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Research Article

A Comparative Assessment of the Effect of Pretreatment Dexamethasone Versus Placebo on Post-Endodontic Pain and Success of Inferior Alveolar Nerve Block in Mandibular Molars with Symptomatic Irreversible Pulpitis: A Blinded Randomized Clinical Trial Therapeutic Study

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Abstract

Objective: The aim of the present study was to evaluate the effect of using a preoperative, single oral dose of dexamethasone versus placebo on postoperative pain and success of inferior alveolar nerve block in mandibular molars with symptomatic irreversible pulpitis.

Methods: Thirty two patients were randomly assigned into two equal groups. Patients were asked to record his/her pain level before starting the endodontic treatment using the [Numerical Rating Scale (NRS)]. Half an hour after oral administration of the tablets, the tooth was anaesthetized by inferior alveolar nerve block. They were instructed to make a mark on the point that was representing their pain level and to complete a pain diary at access cavity, pulp extirpation, immediately after treatment completion, 6, 12, 24 and 48 hours after the commencement of treatment.

Results: Results showed that either pre-operatively, at access, at pulp extirpation, post-operatively, after 6, 12, 24 as well as 48 hours; there was no statistically significant difference between the two groups.

Conclusion: Within the limitation of this study, it could be concluded that preoperative administration of a single dose of 0.5 mg dexamethasone did not seem to affect the intensity of postoperative pain or the anesthetic success of inferior alveolar nerve block using 2% mepivacaine with 1:100,000 epinephrine for patients suffering from symptomatic irreversible pulpitis in mandibular molars.

Keywords: Pretreatment Dexamethasone; Placebo; Post-Endodontic Pain; Inferior Alveolar Nerve Block; Mandibular Molars

Introduction

The primary reason people seek endodontic treatment is for the relief of pain caused by bacterial infection and subsequent inflammation [1]. Odontalgia is the most common form of orofacial pain [2]. Although pain is diminished after treatment, there may be residual symptoms because of the effects of inflammation. Endodontic post-treatment pain continues to be a big dilemma facing the dental clinician [3]. Post-treatment endodontic pain has been reported in 25% - 40% of all endodontic patients. Patients usually experience the most severe pain within 12 hours after the operation [4].

For those patients presenting with preoperative pain, it has been reported that up to 80% of this population will continue to report pain after endodontic treatment, with pain levels ranging from mild to severe [5,6].

Pretreatment analgesia can decrease the establishment of central and peripheral sensitization. Thus, it has the potential to reduce postoperative pain and postoperative analgesic intake. Glucocorticosteroids are hormones that are secreted from the adrenal glands and are known to reduce the acute inflammatory response. Dexamethasone is a potent glucocorticoid with anti-inflammatory efficacy twenty five times more than that of hydrocortisone [7].

Teeth with an inflamed pulp rarely achieve profound anesthesia. In the absence of pulpal or periapical pathosis, inferior alveolar nerve block provides clinically adequate anesthesia for restorative dentistry 85 to 90% of the time. However, in cases of irreversible pulpitis, the rate of success is greatly reduced; reportedly as low as 20% [8].

There is a great controversy in the literature on the effect of dexamethasone on postoperative pain and anesthetic efficacy. This is why the following study was conducted.

Materials and Methods

Ethical considerations

The protocol and the informed consent form had been reviewed and approved by the institutional review boards/ethical committees (IRBs/ECs), Faculty of Dentistry, Cairo University, with respect to scientific content and compliance with applicable research and human subject's regulations.

Participants

Sample size

According to Pochapski (2009) and Bidar [32], the sample size was set at 32 patients (16 in each group), based on probability of type I error 0.05 and power at 0.85. The number of the patients was 13 in each group for non-parametric usage and then this number increased to 16 to compensate for possible losses during follow up. The sample size was calculated by PS program.

Eligibility criteria for participants

Thirty two adult patients (20 - 50 years old) with non-contributory medical history diagnosed with symptomatic irreversible pulpitis in one of their mandibular molars were invited to participate in this study. The included patients were able to understand the categorical tool (points) for measurement and to sign the informed consent. The exclusion criteria were patients who had history of necrosis with or without apical pathosis, or those who had extraoral or intraoral sinus tract or fistula or pain in more than one molar or had taken analgesics in the 12 hours preceding the preparation or having complicating systemic disease and patients with allergies or hypersensitivity to or unable to take dexamethasone. Mandibular molars with grade 2 or 3 mobility were also excluded from the study.

