CONSORT RANDOMIZED CLINICAL TRIAL

The Effects of Calcium Silicate- and Calcium Hydroxide–based Root Canal Sealers on Postoperative Pain: A Randomized Clinical Trial

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SIGNIFICANCE

Calcium silicate– and calcium hydroxide–based root canal sealers resulted in statistically similar postoperative pain levels. Pain intensity in both groups statistically decreased compared with preoperative pain levels at 12 hours after treatment.

ABSTRACT

Introduction: This study aimed to compare the postoperative pain level changes resulting from using calcium silicate- (EndoSeal MTA) and calcium hydroxide–based (Sealapex) root canal sealers in mandibular first and second molar teeth with symptomatic apical periodontitis. **Methods:** A total of 60 patients with symptomatic apical periodontitis in their lower molar teeth were randomly allocated into 2 groups according to sealer type ($n = 30$). Demographic data, including gender, age, and smoking habit, and preoperative pain measures were recorded. Root canal treatments were performed in a single visit. Postoperative pain measurements and analgesic intake were measured at 6, 12, 24, and 48 hours and after 3, 5, and 7 days using the visual analog scale. The data were statistically analyzed using a chi-squared test (to compare gender, age, smoking habit, analgesic intake, and sealer extrusion), the Mann-Whitney *U* test (to compare pain levels), Friedman tests (for the evaluations of the reduction in pain levels over time), and Spearman's correlation test (to analyze the relationships of age, gender, smoking habit factors with postoperative pain) ($P = .05$). **Results:** The statistical analysis showed no significant differences between the groups in postoperative pain and analgesic intake at any of the time intervals evaluated ($P > .05$). **Conclusions:** Patients treated with calcium silicate– and calcium hydroxide–based root canal sealers experienced similar postoperative pain and no statistically significant differences were observed in analgesic intake. *(J Endod 2023;49:1588–1594.)*

KEY WORDS

calcium hydroxide–based sealer; calcium silicate–based sealer; EndoSeal MTA; postoperative pain; Sealapex

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Postoperative pain following endodontic therapy can be defined as a dental experience characterized by discomfort or suffering in the range of 3% to 58%[1]. Postoperative pain is difficult to attribute with certainty to specific factors, as various issues are associated with pain after root canal treatments (RCTs). These factors include age, gender, single or multiple visits, analgesic intake, periapical condition, tooth type, preoperative pain, instrumentation technique, and irrigation and root canal filling protocols[2]. The severity of inflammatory responses is affected by the sealer composition and may be related to the postoperative pain experienced following RCTs[3]. Root canal sealers may activate trigeminal nociceptors, which, along with immune reactions, may cause pain and flare-ups[4].

Calcium silicate–based root canal sealers (CSBSs) have demonstrated cytotoxicity in both *ex vivo* and animal experiments, and a 90.9% success rate was achieved at the 3-year follow-up[5,6]. CSBSs exert an antimicrobial effect by releasing hydroxyl ions and increasing pH[7]. Furthermore, calcium ions in CSBSs stimulate osteoblastic differentiation and bone formation[8]. Lee et al[8] and Zhang et al[3] showed that the Ca^{2+} in CSBSs induces the expression of bone-associated proteins, which is required for apatite genesis. Postoperative pain levels after CSBS use were similar to those following treatment with resin-based sealers[9,10].

Calcium hydroxide–based sealers (CHBSs) have been in use for more than 25 years. Previous studies have shown that CHBSs exert antibacterial effects by releasing hydroxyl ions and decreasing

cytotoxicity[11,12]. Paredes-Vieyra and Enriquez[13] evaluated the results of 1 visit RCTs of teeth with apical periodontitis at 2-year follow-up and showed that postoperative pain was recorded at 1.36% (only 2 cases of 146 teeth) after using CHBS at 2-year follow-up. Postoperative pain intensity was significantly higher in the AH Plus sealer group compared with Sealapex sealer at 24 to 48 hours when the sealer was extruded[14].

