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Postobturation Pain of three Novel Calcium Silicate-based sealers with asymptomatic irreversible pulpitis or necrotic pulp with chronic apical periodontitis: prospective clinical trial

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Abstract

Background Bioceramic-based root canal sealers are increasingly important in root canal treatment because of their biocompatible properties. This study aimed to evaluate postobturation pain incidence and intensity after root canal obturation with NeoSealer Flo, MTA-Bioseal, and GuttaFlow bioseal calcium silicate-based sealers and AH Plus epoxy resin-based sealer in patients with asymptomatic irreversible pulpitis or necrotic pulp with chronic apical periodontitis.

Methods A total of 120 participants with single-rooted teeth were included and randomly divided into four groups according to the root canal sealer used ($n=30$). The patients were subsequently categorised based on the pulp vitality (vital or nonvital) in each group ($n=15$) and all teeth were obturated in a single-visit. The postobturation pain scores were recorded on a visual analogue scale (VAS) at 6 h, 24 h, 48 h, 72 h, 7 d and 30 d. Moreover, analgesic intake was also noted at 24 h and 48 h. The Mann–Whitney *U* test, Kruskal–Wallis H test, Friedman test, and Spearman's correlation test were used, and a p value < 0.05 was considered significant.

Results VAS scores were highest for the 6 h > 24 h > 48 h ≈ 72 h ≈ 7 d ≈ 30 d time intervals for both pulp status in each root canal sealer. A significant decrease in the VAS score was observed for all sealers from 6 h to 48 h (p 0.05). Nonvital cases had lower VAS scores at all time intervals. Analgesic intake was greater in the first 24 h ($p < 0.05$) in vital cases ($p < 0.05$) and also in females than males.

Conclusion The level of pain experienced after obturation was similar in patients with different pulp status for all the root canal sealers. Analgesic intake was greater in vital cases and females within 24 h.

Trial registration ClinicalTrial.gov, NCT06515756, record date: 2024-07-17, retrospectively registered.

Keywords Calcium silicate, Pain, Postobturation, Root canal sealer, Visual analogue scale

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Background

Endodontic treatment is sometimes a source of anxiety and stress for patients when pain is present. Postoperative pain is the result of mechanical, chemical or microbiological injury to the apical region after instrumentation or obturation [1]. Pain management should be a complementary phase of dental treatment, particularly to prevent the exacerbation of pain during the postoperative period [2]. Acute inflammation is believed to be a significant contributor to severe pain following endodontic treatment [3]. However, the occurrence of pain can be influenced by the different stages of treatment, from diagnosis to postobturation. In particular, the content and effectiveness of the root canal sealer is a critical factor that should be considered. Root canal sealers are in contact with the periodontal tissues through the lateral canals and apical foramina and may potentially affect the healing process in the periodontium. If local inflammation is induced by root canal obturation materials, postoperative pain may result. The intensity of the inflammatory response depends on a number of factors, including the composition of the root canal sealer [4].

AH Plus (Dentsply, DeTrey, Konstanz, Germany) is considered to be the gold standard in endodontic treatment, due to its excellent leakage properties, radiopacity, and solubility and present satisfactory results and closer to ideal properties during obturation. However, the AH Plus formula can cause inflammation and pain when sealer exist to periodontal tissues [1]. Due to a number of beneficial bioactive properties, including antibacterial activity supported by alkaline pH, promotion of apical healing through hydroxyapatite formation, mineralisation of the dentine structure and sealing properties [5], the use of bioceramic-based root canal sealers is increasing. In addition, it was showed that they reduce inflammation and facilitate the differentiation of odontoblasts and preosteoblast mineralisation, thereby supporting the healing of periapical tissues [6]. Recent studies have demonstrated the equivalence of resin-based sealers and calcium silicate-based sealers with respect to postobturation pain [5, 7–9]. In a study by Arslan et al., the severity of postobturation pain following single-visit root canal treatment of molar teeth was not significantly different among Endoseal MTA (Maruchi; Wonju, Korea), Endosequence BC Sealer (BC, Brasseler USA) and AH Plus [7]. In another study, no difference was found in the level of postobturation discomfort following single-visit endodontic treatment of teeth with apical periodontitis with a calcium silicate-based sealer [BioRoot RCS (Septodont, Saint-Maur-des-Fosses, France)] compared with a resin-based sealer (AH Plus) at 8 h, 24h and 48 h [8]. Similarly, the use of bioceramic- and resin-based sealers did not result in notable alterations in pain levels in patients with vital or nonvital cases [9].

