ORIGINAL ARTICLE

Turk Endod J 2021;6(1):7–13
doi: 10.14744/TEJ.2021.42714

Evaluation of post-obturation pain in single-visit endodontic treatment after pre-medication with oral anti-inflammatory and antibiotics

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Purpose: The objective of the study was to evaluate post-obturation pain on the 1st, 3rd, and 7th days on single-visit endodontic treatment after taking antibiotics and anti-inflammatory drugs.

Methods: Permanent molars were managed with single-visit root canal treatment after pre-medication in 80 patients. Patients were randomly assigned to four groups (n = 20); Group-1; amoxicillin (500 mg) + clavulanic acid (125 mg), Group-2; aceclofenac (100 mg) + paracetamol (325 mg); Group-3; anti-inflammatory and antibiotics; and Group-4; without pre-medication. Medications were administered 1 h before treatment. Patients filled a visual analog scale form to rate their pain at 1st, 3rd, and 7th days. Kruskal–Wallis test was used to obtain mean rank and the level of significance was set at 0.05.

Results: The mean rank on the 1st and 3rd post-operative days for each group, was; Group-1, 51.78 and 55.70, Group-2, 32.60 and 29.95, Group-3, 17.65 and 19.25, and Group-4, 59.98 and 57.10, respectively. Mean rank value was least in the Group-3, followed by Group-2, Group-1 and Group-4. No statistically significant difference in the mean rank was found on the 7th day.

Conclusion: Pre-medication with antibiotic and anti-inflammatory drugs was the most effective in reducing post-operative pain followed by anti-inflammatory alone and least when antibiotic was given.

Keywords: Post-obturation pain, pre-medication, single-visit root canal treatment, visual analog scale.

Introduction

Pain management during and after root canal treatment is an important aspect of endodontic practice. The incidence and severity of post-operative pain are associated with specific dental treatments; the highest of which is root canal therapy (1). The prevalence of pain after root canal treatment has been reported to be 3–58% of patients (2). There are several factors associated with pain after root canal treatment. Pre-operative factors such as acute exacerbation of chronic lesion, non-vital tooth, unusual root canal anatomy, periapical cysts, and abscess are responsible for flare-ups and pain (3,4). Intraoperative factors such as apical extrusion of filling materials and instruments, irritating canal medications, and irrigation procedural complications, missed canals, and working without rubber dam isolation can increase the pain occcurence (5,6). Post-operative factors such as leaky temporary material and the effect of occlusion can also give rise to pain (7). Various investigations have been performed to evaluate the efficacy of various

Cite this article as: Pathak I, Samant PS, Chauhan R. Evaluation of post-obturation pain in single-visit endodontic treatment after pre-medication with oral anti-inflammatory and antibiotics. Turk Endod J 2021;6:7-13.

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Submitted: August 01, 2020 Accepted: April 26, 2021

pain management strategies and the influence of various techniques, medicaments, irrigants, analgesics, anesthetic agents, and post-operative factors on the amount of post-operative pain after root canal treatment (1). Based on the evidences, several strategies have been described for pain management after root canal treatment such as the administration of long-acting anesthesia and pre-medication with analgesics and antibiotics (1,2,8). Amoxicillin is a moderate spectrum, bacteriolytic, β-lactam antibiotic that represents a synthetic improvement on the original penicillin molecule. It is readily absorbed, resists damage from stomach acids, and has a much broader spectrum against gram-negative bacteria compared to penicillin, but amoxicillin is susceptible to degradation by β-lactamase producing bacteria, so its use is recommended with clavulanic acid. It is a broad-spectrum antibiotic (9).

Nonsteroidal anti-inflammatory drugs (NSAIDs) can reduce inflammation at different levels in the inflammatory process. The mechanism of the action of most NSAIDs occurs by acetylating the cyclooxygenase enzyme, which, in turn, inhibits the synthesis of prostaglandins. Thus, NSAIDs non-specifically prevent both the COX-1 and COX-2 isoenzymes from forming arachidonic acid metabolites. Because there is induction of COX-2 at sites of inflammation, it is believed that the therapeutic properties of NSAIDs account primarily for the inhibition of COX-2. Aceclofenac is an arylacetic acid derivative. It is an analgesic, anti-pyretic, and anti-inflammatory agent. Aceclofenac exerts its analgesic and anti-inflammatory effects by selectively inhibiting the COX-2 (8).

