

Intracanal Medications *versus* Placebo in Reducing Postoperative Endodontic Pain - A Double-Blind Randomized Clinical Trial

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This prospective randomized, double-blind factorial study aimed to compare the efficacy of three different intracanal medicaments with the placebo in controlling the postoperative pain after complete root canal preparation. The study was performed on 64 mandibular molars of 64 patients with diagnosis of pulp necrosis and acute apical periodontitis. After chemomechanical procedures using the stepback technique and 1% sodium hypochlorite, the teeth were randomized into four treatment groups (n=16). In group I, canals were filled with calcium hydroxide paste mixed with 2% chlorhexidine gel, group II received 2% chlorhexidine gel, group III was treated with calcium hydroxide paste, and group IV received no dressing (control). Before dismissal, preoperative pain experience was recorded using a visual analog pain scale. Patients were then instructed to quantify the degree of pain experienced 4 h after treatment and daily for a further 24, 48, 72 and 96 h. Two-way repeated measures ANOVA test and *post hoc* Tukey's HSD test revealed that at each time interval groups I and II were significantly more effective in reducing the postoperative pain values than groups III and IV ($p < 0.05$). Dunnett's test showed that groups I and II differed significantly from control whereas difference between group III and control was not significant ($p > 0.05$). Patients with pulp necrosis and acute apical periodontitis that had been dressed with chlorhexidine alone and calcium hydroxide plus chlorhexidine gave rise to less pain than that experienced by patients who had a calcium hydroxide dressing alone or no dressing at all.

Key Words: calcium hydroxide, chlorhexidine, postoperative pain.

Introduction

Pain of endodontic origin has been a major concern to the patients and clinicians for many years. Torabinajed et al. (1) reported the occurrence of interappointment emergencies in approximately 50% of 2000 patients who had received root canal treatment in pulpless teeth. Pain may occur as a result of various causes such as microbial factors, change in periapical tissue pressure, chemical mediators, change in cyclic mediators and various psychological factors. The presence of microorganisms as a result of failure to properly disinfect the canal is the most important cause of pain. The flora of infected root canals showed the presence of considerable variety of microorganisms. These microorganisms may be responsible for the production of enzymes and endotoxins, the inhibition of chemotaxis and phagocytosis resulting in persistence of painful periapical lesion (2). The elimination of microorganisms from the root canal space is therefore crucial in the treatment of infected root canals. Thus insertion of antimicrobial dressing after preparation is generally recommended.

The antimicrobial dressing must have the greatest possible and most long-lasting effect against various bacterial species without causing irritation of periapical

tissue. The use of calcium hydroxide in reducing intracanal bacteria has been suggested (3). Calcium hydroxide alters bacterial cell walls and denatures a potent endotoxin (4), a lipopolysaccharide, thereby rendering it less antigenic (5). It has been suggested that calcium hydroxide has pain-preventive properties because of its antimicrobial or tissue-altering effects. In addition, it controls inflammatory process and induces repair (6).

Chlorhexidine is a broad spectrum antimicrobial agent and has been advocated as an effective intracanal medicament in endodontics (7). The advantages of chlorhexidine are its retentive character in root canal dentin (8) and its relatively low toxicity (9). In addition, it is also effective against strains resistant to calcium hydroxide (10). Some studies (11) have suggested that chlorhexidine could be used in combination with calcium hydroxide to improve the antimicrobial efficacy against calcium hydroxide resistant microorganisms. Although this combination has been tested for the reduction of postoperative pain (12), there was no control and no attempt was made to quantify the degree of pain relief.

This randomized double-blind factorial study was designed to compare the effectiveness of different intracanal medicaments with placebo in reducing

postoperative pain.

