooth via special equipment.(21) Several systems for IO injection are available with high cost, including Stabident (Fairfax Dental Inc., Miami, FL), X-Tip (Dentsply International Inc, Tulsa, OK, USA), IntraFlow (Pro-Dex Inc, Santa Ana, CA), and Quick Sleeper 5 devices (DHT, Cholet, France).(10-13,15,49) Advantages of IO injection are immediate onset (< 30 seconds), lack of lip and tongue anesthesia (appreciated by most patients), and smaller doses required.(16,32) Clinical studies reporting success rates of pulpal anesthesia from supplement IO following IANB ranged between 68% to 98% (Table 1).(10-15,49) However, in pediatric patients, this IO supplemental technique also has several disadvantages. First, this method is technically more difficult to perform than the other injection techniques and requires special equipment. Secondly, if leakage occurs during injection, patients may suffer from bitter taste of the anesthetic agents. Third, high occurrence (46-93%) of palpitations is reported when the vasopressor-containing local anesthetic is used.(50) Fourth, the perforators which are used to drill a hole in the bone can accidentally penetrate teeth and may induce post-operative pain.(15,32)

Intraligamentary injection (IL) involves the use of high injection pressure to force the local anesthetic solution through the periodontal ligament in order to reach the pulpal nerve supply by entering the cancellous bone through natural perforations in the socket wall, not by travelling down the length of the ligament. Thus, this injection is considered a form of intraosseous anesthesia.(32) The IL technique, as described by Malamed(16) and Walton and Abbott[51], involves slow administration of a small amount (at least 0.2 ml for each surface of the tooth) of anesthetic solution.[52] The needle is forced to maximum penetration until it is wedged between the tooth and the crestal bone.[16] To ensure that the solution is being forced into the tissue, the operator must feel resistance.[9,16] The most critical factor leading to success of the technique is that the injection is performed against resistance (back pressure).[52] The success of supplemental IL in achieving pulpal anesthesia after failed IANB has been reported to be 48% to 84% (Table 1).[14,53,54] The advantage of IL is its rapid onset (immediate or within 30 seconds), smaller doses of anesthetic agent required, and convenience of administration under rubber dam isolation, thus decreasing contamination during the pulp treatment.[32,52] However, disadvantages of IL include its variable and relatively short pulpal anesthetic duration (approximately 23 minutes)[9,52], peri- and post-operative pain due to high pressure during injection, and possibility of tooth extrusion with premature contact.[32] These complications are often a consequence of injecting too fast and with too much force.[55] Additionally, IL was reported to produce a bacteremia in over 96.6% of children.[56] Nevertheless, this rate could be decreased significantly by a preoperative mouthwash with chlorhexidine for 30 seconds.[55]

Supplemental mandibular buccal infiltration (MBI) is performed by retracting the cheek, pulling the tissue taut, and orientating the needle bevel toward the bone. The needle is gently inserted into the height of the mucobuccal fold over the target tooth.[16] Pulpal anesthesia through MBI can be achieved only if the anesthetic solution is able to spread from the periosteum through the thickness of cortical bone to the apexes of the teeth.[57] Recent systematic review and meta-analysis concluded that using articaine is superior to lidocaine for supplementary MBI after failed IANB during endodontic treatment in mandibular posterior teeth with irreversible pulpitis of adult patients.[58] Previous clinical studies have demonstrated that the success rate of pulpal anesthesia in these teeth by IANB alone (14.8-55.6%) can improve to 65.4-91.7% by combination of IANB with supplementary MBI (Table 1).[4,14,29,59] MBI is a simple technique that does not require any special equipment, while providing a long pulpal anesthetic duration (approximately 40 minutes), and does not cause any serious complications.[4] Furthermore, the onset of pulpal anesthesia in mandibular teeth by immediate MBI was significantly faster than that of IANB alone.[4] However, MBI is contraindicated in infected or acute inflamed areas or areas where the apices of the teeth are covered by dense bone. Moreover, it is not recommended for large area because multiple needle insertions would be required, and larger total volumes of local anesthetic would be administered.[16]