The aim of this study was to use anti-inflammatory drugs and antibiotics as a pre-medication to understand the effects on post-obturation pain after single-visit root canal therapy.

Materials and Methods

The study was conducted in the postgraduate clinics of the department of conservative dentistry and endodontics in our institute. The study was conducted after taking an ethical clearance from Institutional Human and Ethical Committee. The study protocol was approved by the Joint Research and Ethics Committee of Health University. A total of 80 patients were selected and treated in this study, which was carried out over a period of nearly 1 year. Maxillary and mandibular molars were treated with single-visit root canal treatment with pre-medication. Inclusion criteria were healthy patients with a mandibular or maxillary molar tooth with acute irreversible pulpitis and normal periapical radiographic appearance without sensitivity to percussion and ages between 18 and 59 years. Exclusion criteria were patients who had taken antibiotics and anti-inflammatory drugs within the past 12 h, systemic diseases that require prophylactic antibiotics, pregnancy and lactating patients, teeth with periapical radiolucency, presence of acute endodontic or periodontal abscess, diabetic patients, weeping canal, and third molars.

For diagnosis of pulpal status, clinical history, clinical examination, electric pulp test, and digital radiographs were evaluated. Patients with a history of pain or trauma in relation to the concerned tooth, deep carious lesion involving the pulp, absence of tenderness, electric pulp test eliciting delayed response and radiographically intact lamina dura, normal or slightly widened periodontal space, and absence of periapical radiolucency were selected for single-visit endodontic treatment.

The treatment plan and the purpose of the study were explained to the patient, and a signed consent form was obtained. Patients were randomly assigned to three experimental and one control group. Each group had a sample size of 20 (n = 20). Patients were asked to place a mark anywhere on the horizontal visual analog scale (VAS), depending on the intensity of pain, and were instructed to use the verbal descriptors as a guide. Values assigned on VAS were between 0 and 10 cm (10,11). Patients marked their pre-operative pain level in the presence of the clinician to ensure that they understood the instructions. Patients were given the VAS form, along with a stamped, addressed envelope for return of the form after the 7th day of the treatment. VAS forms were coded as Group-1, Group-2, Group-3, and Group-4 for identification. Patients were instructed to complete the VAS form to rate their pain at the 1st day, 3rd day, and 7th day after the root canal treatment (12).

The following criteria were outlined for the patients to rate their pain (1,2):

0: No pain

1–3: Mild pain

4–6: Moderate pain

7–9: Severe pain

Patients were randomly divided into four groups based on the type of pre-operative medication given, n = 20.

Group-1: Patients received an antibiotic, that is, amoxicillin 500 mg and clavulanic acid 125 mg (Tab. Augmentin Duo, GlaxoSmithKline, Brentford, UK);

Group-2: Patients received an anti-inflammatory drug , that is, 100 mg aceclofenac and 500 mg of paracetamol (Tab. Aceclo-P, Aristo Pharma Ltd., Mumbai, India);

Group-3: Patients received both anti-inflammatory drugs and antibiotics;

Group-4: Control group (without pre-medication).

Medications were administered 1 h before the single-visit root canal treatment (8,9,13,14).