NeoSealer Flo (Avalon Biomed, Houston, TX, USA) is a bioactive ceramic paste that is premixed and contains a fine grade of inorganic powder made from tricalcium and dicalcium silicate. It is radiopaque, free from resin, and nondiscolouring and was formulated to harden when moisture from dentinal tubules is present. It possesses antimicrobial properties in vitro due to its high initial pH [10]. MTA-Bioseal (ITENA Clinical, Paris, France) recently introduced root canal sealer based on mineral trioxide aggregate (MTA). According to the manufacturer, the product displays minimal expansion upon hardening, low solubility in tissue fluid, and optimal fluidity [11]. GuttaFlow bioseal (Coltene/Whaledent, Altstatten, Switzerland) is a bioceramic silicone-based root canal sealer that contains bioceramic particles and guttapercha powder in a silicone matrix. Its unique hybrid composition enables biointeractivity and apatite-forming abilities, which promote the regeneration of apical tissues [12].

To the best of our knowledge, studies comparing postobturation pain management with these three bioceramic-based root canal sealers in patients with vital and nonvital pulp status are lacking. Therefore, the aim of this study was to evaluate the effects of MTA-Bioseal, GuttaFlow bioseal, and NeoSealer Flo calcium silicate-based root canal sealers on postobturation pain in teeth with asymptomatic irreversible pulpitis (AIP) or necrotic pulp with chronic apical periodontitis (CAP) undergoing single-visit root canal treatment (RCT).

The three null hypotheses were tested in this study: $H_0$1: The type of sealer used does not affect the incidence and intensity of postobturation endodontic pain; $H_0$2: Pulp status does not affect the incidence and intensity of postobturation endodontic pain; and $H_0$3: There is no difference in analgesic intake by patients after RCT between the vital and nonvital experimental groups.

Materials and methods

This prospective clinical study was reported in accordance with the Consolidated Standards Statement on Research Reporting Standards (CONSORT, 2010) and was carried out with the ethical rules of the Declaration of Helsinki. The study was approved by the Ethical Committee of the Kirikkale University and was conducted with a single-blind, randomised design. The required minimum sample size was determined using G*Power v.3.1.9.2 (University of Dusseldorf, Germany) with a 5% type-1 alpha error, 0.40 effect size, and 90% power in accordance with Mehrvarzfar et al. [13]. The minimum sample size required for each study group was 12. Considering the estimated 20% loss resulting from inaccurate or absent data, the final total sample size was established at 120 participants, with 15 participants per group.

Patient enrollment

Adult patients (aged 18–60) who were referred to the Dental Faculty of Kirikkale University for root canal treatment were included in this study. One hundred and twenty single-rooted anterior and premolar teeth that underwent endodontic treatment from July 2023 to November 2023 were selected.

Inclusion criteria

The inclusion criteria were good oral hygiene and not reporting pain before the appointment. Pulpal diagnosis was applied during clinical examination and confirmed upon accessing the teeth according to the AAE consensus. This was an AIP caused by extremely deep carious lesions, which are radiographically detectable and penetrate the entire thickness of the dentin. Pulp exposure would only occur during the removal of the caries, as there is no clinical or radiographic pathology or symptoms present (vital cases). Pulpal diagnosis was performed via clinical examination and radiographs for necrotic pulp with CAP (nonvital cases).

Exclusion criteria

The exclusion criteria were pregnancy, autoimmune diseases, uncontrolled diabetes, smoking, moderate and advanced periodontal disease (with 5 mm or greater probing depth), patients requiring endodontic treatment for more than one tooth, unrestorable coronal destruction, incomplete root formation, systemic or allergic sensitivity to local anaesthetics or NSAIDs, patients with ASA II and analgesic or antibiotic intake within 7 days before the beginning of treatment.

Informed consent

All participants received information about the aim of the study and the treatment protocol. Informed consent was obtained from patients who wanted to participate in the study.

Diagnosis and data record

The vitality was diagnostically examined using both electric pulp testing and thermal tests with the help of a secondary investigator who was not involved in the study. The same investigator recorded gender, age, preoperative pain and periapical index (PAI) scores and contact information.