Intraseptal injection (ISA) is performed by delivering anesthetic solution through the interdental papilla (2-3 mm apical to the apex of the papillary triangle) subperiosteally against the interdental septum. Hence, the needle should contact the underlying bone. Under injection pressure, the anesthetic penetrates porosity of the alveolar cortex, diffuses through the medullary bone, and achieves anesthesia of the dental pulp and adjacent gingival tissues. This injection method is effective because the nature of the dental alveolus, which has openings of intrabony vascular channels at the osseous crests of the interdental septum.[26,60,61] It has been recommended that ISA should be delivered at the mesial and distal aspects (0.2-0.4 ml per side in a minimum of 20 seconds) of the tooth to gain complete pulpal anesthesia.[60] Prevailing resistance to the flow/movement of the anesthetic solution and ischemic discoloration of the neighboring soft tissues are the main signs of success of this technique.[26] According to the literature, the reported armamentarium for ISA has included a variety of syringe types, anesthetics administered, and needle lengths and gauges. This may imply that the materials employed are less important for success than the injection technique itself.[60] Success rates of ISA have ranged between 76% and 90% depending on how success was measured in each dental procedure (extraction, restorative procedure, and evaluation with an electric pulp tester), pulpal diagnosis, preoperative pain scale, pain assessment protocol, and location of teeth as shown in Table 1.[62-66] Dianat *et al.*[66] have shown that IANB with supplemental intraseptal and buccal infiltration of 4% articaine with 1:100,000 epinephrine produced a greater success than IANB and MBI or IANB alone in mandibular molars with symptomatic irreversible pulpitis of adult patients. The efficacy of ISA is similar to that of the IO, and they both have higher success than the IL because a greater amount of anesthetic solution can be delivered. However, injection into inflamed gingival tissue should be avoided.[16] The most common complications of ISA were injection site soreness; pain or bleeding when

Table 1: Clinical studies examining success rates of four different supplemental injection techniques (intraosseous, intraligamentary, mandibular buccal infiltration, and intraseptal injections) following inferior alveolar nerve block in mandibular permanent teeth

Authors, Year	Type of study	Patient age (years)	Teeth studied	local anesthetic agent	Success rates
Reisman *et al.*, 1997[10]	Cohort	18-55 (n=48)	Molar and premolar (Irreversible pulpitis)	IANB with 1.8 ml of 2% lidocaine with 1:100,000 epinephrine + IO with 1.8 ml of 3% mepivacaine plain	- IANB: 25% - IANB + 1st IO: 80% - IANB + 2nd IO: 98%
Nusstein *et al.*, 1998[27]	Cohort	19-68 (n=51)	Molar and premolar, both maxillary and mandibular (Irreversible pulpitis)	IANB with 1.8 ml of 2% lidocaine with 1:100,000 epinephrine + IO with 1.8 ml of 2% lidocaine with 1:100,000 epinephrine	- IANB: 19% - IANB + IO: 88%
Prohić *et al.*, 2005[12]	Retrospective	98 teeth	Molars with clinical indication for extraction	Classical mandibular block (no other information provided) + IO with 2% lidocaine with 1:100,000 epinephrine	- IANB: 74.5% - IANB + IO: 94.9%
Fan *et al.*, 2009[53]	Cohort	18-46 (n=57)	First molars (Irreversible pulpitis)	IANB with 1.7 ml of 4% articaine with 1:100,000 epinephrine + IL with 0.4 ml 4% articaine with 1: 100,000 epinephrine	- IANB + IL: 83.33%
Kanaa *et al.*, 2009[4]	RCT	> 18 (n=36)	First molar, first and second premolar, and lateral incisor	**Group I:** IANB with 2.0 ml of 2% lidocaine with 1:80,000 epinephrine + MBI with 2.0 ml of 4% articaine with 1:100,000 epinephrine **Group II:** IANB with 2.0 ml of 2% lidocaine with 1:80,000 epinephrine + dummy injection added	First molar - **Group I:** IANB + MBI: 91.7% - **Group II:** IANB + dummy: 55.6% First and second premolars - **Group I:** IANB + MBI: 88.9% - **Group II:** IANB + dummy: 66.7% Lateral incisor - **Group I:** IANB + MBI: 77.8% - **Group II:** IANB + dummy: 19.4%
Parirokh *et al.*, 2010[29]	RCT	> 18 (n=84)	First molar (Irreversible pulpitis)	**Group I:** IANB with 1.8 ml of 2% lidocaine with 1:80,000 epinephrine **Group II:** IANB with 3.6 ml of 2% lidocaine with 1:80,000 epinephrine **Group III:** IANB with 1.8 ml and buccal infiltration with 1.8 ml of 2% lidocaine with 1:80,000 epinephrine	- **Group I:** IANB 1.8 ml: 14.8% - **Group II:** IANB 3.6 ml: 39.3% - **Group III:** IANB 1.8 ml + MBI 1.8 ml: 65.4%
Kanaa *et al.*, 2012[14]	RCT	> 18 (n=182)	Molar, premolar, canine, and lateral incisor (Irreversible pulpitis)	After failed IANB with 2.0 ml of 2% lidocaine HCl with 1:80,000 epinephrine (positive response to EPT) **Group I:** + repeated IANB with 2.0 ml of 2% lidocaine HCL with 1:80,000 epinephrine **Group II:** + MBI with 2.0 ml of 4% articaine HCL with 1:100,000 epinephrine **Group III:** + IL with 0.18 ml of 2% lidocaine with 1: 80,000 epinephrine **Group IV:** + MBI with 0.2 ml of 2% lidocaine with 1: 80,000 epinephrine + IO with 1.0 ml of 2% lidocaine with 1: 80,000 epinephrine	- **Group I:** IANB + repeated IANB: 32% - **Group II:** IANB + MBI: 84% - **Group III:** IANB + IL: 48% - **Group IV:** IANB + MBI + IO: 68%