EndoSeal MTA (Maruchi, Wonju, Korea) is a premixed CSBS containing calcium silicate, calcium aluminate, calcium sulfate, and radiopaque material. It has demonstrated good physical properties, biocompatibility, great bond strength, minimal discoloration, and superior sealer distribution[15]. Shim et al[16] demonstrated that EndoSeal MTA and AH Plus yield similar intensities of postoperative pain. Another study also showed that AH Plus and EndoSeal MTA were associated with similar levels of postoperative pain and a similar intake of analgesics[9]. However, no study has evaluated the possible effects of calcium silicate– and calcium hydroxide–based root canal sealers on postoperative pain. According to the population, intervention, comparison, and outcome criteria (PICO) framework, a specific question was structured: "Does calcium silicate–based sealer result in similar postoperative pain levels compared to calcium hydroxide–based sealer?" In this framework, population represents mandibular first and second molar teeth with symptomatic apical periodontitis, intervention represents calcium silicate–based sealer, comparison represents calcium hydroxide–based sealer, and outcome represents postoperative pain levels. The null hypothesis was that there are no significant differences between calcium silicate– and calcium hydroxide–based root canal sealers in terms of postoperative pain levels.

MATERIALS AND METHODS

Sample Size Determination and Ethical Approval

This randomized, controlled clinical trial received ethical approval from the Ethics Committee of the Atatürk University, Faculty of Dentistry (Decision no. 83/2022). In this clinical trial, the Preferred Reporting Items for Randomized Trials in Endodontics 2020 guidelines were followed[17,18], and the study protocol was registered in a clinical trial database (No. TCTR2022118004 at https://www.thaiclinicaltrials.org/). Based on information from a prior investigation[19], a minimum sample size calculation was performed using the G*Power 3.1 software (Heinrich-Heine, Dusseldorf, Germany), with type I error (alfa) of 0.05, power (1-beta) of 0.95, effect size of 1.0997, and 2-sided hypothesis. The minimum required sample size was 27 patients per group at least. To enhance the statistical power of the study and compensate for potential patient loss, 30 patients were enrolled in each group. The patients signed a written informed consent form.

Inclusion and Exclusion Criteria

This study included systemically healthy patients aged 18 to 60 years with symptomatic apical periodontitis in the vital mandibular molars. Pulp sensitivity was confirmed by a positive response to electric pulp testing and a prolonged response, with moderate to severe pain, to cold testing. Patients with preoperative pain levels ranging from 45 to 100 mm (moderate to severe) on the visual analog scale (VAS, 0–100 mm)[20], preoperative percussion values >74 on the VAS, and periapical index (PAI) scores <2 were included. Patients with root resorption, immature teeth, teeth with crown damage, calcified canals, previous root canal fillings, and severe malocclusion, along with pregnant or breastfeeding patients, patients with PAI scores higher than 2, and those who had taken analgesics or anti-inflammatory drugs in the last 4 hours, were excluded.

Treatment Protocols

A simple randomization process was conducted to assign the individuals to treatment groups using web-based randomization software (http://www.random.org/) with a ratio of 1:1 allocation. Sealed, sequentially numbered, opaque envelopes were prepared before recruitment, with ID numbers written on the outside of envelopes before opening, to provide allocation protection. The process and application of randomization were handled by a secretary. Although patients were blinded to the type of sealer used for the treatment of their teeth, the operator could not have been blinded during the trial because of the nature of the process. Teeth were anesthetized by 4% articaine hydrochloride with 1:100,000 adrenaline (Ultracaine DS Forte; Aventis, Istanbul, Turkey) followed by another 1.8 mL with a supplemental buccal infiltration for pulpal anesthesia success. The tooth was isolated with a rubber dam, and an access cavity was performed using high-speed diamond burs spraying cooling water. Bleeding in the pulp chamber was considered a sign of pulp vitality. The working length (WL) was determined via an 8- or 10-K file (Dentsply, Maillefer, Switzerland) using an apex locator (Root ZX; J Morita USA Inc, Irvine, CA), after which it was radiographically verified. A 10-K file (Dentsply) was used to achieve apical patency.

A Reciproc Silver endodontic motor (VDW, Munich, Germany) was programmed to the "RECIPROC ALL" mode for root canal instrumentation using Reciproc R25 files (size 25, 0.08 taper; VDW) with the crown-down shaping procedure. When necessary, additional instrumentation was performed with R40 files (size 40, 0.06 taper) according to the initial apical diameter. Depending on the individual tooth, the final apical preparation size was determined as the first file binding at the WL. Root canals were flushed using a 30-gauge irrigation needle (Maxi Probe; Dentsply Sirona) containing 10 mL of 5% NaOCl (Imicryl, Konya, Turkey). During all irrigation procedures, the irrigation needle was injected into a depth 2 mm shorter than the WL to avoid irrigation complications. For final flushing, the canals were irrigated with 5% NaOCl (Imicryl) for 5 minutes, followed by 17% EDTA (Imicryl, Konya, Turkey) for 1 minute before finishing with 5% NaOCl (Imicryl) and saline. The root canals were dried with paper points, and the gutta-percha master cone fit was verified with a periapical radiograph before root canal filling was initiated.

