Journal of Oral Biology and Craniofacial Research 13 (2023) 218–223

Contents lists available at ScienceDirect

Journal of Oral Biology and Craniofacial Research

journal homepage: www.elsevier.com/locate/jobcr

Comparative evaluation of effect of different premedication agents on efficacy of Articaine: A randomized contol trial

Anjali Sharma [a,*], Rohit Sharma [a], Madhurima Sharma [b], John Johnson Panadan [a], M Abbas Ansari [a], Sasmita Dalai [a,c]

[a] Department of Conservative Dentistry and Endodontics, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, India
[b] Department of Prosthodontics and crown and bridge, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, India
[c] Department of Public Health Detistry, India

ARTICLE INFO

Keywords:
Inferior alveolar nerve block
Root canal treatment
Pain
Pain control
Pain level

ABSTRACT

Type of study: Original Research.
Aims: To comparatively evaluate the effect of different premedication agents on the efficacy of 4% Articaine in teeth with symptomatic irreversible pulpitis.
Materials and methods: The primary objective of our study is to evaluate the effect of premedication agents on efficacy of Articaine as an oral anesthetic. Our secondary objective is to comparatively evaluate the efficacy of Diclofenac patch, Ibuprofen tablet, Paracetamol tablet and Placebo as a premedication agent. Patients with 25–40 years age, no systemic disease, no history of medication for that complaint, with pain on Heft Parker Visual Analog Scale between 55 mm and 170 mm (VAS), no tenderness on percussion, cold test and EPT negative- Positive, giving proper consent, coming to the Department of Conservative Dentistry and Endodontics were allowed to participate. The exclusion criteria include the following- Non-vital teeth, pregnant and lactating women, allergic to Articaine and NSAIDs, active systemic disease, immune-compromised patients, taken analgesics in last 24 h, root fractures, restoration extending to pulp[10] and periapical pathologies (except periodontal ligament widening).
Preoperatively pain was recorded using Heft Parker VAS (Visual Analog Scale). Cold testing, palpation, percussion and EPT were carried out. 40 patients having symptomatic irreversible pulpitis were randomly divided into 4 groups: group 1 Placebo (n = 10), group 2-Diclofenac patch (n = 10), group-3 Ibuprofen tablets (n = 10), group 4-Paracetamol tablets (n = 10). After 1 h of premedication, all patients were administered IANB injection using 4% Articaine (Septanest with adrenaline 1/100000, Septodont, France) containing epinephrine 1:100000. 15 mins after administration of IANB, patients were asked about symptomatic numbness and was tested with Endo frost and EPT and Outcome was recorded. If lip numbness was present, Electric Pulp Testing and Cold Test give negative result then endodontic access opening was performed and pain was recorded using visual analog scale. The study was conducted for a period of 1.5 years.
Results: During the access cavity preparation only 1 subject in the Group III reported pain while in other groups none of the subjects reported pain of any type. When the intergroup comparison was made of intensity of pain 15 min after LA and during access cavity preparation, the difference between the groups was statistically non-significant when analyzed using One Way ANOVA. The intragroup comparison between three time intervals revealed significant reduction in the pain scores from the pre-treatment levels in all the four groups.
Conclusions: The results of the study showed that there is no significant effect of different premedication agents on the efficacy of 4% Articaine in teeth with symptomatic irreversible pulpitis.

* Corresponding author.
E-mail addresses: anjali357512@gmail.com (A. Sharma), rohit.s.0312@gmail.com (R. Sharma), drrohit.dental@tmu.ac.in (M. Sharma), johnpanadan@gmail.com (J.J. Panadan), dr.abbas.ansari@gmail.com (M.A. Ansari), drsasmitad19@gmail.com (S. Dalai).

https://doi.org/10.1016/j.jobcr.2023.01.007
Received 18 November 2022; Received in revised form 18 December 2022; Accepted 6 January 2023
Available online 8 January 2023

Key messages

- Anesthesia is hard to achieve in teeth with symptomatic irreversible pulpitis.
- Cases of symptomatic irreversible pulpitis can be managed by giving premedication 1 h prior to local anesthesia.
- Articaine is found to be more effective than Lidocaine in teeth having symptomatic irreversible pulpitis.