Clinical procedures

After confirming the diagnosis clinically and radiographically treatment of the patients was done in a single visit as follows; Patients were asked after the cold test to record his /her pain level before starting the endodontic treatment using the [Numerical Rating Scale (NRS)]. Half an hour after oral administration of the capsules, the tooth was anaesthetized by inferior alveolar nerve block using 1.8 - 3.6 ml (1 - 2 carpoules) of 2% Mepivacaine HCl with 1:100,000 epinephrine local anesthetic solution using a side-loading cartridge syringe and 27-G long needle. After reaching the target area, aspiration was performed, and the solution was injected at a rate of 1 ml/min. Intra-pulpal injection was the supplemental anesthesia of choice when needed. Fifteen minutes after the initial inferior alveolar nerve block, each patient was asked if his/her lip was numb. If complete lip numbness was not reported within 15 minutes, another block was considered. If complete lip numbness was not reported, block was considered unsuccessful, and the patients were excluded from the study.

In patients with a successful inferior alveolar nerve block, an access cavity was performed using a round bur size 3 for molars then an Endo-Z bur used for flaring and de-roofing. The tooth was isolated with rubber dam. The canals were negotiated using stainless steel hand k-files size 10 and 15. Patients were instructed to raise their hand if they felt any pain during the procedure. In case of pain during the treatment, the procedure was stopped, and the patients were asked to rate their pain on the numerical rating scale. Success was defined as no pain or mild pain during endodontic access preparation and instrumentation. Any pain more than no pain or mild pain was considered a failure.

Working length was determined using an electronic apex locator then confirmed with an intraoral periapical radiograph, to be 0.5 - 1 mm shorter than the radiographic apex. Chemo-mechanical preparation performed using Protaper Universal rotary system. The rotary files were used in the sequence of SX (19/0.035), S1 (17/0.02) is designed to prepare coronal one third of the canal, S2 (20/0.04) is designed to enlarge and prepare the middle third of the canal. The finishing files F1 (20/0.07), F2 (25/0.08) and F3 (30/0.09) were used in a pecking motion to the full working length in mesial and distal canals while F4 (40/0.06) was used to the full working length in case of one distal canal.

Irrigation was done using 2.5% NaOCl 3 ml with each 1ml in 60 sec using gauge 27 side vented needle between successive files. It was prepared by adding 10 ml of sterile distilled water to 10 ml of 5.25% sodium hypochlorite solution. After that, each root canal was rinsed with 17% EDTA solution 1 ml for 3 minute then followed by saline as a final rinse [9].

Master cone corresponding to the master apical file determined and confirmed using periapical x-ray, F3 in mesial and distal canals and F4 in case of one distal canal. Canals were then dried with sterile paper points and obturated using gutta-percha points and AD seal sealer with lateral compaction technique. A spreader of suitable size was selected and used to allow space for auxiliary cones, together with a resin-based root canal sealer. The access cavity was sealed using glass ionomer as a temporary restoration. Postoperative radiograph was performed.

Patients were instructed to make a mark on the point that represents their level of perceived pain and to complete a pain diary

at specific intervals immediately after treatment completion, 6, 12, 24 and 48 hours after the commencement of treatment. All subjects were recalled after 2 days to return the pain diary and for a clinical evaluation. Patients were instructed after 48 hours postoperatively to complete the treatment procedures by placing a permanent restoration followed by a full-coverage restoration in fixed prosthodontics clinic of Faculty of Dentistry, Cairo University.

The operator followed-up with the patients over the phone for reminding and ensuring accurate readings. A rescue medication (ibuprofen 200 mg) was prescribed and the patients were instructed to take it only if they experienced severe pain postoperatively. Another rescue medication (Amoxicillin 500 mg) one capsule every 8 hours for 5 days was prescribed if swelling occurred but after contacting the operator. Finally, the patient was instructed to complete the treatment procedures until placing a full-coverage restoration on the treated tooth.

Pain assessment and outcomes

Primary outcome

Post treatment endodontic pain which is assessed immediately after the treatment, 6, 12, 24 and 48 hours postoperatively.

Secondary outcome

Secondary outcome was success of inferior alveolar nerve block after the use of 1-2 carpoules of anesthesia (binary outcome). It was considered successful in case of no pain or mild pain and failure in case of moderate pain or severe pain at access cavity and pulp extirpation.