Webster *et al.*, 2016[65]	Prospective Cohort	18-65 (n=100)	Premolar or molar (symptomatic irreversible pulpitis)	IANB with 1.8 ml of 2% lidocaine with 1:80,000 epinephrine + ISA with 1.4 ml of 4% articaine with 1:100,000 epinephrine	- IANB + ISA: 29%
Chompu-inwai *et al.*, 2018[67]	Prospective Cohort	6-18 (n=60)	Molar (all pulpal diagnosis)	IANB with 1.7 ml of 4% articaine with 1:100,000 epinephrine **Group I:** + IL with 0.4 ml of 4% articaine with 1:100,000 epinephrine **Group II:** + IL with 0.8 ml of 4% articaine with 1:100,000 epinephrine **Group III:** + IL with 1.2 ml of 4% articaine with 1:100,000 epinephrine	- IANB: 26.7% - **Group I:** IANB + IL 0.4 ml: 63.4% - **Group II:** IANB + IL 0.8 ml: 71.7% - **Group III:** IANB + IL 1.2 ml: 80%
Dianat *et al.*, 2019[66]	RCT	18-65 (n=90)	Molar (symptomatic irreversible pulpitis)	**Group I:** IANB with 1.7 ml of 2% lidocaine with 1:100,000 epinephrine **Group II:** IANB with 1.7 ml of 2% lidocaine with 1:100,000 epinephrine + MBI with 1.7 ml of 4% articaine with 1:100,000 epinephrine **Group III:** IANB with 1.7 ml of 2% lidocaine with 1:100,000 epinephrine + MBI with 1.7 ml of 4% articaine with 1:100,000 epinephrine + ISA with 1.7 ml of 4% articaine with 1:100,000 epinephrine	- **Group I:** IANB: 30.33% - **Group II:** IANB + MBI: 66.66% - **Group III:** IANB + MBI + ISA: 80.00%
Chompu-inwai *et al.*, 2020[68]	Prospective Cohort	6-18 (n=60)	Molar (all pulpal diagnosis)	After IANB with 1.7 ml of 4% articaine with 1:100,000 epinephrine **Group I:** + MBI with 0.425 ml of 4% articaine with 1:100,000 epinephrine **Group II:** + MBI with 0.85 ml of 4% articaine with 1:100,000 epinephrine **Group III:** + MBI with 1.275 ml of 4% articaine with 1:100,000 epinephrine	- IANB: 33.3% - **Group I:** IANB + MBI 0.425 ml: 68.3% - **Group II:** IANB + MBI 0.85 ml: 85% - **Group III:** IANB + MBI 1.275 ml: 95%

RCT: randomized controlled trial; IANB: inferior alveolar nerve block; IO: intraosseous; IL: intraligamentary; MBI: mandibular buccal infiltration; ISA: Intraseptal; +: supplemental injection with

eating, chewing, brushing, or flossing; and gingival bruising or discoloration.[63]

Results from clinical studies in deep carious young permanent mandibular molars

The study of pulpal anesthetic success in deep carious permanent mandibular molars of patients who were younger than 20 years old was reported by Chompu-inwai *et al.* in 2018[67] and in 2020.[68] Both studies[67,68] showed that, the success of preoperative pulpal anesthesia following IANB with 1.7 ml of 4% articaine with 1:100,000 epinephrine in the deep carious permanent mandibular molar diagnosed with all diagnoses (normal pulp, reversible and irreversible pulpitis) were 26.7% and 33.3%, respectively. Moreover, the investigators reported that the success rate of preoperative pulpal anesthesia in teeth, diagnosed with irreversible pulpitis, was as low as 21.4%.[67] Their results supported that the use of IANB alone was not sufficient, especially in young permanent mandibular molars with deep caries. To increase the success rate of preoperative pulpal anesthesia, supplemental injection with ¾ cartridge of 4% articaine with 1:100,000 epinephrine (approximately 1.3 ml) via IL and MBI technique were used in the first[67] and second studies.[68] Success rates of the pre-operative pulpal anesthesia increased significantly to 80% with the supplemental

IL[67] and to 95% with the MBI.[68] However, the success rate of intra-operative pulpal anesthesia in all diagnosis was only 72.9% in supplemental IL[67] and only 66.7% in MBI technique[68], suggesting that these two supplementary techniques cannot provide adequate pulpal anesthesia intraoperatively.

Other than the two studies in Thai children[67,68], pulpal anesthetic success in young permanent teeth was also studied in the French patients who were younger than 16 years old using intra-osseous injection (Quick Sleeper 2 system, DHT, Cholet, France) as a primary injection technique, where the authors found that the success rates were 89.9% for restorative procedures and 92.3% for endodontic procedures.[13] In conclusion, the results from these three studies[13,67,68] suggested that there is a need of highly efficacious technique that can enhance pulpal anesthetic success in the young permanent teeth with deep caries because none of the investigated techniques could reach a 100% success.