1. Introduction

Pain management is the main challenge for the dentists during root canal treatment.[1] For its control, adequate anesthesia is the prime requirement. Pre anesthetic medications and local anesthesia are used for endodontic emergencies management and for controlling pain.[2]

The most common assistance used in dentistry is nerve block. There are many publications in literature telling about the failure rate and modifications in inferior alveolar nerve block technique. There are chances of inferior alveolar nerve block failure not only because of anatomical variations but also due to technical failures.[3] In previous studies, it has been found that there are higher chances of IANB failure during management of teeth having irreversible pulpitis quoting failure rate of 44%–80%.[4] Higher rate of IANB failures are due to improper needle position, infection, pulpal inflammation, variation in anatomy and psychological factors.[5] Combination of pre anesthetic medications along with local anesthesia can better help in management of pain.[6]

Higher success rates are documented with Articaine compared to Lidocaine as IANB in symptomatic irreversible pulpitis of mandibular molars.[7] Higher diffusion through bony tissues, faster onset of action and its longer duration of anesthesia are main advantages of Articaine over Lidocaine.

NSAIDs administered 1 h before administration of anesthesia has been suggested to improve the success rate of IANB in patients of symptomatic irreversible pulpitis.[8] Also, Articaine has been used as an alternative to lignocaine to improve the effectiveness of IANB in cases of symptomatic irreversible pulpitis.[9]

Articaine has been found to be more effective as local anesthetic agent than the widely used lidocaine but in certain situations it does not prove to be effective like in cases of acute inflammatory conditions.[10] In these situations use of premedication is advised. Hence this study was conceived to test whether premedication, enhances the efficacy of Articaine in mandibular molar in cases of symptomatic irreversible pulpitis. Also, this study comparatively evaluates the efficacy of Diclofenac patch, Ibuprofen tablet, Paracetamol and Placebo as a premedication agent.

2. Materials and Methods

The primary objective of our study is to evaluate the effect of premedication agents on efficacy of Articaine as an oral anesthetic. Our secondary objective is to comparatively evaluate the efficacy of Diclofenac patch, Ibuprofen tablet, Paracetamol tablet and Placebo as a premedication agent. Patients aged 25–40 years having moderate to severe pain in mandibular molars were selected irrespective of sex, race and socioeconomic status. Before Starting the study, Ethical clearance was obtained from institutional review board (TMDCRC/IEC/19-20/CD21). Patients coming to the Department of Conservative Dentistry and Endodontics in Dental College were screened and chosen. Informed consent explaining the rationale of the study was read and signed by the patients selected for the study.

2.1. Inclusion and exclusion criteria

Patients with 25–40 years age, free from any systemic disease, having no history of medication for that complaint, with pain on Heft Parker Visual Analog Scale in relation to mandibular 1st and 2nd molar between (55 mm–170 mm) (VAS), no tenderness on percussion, cold test and EPT- Positive, giving proper consent, coming to the Department of Conservative Dentistry and Endodontics were allowed to participate.

The exclusion criteria include the following- Non-vital teeth, pregnant and lactating women, allergic to Articaine and NSAIDs, active systemic disease, immune-compromised patients, taken analgesics in last 24 h, root fractures, restoration extending to pulp[10] and periapical pathologies (except periodontal ligament widening).

2.2. Outcomes measured

Pretreatment and during access opening type of pain, nature of pain, intensity of pain (using Heft Parker Visual Analog scale), lingering pain, spontaneous pain and nocturnal pain was recorded.