Material and Methods

The outline of this study was approved by the Ethics in Clinical Research Committee of Sri Guru Ram Das Institute of Dental Sciences and Research, Amritsar. The study was conducted during March 2011 to October 2011. The sample size was calculated as 16 in each group using G* power 3.1.2 software with type I error of 0.05 and statistical power of 80%. However, allowing for the possible loss of 10% in each group, 18 patients were included. Patients from both genders with ages ranging between 20 and 40 years old, presenting to the department of conservative dentistry and Endodontics of Sri Guru Ram Das Institute of Dental Sciences and Research for emergency relief of pain were selected. The study was confined to the patients with mandibular molar teeth with necrotic pulps and acute apical periodontitis. The diagnosis was performed by negative response to sensitivity pulp tests. Sensitivity pulp test was performed through thermal stimulation with endo-frost spray (Coltene Whaledent, Allstätt, Germany). Further status was confirmed by absence of vital pulp/bleeding during access opening. Clinical and radiographic evidence of apical periodontitis was confirmed by tenderness to percussion and widening of periodontal ligament space. The patient accepted two-visit treatment and criteria for postoperative pain evaluation, the tooth was functional and the patient was in good general health.

Exclusion criteria were teeth associated with fluctuant facial swelling (acute abscess) because it was felt that emergency management should include incision and drainage, teeth from patients who received antibiotic therapy within previous three months, patients having more than one tooth that require root canal treatment to eliminate the possibility of pain referral and false results and patients taking medications for pain or medication that would alter the pain perception. The nature of this study, complications and associated risks were fully explained to the patients and consents were obtained before initial treatment.

Patients were assigned to the medication group randomly using computer generated random number table. Apart from the case selection, all the clinical procedures were performed by a single endodontist (who was not a part of study process). The operator had no involvement with study outcome. To ensure blinding; neither the operator nor the patient had knowledge about the medication used. Allocation sequence was concealed from researchers who were part of study to reduce bias.

All the patients were anaesthetized with standard inferior alveolar nerve block injections by using 1.8 mL of 2% lignocaine with 1:200000 epinephrine (Xylocaine;

Astra Zeneca Pharmaceutical Products, London, UK). The solution was injected by using self aspirating syringes (Septodont, Saint-Maur-des-Fossés Cedex, France). After reaching the target area, aspiration was performed and 1.8 mL of solution was deposited at a rate of 1 mL/min. Teeth were reduced out of occlusion. The teeth were isolated with rubber dam and access gained to root canal. Using EDTA as a lubricant, patency of canal was checked with No. 10 K file (Dentsply Maillefer, Ballaigues, Switzerland) of 0.02 taper. Working length was determined with apex locator and then confirmed radiographically. After access opening chamber was blot dried. Lubricant was placed at the entrance of canal orifice. The patency of canal was checked with No. 10 K file. No. 15 K file was clamped to apex locator (Propex; Dentsply Maillefer, France) to measure the working length. Working length was confirmed with intraoral periapical radiograph. In case of disagreement between radiographic and electronic measurements, the latter was selected. Shaping of the canals was done by stepback technique using K files (Dentsply Maillefer) and Gates-Glidden drills (Dentsply Maillefer). Master apical preparation of 25–30 was done in narrow canals and 35–40 in wide canals. Throughout the treatment the canal system was flushed with 1% sodium hypochlorite alternating with 17% EDTA. At the conclusion of treatment, the canals were irrigated with normal saline, dried and medicated with one of the following medications. Group I: calcium hydroxide paste prepared with 2% chlorhexidine gel in equal parts (w/w), Group II: 2% chlorhexidine gel (Endogel, Itapetinga, SP, Brazil), Group III: commercial calcium hydroxide paste (Calcipulpe, Septodont, France) and Group IV: no dressing (control).

Intracanal medications were inserted into dried canals with the help of lentulo spirals (Dentsply Maillefer). Cavities were sealed with Cavit (ESPE Dental AG, Seefeld, Germany).

At the conclusion of appointment, each patient was given an evaluation sheet and the visual analog pain scale was explained to the patient. Patients were told to evaluate pain experienced 4 h after treatment and daily for additional 24, 48, 72 and 96 h according to the visual analog scale. Values were attributed according postoperative pain characteristics (Table 1).