Clinical Methods

All the patients were treated for approximately 3 h, to provide sufficient time for single-visit root canal procedure (15). Local anesthetic was administered using 2% lignocaine with 1:200,000 adrenaline and teeth were isolated from the rest of the oral cavity with a rubber dam to provide safe and aseptic operating field. Access cavity preparations were done using Endo-access burs (Dentsply Maillefer, Ballaigues, Switzerland) and refined with Endo-z bur (Dentsply Maillefer, Ballaigues, Switzerland) using a high-speed air rotor handpiece. Working length of each canal was determined with electronic apex locator (Root ZX, J Morita, Tokyo, Japan) and confirmed radiographically with size #10 and #15 stainless steel K-file (Dentsply Maillefer, Ballaigues, Switzerland). Working length was kept short of the apex by 0.5–1 mm. Canals were then irrigated with 5.25% sodium hypochlorite, using 10 ml irrigation syringe with 24 gauge side vented needle (Maxi-i-probe, Dentsply, Rinn, Elgin, IL). Canal instrumentation was performed with ProTaper Gold NiTi system (Dentsply Maillefer, Ballaigues, Switzerland) according to the manufacturer's instructions. About 17% EDTA (Aveuprep, Dental Avenue, Mumbai, India) was used as a lubricant during instrumentation. The final irrigation was done with normal saline, using 10 ml irrigation syringe with 24 gauge side-vented needle (Maxi-i-probe, Dentsply, Rinn, Elgin, IL). Canals were dried with paper points and obturated with gutta-percha points (Meta Biomed Co., Chungcheongbuk-do, Korea) and AH Plus sealer (Dentsply, Maillefer, Ballaigues, Switzerland) using cold lateral compaction technique. Access cavity was then sealed with glass ionomer cement (Ionostar Plus, Voco, GmbH, Cuxhaven, Germany) followed by occlusal adjustment. Post-operative radiograph was taken after complete root canal treatment. Analgesics were prescribed in case of severe intolerable pain. Patients were instructed to complete a pain diary on VAS at the 1st, 3rd, and 7th day intervals after root canal treatment (13,16).

Results

Descriptive statistics were performed by calculating mean, standard deviation, frequencies, and percentages for the continuous variables (Table 1). Categorical variables were summarized as frequencies and percentages. The software used for the statistical analysis was SPSS (Statistical Package for the Social Sciences) version 21.0 and Epi-info version 3.0.

Table 1. The above table showed the mean, standard deviation along with the minimum and maximum scores of the VAS for all of the subjects in the study on the 1st, 3rd, and 7th day of post-obturation

	Descriptive statistics for all the subjects on post-obturation day 1, day 3, and day 7				
	n	Mean	Std. deviation	Minimum	Maximum
Day 1	80	5.4875	1.28274	2.00	8.00
Day 3	80	1.8000	1.31592	0.00	4.00
Day 7	80	0.0500	0.31422	0.00	2.00

VAS: Visual analog scale.

Table 2. The mean ranks of the subjects in the four groups for all of the subjects in the study on the 1st, 3rd, and 7th day of post-obturation

Kruskal–Wallis test showing the mean ranks for the four groups on post-obturation day 1, day 3, and day 7		
Groups	**n**	**Mean mark**
Day 1		
Pre-medication with antibiotic drugs	20	51.78
Pre-medication with anti-inflammatory drugs	20	32.60
Pre-medication with both anti-inflammatory and antibiotic drugs	20	17.65
Without pre-medication	20	59.98
Total	80	
Day 3		
Pre-medication with antibiotic drugs	20	55.7
Pre-medication with anti-inflammatory drugs	20	29.95
Pre-medication with both anti-inflammatory and antibiotic drugs	20	19.25
Without pre-medication	20	57.1
Total	80	
Day 7		
Pre-medication with antibiotic drugs	20	39.5
Pre-medication with anti-inflammatory drugs	20	39.5
Pre-medication with both anti-inflammatory and antibiotic drugs	20	39.5
Without pre-medication	20	43.5
Total	80	

All data were recorded and analyzed using Kruskal–Wallis test which compared the mean severity of pain in the four groups at different time points (Table 2). Table 3 shows that there was a highly significant difference ($p < .05$) between the four groups at the 1st post-obturation day. Similarly, there was a highly significant difference ($p < .05$) between the four groups on the 3rd day of post-obturation. However, there was no significant difference ($p > .05$) at the 7th day of post-obturation among the four groups. Table 4 shows the distribution of subjects in the four groups above and below the median values of the

Table 3. Test statistics[a,b] showing p value for Kruskal–Wallis H comparing the four groups on post-obturation day 1, day 3, and day 7

	Day 1	Day 3	Day 7
Kruskal–Wallis H	42.704	43.799	6.077
Df	3	3	3
Asymp. sig.	.000	.000	.108

P< .05. [a]Kruskal–Wallis test. [b]Grouping variable: Groups.