2.3. Sample size calculation

The sample size was calculated using the **nMaster 2.0 software**. The power of the study was taken to be 80% and Confidence Interval (C.I.) of 95% was taken. The sample size calculation was done as per the article by **Wali** et al.[8] The sample size was estimated to be a minimum of 10 per group. The total sample size for the study was estimated to be a minimum of 40 for all groups using these input conditions: power of 0.95 and $p \leq 0.05$.

2.4. Study period

The study was conducted for a period of 1.5 years (11/05/2019–11/12/2020).

2.5. Randomization

2.5.1. Sequence generation

Block randomization was done using computer with a block size of 4. These blocks were generated by a third person who was unaware of the study. The investigator was blinded about allocation and sequencing of the groups. Forty participants were randomly assigned to 4 groups ($n = 10$).

2.5.2. Allocation concealment

Opaque, sequentially numbered, sealed envelopes was used for the allocation concealment that conceals the sequence unless interventions were given. Patients were given study number in a sequence they entered the department by the observer. Depending on the group allotted, treatment was done as given in the procedure.

2.6. Blinding

Double blinding was done. The investigator was knowing regarding the study design as well as pre-medications used in the study but was totally unaware about what premedication was assigned to each sample. Therefore, both the investigator and patient were blinded in the study. A trained person had divided 10 samples of each NSAID into 4 bottles: The bottles were then masked by help of opaque label & then they were randomly assigned-group 1,2,3,4 respectively.

2.7. Procedures

In this study 40 patients with symptomatic irreversible pulpitis were divided randomly in 4 groups. In group 1, patients were administered with a Placebo prior to administration of IANB with 4% Articaine (Septanest with adrenaline 1/100000, Septodont, France). In group 2-Diclofenac patch (Powergesic Patch 100 mg, Jenburkt, India), group-3 Ibuprofen tablets (Ibugesic 400 mg, Cipla, India), group 4-Paracetamol tablets (Dolo 500 mg, Micro Labs Ltd, India) were administered prior to IANB with 4% Articaine.

Cold testing, palpation, percussion, EPT was done. Procedure is given in Fig. 1.

2.8. Treatment

Premedications were given to group 1,2,3,4 1 h before procedure.

After 1 h of premedication, all patients had received IANB injection using 4% Articaine containing epinephrine 1:100000. The solution was deposited using self-aspirating syringe. After 15 min cold test, EPT and lip numbness were checked. If lip numbness was absent, cold test and EPT were positive, block was considered unsuccessful. So, in those cases buccal infiltration should be given. If lip numbness was present, EPT and cold test were negative then access opening was done. If patient was having no pain, block was considered successful.

2.9. Statistical analysis

Data for present study was written in the MS Excel version 2007 and was analyzed using the statistical software (SPSS) version 19.0 V.[8] Descriptive statistics had included standard deviation and mean. The intragroup comparisons among the time intervals were done with the help of Friedmann test to check the differences among the individual time interval. The level of significance for present study was fixed at 5%.

The intergroup differences of the mean scores among independent groups were done with the help of following tests- Chi Square and Kruskal Wallis.

