Comparative assessment of efficacy of two different pretreatment single oral doses of betamethasone on inter-appointment and postoperative discomfort: An *in vivo* clinical evaluation

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Abstract

Aim:

Study aimed to evaluate the efficacy of two different pretreatment single oral doses of betamethasone on the incidence of inter-appointment flare up and postoperative discomfort.

Materials and Methods:

Fifty-four patients aged 18–59 years requiring endodontic treatment were selected and randomly assigned to three groups; single pretreatment oral dose of placebo or betamethasone in two different oral doses of 0.5 mg and 1 mg, respectively. Endodontic therapy was completed in two visits using triple antibiotic paste as intracanal medicament. Patients were given a questionnaire to record their pain at 1, 2, 3, and 7 days after treatment. In the second visit, obturation was done, and the patients were again instructed to record their pain scores after treatment and discharged. The verbal rating scale was used for recording the pain scores. Statistical analysis was done using ANOVA and the Friedman test.

Results:

0.5 mg betamethasone group showed least mean pain scores among all experimental groups; however, there was no statistically significant difference between any of the groups ($P > 0.05$).

Conclusion:

Pretreatment single oral dose of betamethasone is an effective in managing endodontic flare-ups; however, the results were statistically insignificant.

Keywords: Betamethasone, flare up, placebos, root canal therapy

INTRODUCTION

Toothache and swelling are the major complaints reported to the dentist. Literature reveals that nearly 80% of the patients reporting with the complaint of preoperative pain also experienced severe postoperative pain.[1] Overinstrumentation, periapical extrusion of irrigant/medicament, restoration in hyperocclusion are chief causes that often provoke an acute inflammatory response resulting in mid-treatment flare-up.[2,3,4] In addition, the teeth with necrotic pulp and periapical lesions are commonly associated with posttreatment flare-up.[5]

Preoperative medications and intracanal medicaments are one of the effective ways to counteract the endodontic pain. Preoperative single oral dose of anti-inflammatory drug reduces the intake of multiple doses of drug postoperatively for managing endodontic flare-ups.[6] Anti-inflammatory analgesics, systemic steroids, and anxiolytics are few of the commonly used preoperative drugs used during endodontic practice.[7]

Intracanal medicaments such as $Ca(OH)_2$,[8,9] iodine potassium iodide,[10] and combination of antibiotics and steroids have been used with promising results.[11] Owing to polymicrobial nature of the infected root canal space, single empirical antibiotic is inadequate in obtaining thorough disinfection. Triple antibiotic paste, which is a combination of ciprofloxacin, metronidazole, and minocycline, has been successfully employed as an intracanal medicament.[12]

Corticosteroids are the anti-inflammatory, immunosuppressant drugs which if used appropriately can function as a boon in

managing endodontic pain. Corticosteroids have been often used locally as well as systemically during the endodontic treatment.[13] Glucocorticoids interfere at several steps in the inflammatory response, but the most important overall mechanism appears to be the limitation of recruiting inflammatory cells at the affected site.[14]

Preoperative administration of prednisolone and dexamethasone during the root canal treatment has already been evaluated with mixed outcomes.[15,16] Betamethasone is another commonly available longer acting corticosteroid and can be administered through oral, intramuscular, or intravenous route. Owing to its longer duration of action, it may provide better results in treating the mid- or post-treatment endodontic pain. To the best of our knowledge, there are no researches which have reported the preoperative administration of oral betamethasone in managing the mid-treatment flare-up. Therefore, the present study was aimed to evaluate the efficacy of two different preoperative single oral doses of betamethasone for inter-appointment flare-up as well as postoperative discomfort. Research hypothesis postulated that while using triple antibiotic paste as an intracanal medicament during endodontic treatment, betamethasone owing to its higher anti-inflammatory potential might perform better in reducing inter-appointment flare-up as well as postoperative discomfort.