For the CSBS group (EndoSeal MTA; Maruchi, Wonju, Korea), the sealer was applied directly to the root canal using a disposable tip, and a single cone was placed in the canal in accordance with the manufacturer's recommendations. For the CHBS group (Sealapex; Kerr, Bioggio, Switzerland), the root canal filling was completed via cold lateral condensation. Gutta-percha cones were cut from the canal orifice, and a cotton pellet dampened with alcohol was used to clean the pulp chamber. The teeth were restored with composite (Filtek Z250; 3M, ESPE, St Paul, MN). All treatments were performed by a single operator. The patients were prescribed ibuprofen 400 mg (Profen; Dinçtaş Pharmacy, Kızılay, Ankara, Turkey) as an analgesic and were advised to use it only when they experienced severe pain.

Evaluation of Postoperative Pain Levels

Levels of postoperative pain were evaluated at 6, 12, 24, and 48 hours and on days 3, 5, and 7 of using the VAS after the RCTs were completed. The VAS consists of a horizontal 100-mm ruler with no numbers other than 0 at the beginning and 10 at the end of the scale[20]. The scale's use was explained to each participant. A volunteer who did not know about the treatment groups called the patients by phone and reminded them to record their pain scores on the VAS scale provided.

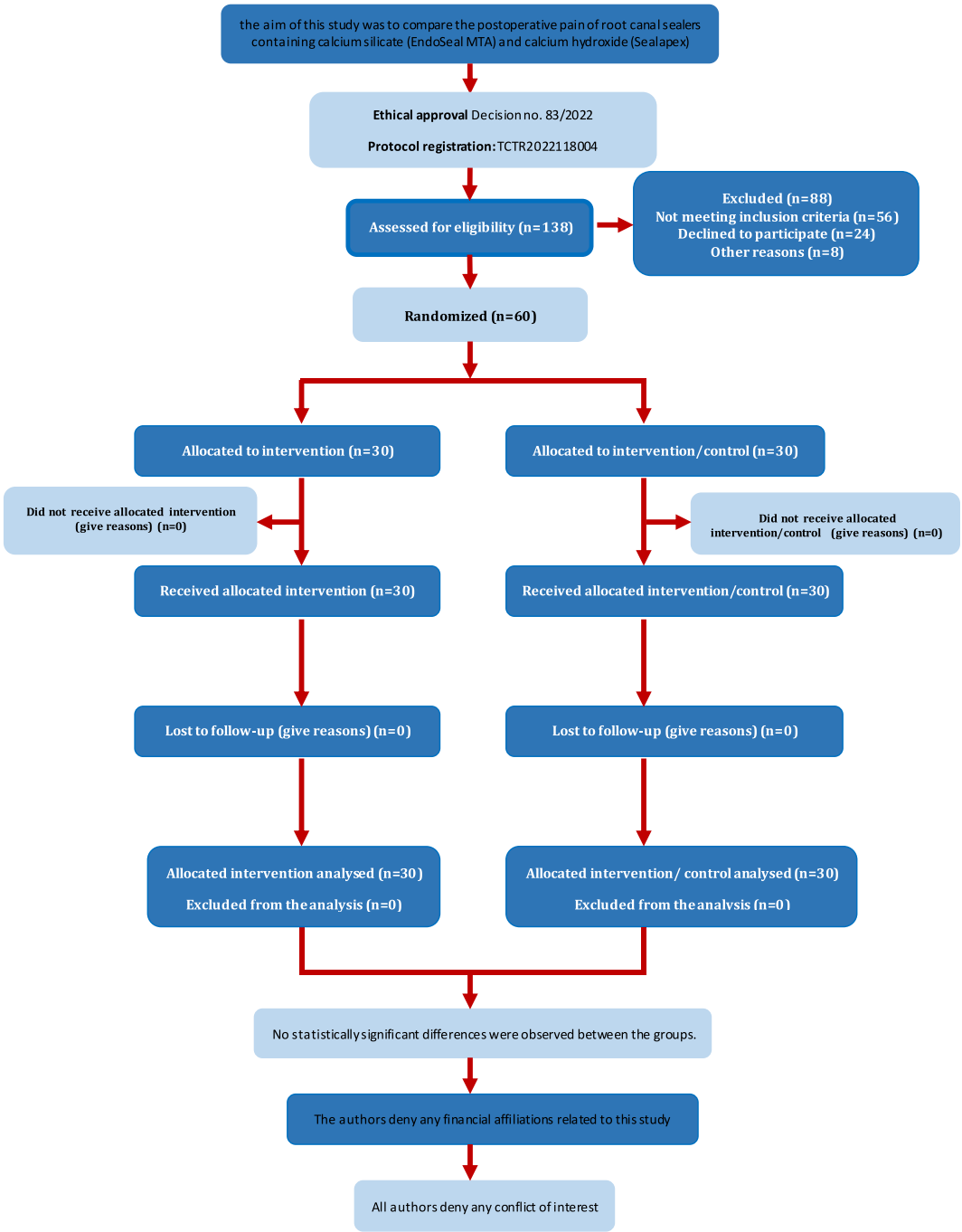

FIGURE 1 – Preferred Reporting Items for Randomized Trials in Endodontics 2020 flowchart.

With the values recorded on the VAS as the bases, pain levels were categorized as follows[21]:

1. No pain = 0 to 4 mm
2. Mild pain = 5 to 44 mm
3. Moderate pain = 45 to 74 mm
4. Severe pain = 75 to 100 mm

All participants were instructed to bring the reports at their next visit to the clinic on the seventh day after treatment and the postoperative percussion scores were recorded at this appointment on the scale.

Statistical Analysis