3. Results

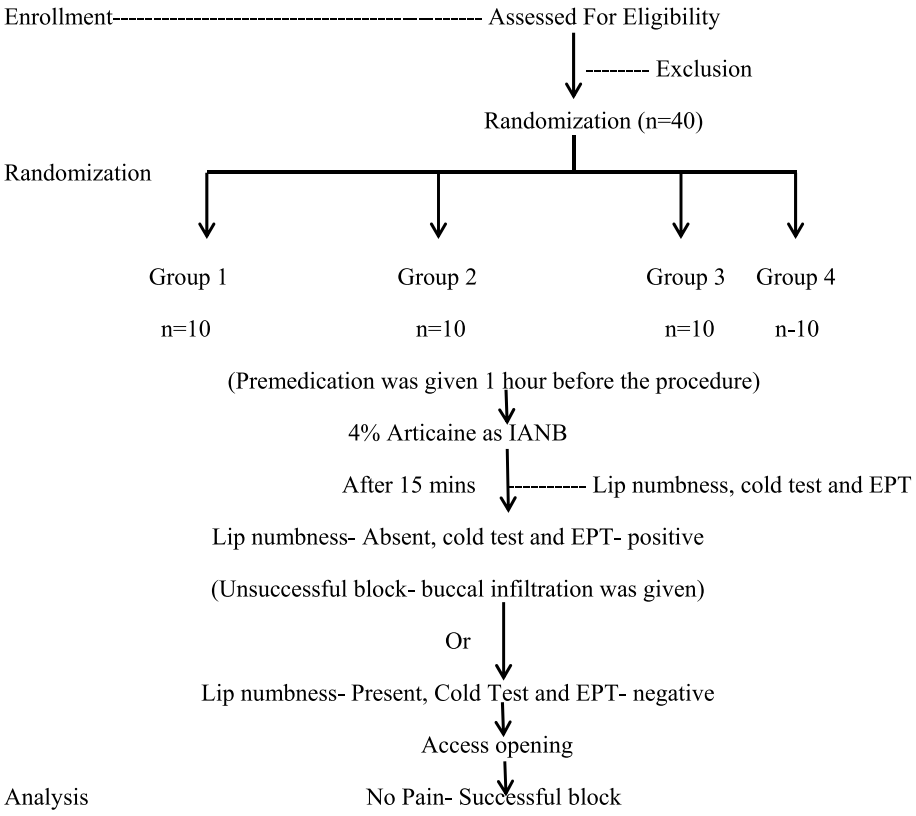
In the present study, forty patients were enrolled and randomized into 4 groups: In group 1, patients were administered with a Placebo prior to administration of IANB with 4% Articaine. In group 2-Diclofenac patch, group-3 Ibuprofen tablets, group 4-Paracetamol tablets were administered prior to IANB with 4% Articaine.

Preoperatively, In Group I, 30% of the subjects was having severe pain and rest 70% were having moderate pain while it was sharp, continuous, lingering and spontaneous in all the patients as seen in Table 1.

15 min after LA injection none of the subjects in all the four Groups reported pain, difficulty in mouth opening and response to electric and cold pulp testing, 100% of the subjects in all the four Groups reported lip numbness and tongue sensation (Tingling) as seen in Table 2.

During the access cavity preparation also only 1 subject in the Group III reported pain while in other Groups none of the subjects reported pain of any type as seen in Table 3.

When the intergroup comparison was made of intensity of pain between the four Groups at pre-treatment, 15 min after LA and during access cavity preparation, the differences among the Groups were statistically non-significant when analyzed using One Way ANOVA as seen in Table 4.



* Patients were checked for eligibility then they were randomly divided into group 1,2,3,4. Premedication was given 1 hour before IANB (Inferior Alveolar Nerve Block). 15 mins later lip numbness; cold test and EPT were carried out. If cold test and EPT were negative and lip numbness was present, access opening was done. If patient felt no pain in access opening, block was considered successful.

Fig. 1. Procedure
*Patients were checked for eligibility then they were randomly divided into group 1,2,3,4. Premedication was given 1 h before IANB (Inferior Alveolar Nerve Block). 15 mins later lip numbness; cold test and EPT were carried out. If cold test and EPT were negative and lip numbness was present, access opening was done. If patient felt no pain in access opening, block was considered successful.

Table 1
Intergroup comparison of pretreatment pain.

