RESEARCH ARTICLE ISSN: 2349-2678

Contents lists available at www.ijpba.in

International Journal of Pharmaceutical and Biological Science Archive

NLM (National Library of Medicine ID: 101732687)

Index Copernicus Value 2019: 71.05

Volume 7 Issue 1; January-February; 2019; Page No. 27-32

EFFECT OF PREMEDICATION WITH SINGLE DOSE ORAL ADMINISTRATION OF NON-STEROID, STEROID AND OPIOID COMBINATION ON POST-ENDODONTIC PAIN IN PATIENTS OF IRREVERSIBLE PULPITIS WITH APICAL PERIODONTITIS: A RANDOMIZED CLINICAL TRIAL

Malik Sartaj[1], Anum Maqbool[2], Rizwan Hamid[3], Mohd Sajad[4], Ab Wahid Zargar[5] and Mushtaq Mohamad[6].

[1]Senior Resident, Department of Conservative Dentistry and Endodontics.

[2]Post Graduate scholar, Department of Conservative Dentistry and Endodontics.

[3]Post Graduate scholar, Department of Oral Medicine and Radiology.

[4]Senior Resident, Department of Conservative Dentistry and Endodontics.

[5]Post Graduate scholar, Department of Conservative Dentistry and Endodontics.

[6]Post Graduate scholar, Department of Conservative Dentistry and Endodontics.

ABSTRACT

Aim: To evaluate the effect on postoperative pain in patients with symptomatic irreversible pulpitis, receiving endodontic treatment after pre-treatment with single oral dose of a NSAID, NSAID-Paracetamol combination, Acetamenophen-opoid combination and a single dose steroid in comparison to a placebo.

Materials and methodology: A total of 150 patents divided into 5 Groups who were diagnosed with irreversible pulpit is with periapical periodontits were selected for the study. In Group1 patients were given a NSAID, Aaceclofenac 100mg (Aceclo; Aristo pharmaceuticals) half an hour before procedure. In Group 2 patients were prescribed NSAID-Aetamenophen combination i.e. Aceclofenac 100mg+Paracetamol 325mg (Aceclo P; Aristo Pharmaceuticals).In Group 3 patients were given a single dose of Acetamenophen-opoid combination i.e. Acetamenophen 325mg+Tramadol 37.5mg (Mega Flexon; Aristo Pharmaceuticals).In group 4 patients were advised to take single dose of Prednisolone 50mg (Deltason; Group Pharmaceuticals).In Group 5 patients were given a single oral dose of a placebo i.e. Dextrose gelatin capsule. VAS scores were recorded at four different time interval at 3,8,12 and 24 hrs.

Results: The results of pain intensity (VAS) were computed as the means and standard deviations (SD). The incidence of moderate to severe pain in the experimental groups was lower than that in the placebo control group, and this difference was significant ($p<0.05$) except with that of Group 4 i.e. steroid (prednisolone) ($p>0.05$). There was no significant difference between NSAID, NSAID-Acetamenophen and Acetamenophen-Opoid combinations ($P > 0.05$). Among the four different experimental groups lowest incidence of pain at all four different time intervals was recorded with Group 3 i.e. acetaminophen and opioid combination.

Conclusion: Within the limitations of the study, pretreatment analgesia with single oral dose of Aceclofenac and acetaminophen or Acetamenophen and tramadol before endodontic treatment showed substantial reduction in postoperative pain when compared with Aceclofenac and Prednisolone.

Keywords: post-endodontic pain, irreversible pulpitis, NSAIDs, Acetamenophen, opioid

**Corresponding author: Abdul Wahid Zargar |*

Introduction:

Most common reason for patient reporting to the dental office is the pain, usually associated with irreversible pulpitis and periapical periodontitis. Among these up to 40-80% of patients continue to report mild to severe pain after endodontic treatment.[1,2] Certain factors such as preoperative pain, number of appointments, use of intracanal medications and tooth position may predispose the development of postoperative pain and flareups.[3,4]This postoperative pain usually commences a few hours or days after treatment, needs both preventive and management strategies to control it.[3]A variety of approaches have been recommended for the management of post-endodontic pain. Preparing patients about the expected postoperative endodontic pain and prescribing medications beforehand can increase patient confidence, pain threshold, and can improve their attitude towards the endodontic therapy. Drugs with different mechanisms of action have been used for the management of post-endodontic pain including non-narcotic analgesics comprising nonsteroidal anti-inflammatory medicines (NSAIDs) and acetaminophen, opioids and steroids.[5] Treatment with an analgesic before a procedure has been shown to have a significant reduction in post-operative pain by many studies.[6,7] For dental pain, nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen, aspirin, flurbiprofen, ketorolacare etc. are most frequently taken analgesic medications. Their popularity is attributed to their abundant over-the-counter availability, efficacy in relieving pain and fever, and low side effect profile at therapeutic doses.[4]Evidence suggests that a combination of paracetamol and an NSAID may offer superior analgesia compared with either drug alone.[8]Management of post endodontic pain usually focusses on peripheral control of inflammation by NSAIDs or NSAID combinations,however it is often required to reduce central hyperalgesia by opoids. In cases of moderate to severe pain, an NSAID may be administered with an opoid.[9]Some authors have sugessted use a preoperative, single oral dose of prednisolone for the control and prevention of postendodontic pain suggesting that it can modulate release of inflammatory mediators and reduce the occurrence pain.[10]However the optimal oral prednisolone dosage for the prevention and control of interappointment endodontic pain is yet to be determined. Since, a definitive anti-inflammatory protocol to prevent and control the occurrence of postendodontic pain has not yet been established,[5,11] so the present study was undertaken with the aim to evaluate the effect on postoperative pain in patients with symptomatic irreversible pulpitis, receiving endodontic treatment after pre-treatment with single oral dose of a NSAID, NSAID-Paracetamol combination, Acetamenophen-opoid combination and a single dose steroid in comparison to a placebo. The null hypothesis tested was that the preoperative consumption of different analgesics or their combinations has no influence on post-operative pain after endodontic therapy in irreversible pulpitis with periapical periodontitis.

Materials and methodology

The research methodology and design was approved by the Institutional Ethical Committee after deliberation about the patient intervention and drugs involved in study. An invigilator of Institutional Ethical Committee monitored the research protocol during course of study. Among the patients visiting the endodontic department one hundred fifty patients who were diagnosed with irreversible pulpitis with periapical periodontits were selected for the study. A written consent was taken from each and the protocol for the study and necessary instructions for the drug dosage was explained to each of them. Patients in the age group 20-40years without any medical history and previous medication for the pain were selected. To remove the gender bias only male patients were included in the study. Baseline pain score was noted on visual analog scale (VAS) for each patient before endodontic intervention and only the patients with VAS score > 4 were selected for the study. Clinical examinations, including thermal (cold) test, electrical pulp testing, periodontal

assessments, and radiographic examinations were performed. Exclusion criteria selected for patients were drugs taken within the last 8 hours, patients under any currently acting analgesics, patients with any systemic or mental illness, patients with acute endodontic abscess, periodontal diseases, and retreatment cases and any known allergy or sensitivity to drugs. The selected patients were divided into five groups randomly before the endodontic treatment of offending tooth was started. In each group 30 patients were given single dose of experimental drug at a prescribed dose half an hour before the endodontic procedure. In Group1 patients were given a NSAID, Aaceclofenac 100mg (Aceclo;Aristo pharmaceuticals) half an hour before procedure. In Group 2 patients were prescribed NSAID-Aetamenophen combination i.e.Aceclofenac 100mg+Paracetamol 325mg(Aceclo P; Aristo Pharmaceuticals)In Group 3 patients were given a single dose of Acetamenophen-opoid combination i.e. Acetamenophen 325 mg+Tramadol 37.5mg(Mega Flexon; Aristo Pharmaceuticals).In group 4 patients were advised to take single dose of Prednisolone 50mg(Deltason;Group Pharmaceuticals)In Group 5 patients were given a single oral dose of a placebo i.e. Dextrose gelatin capsule. In this clinical trial, all medications were provided to patients in coded packets. Apart from the case selection, all the clinical procedures were performed by a four endodontists (who were not a part of study process) in a single visit. The operators had no involvement with study outcome. To ensure blinding; neither the operators nor the patients had knowledge about the medication used. Clinical record diary with the pain scale was delivered to patients and returned in the second session. Patients were instructed to complete a pain diary 3, 8, 12, and 24 hours after root canal instrumentation. The method used to measure clinical pain intensity was the visual analogue scale (VAS), which consists of a 10-cm line anchored by 2 extremes, ‘‘no pain’’ and ‘‘pain as bad as it could be’’. Patients were asked to make a mark on the line that represented their level of perceived pain. Thus, pain intensity was assigned into 4 categorical scores: 1, none (0); 2, mild (1–3); 3, moderate (4–6); and 4, severe. Patients were also asked to make a note of quality of pain as sharp, dull or throbbing. Due to the possibility of pain after the root canal instrumentation, the patients were instructed to use analgesic rescue medication if they had any uncomfortable sensation, regardless of the experimental group. However, these patients were excluded from the analysis. A total of 140 patients completed the study as ten patients were lost to follow up attrition and post-operative medication consumption.

