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Research Article

Influence of Calcium Hydroxide Chlorhexidine Combination vs. Calcium Hydroxide as an Intra Canal Medicaments on Postoperative Flare -up Following Two-Visit Endodontic Retreatment Cases: Single Blinded Randomized Clinical Trial

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Abstract

Introduction: It was hypothesized that post endodontic flare up often follows endodontic treatment in non-vital teeth as well as after retreatment rather than in vital teeth; that requiring an unscheduled appointment and active treatment. The aim of the study was to evaluate the influence of calcium hydroxide chlorhexidine combination and calcium hydroxide intra-canal medicaments on the postoperative flare-up following two visit endodontic retreatment cases.

Methods: Twenty four adult patients, aged from 20-50 years old, suffering from failed previous endodontic treatment were participated in this randomized, controlled, clinical single blinded study. Patients were assigned into two equal groups of 12 patients in each. After removal of the previous root canal filling, root canals were prepared and medicated with calcium hydroxide chlorhexidine combination (CA OH/CHX) in the intervention group, whereas the comparator group was medicated with calcium hydroxide as intra canal medicament for 7 days period. Postoperative pain and swelling were recorded after 6, 12, 24, 48, 72 hours and at 7 days before and after obturation using categorical scale.

Results: Statistically significant difference was detected between the 2 groups at the first 6, 12 and 24 hours with intervention group recording high incidence of postoperative flare-up. As well the intervention group showed statistically significantly higher intake of analgesics than control group.

Conclusion: Calcium hydroxide paste showed favorable results in terms of postoperative pain and swelling.

Keywords: Endodontic Retreatment; Calcium Hydroxide; Calcium Hydroxide Chlorhexidine; Intra-Canal Medicament; Postoperative Flare-Up

Abbreviations

CA OH/CHX: Calcium Hydroxide Chlorohexidine Combination; CA OH: Calcium Hydroxide; CHX: Chlorhexidine; EDTA: Ethylene Diamine Tetra Acetic Acid.

Introduction

The purpose of root-canal treatment (RCT) is thorough mechanical and chemical cleaning of an infected root-canal system, followed by its complete obturation with a filling material. Removal of infected substances and avoidance of further intraoperative/postoperative infection are crucial for successful RCT [1]. Endodontic treatment failure is usually character by the persistence or manifestation of an apical periodontitis [2]. It can be manifested as post endodontic pain which is referred to as flare-up, which is defined as acute exacerbation of asymptomatic pulp or per radicular pathology after the initiation or continuation of root canal treatment. It is represented as occurrence of severe pain and/or swelling, requiring an unscheduled appointment and active treatment [3]. Ercan*., et al,* [4] stated that flare-ups often follow endodontic treatment in non-vital teeth as well as after retreatment rather than in vital teeth. Orth grade retreatments presented a success rate of 81% classified as healed and 93 % as no symptoms and fully functional [5]. Retreatment cases require the use of suitable intra-canal medicaments that simultaneously eliminate bacteria, prevent

their proliferation and act as a barrier against their ingress, thus; cutting off their nutrient supply [6].

Calcium hydroxide (CA OH) is considered the intra-canal medication of choice, mainly because of its high pH, which provides an excellent antibacterial activity and strong capacity of inactivating the bacterial endotoxin [4]. However, the antimicrobial activity of CA OH depends on direct contact with bacteria, Ørstavik and Haapasalo [7] demonstrated that it is not effective in eliminating bacteria harboring the deep part of the dentinal tubules. On the other hand, Chlorhexidine gluconate (CHX) possesses broad spectrum antibacterial activity, substantively and it is also effective against strains resistant to calcium hydroxide [8]. Its antimicrobial effect is caused by the cationic molecule binding to negatively charged bacterial cell walls, thereby altering the cell's osmotic equilibrium [9]. It is an effective agent against gram positive, gram-negative bacteria and against microorganisms resistant to calcium hydroxide as *E. fecalis* [10], anaerobic bacteria and *Candida albicans* [8] and [11]. The advantages of chlorhexidine are its retentive character in root canal dentin [12] and its relatively low toxicity [13]. CHX combined with CA OH has recently been advocated as a suitable intra-canal medicament in endodontic periapical pathology [14]. The purpose of this randomized clinical trial was to evaluate the influence of the calcium hydroxide chlorhexidine combination and calcium hydroxide intra-canal medicaments on postoperative pain and swelling (flare-up) in two visits endodontic retreatment cases.

