Title: Efficacy of four local anesthesia protocols for mandibular first molars with symptomatic irreversible pulpitis. A randomized clinical trial
NCT number: NCT04929522
Date: 5-October- 2021

Subjects and methods

Ethical considerations

This trial was conducted with the approval of the institutional review of board (IRB) of the ethics committee at the Faculty of Dentistry, Ain Shams University, Cairo, Egypt (FDASU-REC772019). The protocol was registered at the clinical trials website (http://www.clinicaltrials.gov, ID: NCT04929522). Subjects were treated in full compliance with the World Medical Association Declaration of Helsinki (2008).

Trial design

This study was designed as a prospective, parallel, triple blinded, and randomized clinical trial with an allocation ratio of 1:1. The trial design is being reported according to the Preferred Reporting Items for Randomized Trials in Endodontics (PRIRATE) 2020 guidelines (Nagendrababu *et al.* 2020).

Sample size calculation

A sample size calculation was performed based on the study by Kanaa *et al.* (2012). This research was based on a type I error of 0.05 and a power of 0.8 and indicated that ideally, a sample size of 36 in each group would be required to detect a 20% difference in the success rate of the test groups. To increase the validity of the study, 40 subjects in each group were considered.

Eligibility criteria

Patients who participated in this trial were allocated from the outpatient emergency clinic of the Endodontic Department, Faculty of Dentistry, Ain Shams University in Cairo, Egypt, between January 1st, 2021, and May 30th, 2021. All the patients were informed about the benefits, risks, and indications for endodontic treatment and possible adverse effects of the proposed interventions. All the included patients signed a written informed consent.

Inclusion criteria

Patients included in the study were healthy males and females (Category: American Society of Anesthesiologists class 1) aged 21-49 years, with no physical disability, facial paresthesia, or psychological problems, presenting with a mandibular first molar, with signs and/or symptoms of symptomatic irreversible pulpitis.

Exclusion criteria

Pregnant women, patients who took analgesics or other medications that would alter the inflammatory response of the pulp or provide analgesia 12- hours pre-operatively, those with known sensitivity to the pharmaceuticals used in this trial were excluded from the study. Also, those with pathological periodontal pockets more than 3 mm depth at the injection site were excluded.

Randomization and blinding

Participants were allocated randomly into four groups with1:1 allocation ratio to ensure random selection by using computer-generated randomization (www.randome.org). The sequence was therefore generated.

Allocation concealment mechanism: The sequentially generated numbers were placed in opaque envelopes until the intervention was conducted. Each participant was asked to select an envelope that determines which group of intervention was assumed.

Implementation: The co-researcher used computer-generated randomization for participants who achieve eligibility criteria. Accordingly, participants were enrolled in either of the groups under study. The participants, the operator who initiated endodontic treatment, monitored the pain and heart rate, and the statistician were blinded to the anesthetic techniques.

Intervention

The diagnosis was confirmed through history reporting spontaneous pain, a moderate to a severe painful response that persists after thermal stimulation, a prolonged response to cold testing with Endo-Ice (1,1,1,2 Tetrafluoroethane; Hygenic Corp, Akron, OH), absence of percussion sensitivity, and the periapical aspect of the tooth in the bidimensional periapical radiograph was normal. Matching vital contralateral teeth were also tested to ensure an accurate diagnosis and to serve as controls. To prevent bias, this diagnostic step was performed by one investigator (AH). In contrast, another investigator (DK) was responsible for administering all anesthetic injections. A third investigator (SS) was responsible for root canal treatment procedures, pain recording and monitoring of heart rate. All investigators have a minimum of 12 years of clinical experience in endodontics.