Results

All the statistical calculations were made through the Statistical Package for Social Science SPSS (Statistical Package for the Social Science) version 17.0 for Windows (SPSS Inc, Chicago, IL)The results of pain intensity (VAS) were computed as the means and standard deviations (SD). Statistically significant differences among groups were evaluated by the Kruskal-Wallis test which was used to determine the differences between groups at each time point. The number of excluded samples was almost equal amongst the groups. Otherwise, excluding the noncompliance samples was not allowed. Table 1 shows the sample size in each group with mean and standard deviations (SDs) of VAS scores for five different groups at different time intervals. The significance levels were set at ($P < .05$).

Table1: Comparison of mean and standard deviations of VAS scores

Group	n	VAS score at different time intervals			
		3hr	8hr	12hr	24hr
Group 1	28	3.2+1.03	0.8+0.1	1.9+0.1	2.2+1.0
Group 2	29	2.4+1.3	3.2+1.7	3.1+1.6	2.1+1.2
Group 3	30	0.3+0.1	0.1+0.12	0.1+0.13	1.1+0.12
Group 4	26	3.5+1.12	5.2+0.17	3.8+0.16	4.1+0.14
Group 5	27	5.8+1.33	6.8+1.48	5.7+1.65	3.9+1.54

The incidence of moderate to severe pain in the experimental groups was lower than that in the placebo control group, and this difference was significant ($p<0.05$) except with that of Group 4 i.e. steroid (prednisolone) ($p>0.05$). There was no significant difference between NSAID, NSAID-Acetamenophen and Acetamenophen-Opoid combinations ($P > 0.05$), Among the four different experimental groups lowest incidence of pain at all four different time intervals was recorded with Group 3 i.e. acetaminophen and opioid combination. The percentage of subjects reporting no pain after a 8 and 12hr period was more than 80% for the Group 3 i.e. acetaminophen and opioid combination group and 60% Group 2 i.e. NSAID-Aetamenophen combination group.

Discussion

Amongst all dental procedures, endodontic treatment produces more frequent and severe postoperative pain. Moreover, postoperative pain is more likely to occur within the first 24 hrs following endodontic treatment.[12] Inflammatory process in periradicular areas due to periapical periodontitis and the irritation to periodontal ligament subsequent to endodontic treatment can produce postoperative pain.[13]Thus the patients with irreversible pulpitis with apical periodontitis were selected for this study. These patients respond well to pulpectomy and need analgesic medication to curtail periapical inflammation. Therefore, it is likely that effective pain relief may result from this procedure and by administering a single dose of analgesic drugs. Patients with no history of taking analgesics in the previous 12 hr or other drugs prior to presenting for treatment were selected to eliminate the interfering effects of these other agents. Optimal pain management combines both pharmacological and non-pharmacological treatment strategies. Thus the effective debridement of infected root canal in these cases is supplemented by preoperative single dose analgesics for predictable pain reduction. In comparison to repeated doses during the postoperative period, a preoperative, single oral dose of anti-inflammatory drugs can modulate release of inflammatory mediators and reduce the occurrence of side effects.[8] The maximum benefit of the anti-inflammatory is obtained when therapeutic levels are reached before tissue manipulation.[5, 8, 14-16] The NSAIDs inhibit the production of inflammatory mediators; thus, they reduce pain, especially moderate to severe pain after root canal treatment.[17,18]Few studies have evaluated the effect of SAIDs and NSAID-Opioids combinations with regard to prevention and control of postendodontic pain after root canal instrumentation.[8,10,14,19]But the comparative efficacy of different regimens in pain control was not elucidated fully. So the present double-blind, placebo-controlled clinical trial compared the analgesic effects of non-steroid, steroid and opioid combination with those of a placebo under controlled clinical conditions. The patients in each group were distributed similarly taking into account age, gender, diagnosis, pain symptomatology, treatment and anxiety rating in each sample. The control of these variables was important to minimize bias as much as possible. Placebo group has been used as control in this clinical trial. Most patients experience pain in the first 24 hrs after root canal treatment and therefore, this longer period for assessment was chosen. Results of our study show that the combination of a

NSAID with other analgesics such as Acetaminophen and Tramadol can reduce moderate to severe endodontic pain more effectively than single dose NSAIDs or SAIDs. These results are in concordance with the studies of Adrian Camargo et al and Holstein A et al.[20,21]A preoperative single dose combination of Aceclofenac and acetaminophen or Acetamenophen and tramadol appears to be a suitable choice for alleviating moderate to severe pain after endodontic treatment or surgery. However, only the effects of these drugs on pain were evaluated in this study and not the adverse effects. Due to short plasma half-life of drugs preoperative single dose may not be sufficient for long term analgesia of 24hr combined effect of pre and post endodontic analgesics need to be studied.