Null hypothesis was that there would be no difference between calcium hydroxide chlorhexidine combination in comparison with calcium hydroxide as intra-canal medicament on postoperative flare-up in retreatment cases at 6, 12,24,48,72 hours and 7 days.

Subjects and Methods

Ethics

The protocol of this randomized clinical trial was approved by the institutional review boards/ethical committees (IRBs/ECs) of the Faculty of Dentistry, Cairo University. The clinical trial was registered on www.clinicaltrials.gov (code: NCT03064191)0.

Sample size

The sample size was calculated by the G power program (Universidad Düsseldorf, Düsseldorf, Germany). We will need to study 10 subjects in each group to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.8 and type I error probability equal to 0.05. This number is to be increased to 12 in each group to correct for non-parametric usage; and to 14 to compensate for possible losses during follow up.

Selection of subjects

All included patients signed an informed consent after the explanation of the involved procedures and the possible risks. Interventions were done by a master's degree student in the Department of Endodontics. Twenty-four participants recruited from the outpatient clinic of the endodontic department, Faculty of Dentistry, Cairo University, in the duration between February 2017 and January 2018.

Inclusion and exclusion criteria

Inclusion criteria involved patients complaining from signs and symptoms of endodontic treatment failure, patients who had defective root canal filling, patients who were in good health with no systemic disease, patients age range between 20 and 50 years, patients who could understand the categorical tool (points) for measurement in the pain diary and were able to sign the informed consent.

Patient exclusion criteria included those with complicated systemic disease; with severe pain and/or acute apical abscesses; Age under 18 years old; those administered antibiotics or corticosteroids; with multiple teeth that requires retreatment to eliminate the possibility of pain referral and who had root canals that could not be retreated.

Diagnostic criteria of retreatment procedure confirmed by the history of the chief complaint, clinical and radiographic examinations. Patients who complained from pain and/or swelling with history of previous treatment or referred from the prosthodontics department for retreatment due to inadequate root canal filling were included in the study according to the eligibility criteria.

Randomization, allocation concealment and blinding

For randomization, a table of random numbers (from 1 to 24) distributed using computer sequence generation (Microsoft Excel) into group I and group II with participants numbers (12 numbers in each group). The table was kept with the assistant supervisor. The patient was blinded (single-blind study). After the subject was confirmed to be enrolled in the trial, the investigator gave a phone call to the co-supervisor who allocated the patient either to the in-

tervention or the control group according to the generated random sequence. The investigator was the one responsible for performing the whole procedure, assessing the outcomes from the patients and recording any abnormal findings such as mishaps or side effects.

Operating Sequence

First Session

Patients were anesthetized using a solution of 4 % articaine with 1:100,000 epinephrine hydrochloride (Alexandria Co. for Pharmaceuticals, Alexandria, Egypt). Isolation was performed using rubber dam. The previous restoration was removed using high-speed hand piece. Modification of the access cavity was performed using an Endo-Z bur (DENTSPLY Maillefer, Ballaigues, Switzerland). Removal of the root canal filling material was performed as follow: Few drops of the Carvene solvent (PREVEST Den Pro, India) were injected at the canal entrance using a 27-gauge open end needle (Endo-Top, Cerkamed, Poland) and left for 2 minutes. Protaper Universal rotary system (DENTSPLY, Maillefer, Ballaigues Switzerland) adjusted in an NSK endo motor (Endo mate, NSK, Japan) with the speed adjusted at 300 rpm with torque 2 adjusted according to the manufacturer's instructions. Protaper Universal System (PTU) finishing files were used in the coronal 2/3 of the canal in an up and down motion, sequentially. All the files were introduced to the point where resistance was felt by the filling materials after which the file was removed, cleaned and reinserted with addition of solvent. Then, Hedstorm hand files (MANI, INC. Industrial Park, Utsunomiya, Tochigi, Japan) was used to complete the removal of the apical part of the canal in a crown down technique. Irrigation was performed using 3 ml 2.5% Na OCl with 27-gauge open end needle. Working length was determined by apex locator (APEXII, NSK, Japan) and confirmed by periapical radiographs 1 mm short from the radiographic apex. Then, Chemo-mechanical preparation was performed. Irrigation with 3ml 2.5% Na OCl between each subsequent file and final irrigation with saline was performed. Protaper special paper points were used to dry the canals. Then, canals were classified to 2 groups according to medicament used into:

- **Group (I):** Control group, a Metapex calcium hydroxide (Meta Biomed Co. Ltd, Korea) was used. The paste was injected directly in the root canal through Meta biomed syringe with disposable tip.
- **Group (II):** Experimental group, Calcium hydroxide chlorhexidine combination (CA OH/CHX) was used. A paste consists of 1.2 g powder of CA OH (Cerkamed, Poland) mixed with GLUCO-CHX 2% chlorhexidine gel (Cerkamed, Poland) mixed in 1:1 ratio on a paper pad and then injected through a special Cerkamed plastic syringe with disposable tip into the root canal system.

For both groups, a lentulo spiral (size 35) (DENTSPLY Maillefer, Ballaigues, Switzerland) connected to low speed headpiece was introduced into the root canal and slowly rotated in a clock wise motion into the canal 2 mm short of the working length [15].

Excess medication was removed from the pulp chamber and a sterile cotton pellet placed and a Den Seal glass ionomer (Prevest Dent Pro, Heidelberg Germany) was used to seal the cavity.

Second session

One week after the initial appointment, the patients were recalled returning for the completion of endodontic treatment. Anesthesia and rubber dam were applied. Glass ionomer filling and the cotton pellet were removed from the pulp chamber. Removal of the intra-canal medicament was performed using a hand K-file and irrigation with 3 ml 2.5% sodium hypochlorite solution. Then, canals were flushed with 3 ml normal saline. Then, each root canal was rinsed with 17% EDTA solution (EDTA, PREVEST Den Pro, India) 1 ml for 3 minute [16]. then followed by saline as a final rinse. Master cone was confirmed using periapical x-ray and obturation was performed using customized gutta-percha points and AD seal resin sealer (Meta Biomed Co. Ltd, Korea) using lateral compaction technique. Glass ionomer was placed as a temporary restoration. Postoperative radiograph was taken to confirm the density and length of the filling material.

Pain assessment and outcomes

Postoperative pain: Subjectively measured using a categorical scale of 4 classes:

1. No pain;
2. Mild pain: recognizable but not discomforting pain that required no analgesics;
3. Moderate pain: discomforting but bearable pain (analgesics if used were effective in relieving pain);
4. Severe pain: difficult to bear (analgesics were effective in relieving pain) [14].

Postoperative swelling: categorized as presence or absence of swelling.

Will be measured after 1st visit at 6h, 12h, 24h, 48h, and 72h and after 7 days from 1st visit: Pre-obturation/ Post-obturation.

Objectively: percussion test (presence or absence of pain).

Primary outcomes: Postoperative flare-up (pain or/and swelling) will be measured using the categorical scale s as mentioned above after 6hrs, 12 hrs., 24 hr., 48hr, 72 hr., and 7 days pre and post obturation. With severe pain and /or swelling considered as flare-up.

Secondary outcomes: Recording analgesic intake as well as number of analgesic tables.

Statistical analysis

Qualitative data were presented as frequencies and percentages. Chi-square test or Fisher's Exact test (when applicable) were used for comparisons between the two groups. Cochran's Q test was used to study the changes by time in each group. Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). Age data showed normal (parametric) distribution while number of analgesic tablets data showed non-normal (non-parametric) distribution. Parametric data were presented as mean and standard deviation (SD) values and compared using Student's t-test while non-parametric data were presented as median and range values and compared using Mann-Whitney U test. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows.

Results

The trial design followed the CONSORT 2010. The flow of the participants throughout the study is presented in (Figure 1).