Table 1. Values attributed according postoperative pain characteristics

Pain values	Characteristics
0-25	No pain to mild pain requiring no analgesics
26-50	Moderate pain requiring analgesics
51-75	Severe pain not relieved by analgesics
76-100	Extreme pain not relieved by any medicine

No antibiotics were prescribed. They were also requested to stop taking analgesics except if pain persisted or recurred.

The results were analyzed by two-way repeated measures ANOVA, with the groups serving as one factor and time as the other. Multiple comparisons of pain reduction values were performed using Tukey's HSD at $\alpha=0.05$. Statistical significance was defined in advance as p less than 0.05 by using the SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA) statistical package. Dunnett's test comparing experimental groups versus control was performed.

Results

Seventy-two teeth, belonging to 72 patients were treated. Eight patients were excluded for different reasons. Four patients did not return for further treatment and there was no evidence that these patients had their teeth extracted (2 from combination group, 1 from chlorhexidine group and 1 from calcium hydroxide group). Three patients had their teeth extracted because of intractable pain. Of these, 1 patient had been treated with calcium hydroxide. This tooth was extracted on the first day of trial whilst the 2 other teeth which had received no medication were extracted on day 2. It was not possible to include these 3 teeth in the results because there were no pain scores for the days after teeth had been extracted. Another patient belonging to the chlorhexidine group was excluded because of language difficulties that compromised the patient's ability to fill the evaluation sheet.

This way, a total of 64 teeth belonging to same number of patients were treated. Table 2 gives the mean pain values of each treatment by time. Preoperative mean pain value for all groups was 58.1, ranging from 56.8 (no dressing) to 59.7 (chlorhexidine). Homogeneity of variance was tested for each period using Barlett's test. It was found that for initial and 4 h, variance was homogeneous while for the remaining periods, i.e. 24, 48, 72, 96 h, variance was non homogeneous. There was a statistically significant difference in pain reduction amongst the four treatment groups ($p<0.001$).

The pain values also decreased significantly with time in all groups ($p=0.001$). The interaction between treatment and time was not significant ($p=0.519$). Post hoc Tukey's test showed that pain reduction in groups I and II was significantly higher ($p<0.05$) than in groups III and IV. Dunnett's test of significance showed that group I and group II differed significantly with control whereas the difference between group III and control was not significant for 24, 48, 72 and 96 h (Table 3). During the study, no complication associated with any of the intracanal medications was detected or reported by any patient.

Discussion

Cases with apical periodontitis were selected for this study. Therefore, certain factors affecting the treatment

Table 3. Comparison of experimental groups versus control (group IV) using Dunnett's test

Period	Experimental vs control group	Calculated t-value	Corrected Dunett's t-value (5% significance)	Remark
24 h	I vs IV	6.5766	2.6542	Sig.
	II vs IV	5.4496	2.6618	Sig.
	III vs IV	1.4594	2.6642	NS
48 h	I vs IV	6.5951	2.6623	Sig.
	II vs IV	5.8159	2.6622	Sig.
	III vs IV	1.2331	2.6163	NS
72 h	I vs IV	5.5315	2.6682	Sig.
	II vs IV	4.4290	2.6691	Sig.
	III vs IV	0.7744	2.6339	NS
96 h	I vs IV	4.1427	2.6764	Sig.
	II vs IV	3.8757	2.6758	Sig.
	III vs IV	0.1255	2.6402	NS

Sig.: Significant. NS: Non-Significant.