The Shapiro-Wilk normality test revealed that the data (pre- and postoperative pain levels) were not normally distributed. Gender, age, smoking habits, analgesic intake, and sealer extrusion were assessed as a categorical variable and analyzed using Pearson's chi-square test. The Mann-Whitney *U* test was used to compare the pre- and postoperative pain between groups for each time interval. The Friedman test was used to evaluate the changes in pain scores over time. Also, the correlation evaluations of age, smoking habit, and gender factors with postoperative pain were done using Spearman's correlation test. Statistical analysis was conducted using SPSS Statistics version 22.0 (IBM, Armonk, NY). A value of $P < .05$ was considered statistically significant.

TABLE 1 - Distribution of Demographic Data According to Groups

	Groups		
	EndoSeal MTA	Sealapex	*P* value
Gender			.795
Female	13	14	
Male	17	16	
Age			.259
20–29	17	13	
30–39	9	15	
40–49	4	2	
Smoking habit			.787
Yes	11	10	
No	19	20	

Clinical baseline parameters of each of the study groups. The chi-squared *P* value is shown.

RESULTS

A total of 60 patients were included in the study from March to October 2022 in the Department of Endodontics. All patients attended the follow-up, as shown in Figure 1. Table 1 presents an overview of the demographic comparisons of gender, age, and smoking habits. The VAS scores revealed no significant difference in postoperative pain between the calcium silicate and calcium hydroxide–based sealer groups at any of the time intervals evaluated ($P > .05$) (Table 2). However, pain intensity in both groups decreased statistically compared with preoperative pain levels at 12 hours after treatment ($P < .05$) (Fig. 2). Two patients reported an intake of nonsteroid analgesics at the 6-hour time point in each group, and no significant differences were observed in terms of analgesic intake between the groups ($P > .05$). Two patients in each group exhibited radiographically visible sealer extrusion, and there was no statistically significant difference between the groups in terms of sealer extrusion ($P > .05$). Also, no significant correlation was detected between age, gender, and smoking habit factors and postoperative pain levels ($P > .05$).