Statistical analysis

Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). Age data showed normal (parametric) distribution while pain scores showed non-normal (non-parametric) distribution. Data were presented as mean, standard deviation (SD), median and range values. For parametric data, Student's t-test was used to compare between mean age values in the two groups. For non-parametric data: Mann-Whitney U test was used to compare between the two groups. Friedman's test was used to study the changes by time within each group. Dunn's test was used for pair-wise comparisons between the time periods.

Qualitative data were presented as frequencies and percentages. Chi-square test or Fisher's Exact test (when applicable) was used for comparisons regarding qualitative data. Friedman's test was used to study the changes by time within each group.

The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows.

Results

Demographic data

Age, Gender and examined teeth had no statistically significant difference between the two groups.

Pain scores

Intergroup comparisons

Either pre-operatively, at access, at pulp extirpation, post-operatively, after 6, 12, 24 as well as 48 hours; there was no statistically significant difference between the two groups with P-value = 0.83, 0.969, 0.419, 0,535, 0.906, 0.094, 0.734, 0.317) respectively.

Time	Intervention (n = 16)	Control (n = 16)	P-value
Pre-operative			0.830
Mean (SD)	7.4 (1.1)	7.5 (1.2)	
Median (Range)	7.5 (6 - 9)	7.0 (6 - 10)	
Pain level at access			0.969
Mean (SD)	4.9 (2.6)	4.9 (1.9)	
Median (Range)	4.5 (0 - 9)	4.5 (2 - 8)	
Pain level at pulp extirpation			0.419
Mean (SD)	4.5 (2.9)	5.2 (2.6)	
Median (Range)	4 (0 - 10)	6 (0 - 9)	
Pain level post-operatively (Immediate)			0.535
Mean (SD)	1.4 (1.6)	2.1 (2.4)	
Median (Range)	0.5 (0 - 4)	2 (0 - 7)	
Pain level after 6 hours			0.906
Mean (SD)	2.3 (2.3)	2.9 (3.5)	
Median (Range)	2 (0 - 8)	1 (0 - 9)	
Pain level after 12 hours			0.094
Mean (SD)	0.7 (1.7)	2.5 (3.3)	
Median (Range)	0 (0 - 6)	0 (0 - 9)	
Pain level after 24 hours			0.734
Mean (SD)	0.7 (1.7)	0.6 (1.2)	
Median (Range)	0 (0 - 6)	0 (0 - 3)	
Pain level after 48 hours			0.317
Mean (SD)	0.1 (0.5)	0 (0)	
Median (Range)	0 (0 - 2)	0 (0 - 0)	

Table 1: Descriptive statistics and results of Mann-Whitney U test for comparison between pain scores of the two groups.

*: Significant at $P \leq 0.05$.

Figure 1: Pain level at different time intervals.

Intra group comparisons

Group 1: Intervention (Dexamethasone group)

There was a statistically significant difference in pain scores in the intervention group by time (P-value < 0.001).

Group 2: Control (Placebo group)

There was a statistically significant difference in pain scores in control group by time (P-value < 0.001).

Figure 2: Line chart representing change by time in pain scores within each group.

Severity of pain

Inter group comparison

Either pre-operatively, at access, at pulp extirpation, post-operatively, after 6, 12, 24 as well as 48 hours; there was no statistically significant difference between the two groups with P-value = 0.685, 0.090, 0.905, 1, 0.071, 0.466, 0.654, 1 respectively.

Intragroup comparison

Group 1 (Intervention group)

There was a statistically significant change in severity of pain by time in intervention group (P-value < 0.001).

Figure 3: Bar chart representing severity of pain in the two groups.

Figure 4: Bar chart representing severity of pain within intervention group.

Group 2 (Control group)

There was a statistically significant change in severity of pain by time in control group *(*P-value < 0.001).

Figure 5

Intake of analgesics

Only 3 cases in Group 2 (control group) used analgesics; 2 cases after 6 hours and one case after 12 hours.

Discussion

The aim of the present study was to evaluate the effect of using a preoperative, single oral dose of dexamethasone versus placebo on postoperative pain and success of inferior alveolar nerve block in mandibular molars with symptomatic irreversible pulpitis.

