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# The Effect of Preoperative Administration of Analgesic, Antihistamine and Combination of Two on Post Operative Pain in Teeth with Symptomatic Apical Periodontitis: A Randomized Controlled Trial

Dr. Champa Chikkamallaiah, Reader, Department of Conservative Dentistry and Endodontics, The Oxford Dental College, Bangalore.

Dr. Srinivas Panchajanya, Reader, Department of Conservative Dentistry and Endodontics, The Oxford Dental College, Bangalore.

Dr. Srirekha A, Professor and Head of the Department, Department of Conservative Dentistry and Endodontics, The Oxford Dental College, Bangalore.

Dr. N. Parvathy Menon, Post graduate student, Department of Conservative Dentistry and Endodontics, The Oxford Dental College, Bangalore.

Dr. Neha Patel, Post graduate student, Department of Conservative Dentistry and Endodontics, The Oxford Dental College, Bangalore.

**Corresponding Author:** Dr. N. Parvathy Menon, Post graduate student, Department of Conservative Dentistry and Endodontics, The Oxford Dental College, Bangalore.

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## Introduction

One of the aims of root canal treatment is to prevent or eliminate pain. Although dental procedures can be performed without producing pain using local anaesthetics, post operative pain is relatively common after some procedures, especially in patients with pre-operative pain. [1]Post operative pain following root canal treatment occurs because of acute inflammation within the periradicular tissues in response to an increase in intensity of stimulants coming from root canal.[2] A recent systematic review showed that between 3 – 58% of the patients were reported to have experienced endodontic post operative pain.[3] Some studies have reported mild pain after chemo-mechanical preparation in about 10 – 30% of the cases and others have reported that the frequencies of interappointment emergencies ranged from 1.4% to 16%.[4] Furthermore, a positive association has been demonstrated between post operative pain and the presence of apprehension and pre operative pain.[5]

The management of post operative pain has been the subject of many research studies, including pre operative explanations and instructions, long acting anaesthesia, glide path, occlusal reduction, medication using salicylic acid, NSAID's, combination of Ibuprofen and Acetaminophen, narcotic analgesics, a combination of narcotic analgesics with Aspirin or Acetaminophen and steroidal anti- inflammatory drugs.[4,6]

Antihistamines have been used in endodontics for a variety of different purposes, including as an intracanal medicament, reducing post-operative pain by local prophylactic Benadryl injection anaesthesia and management of sodium hypochlorite accident.[7,8] The first study of anti-histamines in endodontics was by Stewart[9]. He prepared an antihistamine- antibiotic compound for

root canal medication and found that this compound inhibited the growth of heavy concentrations of mixed microorganism's invitro

No study has been conducted to evaluate the effect of combination of analgesic and antihistamine on post-operative pain levels. Thus the aim of the study was to evaluate the effect of pre operative administration of antihistamine, analgesic and a combination of the two on post operative pain in pre molar teeth with symptomatic apical periodontitis. The null hypothesis was that there would be no difference among the groups in post operative pain.

**Materials and Methods**

The ethical clearance was obtained from the institutional review board.The inclusion criteria were healthy patients, aged between 18 to 45 years, with a maxillary premolar tooth with symptomatic apical periodontitis. Symptomatic apical periodontitis was determined on the basis of clinical symptoms, severe pre operative pain[Visual Analogue Scale {VAS} rating more than 60] and severe percussion pain [Visual AnalougeScale {VAS} rating more than 60].

The exclusion criteria were as follows- patients under the age of 18, any systemic diseases or allergic reactions, patients who had used any type of analgesic or antibiotic within 3 days, patients whose affected tooth had had root canal treatment, sinus tract or showed localized gum swelling, patients with severe periodontal disease, periodontal pockets more than 3mm in the affected tooth or a periapical radiolucency more than 3 cm in diameter. Also excluded were patients whose affected tooth had curved roots, excessive long or short root length, problem in determining working length, broken files, over instrumentation and over or incomplete filling.