DISCUSSION

Many parameters, including WL, number of appointments, preparation technique, and type of root canal sealer, are associated with postoperative pain[22]. The apical foramen and lateral canals allow an endodontic sealer to directly access periapical tissues during the root canal process[23]. The interaction of sealers with periapical tissues may give rise to localized irritation, which may cause postoperative pain[3]. The data available on postoperative pain resulting from calcium silicate–based root canal sealer are limited. Moreover, to the best of our knowledge, no study has compared the effects of calcium silicate– and calcium hydroxide–based root canal sealer on postoperative pain. In this randomized controlled trial investigating the effect of calcium silicate– and calcium hydroxide–based sealers on postoperative pain, because pain levels of the patients experienced and other data compared were not statistically significant between the groups, the null hypothesis was not rejected.

According to the findings of the present study, pain levels in CBCS and CHBS groups were similar in terms of postoperative pain. Graunaite et al[10] compared the effect of resin-based and bioceramic root canal sealers on the occurrence and intensity of postoperative pain in patients with asymptomatic apical periodontitis and reported that postoperative pain levels were similar after RCTs with resin-based and bioceramic root canal sealers. Similarly, Aslan and Dönmez Özkan[9] compared the effect of calcium silicate–based and epoxy resin–based root canal sealers on postoperative pain following single-visit root canal treatment on molar teeth and found that calcium silicate–based and an epoxy resin–based root canal sealers were associated with similar levels of postoperative pain levels. Song et al[24] and Drumond et al[25] observed a low incidence of postoperative pain following RCTs using calcium silicate–based sealer. These findings are consistent with those of the present study.

Calcium hydroxide is well known for its antibacterial and tissue regeneration capacity, which is achieved by the infiltration of calcium and hydroxyl ions into surrounding tissues. Correspondingly, CHBSs have a satisfactory effect on surrounding tissues and advance healing[26]. The results of the study could not be directly compared; there are no clinical trials comparing the effect of bioceramic-based root canal sealers and calcium hydroxide–based sealer on postoperative pain. Some studies revealed that sealer (resin-based and calcium silicate–based) had significantly no effect on postoperative pain[9,10]. Shashirekha et al[14] also reported that pain levels in AH Plus group were higher than the Sealapex group, but not significantly different. Likewise, in the current study, the findings showed that no significant differences were obtained in both groups.

Endodontic postoperative pain is a reflection of the periapical tissues' local inflammatory response[27], which is known to

TABLE 2 - Median (Minimum-Maximum) and Mean Rank Values Regarding Groups

	Group				
	EndoSeal MTA		Sealapex		
	Median (min-max)	Mean rank	Median (min-max)	Mean rank	*P* value
Preoperative pain	60 (50–90)	17.14	60 (46–90)	16.00	.728
Preoperative percussion	80 (60–90)	17.39	75 (70–90)	15.81	.623
Postoperative pain					
Postop 6 h	15 (0–90)	13.93	30 (0–70)	18.50	.166
Postop 12 h	10 (0–50)	15.07	20 (0–50)	17.61	.426
Postop 24 h	0 (0–40)	14.75	0 (0–55)	17.86	.172
Postop 48 h	0 (0–20)	14.64	0 (0–60)	17.94	.147
Postop 3 day	0 (0–20)	15.18	0 (0–60)	17.53	.266
Postop 5 day	0 (0–0)	15.50	0 (0–50)	17.28	.205
Postop 7 day	0 (0–20)	19.07	0 (0–0)	14.50	.180
Postop 7 day percussion	0 (0- 0)	14.00	0 (0–50)	18.44	.193

The Mann-Whitney *U* test indicated significantly similar postoperative pain levels in both groups at any time of intervals ($P > .05$).