		Continuous	Intermittent	Chi Square value	P value
Type of Pain	Group I	10 100%	0 0%	0.000	1.000
	Group II	10 100.0%	0 0%		
	Group III	10 100.0%	0 0%		
	Group IV	10 100.0%	0 0%		
Nature of Pain		Sharp	Throbbing		
	Group I	10 100.0%	0 0%	0.000	1.000
	Group II	10 100.0%	0 0%		
	Group III	10 100.0%	0 0%		
	Group IV	10 100.0%	0 0%		
Intensity of pain		Moderate	Severe		
	Group I	7 70.0%	3 30.0%	9.731	0.021
	Group II	10 100.0%	00 0.0%		
	Group III	10 100.0%	0 .0%		
	Group IV	10 100.0%	0 .0%		
Lingering Pain		Present	Absent		
	Group I	10 100%	0 0%	0.000	1.000
	Group II	10 100.0%	0 0%		
	Group III	10 100.0%	0 0%		
	Group IV	10 100.0%	0 0%		
Spontaneous pain		Present	Absent		
	Group I	10 100%	0 0%	0.000	1.000
	Group II	10 100.0%	0 0%		
	Group III	10 100.0%	0 0%		
	Group IV	10 100.0%	0 0%		
Night Pain		Present	Absent		
	Group I	6 60.0%	4 40.0%	8.627	0.025 (Significant)
	Group II	10 100.0%	0 .0%		
	Group III	8 80.0%	2 20.0%		
	Group IV	10 100.0%	0 .0%		

* Preoperatively, In Group I, 30% of the subjects was having severe pain and rest 70% were having moderate pain while it was sharp, continuous, lingering and spontaneous in all the patients.

Table 2
Intergroup comparison of factors 15 min after LA.

Lip Numbness		Present	Absent	Chi Square values	P values
	Group I	10 100.0%	0 0%		
	Group II	10 100.0%	0 0%		
	Group III	10 100.0%	0 0%	0.000	1.000
	Group IV	10 100.0%	0 0%		
Tongue sensation (Tingling)		Present	Absent		
	Group I	10 100.0%	0 0%	0.000	1.000
	Group II	10 100.0%	0 0%		
	Group III	10 100.0%	0 0%		
	Group IV	10 100.0%	0 0%		
Difficulty in mouth opening		Present	Absent		
	Group I	0 0%	10 100%	0.000	1.000
	Group II	0 0%	10 100%		
	Group III	0 0%	10 100%		
	Group IV	0 0%	10 100%		
Cold Test		Present	Absent		
	Group I	0 0%	10 100%	0.000	1.000
	Group II	0 0%	10 100%		
	Group III	0 0%	10 100%		
	Group IV	0 0%	10 100%		
Electric pulp test		Present	Absent		
	Group I	0 0%	10 100%	0.000	1.000
	Group II	0 0%	10 100%		
	Group III	0 0%	10 100%		
	Group IV	0 0%	10 100%		
Pain		Present	Absent		
	Group I	0 0%	10 100%	0.000	1.000
	Group II	0 0%	10 100%		
	Group III	0 0%	10 100%		
	Group IV	0 0%	10 100%		

* 15 min after LA injection none of the subjects in all the four Groups reported pain, difficulty in mouth opening and response to electric and cold pulp testing, 100% of the subjects in all the four Groups reported lip numbness and tongue sensation (Tingling).

4. Discussion

The perception of pain is very precious for the clinician as well as the patient[12] but the perception of pain varies with different patients having same stimuli of pain. This is because people may express varying emotional response to the same levels of the intensity of the stimulus.[13,14]

Symptoms of odontogenic pain are mostly related to changes in the pulp as well as periapical tissues. In such cases we mostly do endodontic treatment.[14,15] In a study by Francisco S S et al., it was found that the most occurring pulp and periapical pathology requiring emergency treatment were necrosis of pulp (69.3%), acute irreversible pulpitis (25%), acute reversible pulpitis (4.1%) and acute apical periodontitis (30.4%).[2] It was also found that out of 1,481 emergency care patients, 927 patients were having pain of pulpal origin, with diagnosis of irreversible pulpitis in 563 cases, pulp necrosis in 173 cases and reversible pulpitis in 191 cases.[2]

There are many techniques of IANB available in literature but the conventional block technique is the most preferred one. Also, the dentist must know the indications, contraindications, advantages and disadvantages of IANB when implementing anesthesia using this technique.[3]

Table 3
Intergroup comparison of pain during access cavity preparation.