Conclusion

Within the limitations of the study, pre-treatment analgesia with single oral dose of Aceclofenac and acetaminophen or Acetamenophen and tramadol before endodontic treatment showed substantial reduction in postoperative pain when compared with Aceclofenac and Prednisolone. Based on the results of this present study, the null hypothesis that the preoperative consumption of different analgesics or their combinations has no influence on post-operative pain after endodontic therapy in irreversible pulpitis with periapical periodontitis was rejected.

References

1. Pak JG, White SN. Pain prevalence and severity before, during, and after root canal treatment: a systematic review. J Endod 2011; 37, 429–38
2. Marshall JG. Consideration of steroids for endodontic pain. Endodontic Topics.2002;3:41–51.
3. Ng Y-L, Glennon JP, Setchell DJ, Gulabivala K.Prevalence of and factors affecting post-obturation pain in patients undergoing root canal treatment. Int Endod J 2004; 37, 381–91.
4. Mohammed Saadi Alarbeed., et al. “Effect of Combination of Calcium Hydroxide and Chlorhexidine Gel 2% as Intracanal Medication in Comparison to Calcium Hydroxide Paste as Intracanal Medication on Postoperative Pain and Bacterial Endotoxin in Necrotic Teeth: A Randomized Controlled Trial”. Acta Scientific Dental Sciences 3.2 (2019): 124-130.
5. 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
6. Dionne R. Suppression of dental pain by preoperative administration of flurbiprofen. Am J Med Sci 80:41,1986
7. Dionne RA, Campbell RA, Cooper SA, Hall DL, Buckingham B. Suppression of postoperative pain by preoperative administration of ibuprofen in comparison to placebo, acetaminophen, and acetaminophen plus codeine. J Clin Pharmacol. 1983;23:37–43.
1. 8.Cliff K. S. Robin A. Phillip Lirk, Alan F. Merry. Combining Paracetamol (Acetaminophen) with Nonsteroidal Antiinflammatory Drugs: A Qualitative Systematic Review of Analgesic Efficacy for Acute Postoperative Pain Anesth Analg 2010;110:1170–9
8. Dionne R .Additive analgesic effects of oxydone and ibuprofen in oral surgical model.J Oral Maxillofac Surg 57:673,1999
9. Seyed Mohsen Jalalzadeh, Ahmad Mamavi, Shahriar Shahriari, Fa´bio Andre, Marcia Thaıs Pochapski. Effect of Pretreatment Prednisolone on Postendodontic Pain: A Double-blind Parallel-randomized Clinical Trial .J Endod 2010;36:978– 981
10. Mickel AK, Wright AP, Chogle S, Jones JJ, Kantorovich I, Curd F. An analysis of current analgesic preferences for endodontic pain management. J Endod 2006; 32:1146–54.
11. Menhinick KA, Gutmann JL, Regan JD, Taylor SE, Buschang PH. The efficacy of

pain control following nonsurgical root canal treatment using ibuprofen or a combination of ibuprofen and acetaminophen in a randomized, double-blind, placebo-controlled study. Int Endod J. 2004;37:531–41.

12. Siqueira JF, Barnett F. Interappointment pain: Mechanisms, diagnosis,and treatment. Endod Topics. 2004;7:93–109.
13. Pochapski MT, Santos FA, de Andrade ED, Sydney GB. Effect of pretreatment dexamethasone on postendodontic pain. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:790–5.
14. Marshall JG. Consideration of steroids for endodontic pain. Endo Topics 2002;3: 41–51.
15. Menhinick KA, Gutmann JL, Regan JD, Taylor SE, Buschang PH. The efficacy of pain control following nonsurgical root canal treatment using ibuprofen or a combination of ibuprofen and acetaminophen in a randomized, double-blind, placebocontrolled study. Int Endod J 2004;37:531–41.
16. Hargreaves KM, Seltzer S. Pharmacological control of dental pain. In: Hargreaves KM, Goodis HE, eds. Seltzer and Bender's Dental Pulp. Chicago: Quintessence, 2002: 205–226.
17. Madison S, Anderson RW. Medications and temporaries in endodontic treatment. DCNA 1992;36, 343–56.
18. Liesinger A, Marshall FJ, Marshall JG. Effect of variable doses of dexamethasone on posttreatment endodontic pain. J Endod 1993;19:35–9.
19. Adrian C Amaral, Jorge Araújo, Marcelo C Bortoluzzi, Flares B Filho, Fábio A Santos, Márcia T Pochapski. Effect of Premedication with anti-inflammatory drugs on Post-Endodontic Pain: A Randomised clinical trial. Braz Dent J 29(3) 2018
20. Holstein A, Hargreaves KM, Niederman R.Evaluation of NSAID's for treating post-endodontic pain. A systematic review. Endodontic Topics,2002; 3, 3–13.