Randomisation, blinding, and allocation

The participants were blinded and unaware of the specific treatment protocol. They were then randomly assigned to the four groups at a 1:1 ratio using a computer algorithm program (http://randomizer.org). After randomis ation, patients were assigned consecutive numbers from 1 to 4 in the order of enrolment. The root canal sealers were coded (1: GuttaFlow Bioseal, 2: MTA-Bioseal, 3: NeoSealer Flo, 4: AH Plus). Just before the obturation protocol, a secondary investigator notified the clinician about the assigned root canal sealer. The tooth was obturated with this root canal sealer. The main components of the sealers are listed in Table 1.

Treatment protocols

This study was designed with two different pulp status: vital and nonvital pulp. All the teeth that met the inclusion criteria were treated in a single visit by a specialist (S.D.B.) with over five years of clinical experience in the Department of Endodontics. The treatment of the patients who were excluded from the study was conducted by a clinician who was not involved in the research.

In AIP patients, the presence or absence of bleeding in the pulp chamber served as verification. If the bleeding in the pulp could not be stopped by applying pressure to the pulp exposed with a sterile cotton pellet for 5 min, RCT was performed. However, if bleeding could be prevented, vital pulp therapy was applied, and patients were excluded from the study. In necrotic pulp with CAP patients, PAI was used as previously described [14, 15]. According to this index, periapical lesions with scores

Table 1 Sealer formulation, lot number and composition in accordance with the manufacturer

Sealer and Manufacturer	Formulation	Lot	Composition
GuttaFlow Bioseal (Coltene/Whaledent in Altstatten, Switzerland)	Paste-paste	K84938	Gutta-percha powder, polydimethylsiloxane, platinum catalyst, zirconium dioxide, silver (preservative), coloring, bioactive glass ceramic
MTA-Bioseal ITENA Clinical (Paris, France)	Paste-paste	55,765	Base paste: salicylate resin, natural resin, calcium tungstate, nanoparticulated silica, pigments; Catalyst base: diluting resin, mineral trioxide aggregate, nanoparticulated silica, pigments.
NeoSealer Flo (Avalon Nusmile, USA)	Premixed	2,021,030,104	Tantalite (50%), tricalcium silicate (25%), calcium aluminate (25%), dicalcium silicate (10%), tricalcium aluminate (5%), calcium sulfate (1%), PEG *, grossite *
AH Plus (Dentsply, Germany)	Paste–paste	2,109,000,972	Paste A: diepoxide, calcium tungstate, zirconium oxide, aerosil, pigment (iron oxide) Paste B: 1-adamantane amine, N,N'-dibenzyl-5-oxa-nonandiamine-1,9, TCD-diamine, calcium tungstate, zirconium oxide, aerosil, silicone oil

of 3 and 4 (less than 1 cm in diameter) were included in the study to achieve better standardisation. In patients with CAP, the change in bone structure with a noticeable radiolucent area was defined as a score of 3, and a well-defined radiolucent area was defined as a score of 4. The periapical lesion diameter was measured on digital radiographs using a software tool. When there was doubt about the score, a higher score was given. Only one tooth was treated in each patient. Following rubber dam placement and disinfection of the crown, a sterile bur was used to create an access cavity under an operating microscope (OPMI Pico; Carl Zeiss, Gottingen, Germany).

A local anaesthetic solution (containing 40 mg of articaine hydrochloride and 0.006 mg of epinephrine) was administered to all patients. Mandibular anaesthesia was used for the mandibular premolars. Buccal infiltration anaesthesia was used for other teeth. Supplementary anaesthesia was not required for any of the patients. The working length was established using a 15 K-file (Dentsply Maillefer, Ballaigues, Switzerland) and an apex locator (Root ZX Mini, Morita Corp., Kyoto, Japan), which was set 0.5 mm short of the 0.0 signal of the device. Initial instrumentation was performed up to a size of 25 K files, and then a Reciproc R25 (size 25, 0.08 taper) file (VDW, Munich, Germany) was used. If needed, the root canal was enlarged with Reciproc R40 (size 40, 0.06 taper) file (VDW). A total of 10 mL of 5% sodium hypochlorite was used to rinse the root canal during instrumentation with a 30-gauge side-vented needle. The needle tip was inserted 1.5 mm shorter than the working length, and moderate pressure was applied to avoid irrigant extrusion through the apex. The final irrigation mixture included 3 mL of 17% EDTA (Werax, Izmir, Turkiye), 2 mL of distilled water, 3 mL of 5% NaOCl (Werax), and 2 mL of distilled water respectively. Ultrasonic activation (Mini Piezon, EMS, Nyon, Switzerland) was performed by inserting it 2 mm shorter than the working length, and it was activated in 3 cycles of 20 s for both the NaOCl and EDTA solutions during the final irrigation stage. The root canals were subsequently dried with paper points (Sure-Endo, Seoul, Korea).