Table 4. Frequency distribution of the subjects in the four groups based on the scores of the VAS above and below the median on post-obturation day 1, day 3, and day 7

	Group 1	Group II	Group III	Group IV
Day 1				
>Median	17	6	0	17
≤Median	3	14	20	3
Day 3				
>Median	13	1	0	12
≤Median	7	19	20	8
Day 7				
>Median	0	0	0	2
≤Median	20	20	20	18

VAS: Visual analog scale.

score obtained for the particular group on the 1st day, 3rd day, and 7th day of post-operative pain.

Pre-medication with both anti-inflammatory and antibiotic drugs (Group III) has the least mean rank, it has the best result among the four groups on the 1st day and 3rd day of post-obturation, followed by pre-medication with anti-inflammatory drugs (Group II), followed by pre-medication with antibiotic drugs (Group I) and finally the group without pre-medication (Group IV). Since on the 7th day, Groups I, II, and III had the same mean ranks, it implies that they all have the same effect on the 7th day of post-obturation. However, since Group IV had a mean rank of 43.50 (Table 2), it implies that it has the least ranks among all of the four groups, or the least effect on the 7th day of post-obturation.

Discussion

Pain is the most common reason for physical consultation in most dental clinics. It is a major symptom in many medical conditions and can interfere with the person's quality of life and general functioning. A recent survey conducted by the American Association of Endodontists suggests that 67% of Americans declared the "fear of pain" as their primary concern regarding root canal procedure (17). Endodontic pain arises as a result of the pulp tissue response to any causative agents like dental caries or other irritants like trauma or restorative procedures.

Post-obturation pain is considered to be related with several factors, including pre-operative pain, infection, retreatment, intracanal medications, and physical and chemical damage to periapical tissues. Incidence of post-obturation pain can be explained as, in the case of peripheral sensitization, where a bacterial endotoxin may also trigger genomic changes in the pulp nociceptors, leading to upregulation of the expression of the transient receptor potential vanilloid type 1 channels, which is a crucial inflammatory pain signaling molecule and is linked with the excitation of nociceptor. Therefore, pulp inflammation may lead to long-lasting changes and persistent pain following treatment after the removal of the noxious stimuli (18). The lower incidence of post-operative pain in single-visit root canal treatment might be attributed to immediate obturation, thereby avoiding passage to medications, repeated instrumentation and irrigation. The reported prevalence of post-obturation pain ranges widely from 0% (after 1 week) to 65% (1st day) and generally declines overtime and should, therefore, be qualified by duration after last treatment episode (19).

The descriptive statistics for all the subjects on post-obturation day 1, day 3, and day 7 were compared according to VAS scale measurement where it shows the mean, standard deviation along with the maximum and minimum scores of the VAS scale. Each group has 20 samples, so the number of patients 1st day, 3rd day, and 7th day were 80. The mean was highest in the 1st day and lowest on the 7th day. Maximum score was 8 and the minimum score was 2. Fox et al. (20) reported that 90% of teeth treated in a single visit had little or no spontaneous pain at the end of the 1st day and 99% had no spontaneous pain at the end of 1 week. Oliet (21) treated 264 teeth and found 10.6% incidence of pain following obturation after 24 h and no pain at all after 1 week.

Kruskal–Wallis test showed the mean ranks for the four groups on post-obturation day 1, day 3, and day 7. On day 1, the mean rank was highest in Group-4 and lowest in Group-3. Similarly on day 3, the control group had the highest mean rank and the lowest was in Group-3 (antibiotic and anti-inflammatory). However, on the 7th day, mean rank was almost equal in all four groups. Jabeen and Khurshiduzzaman (22) showed a statistically significant difference in the occurrence and degree of post-endodontic pain between 2 follow-up days. The incidence of pain was reported to be more on the 1st day after obturation and tended to decrease thereafter.