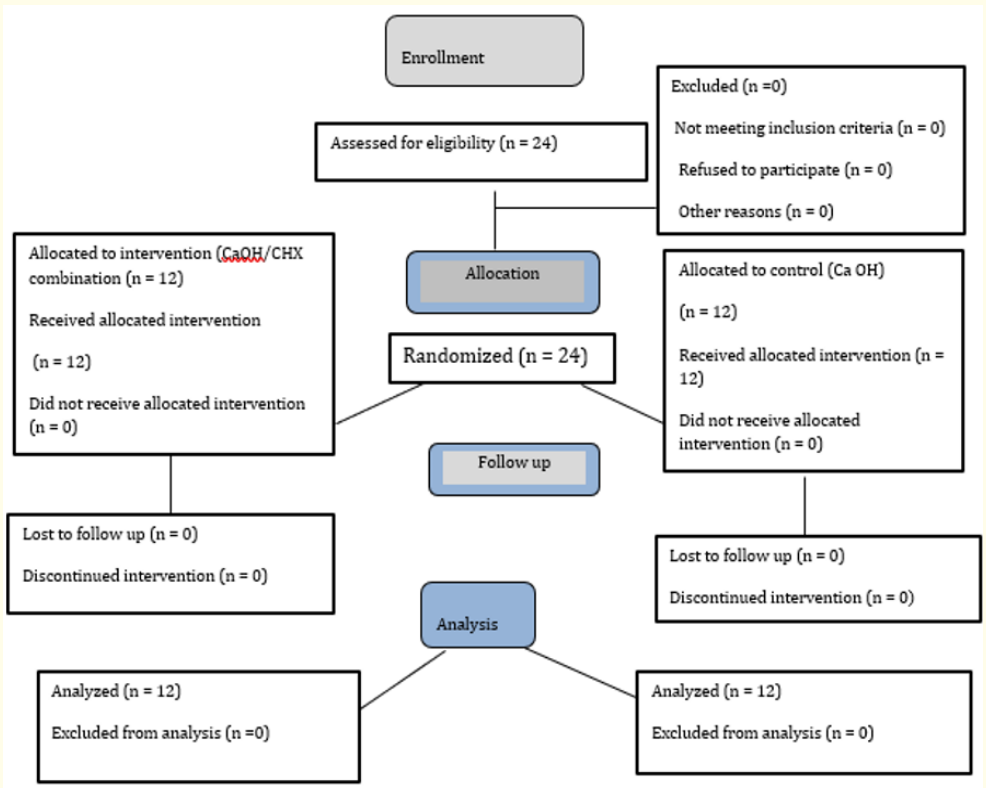

Figure 1: Consort 2010 Flow diagram of the trial design.

Postoperative pain

Demographic data (age, gender and tooth type distribution) illustrated in table 1.

Intragroup compassion

Pain severity in the intervention group (CA OH/CHX) at different time interval: There was a statistically significant change in

	Intervention (Ca OH/CHX) (n = 12)	Control (Ca OH) (n = 12)	P-value
Age (Years) Mean (SD)	37.5 (8)	37.6 (8.3)	0.968
Gender [n (%)]			
Male	9 (75%)	5 (41.7%)	0.098
Female	3 (25%)	7 (58.3%)	
Tooth type [n (%)]			
Maxillary anterior	2 (16.7%)	1 (8.3%)	0.046*
Maxillary premolar	4 (33.3%)	6 (50%	
Maxillary molar	0 (0%)	2 (16.7%)	
Mandibular anterior	5 (41.7%)	0 (0%)	
Mandibular premolar	0 (0%)	2 (16.7%)	
Mandibular molar	1 (8.3%)	1 (8.3%)	

Table 1: Mean, standard deviation (SD), frequencies (n), percentages and results of Student's t-test, chi-square and Fisher's exact tests for comparisons of demographic data between the two groups.

**: Significant at P ≤ 0.05*

the severity of pain by time (P < 0.001). After 72 hours there was a statistically significant decrease in prevalence of severe pain in comparison to the previous time periods. At day 7, there was statistically significantly higher prevalence of no pain as illustrated in figure 2 Pain severity in the control group (COH) at different time interval: There was no statistically significant change (P = 0.051) as illustrated in figure 3.

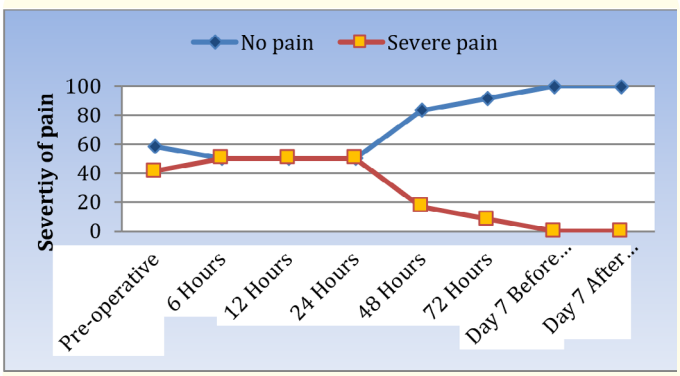

Figure 2: Line chart representing change by time in severity of pain within intervention group.