During obturation, a single tapered gutta-percha cone was adapted to the root canal, and its position was confirmed by periapical radiography. The gutta-percha cone used was either the Reciproc R25 (VDW) or Reciproc R40 (VDW). All the root canal sealers were applied using the same technique. The technique outlined by Castelo-Baz et al. [16] was subsequently employed to apply sealer with appropriate paper point cones (1 mm shorter than the working length) in the following manner: First, the sealer was administered to the root canal with the initial paper point and then uniformly distributed with a second paper point before any excess sealer with a third paper point was removed. Once the sealer was applied, Reciproc R25 or Reciproc R40 was adjusted to fit the root canal. The excess gutta-percha cone was subsequently removed, and the pulp chamber was cleaned. The coronal access cavities were restored with a composite resin material (Charisma Smart; Kulzer GmbH, Hanau, Germany).

Postobturation pain assessment

Pain was assessed using a visual analogue scale (VAS) card at 6 h, 24 h, 48 h, 72 h, 7 d and 30 d postoperatively. All the participants were asked to rate their perceived pain on the scale, with 0 indicating no pain and 10 indicating the highest possible pain. Pain levels were classified as none (0), mild (1 to 3), moderate (4 to 7), or severe (8 to 10). Patients were informed that they might experience mild postobturation pain and were instructed to take 400 mg of ibuprofen only when they experienced severe pain, as previously suggested [17]. The patients recorded the number of pain relief tablets taken on the back of the VAS score card, and the patients were advised to contact their healthcare providers if they needed to make additional appointments for pain management. Patients were recalled for clinical observation at 7 d, and VAS scores were recorded at the same time. Patients submitted their last VAS score for 30 d via their phones, and data were recorded.

Statistical analysis

Pain scores were statistically analysed with IBM SPSS Statistics version 22.0 (IBM, Armonk, NY, USA). The Mann–Whitney *U* and Kruskal–Wallis H tests, along with post hoc multiple comparison tests, were used to investigate the differences between groups. The Friedman test was used to compare changes in pain scores over time. Spearman's correlation test was also used. A p value < 0.05 was considered significant.

Results

In patients with CAP, flare-up was observed in two patients. In the AIP group, the VAS score of one patient was unreachable at the beginning of the study. These patients were excluded from the study, and three new patients were recruited. Therefore, the study achieved full follow-up, ensuring that there was no loss of statistical power. Figure 1 shows the flow chart of this study. All the treatments were completed at one visit. All the participants provided their VAS ratings at any given point. A total of 120 single-rooted teeth (68 anterior and 52 premolar) with vital or nonvital pulp were treated.

Pain assessment

After the completion of the RCTs, the VAS scores decreased significantly for all sealers between 6 h and 48 h ($p < 0.001$). None of the participants reported