MATERIALS AND METHODS

Prior permission was taken from the Institutional Ethics Committee, and informed consent was obtained from the participating patients before the commencement of the study. Fifty-four patients reporting to the Department of Conservative Dentistry and Endodontics with an age range of 18–59 years were selected according to the inclusion and exclusion criteria, and meticulous case history was recorded and thorough clinical and radiographic examination was done. The inclusion criteria for the case selection were defined as follows: (1) Patient's age was between 18 and 59 years; (2) patients with asymptomatic periapical periodontitis; (3) Anterior and posterior teeth (incisors, canine, premolars, and molars); (4) presence of radiographic periapical lesion; and (5) nonvital teeth. However, the exclusion criteria included: (1) Any analgesic and anti-inflammatory drugs taken within last 6 h; (2) any known sensitivity or adverse reaction to the steroid; (3) teeth with acute periodontal abscess; (4) patients requiring prophylactic antibiotic; (5) pregnancy or lactation; (6) patients with mental disability; (7) any known systemic diseases/conditions that contraindicate endodontic therapy. Patients were randomly assigned to any of the three groups ($N = 18$ for each group): Group A: Single pretreatment oral dose of placebo (Vitamin C tablet); Group B: Single pretreatment oral dose of betamethasone 0.5 mg tablet; Group C: Single pretreatment oral dose of betamethasone 1.0 mg tablet. Pretreatment drugs in all the groups were administered 30 min before the commencement of root canal therapy. All the drugs were kept in a paper cover for blinding purpose before dispensing to the patients.

Treatment in all the cases was completed by primary investigator following standardized protocol. Each patient was anesthetized using 1:200,000 lignocaine solution followed by rubber dam isolation and access preparation. Working length was calculated with the help of electronic apex locator as well as radiographic method. Root canal preparation was done in crown down manner using nickel titanium rotary files (Neoniti, Neolix SAS, France). The canals were enlarged to a minimum of apical size 25 or larger (three sizes larger than initial apical file). 17% ethylenediaminetetraacetic acid (EDTA) paste was used as a lubricant during rotary instrumentation. 1 ml of 3% sodium hypochlorite was used as an irrigant during instrumentation.

Preparation of triple antibiotic paste

The ciprofloxacin 250 mg (Powder form – Active pharmaceuticals ingredients - Balaji Drugs, Mumbai, Maharashtra, India), metronidazole 400 mg (Powder form – Active pharmaceuticals ingredients – Balaji Drugs, Mumbai, Maharashtra, India), and minocycline 100 mg (Powder form– Active pharmaceuticals ingredient– Sigma-Aldrich, Bengaluru, Karnataka, India) were weighed separately and mixed in a 1:3:3 proportions. A total of 100 g of this Triple antibiotic mixture was dispensed and mixed with 40 ml of vehicle (macrogol ointment and propylene glycol) to obtain a thick paste-like consistency.

Placement of triple antibiotic paste

Canals were dried with paper points, and triple antibiotic paste was placed using lentulo spiral and gently compacted using finger plugger. Access opening was restored using temporary restorative material (Samfil G, Dentokem, India). All treated patients were prescribed Ketorolac (Ketorol DT, Dr. Reddy's, India) tablets to be taken in the event of developing pain related to the concerned tooth. All the patients were given a questionnaire to record their pain at 1, 2, 3, and 7 days after treatment and discharged. Inter-appointment flare-up was assessed using verbal rating scale (VRS):[17]

- VRS-0 (the treated tooth felt normal)
- VRS-1 (the treated tooth was slightly painful for a time, regardless of the duration, but there was no need to take analgesics)
- VRS-2 (the treated tooth caused discomfort and/or pain, which was rendered comfortable by taking one tablet of Ketorolac)
- VRS-3 (the treated tooth caused discomfort and/or pain, which was rendered comfortable by taking two tablets of Ketorolac at a 6-h interval)
- VRS-4 (the treated tooth caused discomfort and/or pain, which was rendered tolerable by taking two tablets of Ketorolac at every 6 h for 3 days)
- VRS-5 (severe pain and/or swelling caused by the treated tooth that disturbed normal activity or sleep and Ketorolac tablet had little or no effect).