		Present	Absent	Chi Square value	P value
Pain	Group I	0	10	0.101	0.912
		0%	100.0%		(Non-Significant)
	Group II	0	10		
		0%	100.0%		
	Group III	1	09		
		10%	90.0%		
	Group IV	0	10		
		0%	100.0%		

*During access cavity preparation only 1 subject in the Group III reported pain while in other Groups none of the subjects reported pain of any type.

Nowadays, it is said that the acetaminophen is too much COX-2 selective.[2,16] Therefore, it will have reduced side effects. Enzyme COX should be oxidized to make it active as this is the site where NSAIDs bind.[17,18] Acetaminophen stops COX from the pro-inflammatory mediators by reducing COX oxidized form.[3] Therefore, it is effective in reducing inflammation.

Acetaminophen affects cannabinoid endogenous system and thereby relieves inflammatory pain. The AM404 blocks the tetrodotoxin sensitive Na channels of lower micromolar range like L.A (local anesthesia). Therefore, it provides with some analgesic effect. Analgesic effect by the Acetaminophen in the rats may be stopped if we add the CB1.[4]

The COX-2 selective inhibitors generally bind to the COX2 because of reduction in ionic as well as steric crowding in mouth of channel i.e. the site where Arg-120 binds.[19–21]

Cohen studied irreversible pulpitis of posterior teeth of mandible and found 23 out of 61 i.e. 38% patients required the supplemental anesthesia as IANB was not able to give adequate anesthesia. The IANB was having the success rate of 62%.[22]

In the present study, when intergroup comparison was made of intensity of pain between the four groups at pre-treatment, 15 min after LA and during access cavity preparation, the variations among the groups were statistically non-significant when using One Way ANOVA.

Claffey E et al. in their study reported that four percent Articaine (1:1 lakh epinephrine) will not improve success in inferior alveolar block when compared with two percent lidocaine with 1:100,000 epinephrine which is opposite to our study which can be due to smaller number of participants.[7] However, there are numerous studies showing equal anesthetic efficiency of the Lidocaine and the Articaine.[11,23,24,25] Results of the study ensure that Articaine has good anesthetic efficacy in cases of irreversible pulpitis (symptomatic) in the mandibular molars.

In the study, after giving anesthesia and administration of the drug, the pain decreased significantly in all 4 groups 15 min after LA injection. None of the subjects in all the four groups reported pain, difficulty in mouth opening and response to electric and cold pulp testing. 100% of the subjects in all the four groups reported lip numbness. During the access cavity preparation also most of the subjects do not reported pain of any type.

This study demonstrated that 4% Articaine with 1:00000 epinephrine always resulted in adequate lip anesthesia 15 min after the administration of L.A.

Several studies have checked the effects of the pre-medicines on IANB's success in teeth having irreversible pulpitis.[11,26] Modaresi et al.[11] reported less sensitivity in EPT after premedication using 400 mg of the Ibuprofen drug or the combination of 40 mg codeine with 600 mg acetaminophen when checked with placebo group. So, in our study we use premedication before giving local anesthesia to patients requiring root canal treatment. In many studies, the RCT was done and the patient's responses during treatment were observed, that was very similar with the clinical situations.[27–29] So, in our study, RCT was done, and the pain experiences of the patient while doing access cavity preparation were checked and cold pulp sensibility test was carried out.

4.1. Strength

25–40 years old patients were taken of both the genders. Therefore, results of our study can be applied to wide population with symptomatic irreversible pulpitis of mandibular molars. . We had used randomized control clinical trial that has further standardized our article.

4.2. Limitation

The limitation of our study was the small sample size taken. Also different level of preoperative pain can also have some effect on the outcome results.