Patients were randomly divided into four groups on basis of Chit system. The patient number and group number were recorded. Informed consent was obtained from each patient, possible discomfort and risks were fully explained. A total of 40 patients were divided into 4 groups [ n = 10 ], according to the type of pre-operative drug administered is as follows:

**Group 1 - Analgesic** [Diclomol – Diclofenac sodium + Paracetamol]{n=10}[Endolabs Limited, Batch no: ETQ0631]

**Group 2 - Antihistamine** [Avil - 22.7 mg Pheniramine hydrogen maleate]{n= 10}[Sanofi India Limited, Batch no: 528304]

**Group 3 - Combination of the two**{n=10}

**Group 4 - Placebo** [Capsule filled with sugar]{n=10}

Baseline Visual analogue scores were recorded {Pre-operative}. The selected patients were explained about the VAS scale rating and were given sheets of VAS scale to mark at 12 hours, 24 hours and 3 days. The administration of drugs and the root canal treatments were performed by two different researchers. The drugs were powdered and placed into capsules of the same size and colour. One researcher knew the allocation and drug type in capsules, but the operator and the patient did not know which drug type was administered. Fifteen minutes after drug administration, all patients received 2 ml of anaesthetic with 2% lignocaine with 1:200000 adrenaline. All procedures were completed under rubber dam isolation. After access opening was done,working length was determined 1mm from the radiographic apex using radiographic methodwhich was confirmed byelectronic determination with an apex locator [Coletene Canal pro]. Neo-endo rotary files were used to complete root canal preparation as per manufacturer's instructions{17, 4%; 20,4%;25,4%}using new instruments for each patient.A size 10 K file was used to maintain apical patency.

During instrumentation, irrigation was carried out with 2 ml of 5.25% Sodium hypochlorite and a final rinse was performed with 5 ml of 17% EDTA for 1 minute to

remove the smear layer. After final irrigation, the root canals were dried with absorbent paper points and then filled with matched single cone gutta percha points and zinc oxide eugenol sealer. The pulp chamber was filled with a nano hybrid composite resin and then light cured.

If patients experienced pain, they were advised to take Diclomol [Endolabs Limited, India]. Patients recorded their pain experience on a customized form, which they also used to record any analgesic intake. The investigator made a phone call at time points of 12 hours, 24 hours and 3 days to remind the patient to mark his/her readings.

**Statistical Analysis**

Data was analysed usingFriedman's test, chi square test and Wilcoxon Sign rank test (Level of significance $p<0.05$) for assessing the pain levels at 12 hours, 1 day and 3 days.

Kruskal-wallis test was used for inter-group comparisons. ($p<0.05$).

**Results**

According to the results, it was found that there was a significant difference in the VAS scoresof postoperative pain levels for the analgesic, anti-histamine and the combination group of drugs assessed at 12 hrs, 1 day and 3 days as demonstrated in Table 1.

However, there was no significant difference in the pain levels obtained between inter group drug administration in the tested time periods. ($p>0.05$). Table 2

Table 1: Comparison of VAS score between different time intervals in each study group.

| Group | | N | Mean (SD) | Range | Median (Q1-Q3) | Friedman test | | Wilcoxon Sign rank test (p-value) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Chi square value | p-value | 1 vs 2 | 1 vs 3 | 2 vs 3 |
| Analgesic | 12 Hours | 10 | 1.6 (0.97) | 0 – 3 | 1.5 (1- 2.25) | 15.20 | 0.001* | 0.01* | 0.006* | 0.03* |
| | Day 1 | 10 | 0.8 (0.79) | 0 – 2 | 1(0-1.25) | | | | | |
| | Day 3 | 10 | 0.3 (0.48) | 0 – 1 | 0(0-1) | | | | | |
| Anti-Histamine | 12 Hours | 10 | 1.9 (1.10) | 1 – 4 | 1.5 (1-3) | 15.20 | 0.001* | 0.03* | 0.006* | 0.01* |
| | Day 1 | 10 | 1.3 (0.67) | 0 – 2 | 1(1-2) | | | | | |
| | Day 3 | 10 | 0.5 (0.53) | 0 – 1 | 0.5 (0-1) | | | | | |
| Combination | 12 Hours | 10 | 1.5 (1.08) | 0 – 3 | 1.5 (0.75-2.25) | 12.09 | 0.002* | 0.01* | 0.01* | 0.18(NS) |
| | Day 1 | 10 | 0.9 (0.74) | 0 – 2 | 1(0-1.25) | | | | | |
| | Day 3 | 10 | 0.6 (0.70) | 0 – 2 | 0.5 (0-1) | | | | | |
| Placebo | 12 Hours | 10 | 2.9 (1.85) | 0 – 6 | 2.5 (1.75-4.25) | 14.21 | 0.001* | 0.01* | 0.01* | 0.04* |
| | Day 1 | 10 | 1.9 (1.20) | 0 - 4 | 2 (1-3) | | | | | |
| | Day 3 | 10 | 1.1 (0.88) | 0 - 3 | 1(0.75-1.25) | | | | | |