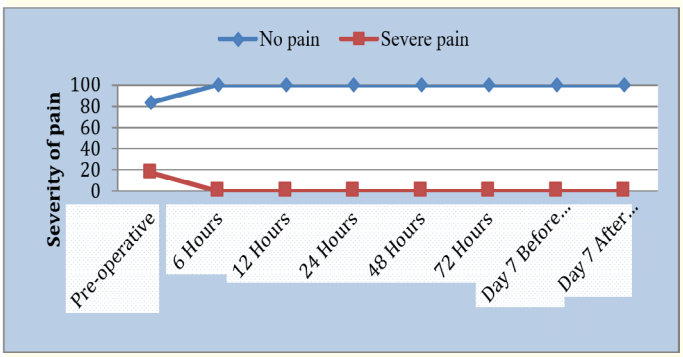

Figure 3: Line chart representing changes by time in severity of pain within control group.

Intergroup Comparison

After 6, 12 and 24 hours, there was a statistically significant difference between the two groups with, the intervention group (CA OH/CHX) showed higher prevalence of severe pain than control group (P = 0.014). After 48 and 72 hours there was no statistically significant difference between the two groups (P = 0.478) as shown in figure 4.

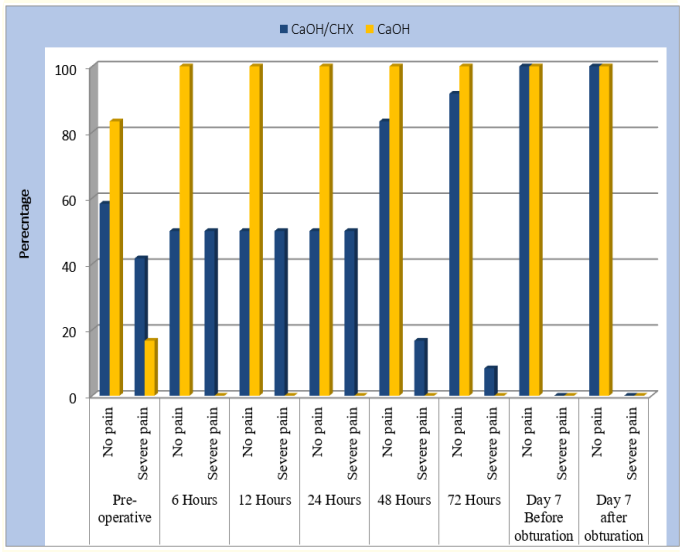

Figure 4: Bar chart representing severity of pain in the two groups.

®IBM Corporation, NY, USA.

®SPSS, Inc., an IBM Company.

Postoperative swelling

Only 2 cases experienced swelling in the intervention group (CA OH/CHX) between 24 to 72 hours period of time.

Intake of analgesics

Intervention group showed statistically significantly higher intake of analgesics than control group (P-value = 0.037) as illustrated in table 2.

	Ca OH/CHX (n = 12)		Ca OH (n = 12)		P-value
	n		%		
Intake of analgesics					
Yes	5	41.7	0	0	**0.037***
No	7	58.3	12	100	

Table 2: Frequencies (n), percentages (%) and results of Fisher's exact test for comparison between intakes of analgesics in the two groups.

*: Significant at P ≤ 0.05

Discussion

Retreatment procedure possess a great challenge because teeth with poor endodontic treatment contain a great number of bacterial species [14] in which *E. faecalis* has been detected in 77% of failed endodontic cases [17] and 30 % of all endodontic ally treated teeth are associated with post treatment disease [18]. The aim of the present study was to evaluate the influence of the calcium hydroxide chlorhexidine combination and calcium hydroxide as an intra-canal medicament on postoperative pain and swelling (flare-up) in two visits endodontic retreatment cases.

In our study intra-canal medicaments were used between visits to prevent postoperative pain caused by persistent intra-canal microorganisms or by secondary microbial invaders. Also, to deny space for microbial proliferation between visits preventing the re-contamination of the root canals [14].