One hundred and eighty-five patients consecutively visited were assessed for eligibility. Twenty-five patients were excluded for different reasons, and the others 160 (eighty-four female and seventy-six male patients) were allocated to the trial and randomly assigned into four groups (n=40) as follows (Figure 1):

Group 1 (IANB): After determining the injection site and aspiration, 3.6ml of the anesthetic solution was administered using the standard inferior alveolar nerve block (IANB) injection. This was considered the control group.
Group 2 (IANB + IO): A standard IANB was administered using 1 carpule (1.8 ml) of the anesthetic solution followed by another carpule (1.8 ml) using the supplemental intraosseous infusion (IO) injection with the Anesto system (W&H Dentalwerk Bürmoos, Austria). To ensure comfort during the procedure, 0.1ml of the anesthetic solution was infiltrated at the perforation site using the standard syringe. The perforation site was selected near the junction of the attached and unattached gingival tissues, immediately distal to the first molar. Perforation was accomplished by operating the Anesto handpiece at full speed, with constant moderate pressure maintained until the perforator was felt to 'drop' into the cancellous bone. The anesthetic solution was then deposited over 60 seconds. The Anesto handpiece was again retracted and, with the perforator rotating, removed from the injection site. **Group3(IANB+PDL):**AstandardIANBwasadministeredusing1carpule(1.8ml)ofthe anesthetic solution, followed by another carpule (1.8 ml) using the supplemental periodontal ligament (PDL) injection. The needle was wedged with force into the PDL space between the tooth and the alveolar

crest of the bone, at 30-degrees to the long axis of the tooth. The thumb and index fingers of the left hand supported the needle to prevent buckling. The handle of the syringe was squeezed firmly until backpressure was achieved. The anesthetic solution was injected mesially and distally to the treated molar.

Group 4 (IANB + BI): A standard IANB was administered using 1 carpule (1.8 ml) of the anesthetic solution, followed by another carpule (1.8 ml) using the supplemental buccal infiltration at the buccal side of the affected tooth. The anesthetic solution was injected halfway to the mesiodistal width of the clinical crown.

IANB, PDL, and BI injections were performed with a conventional aspirating dental syringe (Patterson Dental Co, Montana, USA) and a 27-G needle at a rate of 1.8 mL/min. The anesthetic solution used for all techniques was Articaine HCL 4% with 1:100,000 adrenaline (Artinibsa, Inibsa, Barcelona, Spain).

Outcome assessment

Anesthesia was confirmed 15 minutes post-injection by the following responses: (1) confirmation of lip numbness, (2) negative response to Endo-Ice, (3) negative response to the maximum output of the electric pulp tester (Parkell, Edgewood, NY, USA). Root canal treatment procedure was later initiated. The patients were asked to rate their pain score once using a verbal rating scale (VRS) from 0 to 3. The pain was scored as follows: Score 0, no pain; Score 1, mild pain; Score 2, moderate pain; or Score 3, severe pain. After rubber dam placement and during caries removal, access preparation, and pulpectomy, the success of the anesthetic technique was determined by VRS. The technique was considered as a 'success' when the patient reported no pain (VRS = 0 or 1) and as a 'failure' otherwise (VRS >1).

Heart rate changes were monitored with a finger pulse oximeter (Medlinket, Shenzhen Med-link Electronics, Shenzhen, China). It was recorded from 2 min before to 5 min after injection, at 30-s intervals.

Statistical analysis

All analyses were undertaken with IBM SPSS Statistics (SPSS 26.0; SPSS Inc., Chicago, IL). The anesthetic success rates were analyzed using the chi-square test. Age differences were analyzed using One Way ANOVA; gender differences were analyzed using the Fischer Exact test, while heart rate changes were analyzed with the Kruskal Wallis test, being non-normally distributed. Statistically significant differences were set at the $P < 0.05$ level.

Results

Every tested contralateral teeth used as control, responded positively to the thermal and electrical pulp testing during the diagnostic phase. All the participants had a positive lip sign (numbness) and a negative response to thermal and electrical testing 15 minutes post-injection of all techniques and 100% of the anaestethic block was considered effective. No supplemental anaesthetic infiltration was administrated. No paresthesia or adverse effects associated with the use of Articaine IANBs were found in this trial.

Table 1. shows the distribution of the participants. There were no differences in the success rate related to the age or gender ($P > 0.05$) so the participants were homogenously distributed among the study groups.

Table 2 represents the anesthetic efficacy of the different tested injection protocols. IANB +IO injection had a statistically higher success rate 92.5% ($p>0.05$), followed by IANB + PDL injection (72.5%), IANB + BI injection (65.0%), respectively with no statistical differences between them ($p<0.05$). In comparison, IANB injection alone had a success rate of (40%) which was statistically the lowest compared to other techniques ($p>0.05$).