Discussion

What are the important steps for clinicians to provide adequate pulpal anesthesia in pediatric patients with deep carious young permanent mandibular molars?

Evidently, it is difficult to achieve successful pulpal anesthesia in deep carious young permanent molars due to their unique characteristics as previously mentioned. Hereby, a summary of important clinical steps for increasing pulpal anesthetic success is discussed.

In young permanent teeth with deep caries, pulpal diagnosis should be acquired after taking a thorough history, oral and radiographic examination. A major, and essential, step of pulpal diagnostic process is the use of pulp sensibility tests which was defined as the ability of nerve fiber in the dental pulp to respond to stimuli. Positive response to sensibility tests indicates that the nerve fibers are functioning and may indirectly determine that the tooth is vital. The most common methods of pulp sensibility tests are cold and electric pulp testing.[69] Importantly, immature permanent teeth contained fewer myelinated axons within the pulp, and thus had incomplete innervation at the pulpo-odontoblast layer[70] and an incomplete formation of the Raschkow's plexus. Consequently, these immature teeth will have a higher threshold to electric pulp testing and can give a higher rate of false negative results.[69] Therefore, unlike in adult patients, EPT should not be used as routine sensibility test in pediatric patients. Cold testing with refrigerant sprays cold test has proved to be more reliable than EPT[71,72] and was used in published clinical studies of vital pulp therapy in young permanent teeth.[46,67,68,73,74]

After pulpal diagnosis, i.e., normal pulp, reversible pulpitis, and irreversible pulpitis, is obtained, clinicians should be aware that there is no 'one shot fit all' that can give predictable pulpal anesthesia, especially in pediatric patients. Young permanent teeth are likely to have more anesthetic failure than adult teeth. The more severe the pulpal diagnosis, the higher failure rate of pulpal anesthesia can be anticipated.[46,67,68] Moreover, even in young permanent teeth with normal pulp, pulpal anesthetic failure after IANB was reported at 62.1%.[67] Consequently, supplemental injection after IANB is advocated prior to any treatment that may provoke pain. Based on physiology and clinical studies, the most promising supplemental injection techniques are in order as IO, ISA followed by IL and MBI, accordingly.[9,16]

Many clinical studies in pediatric patients chose 4% articaine with 1:100,000 epinephrine over other types of anesthetic agents for anesthetizing the young permanent mandibular molars.[46,67,68,73,74] The unique features of articaine, as it contains thiophene ring resulting in superior bone penetrating ability[34], especially the thick mandibular cortical bone, may increase success of pulpal anesthesia. However, it is important to remember that articaine is prepared in a 4 % solution, and maximum dosage should be carefully calculated from the body weight of patients on the day of treatment, that is not exceed 7 mg/kg and maximum total dosage should not exceed 500 mg.[37]

IANB should be administered correctly and carefully.[24] After administration of IANB, soft tissue anesthesia should occur within 4.5 to 6 minutes and pulpal anesthesia should occur within 5 to 19 minutes.[9] The soft tissue anesthesia is the confirming sign that clinician had performed IANB accurately. Nevertheless, clinicians should be aware that profound lip and tongue numbness does not represent profound pulpal anesthesia. Studies in pediatric patients reported that after IANB and confirmation of soft tissue anesthesia, 73.3% of the patients responded positively to refrigerant cold test, implying that pulpal anesthesia was not obtained.[67] Consequently, after IANB and confirmation of soft tissue anesthesia, the selected supplemental injection can be subsequently performed with proper technique and equipment.

Evaluation of pulpal anesthesia by using refrigerant cold test prior to operative treatment is highly recommended. If the tooth responded negative to cold test, the treatment can be initiated. If the tooth responded positive to cold test, waiting for 15 minutes maximum is recommended because this may be the case of delayed onset of pulpal anesthesia after IANB.[21,57,75,76] However, if the tooth still responds positively to cold test after maximum waiting time, additional supplemental injection can be given but should not exceed maximum calculated dosage, or rescheduling the patient for treatment under other adjuncts such as preemptive medication and inhalation sedation may be a viable option.

Although pre-operative pulpal anesthesia was achieved, patients may experience pain intra-operatively. Recently, Murillo-Benítez *et al*. reported that dental anxiety in adult patients who received endodontic treatment is significantly correlated to intra-operative pain. Patients with high levels of anxiety are 2 to 9 times more likely to feel moderate or intense intra-operative pain during root canal treatment.[77] Notably, patients' expectations of pain during treatment was higher than that perceived, and anxiety may play a key role in such an "over-expectancy" of pain.[78] It is important that dentists should be able to assess the child patients' dental anxiety as early as possible, so that they may identify the patients who require special attention and treatment protocol modifications with regards to their fear.[79]

Pain assessment intra-operatively is also important. Previous studies have reported that pediatric patients still experience pain intra-operatively at 27.1% to 33.33%, despite none of these teeth responding to the cold test prior to the treatment.[67,68] Pediatric patients should have a sense of control by giving them opportunity to express their level of pain during treatment. The Wong-Baker Faces Pain Rating Scale (WBFPS) is recommended for pain assessment in children.[80] This scale has adequate psychometric properties, and is easy, quick to use and inexpensive to reproduce. The child patients should be informed that if they experienced any pain during treatment, they could express their feelings to their dentists. In some instances, supplemental injection may be necessary, especially in some invasive procedure, such as pulp excavation. Intrapulpal injection is the last resource for providing pulpal anesthesia to allow completion of pulp treatment. This technique could be done by directly administered the anesthetic solution into the pulp tissue and wait for 30 seconds prior to continuation of treatment.