Table 2. Postoperative pain mean values and standard deviations according to the experimental and control groups

Period	Intracanal medication				Total
	CHX + Ca(OH) ₂	CHX	Ca(OH) ₂	Control	
Initial	58.6 ± 5.42	59.7 ± 5.82	57.3 ± 4.70	56.8 ± 5.21	58.1 ± 5.30
4 h	33.5 ± 5.44	34.5 ± 3.67	40.9 ± 3.25	42.1 ± 3.59	37.7 ± 5.52
24 h	20.6 ± 3.03	22.3 ± 3.00	28.6 ± 2.30	30.7 ± 5.13	25.5 ± 5.46
48 h	14.2 ± 2.51	14.6 ± 2.52	21.1 ± 5.00	23.4 ± 5.25	18.3 ± 5.63
72 h	6.31 ± 3.02	8.81 ± 2.88	16.5 ± 6.46	18.5 ± 8.02	12.5 ± 7.48
96 h	1.31 ± 1.53	2.00 ± 1.86	12.3 ± 7.92	12.8 ± 10.6	7.13 ± 8.58
Total	Mean value (SD) A	Mean value (SD) A	Mean value (SD) B	Mean value (SD) B	

CHX= Chlorhexidine. Different letters indicate significant differences ($p<0.05$).

outcome were eliminated. Occlusal reduction was done in the first visit and apical patency was determined. Apical patency was not maintained during root canal preparation, although Arias et al. (13) reported that there was significantly less postoperative pain when apical patency was maintained in non-vital teeth. However, this concept is controversial and not established yet. Moreover, Arias et al. (13) also suggested that patient with preclinical symptoms results in longer duration of pain when apical patency was maintained. The results of the present study revealed significant information on intracanal medications in controlling postoperative pain. There was greatest reduction in the pain values with chlorhexidine containing medications. It became apparent that the greatest reduction in pain took place when chlorhexidine alone or in combination with calcium hydroxide was used, with the greatest effect occurring during the first four hours after treatment followed by gradual decrease during subsequent days. Although the initial pain scores in cases treated with chlorhexidine (59.7) was more than that for the other drugs (58.6, 57.3), it had moved well below the other two from the 4th h postoperatively; the pain value of chlorhexidine remained well below that of other two over the next four days.

The fast and continuous action of chlorhexidine in controlling postoperative pain is striking. Its effect was measurable in 4 h after placement, even though medication had to diffuse into the dentinal tubules and the periapical tissues. It corroborates with the findings of previous studies (14,15), that found that chlorhexidine gel provided 100% inhibition of microorganisms at the depth of 200 μm as well as 400 μm from the day 1 and thus demonstrating its high diffusibility. Moreover, the effectiveness of chlorhexidine as intracanal medication in controlling the postoperative pain might be because of its ability to reduce or eliminate the endotoxins associated with the development of spontaneous pain. However, Gomes et al. (16) evaluated that 2% chlorhexidine gel was not effective in eliminating endotoxins from the primary infected root canals. However, in their study chlorhexidine was used as an irrigant and not as an intracanal medication. Furthermore, the present study is not in concurrence with that of Gama et al. (17), who reported that intracanal dressings with 0.2% chlorhexidine gluconate or calcium hydroxide in combination with CPCM were equally effective in reducing the postoperative pain. The difference in results could be because of lower percentage of chlorhexidine used.

Chlorhexidine has a broad-spectrum antimicrobial effect targeting both Gram positive and Gram negative microorganisms (18). Chlorhexidine has marked effect against resistant microorganisms in the root canal such as *E. fecalis* (19), anaerobic bacteria (20) and *Candida albicans*

(14). Apart from the positive antimicrobial efficacy of chlorhexidine, it is important that 0.1% to 2% chlorhexidine preparations were considered as toxicologically safe (21).