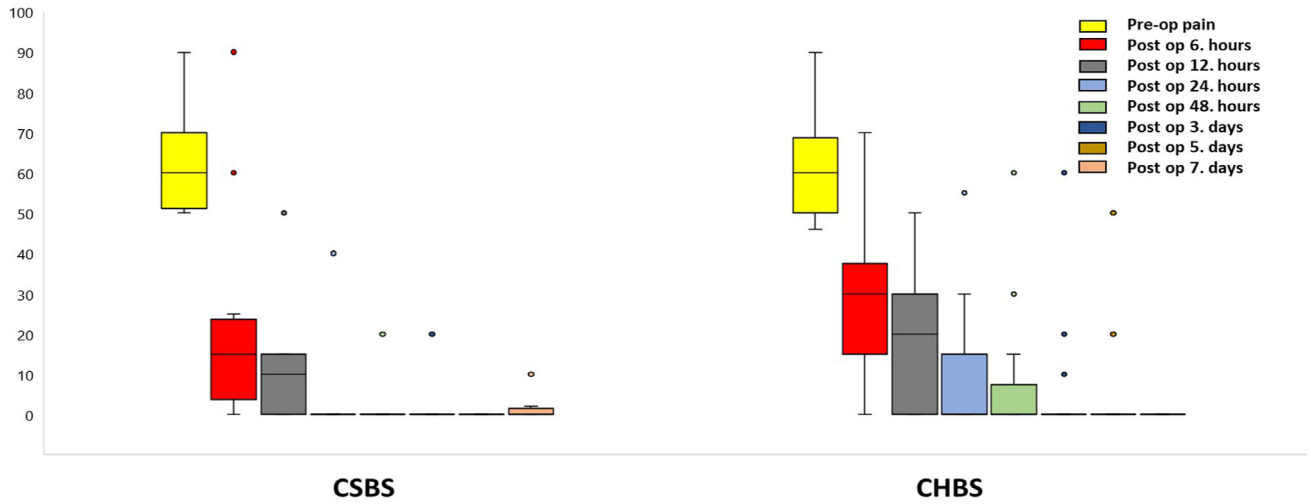

FIGURE 2 – Minimum and maximum pain values, medians, quartiles, and pain reduction over time are shown in the boxplot chart. CHBS, calcium hydroxide–based sealer; CSBS, calcium silicate–based sealer.

be linked to the release of biochemical mediators, including reactive oxygen species, especially induced by resin residues[28]. It is known that oxidative stress is not involved in the cytotoxicity of Sealapex[29] and cytocompatibility of EndoSeal MTA[30]. Biocompatible ingredients of resin-free EndoSeal MTA and low cytotoxicity of Sealapex could be correlated to minimal postoperative pain.

The appropriate radiopacity is a critical need for root canal sealers. A common radiopacifier called zirconium oxide (ZrO_2) promoted the proliferation of fibroblasts and had no cytotoxic effects[31]. EndoSeal MTA is a premixed calcium silicate root canal sealer containing ZrO_2 as a radiopacifier and has a fast setting time[32]. Previous studies have demonstrated that ZrO_2-containing materials hastened the resolution of inflammatory responses[33]. ZrO_2 in EndoSeal MTA may have reduced postoperative pain by suppressing inflammation. In addition, the pain feeling could reduce due to the decrease in inflammatory activity and because most materials lose their irritating components after final setting and become rather inert[3]. The reduction of pain can be attributed to the rapid setting time of EndoSeal MTA.

Root canal sealer extrusion has no effect on the success of endodontic treatment[34], but tissue reactions depend on the type of root canal sealer used in such therapy[35,36]. In this study, the small number of patients with sealer extrusion may be related to the inclusion of patients with PAI scores of less than 2. In addition, contradictory studies have been reported in the literature with regard to the effect of sealer extrusion on postoperative pain[25,37]. In the present study, sealer was extruded in 2 patients in both groups. It could be difficult to interpret the result, considering as a limitation of the study. The effects of canal obturation materials in overfilled situations require further research. In the literature, increased analgesic intake has been observed in symptomatic cases[38]. Among the patients (who suffered moderate to severe preoperative pain) in the current study, few needed anti-inflammatory drugs in the postoperative period.

Smoking may increase the rate of developing apical periodontitis because it causes a systemic inflammatory response and secretes mediators that could damage tissue, including collagenases and pro-inflammatory cytokines[39]. But, in the present study, Spearman's correlation test revealed that there was no correlation between smoking habit and postoperative pain levels at any time after treatment. Also, there was no correlation between gender factor and postoperative pain levels and age factor and postoperative pain levels. The results may be caused by the small sample size, which could be considered as a limitation of the study.

Evaluating postoperative pain intensity and incidence among different cases in clinical trials is very difficult. Therefore, similar treatment protocols should be adopted to reduce the number of variables that may cause postoperative pain in different groups. In this study, the crown-down protocol was used to ensure less extrusion of debris[40]. Aside from the obturation technique, the treatments were completed in a single visit to reduce variety in the treatments applied.

CONCLUSION

Within the limitations, calcium silicate– and calcium hydroxide–based root canal sealers resulted in statistically similar postoperative pain levels and the use of analgesics. Postoperative pain was not related to age, gender, or smoking habit.

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The authors deny any conflicts of interest related to this study.

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