Conclusions

Solely anesthetizing young permanent teeth by inferior alveolar nerve block is not effective enough to acquire adequate pulpal anesthesia in young permanent mandibular molars with deep caries due to their uniqueness in terms of innervation, vascularization, and composition. To provide a pain free quality care to the vulnerable pediatric patients, not only the fundamental understanding of the routinely used IANB, but also the up-to-date information regarding additional techniques suggested to improve the pulpal anesthetic efficacy is crucial for dental practitioners. To date, there is no single approach that can provide a high success rate of pulpal anesthesia in deep carious young permanent mandibular molars. Theoretically intraosseous and intraseptal supplemental injection following IANB may considerably improve the pulpal anesthetic efficacy. Consequently, a well-controlled randomized controlled trial regarding these supplemental injection techniques is necessary to complete this missing piece of information.

References

1. Wilson S, Montgomery RD. Local anesthesia and oral surgery in children. In: Pinkham JR, Casamassimo PS, Fields HW Jr, McTigue DJ, Nowak AJ, eds. *Pediatric Dentistry: Infancy through Adolescence.* 4th ed. St. Louis: Mosby; 2005: 454-461.
2. Potočnik I, Bajrović F. Failure of inferior alveolar nerve block in endodontics. *Dent Traumatol* 1999; 15(6): 247-251.
3. Hargreaves KM, Keiser K. Local anesthetic failure in endodontics: mechanisms and management. *Endod Topics* 2002; 1(1): 26-39.
4. Kanaa MD, Whitworth JM, Corbett IP, Meechan JG. Articaine buccal infiltration enhances the effectiveness of lidocaine inferior alveolar nerve block. *Int Endod J* 2009; 42(3): 238-246.
5. Foster W, Drum M, Reader A, Beck M. Anesthetic efficacy of buccal and lingual infiltrations of lidocaine following an inferior alveolar nerve block in mandibular posterior teeth. *Anesth prog* 2007; 54(4): 163-169.