Cases with VRS scores 4 and 5 were regarded as inter-appointment flare-up.

The patient was recalled after 7 days; canals were irrigated by alternate use of 3% sodium hypochlorite and 17% EDTA solution and final rinse with 5 ml of 3% sodium hypochlorite. Finally, the canals were flushed with distilled water to eliminate any residues of chemical agents. Roots canals were dried using absorbent paper points followed by obturation of the root canal using Guttapercha (Sure Endo, Korea) and AH Plus sealer (Dentsply De Trey, Konstanz, Germany). All the participating patients were again prescribed Ketorolac tablets and given a questionnaire to record their pain at 1, 2, 3, and 7 days after endodontic treatment. Postoperative discomfort was also assessed using VRS as described above. The collected data was subjected to one-way ANOVA and the Friedman test.

RESULTS

The study encountered loss of samples due to various reasons. Out of those, two patients were excluded from Group A, one patient from Group B, and two patients from Group C. In Group A, 1 patient experienced interappointment flare-up in the form of severe pain and swelling, which was not relieved even after intake of rescue medication and other patient did not report back for follow-up. In Group B, 1 patient was excluded from the study owing to the intake of medication other than specified whereas, from Group C two patients reported with the loss of temporary restoration.

Group B demonstrated least mean pain scores at all the time intervals with minimal/no pain experienced by the patient. Group C demonstrated lesser mean pain scores as compared to Group A but was inferior as compared to Group B. At Day 1, Group A and Group C showed similar mean pain scores with Group B outperforming both. At Day 2, Group B and Group C showed similar mean pain scores with Group A performing inferior to both the groups. At Day 3 and 7, all the three groups showed similar mean pain scores [Table 1]. Postobturation pain scores recorded by the patients were similar to the inter-appointment pain score with Group B outperforming Group C and Group A [Table 2].

Table 1
ANOVA values (inter-appointment mean pain score)

Table 2
ANOVA values (postobturation mean pain score)

At Day 1, Group B performed best with least mean pain scores experienced by the patients, whereas at day 2, Group B and Group C showed similar mean pain scores with Group A performing inferior to both the groups. At day 3 and day 7, all the experimental groups performed similarly. In all the experimental groups, there was reduction in the pain scores as experienced by the patient; pain scores gradually reduced from day 1 to day 7 indicating the positive relationship of intake of premedication on the incidence of interappointment or postoperative discomfort. In Group A and Group C reduction in the pain scores from day 1 to day 7 were

statistically significant ($P < 0.05$), whereas for Group B reduction in pain scores were statistically insignificant [Tables 1 and 2].

DISCUSSION

The present study evaluated the effect of two different pretreatment doses of betamethasone, i.e., 0.5 and 1 mg, respectively. The results showed no statistically significant difference among the tested drugs. However, betamethasone groups performed better as compared to placebo group for both the parameters, i.e., inter-appointment flare-up as well as postoperative discomfort. The probable reason for slightly better performance may be the various anti-inflammatory mechanisms associated with steroid, the most important among them being the production of protein, "vasocortin," which can suppress edema that is not suppressed by nonsteroidal anti-inflammatory drug.[18]

Although statistically insignificant, Group B was slightly more effective than Group C in minimizing the incidence of both the inter-appointment as well as postoperative discomfort. However, owing to the differences in inherent pain bearing capacity of the individual and smaller sample size, the groups showed insignificant statistical correlation.[19] Hence, the results of this clinical evaluation should be validated by further randomized controlled trials.