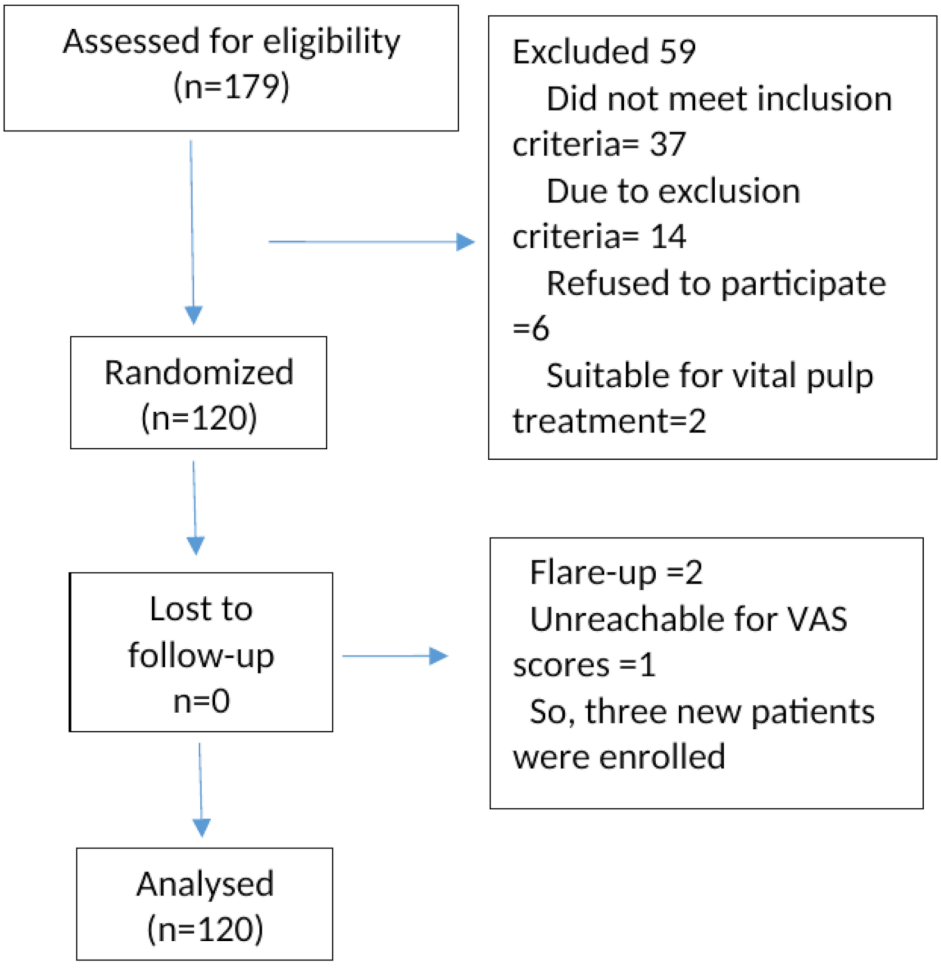

Fig. 1 Flow chart

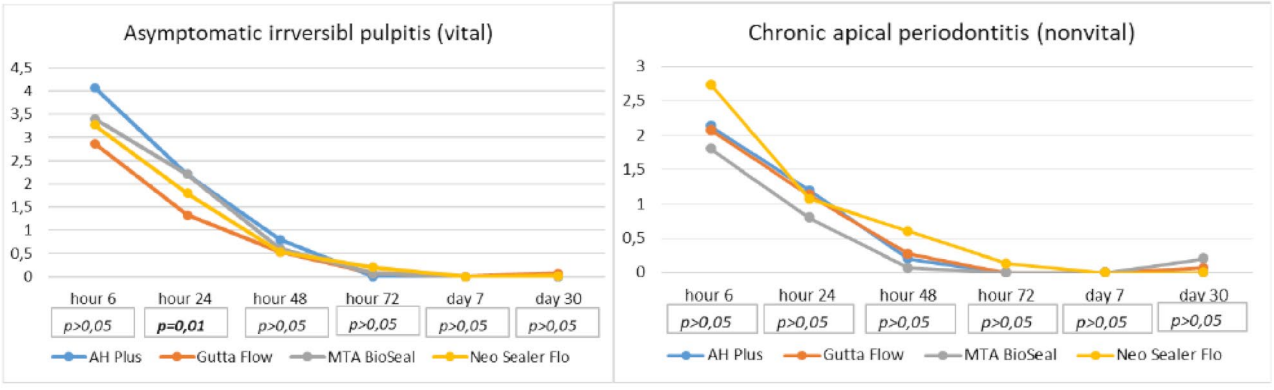

Fig. 2 Comparison of pain levels in the root canal sealer based on pulp status

any pain at 72 h postobturation. The time-dependent decrease in pain level and comparison of sealers according to pulp vitality are shown in Fig. 2. In both pulp status, the mean VAS scores of the three silicate-based and a epoxy-resin based root canal sealers are similar ($p>0.05$). The comparison of pain levels between vital and nonvital teeth for each sealer at each time point is shown in Fig. 3. The vital cases had more VAS scores than nonvital cases at 6 h–48 h when MTA BioSeal or AH Plus were applied ($p<0.05$).