Since age was found to have a significant effect on the postoperative pain, patients aging between 20 and 50 years old were selected. The re-treatment procedures were performed over two visits, aiming to reduce postoperative pain, decrease the number of flare-ups and provide antibacterial effect through the use of intra-canal medicament [14].

Various methods have been used for the removal of root canal filling materials, which are broadly classified into thermal, mechanical, chemical and a combination of the three [19]. In this study, a combination of chemical (Carvene solvent) and mechanical (Protaper universal rotary system (PTU) and Hedstorm files) were used. Where, solvents can soften and dissolve gutta-percha present in the root canal to facilitate its removal and allow for the penetration of manual and rotary instruments. Rotary files have proven their efficiency in removing gutta-percha especially Pro Taper rotary files, with no difference between using Universal system and retreatment system [20]. The effectiveness of PTU in cleaning the root canals is augmented by using the solvent with the instrument rotation, which causes the dilution and plasticization of gutta-percha [21]. On the other hand, De Valo., *et al.* [22] emphasized the importance of hand files for removing filling material.

The working length was determined by IPEX electronic apex locator, because of its reliability [23]. Root canals were irrigated with 2.5% sodium hypochlorite (Na OCl) due to its competence in the reduction of intra-canal microbiota [24]. Side vented needle was used to lower the incidence of irrigant extrusion into the periapical space [25].

Though Calcium hydroxide is one of the most commonly used intra canal medicaments, owing to its high pH and potent antibacterial activity [9] was reported to be ineffective against all bacteria species especially Enterococcus faecalis found in the root canal [26]. On the other hand [27], stated that the mixture of CA OH/CHX combination showed synergistic action and greater efficacy than calcium hydroxide alone [28,29]. Lentulo spiral used after insertion of the intra-canal medicament would help in activation of the paste and thus better penetration of the paste [15]. Pain measurement was performed using categorical scale of 4 classes as a modification to the visual analog scale (VAS) for its validity and simplicity in pain rating [14].

The results of this study showed that after 6, 12, 24 hours, there was a statistically significant difference between the CA OH/CHX combination group and CAOH group. Where CA OH/CHX group showed higher prevalence of severe pain (postoperative flare-up) than CA OH group. Our findings are in agreement with [30] who reported low effectiveness of Ca OH/CHX group against candida albicans and Enterococcus faecalis. This might be due to the difference in pH of CHX than that of CA OH and also due to the binding of chlorhexidine molecule to calcium hydroxide ions and hence

inhibiting the free release of chlorhexidine molecule. This in turn attributed to the higher intake analgesic in the intervention group in compare to control group. Our results showed no statistically significant difference in postoperative flare-up between both group, after 48 and 72 hours. At day 7 either all cases in both groups showed no pain, whether before or after obturation. This finding was also in agreement with [30,31] and [33]. The limited action of calcium hydroxide could be attributed to the buffer effect that the dentin exerts over calcium hydroxide, reducing its antimicrobial action which is reflected on the action of chlorhexidine, thereby; reducing its anti-inflammatory action [34].

In contrast [27], reported that combination of CA OH and 2% CHX was significantly different in reducing inter-appointment pain than that of CA OH and saline group. However, the variation in results could be related to different material formulation and different inclusion criteria of the cases. Similarly [35] who reported that the combination of calcium hydroxide with 2% chlorhexidine reduce the postoperative pain more than calcium hydroxide group. This difference in results may be related to different selection of cases, as the previous study included necrotic mandibular molar with acute apical periodontitis and the participants were sensitive to percussion and so the pain will normally decrease after application of medicament during the first hours after treatment followed by gradual decrease during subsequent days, which result in difference in the pain records postoperatively. In our study, analgesics were only prescribed on-demand and not as a regular prescription of medication since it would influence the outcome measures of the study [14] and [29,31]. Among the non-steroidal anti-inflammatory drugs, Ibuprofen was selected because of its efficiency in treating acute pain and inflammation related to endodontic treatment, rapid absorption and metabolism by the liver [36].

Conclusion

Within the limitations of this study, it can be concluded that calcium hydroxide paste resulted in better pain control as well as absence of postoperative swelling in the first 24 hour and also, recorded no analgesic intake needed in all cases in compare to calcium hydroxide chlorhexidine combination as an intra-canal medicament.

Conflict of Interest

The authors deny any conflicts of interest in this study.

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