Symptomatic irreversible pulpitis cases were selected as a main inclusion criterion as pain of pulpal origin (irreversible pulpitis) is the most feared among patients due to its intensity and severity. The management of such cases was always a challenge to the clinician as they showed significantly lower success rate of inferior alveolar nerve block anesthesia [10] and higher incidence of postoperative pain compared to asymptomatic teeth [11].

In the present study, patients with a non-contributory history who did not take analgesic medication during the preceding 12 hours before treatment, were included to avoid any drug interaction and to prevent any variable from influencing the results of the study [12]. Mandibular multi-rooted teeth were chosen because they are more significantly more susceptible to cause intraoperative pain as well as postoperative pain [13,14].

Single visit root canal treatment was performed as it had been reported that there was no difference in treatment complications or success rates when compared with teeth treated in multiple visits [15]. The advantages of single visit include, less number of appointments, less stress for an anxious patient and no risk of inter-appointment leakage [16]. In addition, a systematic review and meta-analysis showed that patients after single visit endodontic treatment exhibited significantly lower frequency of pain than those who received multiple-visit endodontic treatment [17].

Pretreatment analgesia aims at providing analgesia to patients before endodontic treatment is started. This technique can decrease the establishment of central and peripheral sensitization, which has the potential to reduce postoperative pain, postoperative analgesic intake and increase the success of anesthesia. In this context, drugs that modulate the inflammatory response are steroidal (corticosteroids) and nonsteroidal anti-inflammatory drugs (NSAIDs) [18].

Glucocorticoids (dexamethasone) was used to inhibit the breakdown of arachidonic acid, resulting in inhibition of the formation of inflammatory mediators (prostaglandins) which significantly increased in inflamed pulp [19]. These high levels of prostaglandins can affect Tetrodotoxin (TTX) resistant receptors and decrease nerve responses to anesthetic agents. Tetrodotoxin-resistant (TTX-R) Na(+) channels play a key role in the generation of action potentials in nociceptive dorsal root ganglion (DRG) neurons and are an important target for the proinflammatory mediator prostaglandin E(2), which augments these currents. Therefore, using a medication that can affect the amount of prostaglandins may increase the success rate of anesthesia [20].

It has been stated that a single systemic dose of glucocorticoid, even a large one, is virtually without harmful effects, and a short course of therapy up to one week in the absence of specific contraindications, is unlikely to be harmful [21-23].

In the present study, the lack of efficacy of preoperative dexamethasone on local anesthetic success which is the secondary outcome has been attributed to several factors. Prostaglandins are one of multiple inflammatory mediators found in the dental pulp in patients experiencing irreversible pulpitis. It was found that when inflammatory mediators, e.g. prostaglandins, serotonin, and histamine were combined and then applied to the neuron, the Nav 1.9 isoform was up regulated that carry Tetrodotoxin (TTX) resistant nociceptors resulting in inflammatory mediator-induced hyperalgesia. Therefore, the synergistic action of multiple inflammatory mediators was most likely responsible for the up-regulation of the Nav 1.9 isoform. So, the removal of a single inflammatory mediator might not be enough to overcome the effects of other inflammatory mediators involved [24].

Another possible explanation is the degree and duration of the damage occurring before the prostaglandins was inhibited by dexamethasone. Oleson., *et al*. [25] stated that, although preoperative medication inhibit prostaglandins, inflammatory mediators that already exist because of the presenting irreversible pulpitis along with the action of multiple other inflammatory mediators may explain why the preoperative dexamethasone can be ineffective in patients with symptomatic irreversible pulpitis. So, prostaglandins may be effectively inhibited by dexamethasone premedication, however the inflammatory damage previously created is still present, as well as the concerted action of the other inflammatory mediators. Therefore, in the current study, even if preoperative dexamethasone inhibited prostaglandin production, the previous damage, besides the action of multiple other inflammatory mediators, might explain why it did not improve the success rate of inferior alveolar nerve block.

After 6 hours, for both the drug and the placebo, there was a statistically significant increase in pain scores compared to postoperative pain score. The result agrees with the findings of Wang., *et al.* [26] and Attar., *et al.* [27] who registered the maximum postoperative pain level six hours after the treatment, after the disappearance of the anesthetic effect.

Pain scores after 12, 24 and 48 hours for both the drug and the placebo showed statistically significantly lower values compared to pain scores pre-operatively, at access, at pulp extirpation and at 6 hours. This may be due to the resolution of inflammation resulting from pulp extirpation and instrumentation with time and reduction of inflammatory mediators in the periapical area [28].