In the present study, calcium hydroxide was the least effective medication in reducing the postoperative pain. Despite good antibacterial properties shown by previous studies, many later studies have demonstrated the inability of calcium hydroxide to eliminate bacteria commonly found in the root canals (20) and those penetrated in dentinal tubules (22). The limited action of calcium hydroxide could be because of the buffer effect that dentin exerts over calcium hydroxide, reducing its antimicrobial action (23). In addition, few studies (20,22) found that certain bacteria present in root canal system were resistant to high pH of calcium hydroxide. In this study, the combination of calcium hydroxide and chlorhexidine was found to be the most effective in reducing the postoperative pain. Yoldas et al. (12) reported that two-visit endodontic treatment with intracanal medication with calcium hydroxide in combination with chlorhexidine decreased the postoperative pain in retreatment cases. It might be due to its high pH (12.8), suggesting an increase of the ionized capacity of the chlorhexidine molecule (24). Moreover, the addition of chlorhexidine to calcium hydroxide lowers its contact angle and improves the wettability of the medication on the root canal (11). This could also be because of synergistic effect of calcium hydroxide and chlorhexidine on liposaccharides/endotoxins produced by gram negative bacteria. Hence, both the intracanal medications complement their actions. This corroborates the findings of another study (25), which found that the antimicrobial efficacy of calcium hydroxide is increased when used in combination with chlorhexidine. However, according to Schafer and Bossmann (14), chlorhexidine alone was a more effective antimicrobial than its combination with calcium hydroxide whereas Delgado et al. (19) concluded that there was no difference between the antimicrobial activity of chlorhexidine with or without calcium hydroxide.

Haapasalo et al. (23) and later Krithikadatta et al. (15) have shown in independent studies that dentin matrix and collagen type I have an inhibitory effect on chlorhexidine. Nevertheless, both studies tested 0.2% chlorhexidine, which is much lower than the concentration used in the present study. The inhibitory effect of dentin on chlorhexidine can be overcome by increasing the concentration. However, caution must be exerted when drawing conclusions to *in vivo* situations. There is plausibility of negative interactions between endodontic disinfecting agents and the various compounds present in the root canal environment. This might have a vital role in deciding the clinical effectiveness of antibacterial agents.

The use of intracanal medications inhibits the growth of bacteria resulting in the reduction of microbial factors responsible for pain and inflammation. Under the conditions of the present study, it was concluded that pain associated with teeth having necrotic pulps, which were dressed with chlorhexidine alone or in combination with calcium hydroxide experienced less pain after the first appointment than patients whose teeth had been dressed with calcium hydroxide or received no intracanal dressing.

Resumo

Este estudo prospectivo randomizado, duplo-cego, fatorial teve como objetivo comparar a eficácia de três diferentes medicamentos intracanal com o placebo no controle da dor pós-operatória após a preparação completa do canal radicular. O estudo foi realizado em 64 molares inferiores de 64 pacientes com diagnóstico de necrose pulpar e periodontite apical aguda. Após os procedimentos químico-mecânicos com a técnica escalonada (*stepback*) e hipoclorito de sódio a 1%, os dentes foram divididos aleatoriamente em quatro grupos de tratamento (n=16 por grupo). No grupo I, os canais foram preenchidos com pasta de hidróxido de cálcio misturado com 2% de clorexidina gel, grupo II receberam 2% de clorexidina gel, grupo III foi tratado com uma pasta de hidróxido de cálcio e do grupo IV não receberam curativo (controle). Antes de liberar o paciente, a sensação de dor pré-operatória foi registrada com uma escala visual analógica. Os pacientes foram instruídos para quantificar o grau de dor experimentada após 4 h de tratamento e diariamente após 24, 48, 72 e 96 h. Os testes ANOVA a dois critérios para medidas repetidas e teste de Tukey *post hoc* HSD revelaram que, a cada intervalo de tempo, o grupo I e grupo II foram significativamente mais ($p < 0,05$) eficazes na redução da dor pós-operatória que os grupos III e IV. Além disso, o teste de Dunnett mostrou que o grupo I e grupo II diferiram significativamente com o controle enquanto que a diferença entre o grupo III e controle foi não significativo. Pacientes com necrose pulpar e periodontite apical aguda que receberam curativos de demora de clorexidina e hidróxido de cálcio mais clorexidina apresentaram menos dor do que aqueles que receberam curativo de hidróxido de cálcio ou não receberam qualquer curativo.

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