In Group-1, 30% of the total patient had severe pain on the 1st day of post obturation, 60% had moderate pain. In Group-2, 5% had severe pain on the 1st day of post obturation. In Group-3, 90% had moderate pain. In the control group, 55% of total patients had severe pain. Bour-

reau et al. (23) studied that in immediate post-operative period, 16.6% of all patients presented with spontaneous pain, although the incidence of severe pain and flare-ups was 3.3%. Ali et al. (19) evaluated post-obturation pain incidence and factors associated with pain experience following endodontic procedure. One thousand three hundred and twenty-eight patients participated in the study. Root canal treatment was done in a single visit. Pain was recorded at 3 time intervals of 12 h, 24 h, and 48 h. The prevalence of post-obturation pain in the study was 4% at 48 h. The incidence of post-operative pain in RCT was 9% after 12 h, which was reduced to 8.6% after 24 h and drastically to 4% after 48 h.

Table 2 shows the mean ranks of the four groups on the 1st, 3rd, and 7th days of post-obturation. Pre-medication with both anti-inflammatory and antibiotic drug (Group-3) has the least mean rank (an increase in rank corresponds to an increase in the VAS score value). It has the best result among the four groups on the 1st day of post obturation, followed by pre-medication with anti-inflammatory drugs (Group-2), pre-medication with antibiotic drugs (Group-1), and finally the control group (Group-4).

Therefore, on day 1, the ascending order for pain was Group-3< Group-2< Group -1< Group-4.

On the 3rd day of post-obturation, pre-medication with both anti-inflammatory and antibiotic drugs (Group-3) had the least mean rank, which means, it has the best result among the four groups on the 3rd day post-obturation, followed by pre-medication with anti-inflammatory drugs (Group-2), pre-medication with antibiotic drugs (Group-1), and finally the control group (Group-4). Hence, for day 3, the ascending order for pain was Group-3< Group-2< Group-1< Group-4.

Since, on day 7, Groups-1, 2, and 3 had the same mean ranks (39.50), it implies that they all had the same results on the 7th day post-obturation. However, Group-4 had a mean rank of 43.50 (Table 2) which indicates that it has the highest ranks among all of the four groups, or the least effect on the 7th day of post-obturation period.

Hence, for day 7, the ascending order of pain was Group-3= Group-2= Group-1< Group-4. Alsomadi and Habahbeh (24) concluded that antibiotic pre-medication (amoxicillin and clavulanic acid) resulted in less number of analgesic tablets consumed in experimental group after 24, 32, 40, and 48 h post-treatment with less pain recorded on pain scale. He concluded that amoxicillin with clavulanic acid pre-medication had an impact on degree of post-operative pain.

Abielhassan et al. (9) established that amoxicillin with clavulanic acid pre-medication could be prescribed to lessen the degree of post-operative pain after endodontic treatment. Ramazani et al. (25) assessed post-operative pain after endodontic treatment of molar teeth with irreversible pulpitis and noticed that pre-medication with ibuprofen caused significantly greater pain reduction compared to zintoma and placebo at point of time.

In our study, Group-3 (antibiotic and anti-inflammatory) had the least mean rank on the both 1st day and 3rd day of post-obturation. Amoxicillin and clavulanic acid gives the synergistic effect and helps in reducing post-operative infections and lessens the degree of pain.

Before endodontic therapy, the pre-operative use of NSAIDs such as aceclofenac and paracetamol could block the COX pathway and, consequently, the sensation of pain before it started, thus resulting in a decreased pain level after root canal therapy.

After Group-3, Group-2 had the least mean rank for the 1st and 3rd day of post-obturation. Arslan et al. (26) concluded that administration of pre-operative NSAIDs reduced post-operative pain after 6 h. Mokhtari et al. (27) evaluated the effect of pre-medication with ibuprofen and indomethacin on post-endodontic pain and concluded that both medications were effective for pain control but ibuprofen had greater analgesic efficacy.