In the present study, there was no statistically significant difference on post-operative pain which is the primary outcome; it may be related to the potential of preoperative pain due to preexisting pulpal pathosis to significantly confound the results of preemptive analgesic clinical trials in emergent endodontic patients. Preexisting pulpal and/or periradicular pain, resulting from acute inflammation of the associated anatomic structures, can cause neuroplastic changes in the dorsal horn [27]. In animal models, the peripheral nociceptive barrage from inflamed pulps has been shown to be sufficient enough to cause a 5-fold increase in dorsal horn neuron discharge rate and up to a 3-fold increase in the size of the receptive field of A-delta fibers [29].

Our findings are in agreement with Jorge-araújo., *et al*. [30] who stated that there was no significant difference among groups considering the pain intensity measured with a numerical rating scale (4, 8, 12, 24, and 48h). It might be related to the consequence of the time required for changes in gene expression and protein synthesis; most effects of corticosteroids are not immediate. This fact is of clinical significance, because a delay generally is seen before the beneficial effects of corticosteroid therapy become evident. Also dexamethasone needs patient cooperation to take 1 hour before the dental appointment as dexamethasone has a plasma half-life approximately 1.5 - 4 hours and duration of action of 36 - 54 hours so it must be administered before the infliction of tissue damage, not during or after endodontic treatment. This can be overcomed by early administration of the drug or using other routes of administration as injection or intracanal medication.

In contrast with our results, Sharma., *et al*. [31] and Bidar., *et al*. [32] who demonstrated significant reduction with preoperative administration of dexamethasone than placebo. It could be due to the glucocorticoids inhibition of the breakdown of arachidonic acid which results in inhibition of the formation of inflammatory mediators while the placebo group did not possess any of the anti-inflammatory/analgesic characteristic as those of dexamethasone, and is not expected to influence the inflammatory cascade.

Conclusion

Within the limitation of this study, it could be concluded that preoperative administration of a single dose of 0.5 mg dexamethasone did not seem to affect the intensity of postoperative pain or the anesthetic success of inferior alveolar nerve block using 2% mepivacaine with 1:100,000 epinephrine for patients suffering from symptomatic irreversible pulpitis in mandibular molars.

Bibliography

1. Smith E. "NSAIDS for managing post-operative endodontic pain in patients who present with pre-operative pain: A systematic review and meta-analysis (2016).
2. Keiser K and Hargreaves KM. "Building effective strategies for the management of endodontic pain". *Endodcopy Top* 3 (2002): 93-105.
3. Mohan S., *et al.* "Management of Post Treatment Endodontic Pain". *Journal of Dental Sciences and Oral Rehabilitation* (2013): 8-9.
4. Seymour RA., *et al.* "Post-operative dental pain and analgesic efficacy". *British Journal of Oral Surgery* 21 (1983): 290-297.
5. Mohammadi Z., *et al.* "Pharmacological strategies to control post-operative endodontic pain". *Journal of Dental Research* 4.2 (2008): 61-68.
6. Liesinger A., *et al.* "Effect of variable doses of dexamethasone on posttreatment endodontic pain". *Journal of Endodontics* 19.1 (1993): 35-39.
7. Kissin I. "Preemptive Analgesia". *Journal of Anesthesiology* 93 (2000):1138-1143.
8. Ianiro SR., *et al.* "The Effect of Preoperative Acetaminophen or a Combination of Acetaminophen and Ibuprofen on the Success of Inferior Alveolar Nerve Block for Teeth with Irreversible Pulpitis". *Journal of Endodontics* 33.1 (2007): 11-14.
9. Renata CRodrigues and M Henrique A. "Infection control in retreatment cases: *In Vivo* Antibacterial effects of 2 instrumentation systems". *Journal of Endodontics* 4 (2015): 1600-1605.
10. Shantiaee Y., *et al.* "Efficacy of preoperative ibuprofen and meloxicam on the success rate of inferior alveolar nerve block for teeth with irreversible pulpitis". *International Dental Journal* 67 (2017): 85-90.
11. El Mubarak AHH., *et al.* "Postoperative pain in multiple-visit and single-visit root canal treatment". *Journal of Endodontics* 36 (2018): 36-39.
12. Ramamoorthi S., *et al.* "Comparative evaluation of postoperative pain after using endodontic needle and Endo Activator during root canal irrigation: A randomised controlled trial". *Australian Endodontic Journal* (2015): 1-10.