5. Conclusion

Conclusion of current study is that there is no significant effect of different premedication agents on efficacy of 4% Articaine on teeth having symptomatic irreversible pulpal inflammation. So, premedication given 1 h before local anesthesia do not have any significant effect on pain in cases of symptomatic irreversible pulpitis of mandibular molars.

Source of support

Nil.

Table 4
Intergroup comparison of intensity of pain at three intervals.

	Groups	Mean	*Std. Deviation	Std. Error	P value	Significance
Pain before treatment	Group I	2.100	0.737	0.233	0.679	Non-Significant
	Group II	2.000	0.000	0.001		
	Group III	2.200	0.421	0.133		
	Group IV	2.000	0.000	0.001		
Pain 15 min after LA	Group I	1.000	0.000	0.001	0.404	Non-Significant
	Group II	1.000	0.000	0.001		
	Group III	1.100	0.316	0.100		
	Group IV	1.000	0.000	0.001		
Pain in access opening	Group I	1.000	0.000	0.001	0.404	Non-Significant
	Group II	1.000	0.000	0.001		
	Group III	1.100	0.316	0.100		
	Group IV	1.000	0.000	0.001		

* When the intergroup comparison was made of intensity of pain between the four Groups at pre-treatment, 15 min after LA and during access cavity preparation, the differences among the Groups were statistically non-significant when analyzed using One Way ANOVA.
* Std. - Standard.

Declaration of competing interest

None declared.