*$p<0.05$ Statistically significant, $p>0.05$ Non Significant, NS

Table 2: Comparison of VAS score between different study groups at each time intervals.

| | Group | | Mean (SD) | Range | Median (Q1-Q3) | Kruskal wallis test | |
|---|---|---|---|---|---|---|---|
| | | | | | | Chi square value | p-value |
| 12 Hours | Analgesic | 10 | 1.6 (0.97) | 0 - 3 | 1.5 (1- 2.25) | 4.46 | 0.22(NS) |
| | Anti-Histamine | 10 | 1.9 (1.10) | 1 - 4 | 1.5 (1-3) | | |
| | Combination | 10 | 1.5 (1.08) | 0 - 3 | 1.5 (0.75-2.25) | | |
| | Placebo | 10 | 2.9 (1.85) | 0 - 6 | 2.5 (1.75-4.25) | | |
| Day 1 | Analgesic | 10 | 0.8 (0.79) | 0 - 2 | 1(0-1.25) | 6.99 | 0.07(NS) |
| | Anti-Histamine | 10 | 1.3 (0.67) | 0 - 2 | 1(1-2) | | |
| | Combination | 10 | 0.9 (0.74) | 0 - 2 | 1(0-1.25) | | |
| | Placebo | 10 | 1.9 (1.20) | 0 - 4 | 2 (1-3) | | |
| Day 3 | Analgesic | 10 | 0.3 (0.48) | 0 - 1 | 0(0-1) | 6.18 | 0.10(NS) |
| | Anti-Histamine | 10 | 0.5 (0.53) | 0 - 1 | 0.5 (0-1) | | |
| | Combination | 10 | 0.6 (0.70) | 0 - 2 | 0.5 (0-1) | | |
| | Placebo | 10 | 1.1 (0.88) | 0 - 3 | 1(0.75-1.25) | | |

*p<0.05 Statistically significant, p>0.05 Non Significant, NS

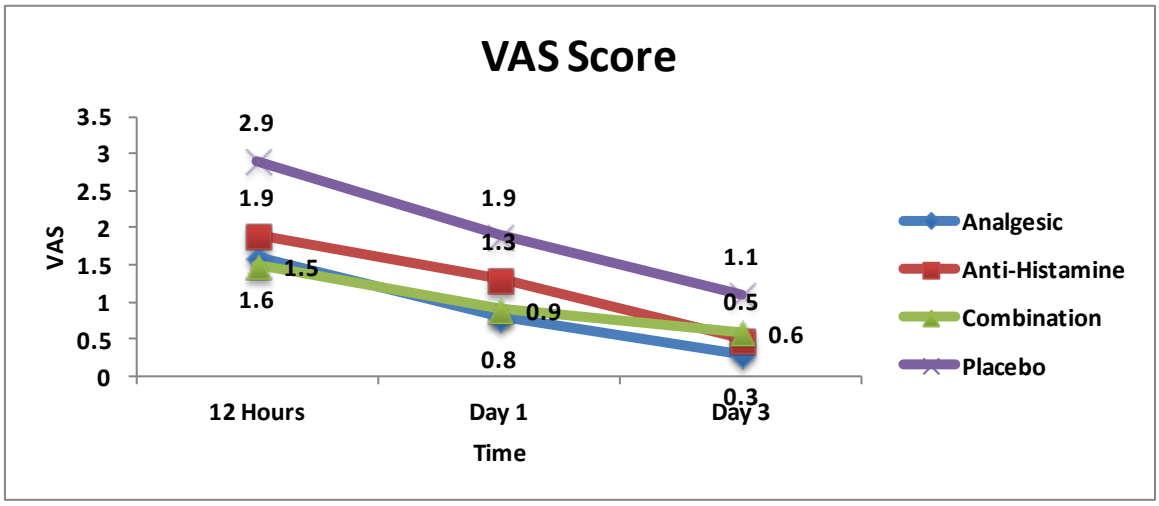


Figure 1: showing graphical representation of change in pain levels from 12 hours through day 3.