13. Siqueira JF., *et al.* "Chemomechanical reduction of the bacterial population in the root canal after instrumentation and Irrigation with 1%, 2.5%, and 5.25% Sodium Hypochlorite". *Journal of Endodontics* 26 (2000): 331-334.

14. Ali S., *et al.* "Prevalence of and factors affecting post-obturation pain following single visit root canal treatment in Indian population: A prospective, randomized clinical trial". *Journal of Contemporary Clinical Dentistry* 3 (2012): 459.

15. Yoldas O., *et al.* "Postoperative pain after endodontic retreatment : Single- versus two-visit treatment". *Journal of Endodontics* 98 (2004): 483-487.

16. Shibu TM. "Post operative pain in endodontics: A systemic review". *Journal of Dentistry and Oral Hygiene* 7 (2015): 130-137.

17. Su Y., *et al.* "Healing rate and post-obturation pain of single-versus multiple-visit endodontic treatment for infected root canals : A systematic review". *Journal of Endodontics* 372 (2011): 125-132.

18. Praveen R., *et al.* "Comparative Evaluation of premedication with ketorolac and prednisolone on postendodontic pain: A Double-blind randomized controlled trial". *Journal of Endodontics* 43 (2017): 667-673.

19. Remmers T., *et al.* "The Efficacy of intraflow intraosseous injection as a primary anesthesia technique". *Journal of Endodontics* 34 (2008): 280-283.

20. Parirokh M and Abbott PV. "Various strategies for pain-free root canal treatment". *Iranian Endodontic Journal* 9 (2013): 1-14.

21. Marshall JG. "Consideration of steroids for endodontic pain". *Endodontic Topics* 3 (2002): 41-51.

22. Holte K and Kehlet H. "Perioperative single-dose glucocorticoid administration: Pathophysiologic effects and clinical implications". *Journal of the American College of Surgeons* 195 (2002): 694-712.

23. Iranmanesh F., *et al.* "Effect of Corticosteroids on Pain Relief Following Root Canal Treatment : A Systematic Review". *Iranian Endodontic Journal* 12 (2017): 123-130.

24. Maingret F., *et al.* "Inflammatory Mediators Increase Nav1.9 Current and Excitability in Nociceptors through a Coincident Detection Mechanism". *The Journal of General Physiology* 131 (2008): 211-225.

25. Oleson M., *et al.* "Effect of Preoperative Ibuprofen on the Success of the Inferior Alveolar Nerve Block in Patients with Irreversible Pulpitis". *Journal of Endodontics* 36 (2010): 379-382.

26. Wang C., *et al.* "Comparison of post-obturation pain experience following one-visit and two-visit root canal treatment on teeth with vital pulps : a randomized controlled trial". *International Endodontic Journal* 43 (2010): 692-697.

27. Attar S., *et al.* "Evaluation of Pretreatment Analgesia and Endodontic Treatment for Postoperative Endodontic Pain". *Journal of Endodontics* 34 (2008): 652-655.

28. Figini L., *et al.* "Single Versus Multiple Visits for Endodontic Treatment of Permanent Teeth: A Cochrane Systematic Review". *Journal of Endodontics* 34 (2008): 1041-1047.

29. Chiang CY., *et al.* "NMDA Receptor Mechanisms Contribute to Neuroplasticity Induced in Caudalis Nociceptive Neurons by Tooth Pulp Stimulation". *Journal of Neurophysiology* 80 (1998): 2621-2631.

30. Jorge-araújo ACA and Bortoluzzi MC. "Effect of Premedication with anti-inflammatory drugs on post-endodontic pain : A randomized Clinical Trial". *Brazilian Dental Journal* 29 (2018): 254-260.

31. Sharma N., *et al.* "Effect of preoperative administration of steroid with different routes on post endodontic pain : A randomized placebo controlled clinical trial". *The Journal of Endodontics* 27 (2015): 107-112.

32. Bidar M., *et al.* "Comparison of Effect of Oral Premedication with Ibuprofen or Dexamethasone on Anesthetic Efficacy of Inferior Alveolar Nerve Block in Patients with Irreversible Pulpitis: A Prospective, Randomized, Controlled, Double-blind Study". *The Bulletin of Tokyo Dental College Journal* 58 (2017): 231-236.