6. Nagendrababu V, Pulikkotil SJ, Veettil SK, Teerawattanapong N, Setzer FC. Effect of nonsteroidal anti-inflammatory drug as an oral premedication on the anesthetic success of inferior alveolar nerve block in treatment of irreversible pulpitis: a systematic review with meta-analysis and trial sequential analysis. *J Endod* 2018; 44(6): 914-922. e2.
7. Minea L, Ricci D, Safaei M, Khan M, Dent M, Tjandra S. What is the best approach to achieve anesthesia of a hot tooth? An evidence based report [monograph on the internet]. Department of Community Dentistry, Faculty of Dentistry, University of Toronto, Toronto, Canada; 2009 [cited 2020 Oct 9] Available from https://www.yumpu.com/en/document/view/4577653/what-is-the-best-approach-to-achieve-anesthesia-of-a-hot-tooth-an-.
8. Claffey E, Reader A, Nusstein J, Beck M, Weaver J. Anesthetic efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible pulpitis. *J Endod* 2004; 30(8): 568-571.
9. Reader A, Nusstein J, Drum M. *Successful local anesthesia for restorative dentistry and endodontics*. Hanover, IL: Quintessence Publishing Company; 2011.
10. Reisman D, Reader A, Nist R, Beck M, Weaver J. Anesthetic efficacy of the supplemental intraosseous injection of 3% mepivacaine in irreversible pulpitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997; 84(6): 676-682.
11. Parente SA, Anderson RW, Herman WW, Kimbrough WF, Weller RN. Anesthetic efficacy of the supplemental intraosseous injection for teeth with irreversible pulpitis. *J Endod* 1998; 24(12): 826-828.
12. Prohić S, Sulejmanagić H, Šečić S. The efficacy of supplemental intraosseous anesthesia after insufficient mandibular block. *Bosn J Basic Med Sci* 2005; 5(1): 57-60.
13. Sixou JL, Barbosa-Rogier ME. Efficacy of intraosseous injections of anesthetic in children and adolescents. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008; 106(2): 173-178.
14. Kanaa MD, Whitworth JM, Meechan JG. A prospective randomized trial of different supplementary local anesthetic techniques after failure of inferior alveolar nerve block in patients with irreversible pulpitis in mandibular teeth. *J Endod* 2012; 38(4): 421-425.
15. Peñarrocha-Oltra D, Ata-Ali J, Oltra-Moscardó MJ, Peñarrocha-Diago M, Peñarrocha M. Side effects and complications of intraosseous anesthesia and conventional oral anesthesia. *Med Oral Patol Oral Cir Bucal* 2012; 17(3): e430-434.
16. Malamed SF. *Handbook of local anesthesia.* 6th ed. California: Elsevier Health Sciences; 2019.
17. Jain N, Gupta A. An insight into neurophysiology of pulpal pain: facts and hypotheses. *The Korean J Pain* 2013; 26(4): 347.
18. Bernick S. Effect of aging on the nerve supply to human teeth. *J Dent Res* 1967; 46(4): 694-699.
19. Bernick S, Nedelman C. Effect of aging on the human pulp. *J Endod* 1975; 1(3): 88-94.
20. Tranasi M, Sberna MT, Zizzari V, *et al.* Microarray evaluation of age-related changes in human dental pulp. *J Endod* 2009; 35(9): 1211-1217.
21. Nusstein JM, Reader A, Drum M. Local anesthesia strategies for the patient with a “hot” tooth. *Dent Clin North Am* 2010; 54(2): 237-247.
22. Massler M. Pulpal reactions to dental caries. *Int Dent J* 1967; 17: 441-460.
23. Norton NS. *Netter's head and neck anatomy for dentistry*. 2nd ed. Philadelphia: Elsevier Health Sciences; 2016.
24. Malamed SF. Is the mandibular nerve block passé?. *J Am Dent Assoc* 2011; 142: 3S-7S.
25. Feigal R, Wandera A, Strange M. Bilateral versus unilateral mandibular block anesthesia in a pediatric population. *Pediatr Dent* 2000; 22(6): 453-457.
26. Gazal G, Fareed WM, Zafar MS. Role of intraseptal anesthesia for pain-free dental treatment. *Saudi J Anaesth* 2016; 10(1): 81.
27. Nusstein J, Reader A, Nist R, Beck M, Meyers WJ. Anesthetic efficacy of the supplemental intraosseous injection of 2% lidocaine with 1: 100,000 epinephrine in irreversible pulpitis. *J Endod* 1998; 24(7): 487-491.
28. Aggarwal V, Jain A, Kabi D. Anesthetic efficacy of supplemental buccal and lingual infiltrations of articaine and lidocaine after an inferior alveolar nerve block in patients with irreversible pulpitis. *J Endod* 2009; 35(7): 925-929.
29. Parirokh M, Satvati SA, Sharifi R, *et al.* Efficacy of combining a buccal infiltration with an inferior alveolar nerve block for mandibular molars with irreversible pulpitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010; 109(3): 468-473.
30. Shahi S, Rahimi S, Yavari HR, Ghasemi N, Ahmadi F. Success rate of 3 injection methods with articaine for mandibular first molars with symptomatic irreversible pulpitis: a CONSORT randomized double-blind clinical trial. *J Endod* 2018; 44(10): 1462-1466.
31. Meechan JG. How to overcome failed local anaesthesia. *Br Dent J* 1999; 186(1): 15-20.
32. Meechan JG. Supplementary routes to local anaesthesia. *Int Endod J* 2002; 35(11): 885-896.
33. Poorni S, Veniashok B, Senthilkumar AD, Indira R, Ramachandran S. Anesthetic efficacy of four percent articaine for pulpal anesthesia by using inferior alveolar nerve block and buccal infiltration techniques in patients with irreversible pulpitis: a prospective randomized double-blind clinical trial. *J Endod* 2011; 37(12): 1603-1607.
34. Malamed SF, GAGNON S, Leblanc D. Efficacy of articaine: a new amide local anesthetic. *J Am Dent Assoc* 2000; 131(5): 635-642.