**Discussion**

This double blinded clinical trial compared the effect of anti-histamines, analgesics, combination of the two and placebo under controlled clinical conditions. Only patients with moderate to severe pain were selected for 2 reasons – first, controlling this type of pain is challenging for clinicians and secondly, because the greatest predictor for post operative pain intensity is the severity of pre operative pain. Most often endodontic patients come to the office already in pain, a more clinically relevant term to use in endodontics would be pretreatment analgesia, providing analgesia to patients before endodontic

treatment is started. This technique may decrease the establishment of central sensitization, a mechanism whereby spinal neurons increase their responsiveness to peripheral nociceptive input.[10]

In this study, the effects of the drugs were assessed upto 3 days. Most of the studies[11,12] haveonly assessed the effects of drugs for upto 8 hours. Majority of the patients experience pain in the first 24 hours after root canal treatment and thereforethis longer period of assessment were chosen, even though the drugs tested would not be expected to provide ongoing analgesia for this entire time period, owing to their relatively short plasma half lives.[4,]

Pain perception is a highly subjective and variable experience modulated by multiple physical and psychological factors.[13] Activation of nociceptive sensory nerve fibres may also be related to concentration of inflammatory mediators like histamine.[14] Also, histamine, an inflammatory mediator is capable of sensitizing and activating nociceptive sensory nerve fibres.[15]Oliveira et al[16] demonstrated that pre-treatment with anti-histamines decreased post-operative nociception in mice.

In the present study,it was found that anti-histamines and analgesics showed a statistically significant difference with p value being 0.001. The combination group was also found to be statistically significant with the p value being 0.002. The synergistic effect of the anti-histamine and analgesic could be the reason behind the success of the combination group.

Histamine facilitates migration of cells to inflammatory sites, stimulates lymphocyte activity, modulates aspects of eosinophil, neutrophil and mast cell behaviour. The effect of histamine is mediated by H1, H2, H3 and H4 receptors. Among these, H1 receptor plays a major role in potentiation of pro inflammatory immune cell activity.[17]In the present study, Pheniramine hydrogen maleate – an H1 receptor antagonist was administered. H1 receptor antagonist antihistamines reduce inflammation by inhibiting NF- kappaB production and also play an important role in central pain processing.[18]

Wells et al.[5] found that there were decreases in postoperative pain levels with the preoperative use of ibuprofen. Since there have not been any studies on the effect of preoperative administration of antihistamine on postoperative pain, a direct comparison here between present and previous findings here is not possible. The decreased pain levels in the antihistamine group can be explained by the ability of antihistamine to eliminate effects mediated by histamine resulting in sensitization and activation of nociceptive sensory nerve fibers.

The teeth were treated in a single visit because, given the combination of effective mechanical instrumentation, use of antimicrobial irrigant and three-dimensional obturation of the root canal, the single-visit treatment can effectively reduce the intracanal microbiota and allow a favourable outcome.[19]

Patients' individual pain thresholds and emotional factors may also have influenced outcomes. Patients can experience a wide range of different emotional responses for very similar levels of stimuli intensity, depending on their perceptions of the event.[20]

An interesting finding in the present study was that there was a significant difference in post operative pain levels assessed at 12 hours, 1 day and 3 days, but there was no significant difference between inter group drug administration at the same time intervals.

Pain is a very subjective experience. Quantifying and standardizing pain objectively across a group of individuals can be challenging. Numeric and verbal rating scales or behavioural observation scales have been used, traditionally in clinical studies.[21, 22]

Coll et al.[23, 24] critically reviewed nursing and health care publications for some of the available objective and

subjective measures of pain and established the suitability of a VAS for measuring the intensity of pain after day surgery. On the basis of their established criteria, the VAS score was found to be methodologically sound, conceptually simple, easy to administer and unobtrusive to the respondent. In this study VAS scale was used, but further studies could be carried out with a combined metric scale VAS HP [ Heft Parker].

There was no loss of participants at the end of the study.Two patients from the analgesic group, one from the combination of analgesic and anti-histamine group and four patients from the placebo group reported to the investigator complaining of pain and they were advised to take Diclofenac sodiumand paracetamol combination. These patients were not excluded from the study.

The main limitation of small studies is that they produce underpowered results. Since this was a pilot study, the sample size was comparatively small and the study is being continued in the department.

**Conclusion**

Within the limitations of our study, it can thereby be concluded that pre-operative administration of an antihistamine and combination of anti-histamine and analgesic can also be beneficial in reducing the post operative pain during endodontic treatments.

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