Most of the effects mediated by glucocorticoids are not immediate since time is required for changes in gene expression and protein synthesis to occur.[20] Therefore, the premedications were given to the subjects 30 min before the initiation of endodontic therapy. Glucocorticoids may have effects on many organ systems but these effects are typically seen at supraphysiological doses given over a long-term period, usually more than 2 weeks. Literature reveals that a single dose of glucocorticoid, even a large one, is virtually without harmful effects.[21]

One of the important findings experienced in this study was that only one patient (Group A), experienced flare-up or emergency appointment for relief of clinical symptoms. Various experimental researches indicate that combination of placebo and biopulpectomy leads to pain relief in 71% of individuals.[22] The main etiologic factor for endodontic pain is the inflammatory mechanism in the altered pulpal tissue; hence, removal of this inflammatory tissue through biopulpectomy may provide adequate pain relief. In addition, we utilized crown-down technique for cleaning and shaping of the root canal. The literature reveals that the use of crown-down technique leads to less extrusion of debris periapically and subsequently the lesser incidence of postoperative discomfort.[23]

In the present study, the triple antibiotic paste used as intracanal medicament may have had a significant role in the reduction of flare-up.[24] Metronidazole exhibits broad spectrum of activity, it binds to the DNA, disrupts the helical structure, and leads to rapid cell death. Minocycline is primarily bacteriostatic, inhibiting protein synthesis by binding to 30 S ribosome.[25] Ciprofloxacin inhibits the enzyme bacterial DNA gyrase, leading to damage to DNA.[25,26] Various researches have shown that the penetration of medicament was greater when propylene glycol and macrogol were used as vehicle as compared to other vehicles used for the delivery of the same.[27] One of the important parameters taken into consideration in this research was that active pharmacological ingredients of drugs were selected for preparation of triple antibiotic paste. On the contrary, if over-the-counter tablet drugs are used, it may consist of various other ingredients (excipients) other than the active products; also the coating may interfere with the formation of homogenous mixture of the drugs.

Oral route of administration was preferred; the use of intramuscular or intravenous injection might lead to discomfort and fear.[16] Among the various methods for evaluation of pain, the VRS was selected in this study. The probable reason for this response might be that subjective perceptions, such as pain, could be more easily expressed in words than by a mark on a continuous line without operational definition or by numbers.[28]

CONCLUSION

Based on the outcome of the research, it can be concluded that there was no statistically significant difference between any of the tested groups; however, the pretreatment single oral dose of betamethasone, as well as triple antibiotic paste as an intracanal medicament, were effective in minimizing the occurrence of inter-appointment and postoperative discomfort nevertheless further clinical trials are essential to validate the outcome of the present research.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. 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. [PMC free article] [PubMed] [Google Scholar]

2. 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. [PubMed] [Google Scholar]

3. Torabinejad M, Cymerman JJ, Frankson M, Lemon RR, Maggio JD, Schilder H. Effectiveness of various medications on postoperative pain following complete instrumentation. J Endod. 1994;20:345–54. [PubMed] [Google Scholar]

4. Genet JM, Hart AA, Wesselink PR, Thoden van Velzen SK. Preoperative and operative factors associated with pain after the first endodontic visit. Int Endod J. 1987;20:53–64. [PubMed] [Google Scholar]

5. Walton R, Fouad A. Endodontic interappointment flare-ups: A prospective study of incidence and related factors. J Endod. 1992;18:172–7. [PubMed] [Google Scholar]

6. Aminoshariae A, Kulild JC, Donaldson M, Hersh EV. Evidence-based recommendations for analgesic efficacy to treat pain of endodontic origin: A systematic review of randomized controlled trials. J Am Dent Assoc. 2016;147:826–39. [PubMed] [Google Scholar]

7. Sethi P, Agarwal M, Chourasia HR, Singh MP. Effect of single dose pretreatment analgesia with three different analgesics on postoperative endodontic pain: A randomized clinical trial. J Conserv Dent. 2014;17:517–21. [PMC free article] [PubMed] [Google Scholar]

8. Sathorn C, Parashos P, Messer H. Antibacterial efficacy of calcium hydroxide intracanal dressing: A systematic review and meta-analysis. Int Endod J. 2007;40:2–10. [PubMed] [Google Scholar]

9. Pai S, Vivekananda Pai AR, Thomas MS, Bhat V. Effect of calcium hydroxide and triple antibiotic paste as intracanal medicaments on the incidence of inter-appointment flare-up in diabetic patients: An *in vivo* study. J Conserv Dent. 2014;17:208–11. [PMC free article] [PubMed] [Google Scholar]