35. Elheeny AAH. Articaine efficacy and safety in young children below the age of four years: An equivalent parallel randomized control trial. *Int J Pediatr Dent* 2020; 30(5): 547-555.
36. Wright GZ, Weinberger SJ, Friedman CS, Plotzke OB. The use of articaine local anesthesia in children under 4 years of age—a retrospective report. *Anesth prog* 1989; 36(6): 268-2671.
37. American Academy of Pediatric Dentistry. Guideline on use of local anesthesia for pediatric dental patients. *Pediatr Dent* 2016; 38(6): 204-210.
38. Abazarpoor R, Parirokh M, Nakhaee N, Abbott PV. A comparison of different volumes of articaine for inferior alveolar nerve block for molar teeth with symptomatic irreversible pulpitis. *J Endod* 2015; 41(9): 1408-1411.
39. Aggarwal V, Singla M, Miglani S, Kohli S, Singh S. Comparative evaluation of 1.8 mL and 3.6 mL of 2% lidocaine with 1: 200,000 epinephrine for inferior alveolar nerve block in patients with irreversible pulpitis: a prospective, randomized single-blind study. *J Endod* 2012; 38(6): 753-756.
40. Tupyota P, Chailertvanitkul P, Laopaiboon M, Ngamjarus C, Abbott PV, Krisanaprakornkit S. Supplementary techniques for pain control during root canal treatment of lower posterior teeth with irreversible pulpitis: A systematic review and meta-analysis. *Aust Endod J* 2018; 44(1): 14-25.
41. Fowler S, Reader A. Is a volume of 3.6 mL better than 1.8 mL for inferior alveolar nerve blocks in patients with symptomatic irreversible pulpitis? *J Endod* 2013; 39(8): 970-2.
42. Nusstein J, Reader A, Beck FM. Anesthetic efficacy of different volumes of lidocaine with epinephrine for inferior alveolar nerve blocks. *Gen Dent* 2002; 50(4): 372-375.
43. Sisk AL. Vasoconstrictors in local anesthesia for dentistry. *Anesth prog* 1992; 39(6): 187.
44. Dagher FB, Yared GM, Machtou P. An evaluation of 2% lidocaine with different concentrations of epinephrine for inferior alveolar nerve block. *J Endod* 1997; 23(3): 178-180.
45. Ehrich DG, Lundgren JP, Dionne RA, Nicoll BK, Hutter JW. Comparison of triazolam, diazepam, and placebo as outpatient oral premedication for endodontic patients. *J Endod* 1997; 23(3): 181-184.
46. Chompu-inwai P, Simprasert S, Chuveera P, Nirunsittirat A, Sastraruji T, Srisuwan T. Effect of nitrous oxide on pulpal anesthesia: a preliminary study. *Anesth prog* 2018; 65(3): 156-161.
47. de Geus JL, Wambier LM, Boing TF, Loguercio AD, Reis A. Effect of ibuprofen on the efficacy of inferior alveolar nerve block in patients with irreversible pulpitis: A meta-analysis. *Aust Endod J* 2019; 45(2): 246-258.
48. American Academy of Pediatric Dentistry. Use of nitrous oxide for pediatric dental patients. *Pediatr Dent* 2018; 40(6): 281-286.
49. Nusstein J, Kennedy S, Reader A, Beck M, Weaver J. Anesthetic efficacy of the supplemental X-tip intraosseous injection in patients with irreversible pulpitis. *J Endod* 2003; 29(11): 724-728.
50. Bigby J, Reader A, Nusstein J, Beck M, Weaver J. Articaine for supplemental intraosseous anesthesia in patients with irreversible pulpitis. *J Endod* 2006; 32(11): 1044-1047.
51. Walton RE, Abbott BJ. Periodontal ligament injection: a clinical evaluation. *J Am Dent Assoc* 1981; 103(4): 571-575.
52. Moore PA, Cuddy MA, Cooke MR, Sokolowski CJ. Periodontal ligament and intraosseous anesthetic injection techniques: alternatives to mandibular nerve blocks. *J Am Dent Assoc* 2011; 142: 13S-18S.
53. Fan S, Chen WL, Pan CB, *et al.* Anesthetic efficacy of inferior alveolar nerve block plus buccal infiltration or periodontal ligament injections with articaine in patients with irreversible pulpitis in the mandibular first molar. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009; 108(5): e89-e93.
54. Zarei M, Ghoddusi J, Sharifi E, Forghani M, Afkhami F, Marouzi P. Comparison of the anaesthetic efficacy of and heart rate changes after periodontal ligament or intraosseous X-Tip injection in mandibular molars: a randomized controlled clinical trial. *Int Endod J* 2012; 45(10): 921-926.
55. Burtscher D, Dalla Torre D. Intraligamentary anesthesia–A brief review of an underestimated anesthetic technique. *Oral Health care* 2019; 4: 1-3.
56. Roberts G, Holzel H, Sury M, Simmons N, Gardner P, Longhurst P. Dental bacteremia in children. *Pediatr Cardiol* 1997; 18(1): 24-27.
57. Salomon E, Mazzoleni S, Sivolella S, *et al.* Age limit for infiltration anaesthesia for the conservative treatment of mandibular first molars. A clinical study on a paediatric population. *Eur J Paediatr Dent* 2012; 13(3): 259-262.
58. Kung J, McDonagh M, Sedgley CM. Does articaine provide an advantage over lidocaine in patients with symptomatic irreversible pulpitis? A systematic review and meta-analysis. *J Endod* 2015; 41(11): 1784-17894.
59. Haase A, Reader AL, Nusstein J, Beck M, Drum M. Comparing anesthetic efficacy of articaine versus lidocaine as a supplemental buccal infiltration of the mandibular first molar after an inferior alveolar nerve block. *J Am Dent Assoc* 2008; 139(9): 1228-1235.
60. Woodmansey K. Intraseptal anesthesia: a review of a relevant injection technique. *Gen Dent* 2005; 53(6): 418-420.
61. Saadoun AP, Malamed S. Intraseptal anesthesia in periodontal surgery. *J Am Dent Assoc* 1985; 111(2): 249-256.
62. Brkovic BM, Savic M, Andric M, Jurisic M, Todorovic L. Intraseptal vs. periodontal ligament anaesthesia for maxillary tooth extraction: quality of local anaesthesia and haemodynamic response. *Clin Oral Investig* 2010; 14(6): 675-681.