References

1 Udoye CI, Jafarzadeh H. Pain during root canal treatment: an investigation of patient modifying factors. *J Contemp Dent Pract*. 2011;12(4):301–304.
2 Francisco SS, Suzuki CLS, Lima APS, Maciel MCR, Murrer RD. Clinical strategies for managing emergency endodontic pain. *RSBO*. 2016;13(3):209–216.
3 Khalil H. A basic review on the inferior alveolar nerve block techniques. *Anesth Essays Res*. 2014;8(1):3–9.
4 Simpson M, Drum M, Nusstein J, Reader A, Beck M. Effect of combination of preoperative ibuprofen/acetaminophen on the success of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis. *JOE*. 2011;37(5):593–597.
5 Jena A, Shashirekha G. Effect of preoperative medications on the efficacy of inferior alveolar nerve block in patients with irreversible pulpitis: a placebo-controlled clinical study. *J Conserv Dent*. 2013;16(2):171–174.
6 Shetkar P, Jadhav GR, Mittal P, et al. Comparative evaluation of effect of preoperative alprazolam and diclofenac potassium on the success of inferior alveolar, Vazirani-Akinosi, and Gow-Gates techniques for teeth with irreversible pulpitis: randomized controlled trial. *J Conserv Dent*. 2016;19(5):390–395.
7 Claffey E, Nusstein J, Beck M, Weaver J. Anesthetic efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible pulpitis. *JOE*. 2004;30(8):568–571.
8 Wali A, Siddiqui TM, Qamar N, Khan R, Jawaid N. Effectiveness of premedication with analgesics vs placebo for success of inferior alveolar nerve block in irreversible pulpitis. *Int J Prosthodont Restor Dent*. 2012;2(1):5–9.
9 Gandhi SA, Das S, Das A, Agnihotri Y, Mohan RV, Subramanian VRD. Anaesthetic efficacy of lidocaine and articaine in inferior alveolar nerve block combined with buccal infiltration in patients with irreversible pulpitis. *J Pharm BioAllied Sci*. 2021;13(Suppl 1):S731–S734.
10 Kazandag MK, Tanalp J, Ersev H. Effect of premedication on the success of inferior alveolar nerve block in patients with irreversible pulpitis: a systematic review of the literature. *BioMed Res Int*. 2019:1–25.
11 Modaresi J, Dianat O, Mozayeni MA, Yazd, Isfahan. The efficacy comparison of ibuprofen, acetaminophen and placebo premedication therapy on the depth of anesthesia during treatment of inflamed teeth. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102:399–403.
12 Eli I, Bar-Tal Y, Fuss Z, Korff E. Effect of biological sex differences on the perception of acute pain stimulation in the dental setting. *Pain Res Manag*. 1996;1(4):201–206.
13 Gracely RH, Kwilosz DM. *The Descriptor Differential Scale: Applying Psychophysical Principles to Clinical Pain Assessment*. vol. 35. 1988:279–288, 3.
14 Price DD, Harkins SW, Baker C. Sensory-affective relationships among different types of clinical and experimental pain. *Pain*. 1987;28(3):297–307.
15 Michaelson LP, Holland RG. Is pulpitis painful? *J Int Endod*. 2002;35(10):829–832.
16 Oscier CD, Milner QJ. Peri-operative use of paracetamol. *Anaesthesia*. 2009;64(1):65–72.
17 Palti DG, Almeida CM, Rodrigues Ade C, Andreo JC, Lima JE. Anesthetic technique for inferior alveolar nerve block: a new approach. *J Appl Oral Sci*. 2011;19(1):11–15.
18 Buch HA. Clinical anatomy of inferior alveolar nerve block anesthesia. *Clin Anat*. 2011;24(4):515–517.
19 Bhattacharya DK, Lecomte M, Rieke CJ, Garavito RM, Smith WL. Involvement of arginine 120, glutamate 524 and tyrosine 355 in the binding of arachidonate and 2-phenylpropionic acid inhibitors to the cyclooxygenase active site of ovine prostglandin endoperoxide H synthase-1. *J Biol Chem*. 1996;271:2179–2184.
20 Mancini JA, Riendeau D, Falgueyret JP, Vickers PJ, Neill GP. Arginine 120 of prostaglandin G/H synthase-1 is required for the inhibition by nonsteroidal anti-inflammatory drugs containing a carboxylic acid moiety. *J Biol Chem*. 1995;270:29372–29377.
21 Kurumbail R, Stevens A, Gierse J, et al. Structural basis for selective inhibition of cyclooxygenase-2 by anti-inflammatory agents. *Nature*. 1996;384:644–648.
22 Cohen HP, Cha BY, Spangberg LS. Endodontic anesthesia in mandibular molars: a clinical study. *J Endod*. 1993;19:370–373.
23 Malamed SF, Gagnon S, Leblanc D. A comparison between articaine HCl and lidocaine HCl in pediatric dental patients. *Pediatr Dent*. 2000;22:307–311.
24 Donaldson D, James-Perdok L, Craig BJ, Derkson GD, Richardson AS. A comparison of Ultracaine DS (articaine HCl) and Citanest forte (prilocaine HCl) in maxillary infiltration and mandibular nerve block. *J Can Dent Assoc*. 1987;53:38–42.
25 Haas DA, Harper DG, Saso MA, Young ER. Lack of differential effect by Ultracaine (articaine) and Citanest (prilocaine) in infiltration anaesthesia. *J Can Dent Assoc*. 1991;57:217–223.
26 Malamed SF. *Handbook of Local Anesthesia*. 5th ed. St Louis, MO: Mosby; 2004:227–254.
27 Ianiro Staci R, Jeansonne Billie G, McNeal Sandre F, Eleazer Paul D. The effect of preoperative acetaminophen and ibuprofen on the success of inferior alveolar nerve block for teeth with irreversible pulpitis. *JOE*. 2007;33(1):11–14.
28 Aggarwal V, Singla M, Kabi D. Comparative evaluation of effect of preoperative oral medication of ibuprofen and ketorolac on anesthetic efficacy of inferior alveolar nerve block with lidocaine in patients with irreversible pulpitis: a prospective, double-blind, randomized clinical trial. *JOE*. 2010;36(3):375–378.
29 Oleson M, Drum M, Nusstein J, Beck Mike. Effect of preoperative ibuprofen on the success of inferior alveolar nerve block in patients with irreversible pulpitis. *J Endod*. 2010;36:379–382.