An increase in the heart rate was noted in patients who received IANB + IO injection, and this was statistically significant compared to the other injection techniques (p>0.01). Differences in heart rate changes among the other injection technique were non-significant (P < 0.05). Relative risk values are reported in Table 2. The relative risk for all the supplemental anaesthesia techniques was less than 1 indicating that the risk of the outcome (high VRS numbers) was decreased by using supplemental anaesthesia protocol. The actual difference in the observed risk of events between the experimental and IANB (Control) techniques is shown in Table 2. The risk in the intervention group was decreased between 25 and 52% by using supplemental anaesthesia.

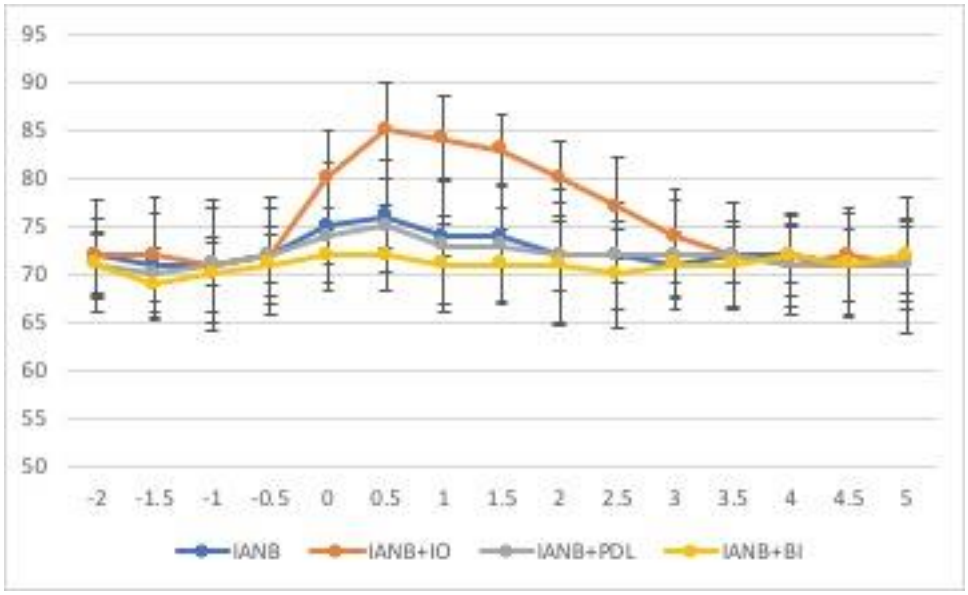
Table 1. Demographic data of the patients for each anaesthetic group.

	IANB n = 40	IANB+IO n = 40	IANB+PDL n = 40	IANB+BI n = 40	P-value
Gender n (%)					
Female	25 (62.5%)	28 (70%)	26 (65%)	23(57.5%)	0.740
Male	15 (37.5%)	12 (30%)	14 (35%)	17 (42.5%)	
Age (Mean ±SD)	29 ± 9.1	31 ± 6.8	33 ± 5.5	29 ± 8.2	0.055

Table 2: Success and failure rates for the four local anaesthesia protocols.

Group	**Success n(%)**	**Failure n(%)**	**OR [95% CI]**	**Relative risk [95% CI]**	**Risk difference**
IANB (control)	16(40%) [a]	24(60%)	---	---	---
IANB +IO	37(92.5%) [c]	3(7.5%)	0.05[0.01-0.21]	0.13[0.04-0.38]	-0.52
IANB + PDL	29(72.5%) [b]	11(27.5%)	0.25[0.10-0.65]	0.46[0.26-0.81]	-0.32
IANB + BI	26(65.0%) [b]	14(35.0%)	0.36[0.15-0.89]	0.58[0.36-0.95]	-0.25

Different superscript letters indicate a statistically significant difference within the same vertical column (p > 0.05)


95
90
85
80
75
70
65
60
55
50
-2
-1.5
-1
-0.5
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
IANB
IANB+IO
IANB+PDL
IANB+BI