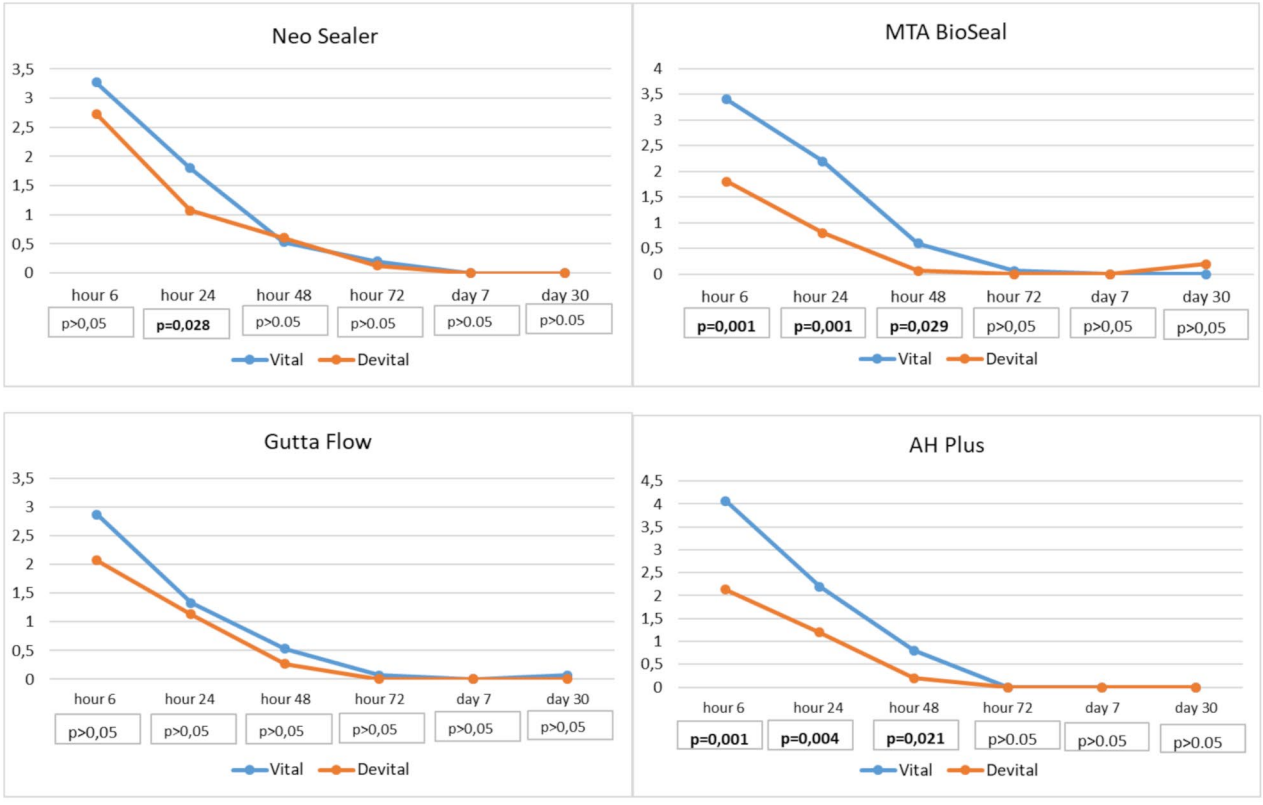

Fig. 3 Comparison of pain levels according to pulp status based on the use of root canal sealers

Pain intensity and analgesic intake

In the first 24 h, 36 (30%) of the patients used analgesic tablets, and in the second 24 h (24 h–48 h), 9 (7.5%) of the patients did so. Among the patients who used analgesics in the first 24 h, 18 (50%) reported using two tablets. Females reported experiencing more pain and taking more analgesics than males within the first 24 h.. The lowest analgesic intake was observed after the use of the GuttaFlow bioseal root canal sealer. Demographic and clinical features of the participants are presented in Table 2. Spearman's correlation test results for the correlation assessments of the age and gender factors with postobturation pain and analgesic intake are shown in Tables 3 and 4.

A statistically significant difference was observed between vital and nonvital teeth in terms of analgesic use at both 24 and 48 h ($p<0.05$ for both). In both pulp status, analgesic intake was more frequent during the initial 24 h than 48 h and greater in vital teeth ($p<0.001$).

Discussion

Postoperative pain following endodontic treatment is correlated with the local inflammatory response that arises due to the root canal sealer content and the method for obturation in periapical tissues [12]. Preventing postobturation pain remains a challenge for clinicians. According to some studies, moderate to severe postobturation pain occurs in only 4–10% of all endodontic patients [18], with studies reporting pain rates as high as 50% [19]. Primary pain conditions may develop in patients that can have a considerable impact on their quality of life. A few clinical studies showed that persistent pain after RCT can be experienced in 5–12% of patients from months to years [20, 21].