10. Law A, Messer H. An evidence-based analysis of the antibacterial effectiveness of intracanal medicaments. J Endod. 2004;30:689–94. [PubMed] [Google Scholar]

11. Ehrmann EH, Messer HH, Adams GG. The relationship of intracanal medicaments to postoperative pain in endodontics. Int Endod J. 2003;36:868–75. [PubMed] [Google Scholar]

12. Carreira Cde M, dos Santos SS, Jorge AO, Lage-Marques JL. Antimicrobial effect of intracanal substances. J Appl Oral Sci. 2007;15:453–8. [PMC free article] [PubMed] [Google Scholar]

13. Mohammadi Z. Systemic and local applications of steroids in endodontics: An update review. Int Dent J. 2009;59:297–304. [PubMed] [Google Scholar]

14. Dall AQ, Jouhar R, Khoso NA. Comparison of inter-appointment pain between ledermix and no intracanal medicament in acute apical periodontitis. J Liaquat Univ Med Health Sci. 2011;10:106–11. [Google Scholar]

15. Jalalzadeh SM, Mamavi A, Shahriari S, Santos FA, Pochapski MT. Effect of pretreatment prednisolone on postendodontic pain: A double-blind parallel-randomized clinical trial. J Endod. 2010;36:978–81. [PubMed] [Google Scholar]

16. 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. [PubMed] [Google Scholar]

17. Schimmer BP, Parker KL. In: Adrenocorticotropic hormone. Adrenocortical steroids and their synthetic analogs; inhibitors of the synthesis and actions of adrenocortical hormones. Goodman and Gilman's the Pharmacological Basis of Therapeutics. Hardman JG, Limbird LE, editors. New York: McGraw-Hill; 1996. [Google Scholar]

18. Ng YL, 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. [PubMed] [Google Scholar]

19. Nobuhara WK, Carnes DL, Gilles JA. Anti-inflammatory effects of dexamethasone on periapical tissues following endodontic overinstrumentation. J Endod. 1993;19:501–7. [PubMed] [Google Scholar]

20. Mohammadi Z, Farhad A, Khalesi M. Pharmacological strategies to control post-operative endodontic pain. Dent Res J. 2007;4:61–8. [Google Scholar]

21. 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. [PubMed] [Google Scholar]

22. Kustarci A, Akpinar KE, Er K. Apical extrusion of intracanal debris and irrigant following use of various instrumentation techniques. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;105:257–62. [PubMed] [Google Scholar]

23. Trope M. Relationship of intracanal medicaments to endodontic flare-ups. Endod Dent Traumatol. 1990;6:226–9. [PubMed] [Google Scholar]

24. Dunston CR, Griffiths HR, Lambert PA, Staddon S, Vernallis AB. Proteomic analysis of the anti-inflammatory action of minocycline. Proteomics. 2011;11:42–51. [PMC free article] [PubMed] [Google Scholar]

25. Hoshino E, Kurihara-Ando N, Sato I, Uematsu H, Sato M, Kota K, et al. *In-vitro* antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. Int Endod J. 1996;29:125–30. [PubMed] [Google Scholar]

26. Alam T, Nakazawa F, Nakajo K, Uematsu H, Hoshino E. Susceptibility of *Enterococcus faecalis* to a combination of antibacterial drugs (3 mix) *in vitro*. J. Oral Biosci. 2005;47:315–20. [Google Scholar]

27. Shaik J, Garlapati R, Nagesh B, Sujana V, Jayaprakash T, Naidu S. Comparative evaluation of antimicrobial efficacy of triple antibiotic paste and calcium hydroxide using chitosan as carrier against *Candida albicans* and *Enterococcus faecalis*: An *in vitro* study. J Conserv Dent.

2014;17:335–9. [PMC free article] [PubMed] [Google Scholar]

28. Holdgate A, Asha S, Craig J, Thompson J. Comparison of a verbal numeric rating scale with the visual analogue scale for the measurement of acute pain. Emerg Med (Fremantle) 2003;15:441–6. [PubMed] [Google Scholar]