Gopikrishna and Parameswaran (28) showed that single-dose prophylactic prescription of rofecoxib (50 mg) or ibuprofen tablet (600 mg) significantly reduced post-operative endodontic pain. On the contrary, Attar et al. (29) found that pre-operative administration of NSAIDs treatment did not significantly reduce post-operative pain after RCT.

In Group-1, only antibiotic was used as pre-medication and found that 30% of the total patients had severe pain and 60% had moderate pain on the 1st day of post-obturation, but in Group-3 patients had much lesser pain. Hence, individual use of antibiotic as a pre-medication has less effect on post-obturation pain. Abielhassan et al. (9) concluded that amoxicillin with clavulanic acid antibiotic pre-medication could be prescribed to lessen the degree of post-operative pain after endodontic treatment. On the contrary, Pickenopaugh et al. (14) determined the effect of amoxicillin on endodontic flare-up in asymptomatic necrotic teeth and concluded that prophylactic amoxicillin had no effect on the occurrence of flare-up.

In the control group (Group-4), 55% of the total patients had severe pain on the 1st day of post-obturation. In this group, patients had maximum severe pain as compared to other groups. Mehrvarzfar et al. (30) found that the incidence of moderate-to-severe pain in the experimental groups was lower than that in the control group, and this difference was significant.

Statistically significant difference in pain perception was found among the groups on the 1st and 3rd day of post-obturation ($p < .05$), but on the 7th day, the difference was statistically insignificant (Table 3). Gotler et al. (31) analyzed the incidence and severity of post-endodontic treatment pain subsequent to root canal treatment in vital and necrotic pulps in 274 patients. The study concluded that the mean incidence of post-operative pain was 54.7% at 6 h post-treatment and was 46.4% at 18 h post root canal. The incidence of post-operative pain in vital teeth was 63.8%, at 6 h post-treatment and 51.8%, at 18 h. Similar results, were obtained by Alsomadi et al. (24) who concluded that post-obturation pain can be effectively controlled using pre-medication with both antibiotics and anti-inflammatory together.

The principle purpose of prescribing antibiotics is to limit the local spread of infection, treat systemic infection, and bring about symptomatic relief. Combination of drugs must be used to increase the antibacterial spectrum. This combination results in more powerful bactericidal action against certain organisms because of synergistic action. Use of antibiotics results in more rapid healing and repair of bone defects, in cases of chronic and acute abscess.

No single antibiotic by itself will sterilize the root canal in every instance because each antibiotic has a specific and limited antibacterial spectrum. Indiscriminate use of antibiotics must be avoided as this could result in antibiotic resistance. Sensitivity reactions can also occur during the treatment with antibiotics. Usual manifestations are pruritus, localized or generalized urticaria, dermatitis, edema, sore throat, and nausea. Most reactions are not serious, but sometimes severe reactions may occur which require hospitalization (32). As a general rule, in the absence of signs and symptoms of infection, medical practitioners should refrain from prescribing antibiotics as a means of alleviating pain (33).

The potential confounding factors, such as sex, different age groups, smaller sample size, different file size and taper, obturation quality and experience of the endodontist, and number of endodontists involved in this procedure, were not taken into the account. Because of this limitation, our findings have to be interpreted with care. In the future, studies have to be carried out in endodontic clinical settings with adequately longer follow-up periods since complications are usually expected to arise in the long term.

Our study shows potential benefit of antibiotic and anti-inflammatory pre-treatment in single-visit endodontics to manage post-operative pain, although our result needs to be corroborated by larger comparative study with bigger sample size.

Conclusion

Within the limitations of the study, it can be concluded that single dose of antibiotic and anti-inflammatory premedication reduces the post-operative pain in single-visit root canal treatment as compared to giving only antibiotics or anti-inflammatory drugs. Further long-term clinical studies are required to validate our results.

Authorship Contributions: Concept: I.P., P.S.S., R.C.; Design: I.P., P.S.S., R.C.; Supervision: I.P., P.S.S., R.C.; Materials: I.P., P.S.S.; Data: P.S.S., R.C.; Analysis: I.P., R.C.; Literature search: I.P., P.S.S.; Writing: I.P., R.C.; Critical revision: R.C.