63. Bonar T, Nusstein J, Reader A, Drum M, Fowler S, Beck M. Anesthetic efficacy of articaine and lidocaine in a primary intraseptal injection: a prospective, randomized double-blind study. *Anesth prog* 2017; 64(4): 203-211.
64. Biocanin V, Brkovic B, Milicic B, Stojic D. Efficacy and safety of intraseptal and periodontal ligament anesthesia achieved by computer-controlled articaine+ epinephrine delivery: a dose-finding study. *Clin Oral Investig* 2013; 17(2): 525-533.
65. Webster Jr S, Drum M, Reader A, Fowler S, Nusstein J, Beck M. How effective is supplemental intraseptal anesthesia in patients with symptomatic irreversible pulpitis? *J Endod* 2016; 42(10): 1453-1457.
66. Dianat O, Mozayeni MA, Layeghnejad MK, Shojaeian S. The efficacy of supplemental intraseptal and buccal infiltration anesthesia in mandibular molars of patients with symptomatic irreversible pulpitis. *Clin Oral Investig* 2020; 24(3): 1281-1286.
67. Chompu-Inwai P, Sutharaphan T, Nirunsittirat A, Chuveera P, Srisuwan T, Sastraruji T. How effective are inferior alveolar nerve block and supplemental intraligamentary injections in pediatric patients with deep carious permanent mandibular molars? *Pediatr Dent* 2018; 40(7): 437-442.
68. Chompu-inwai P, Bua-on P, Nirunsittirat A, Chuveera P, Louwakul P, Sastraruji T. Pulpal anesthesia in pediatric patients following supplemental mandibular buccal infiltration in vital permanent mandibular molars with deep caries. *Clin Oral Investig* 2020; 24(2): 945-951.
69. Gopikrishna V, Pradeep G, Venkateshbabu N. Assessment of pulp vitality: a review. *Int J Pediatr Dent* 2009; 19(1): 3-15.
70. Johnsen DC, Harshbarger J, Rymer HD. Quantitative assessment of neural development in human premolars. *Anat Rec* 1983; 205(4): 421-429.
71. Fuss Z, Trowbridge H, Bender IB, Rickoff B, Sorin S. Assessment of reliability of electrical and thermal pulp testing agents. *J Endod* 1986; 12(7): 301-305.
72. Fulling HJ, Andreasen JO. Influence of maturation status and tooth type of permanei teeth upon electrometric and thermal pulp testing. *Eur J Oral Sci* 1976; 84(5): 286-290.
73. Parinyaprom N, Nirunsittirat A, Chuveera P, *et al.* Outcomes of direct pulp capping by using either ProRoot Mineral Trioxide Aggregate or Biodentine in permanent teeth with carious pulp exposure in 6-to 18-year-old patients: a randomized controlled trial. *J Endod* 2018; 44(3): 341-348.
74. Uesrichai N, Nirunsittirat A, Chuveera P, Srisuwan T, Sastraruji T, Chompu-inwai P. Partial pulpotomy with two bioactive cements in permanent teeth of 6-to 18-year-old patients with signs and symptoms indicative of irreversible pulpitis: a noninferiority randomized controlled trial. *Int Endod J* 2019; 52(6): 749-759.
75. Matthews R, Drum M, Reader A, Nusstein J, Beck M. Articaine for supplemental buccal mandibular infiltration anesthesia in patients with irreversible pulpitis when the inferior alveolar nerve block fails. *J Endod* 2009; 35(3): 343-346.
76. Robertson D, Nusstein J, Reader A, Beck M, McCartney M. The anesthetic efficacy of articaine in buccal infiltration of mandibular posterior teeth. *J Am Dent Assoc* 2007; 138(8): 1104-1112.
77. Murillo-Benítez M, Martín-González J, Jiménez-Sánchez M, Cabanillas-Balsera D, Velasco-Ortega E, Segura-Egea J. Association between dental anxiety and intraoperative pain during root canal treatment: a cross-sectional study. *Int Endod J* 2020; 53(4): 447-454.
78. Lin CS, Wu SY, Yi CA. Association between anxiety and pain in dental treatment: a systematic review and meta-analysis. J Dent Res 2017; 96(2): 153-162.
79. Buchanan H, Niven N. Validation of a facial image scale to assess child dental anxiety. *Int J Pediatr Dent* 2002; 12(1): 47-52.
80. Tomlinson D, von Baeyer CL, Stinson JN, Sung L. A systematic review of faces scales for the self-report of pain intensity in children. *Pediatrics* 2010; 126(5): e1168-e1198.