Source of Funding: None declared.

Conflict of Interest: None declared.

Ethical Approval: The study protocol was approved by the Saraswati Dental College Institutional Human Ethical Committee (date: 18.01.208; protocol no: 226028).

Informed consent: Written informed consent was obtained from patients who participated in this study.

References

1. Parirokh M, Sadr S, Nakhaee N, Abbott PV, Manochehrifar H. Comparison between prescription of regular or on-demand ibuprofen on postoperative pain after single-visit root canal treatment of teeth with irreversible pulpitis. J Endod 2014; 40: 151–4. [CrossRef]
2. Parirokh M, Rekabi AR, Ashouri R, Nakhaee N, Abbott PV, Gorjestani H. Effect of occlusal reduction on postoperative pain in teeth with irreversible pulpitis and mild tenderness to percussion. J Endod 2013; 39: 1–5. [CrossRef]
3. Smith CS, Setchell DJ, Harty FJ. Factors influencing the success of conventional root canal therapy-a five-year retrospective study. Int Endod J 1993; 26: 321–33. [CrossRef]
4. Imura N, Zuolo ML. Factors associated with endodontic flare-ups: a prospective study. Int Endod J 1995; 28: 261–5. [CrossRef]
5. O'Keefe EM. Pain in endodontic therapy: preliminary study. J Endod 1976; 2: 315–9. [CrossRef]
6. Maddor DL, Richard EW, Davis CO. Incidence of postendodontic pain related to medicaments & other factors. J Endod 1977; 3: 447–52. [CrossRef]
7. Tarale K. Post-operative pain analysis between single visit and two visit root canal treatments using visual analogue scale: an in-vivo study. J Dent Allied Sci 2013; 2: 8–15.
8. Zare Jahromi M, Ahmadpour E. Efficacy of premedication with oral dextromethorphan and ibuprofen for pain relief after root canal therapy in patients with irreversible pulpitis. J Islam Dent Assoc Iran 2016; 28: 92–7. [CrossRef]
9. Abielhassan MM, Ezzat KM, Ahmed GM. Effect of

amoxicillin with clavulanic acid antibiotic premedication on pre-treatment and post-endodontic pain in teeth with irreversible pulpitis: A randomized controlled trial. Mod App Dent Oral Health 2018; 2. [CrossRef]
10. Alomaym MAA, Aldohan MFM, Alharbi MJ, Alharbi NA. Single versus multiple sitting endodontic treatment: incidence of postoperative pain - a randomized controlled trial. J Int Soc Prev Community Dent 2019; 9: 172–7.
11. DiRenzo A, Gresla T, Johnson BR, Rogers M, Tucker D, BeGole EA. Postoperative pain after 1- and 2-visit root canal therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 93: 605–10. [CrossRef]
12. Alonso-Ezpeleta LO, Gasco-Garcia C, Castellanos-Cosano L, Martín-González J, López-Frías FJ, Segura-Egea JJ. Postoperative pain after one-visit root-canal treatment on teeth with vital pulps: comparison of three different obturation techniques. Med Oral Patol Oral Cir Bucal 2012; 17: e721–7. [CrossRef]
13. Jorge-Araújo ACA, Bortoluzzi MC, Baratto-Filho F, Santos FA, Pochapski MT. Effect of premedication with anti-inflammatory drugs on post-endodontic pain: a randomized clinical trial. Braz Dent J 2018; 29: 254–60. [CrossRef]
14. Pickenpaugh L, Reader A, Beck M, Meyers WJ, Peterson LJ. Effect of prophylactic amoxicillin on endodontic flare-up in asymptomatic, necrotic teeth. J Endod 2001; 27: 53–6. [CrossRef]
15. Penesis VA, Fitzgerald PI, Fayad MI, Wenckus CS, BeGole EA, Johnson BR. Outcome of one-visit and two-visit endodontic treatment of necrotic teeth with apical periodontitis: a randomized controlled trial with one-year evaluation. J Endod 2008; 34: 251–7. [CrossRef]
16. Metri M, Hegde S, Bhandi S. Effect of pretreatment diclofenac sodium on postendodontic pain: A randomised controlled trial. J Conserv Dent 2016; 19: 7–10. [CrossRef]
17. Chandraweera L, Goh K, Lai-Tong J, Newby J, Abbott P. A survey of patients' perceptions about, and their experiences of, root canal treatment. Aust Endod J 2019; 45: 225–32.
18. Yu CY, Abbott PV. Pulp microenvironment and mechanisms of pain arising from the dental pulp: From an endodontic perspective. Aust Endod J 2018; 44: 82–98. [CrossRef]
19. Ali SG, Mulay S, Palekar A, Sejpal D, Joshi A, Gufran H. Prevalence of and factors affecting post-obturation pain following single visit root canal treatment in Indian population: A prospective, randomized clinical trial. Contemp Clin Dent 2012; 3: 459–63. [CrossRef]
20. Fox J, Atkinson JS, Dinin AP, Greenfield E, Hechtman E, Reeman CA, *et al.* Incidence of pain following one-visit endodontic treatment. Oral Surg Oral Med Oral Pathol 1970;30:123–30. [CrossRef]
21. Oliet S. Single-visit endodontics: a clinical study. J Endod 1983;9:147–52. [CrossRef]
22. Jabeen S, Khurshiduzzaman M. Incidence of post obturation pain following single and multi visit root canal treatment in a teaching hospital of Bangladesh. Mymensingh Med J 2014; 23: 254–60.
23. Bourreau MLS, Soares ADJ , Souza-Filho FJD. Evaluation of postoperative pain after endodontic treatment with foraminal enlargement and obturation using two auxiliary chemical protocols. Rev Odontol UNESP 2015; 44: 157–62. [CrossRef]
24. Alsomadi L, Al Habahbeh R. Role of prophylactic antibiotics in the management of postoperative endodontic pain. J Contemp Dent Pract 2015; 16: 939–43. [CrossRef]
25. Ramazani M, Hamidi MR, Moghaddamnia AA, Ramazani N, Zarenejad N. The prophylactic effects of zintoma and ibuprofen on post-endodontic pain of molars with irreversible pulpitis: a randomized clinical trial. Iran Endod J 2013; 8: 129–34.
26. Arslan H, Topcuoglu HS, Aladag H. Effectiveness of tenoxicam and ibuprofen for pain prevention following endodontic therapy in comparison to placebo: a randomized double-blind clinical trial. J Oral Sci 2011; 53: 157–61. [CrossRef]
27. Mokhtari F, Yazdi K, Mahabadi AM, Modaresi SJ, Hamzeheil Z. Effect of premedication with indomethacin and ibuprofen on postoperative endodontic pain: a clinical trial. Iran Endod J 2016; 11: 57–62.
28. Gopikrishna V, Parameswaran A. Effectiveness of prophylactic use of rofecoxib in comparison with ibuprofen on postendodontic pain. J Endod 2003; 29: 62–4. [CrossRef]
29. Attar S, Bowles WR, Baisden MK, Hodges JS, McClanahan SB. Evaluation of pretreatment analgesia and endodontic treatment for postoperative endodontic pain. J Endod 2008; 34: 652–5. [CrossRef]
30. Mehrvarzfar P, Abbott PV, Saghiri MA, *et al.* Effects of three oral analgesics on postoperative pain following root canal preparation: a controlled clinical trial. Int Endod J 2012; 45: 76–82. [CrossRef]
31. Gotler M, Bar-Gil B, Ashkenazi M. Postoperative pain after root canal treatment: a prospective cohort study. Int J Dent 2012; 2012: 310467. [CrossRef]
32. Bender IB, Seltzer S. The advantages and disadvantages of the use of antibiotics in endodontics. Oral Surg Oral Med Oral Pathol 1954; 7: 993–7. [CrossRef]
33. Abbott PV. Selective and intelligent use of antibiotics in endodontics. Aust Endod J 2000; 26: 30–9. [CrossRef]