Calcium silicate-based materials are classified as bioactive materials because of their capacity to induce hard tissue formation in both dental pulp and bone. Owing to their bioactive properties, these materials offer a new treatment approach for dentin remineralisation, vital pulp treatment, and bone regeneration [22]. The biocompatibility, bioactivity, and osteoconductive properties of the MTA have encouraged the development of new calcium silicate-based endodontic materials.

Resin-based AH Plus is mildly cytotoxic and releases toxic monomers, such as bisphenol A diglycidyl ether [4]. Compared with resin-based AH Plus, bioceramic sealers have lower cytotoxicity [23]. Previous studies have demonstrated positive results for the use of these new generations of bioceramic root canal sealers used in the present study [22, 24]. However, a comparative analysis could not be performed due to the lack of postoperative pain studies that have used some or all of these root canal sealers.

Table 2 Demographic and clinical features of the participants

Variables	Irreversible Pulpitis ($n=60$)	Chronic Apical Periodontitis ($n=60$)	*p* value
Gender, ***n*(%)**			0.264†
Female ($n=72$)	39	33	
Male ($n=48$)	21	27	
Age (**years**), mean ± SD			0.609§
	45,93 ± 12,86	44,73 ± 12,78	
Teeth treated (n)			0.065†
Anterior ($n=68$)	29	39	
Posterior ($n=52$)	31	21	
VAS, **Initial**			1.0§
mean ± SD	0	0	
Analgesic intake (n)			
24 h	27	9	**0.001†**
48 h	7	2	**.006†**
PAI scores (n)			
PAI 3		31	
PAI 4		29	

†Chi Square test,

§Independent sample t test

Table 3 Correlation assessments of age and gender with postobturated pain

	6 h	24 h	48 h	72 h	7 d	30 d
Age	$r=-0.066$	$r=0.021$	$r=0.035$	$r=0.160$	n/a	$r=-0.084$
	$p=0.472$	$p=0.821$	$p=0.707$	$p=0.081$		$p=0.364$
Gender	$r=-0.183$	$r=-0.180$	$r=-0.131$	$r=-0.131$	n/a	$r=0.025$
	$p=0.045^{*}$	$p=0.049^{*}$	$p=0.069$	$p=0.155$		$p=0.782$

*Correlation is significant at the 0.05 level (2-tailed)

n/a (not applicable): cannot be computed for any variable because all the data have a '0' value

Age groups: 18–39, 40–60. h: hour, d: day

Table 4 Correlation assessments of analgesic intake according to time interval in 48 h

	Analgesic intake 24 h	Analgesic intake 48 h
Age	$r=0.141$	$r=0.166$
	$p=0.123$	$p=0.070$
Gender	$r=0.338$	$r=-0.131$
	$p<0.001$*	$p=0.155$

* Correlation is significant at the 0.01 level (2-tailed)

Age groups: 18–39, 40–60

It was reported that no noticeable differences in postobturation pain or analgesic intake in the study analysed AH Plus, Endoseal MTA (Maruchi, Wonju, Korea), and EndoSequence BC Sealer (Brasseler, USA; Savannah, GA) [7]. Another report revealed that resin-based AH Plus and bioceramic-based Total Fill (FKG Dentaire SA, La Chaux-de-Fonds, Switzerland) did not significantly differ in postobturation painwhen acute apical periodontitis was present [4]. Cosar et al. compared the effects of the MTA-based bioceramic root canal sealer MTA Fillapex (Angelus, Londrina, PR, Brazil) and AH Plus on postobturation pain for 30 d in molars with AIP and reported similar pain incidence rates and intensities for these two different types of root canal sealers [5].

The studies have been carried out not only on postoperative pain in relation to a single pulpal or periapical condition but also on comparisons between different pulpal and periapical conditions. In a study compared bioceramic-based iRoot SP (Innovative Bioceramix, Vancouver, BC, Canada) with AH Plus, no significant difference was found between the groups concerning postobturation pain in premolar and molar teeth with vital and nonvital pulp. Nevertheless, patients whose teeth were obturated with iRoot SP needed less analgesic use following treatment [9]. The teeth diagnosed with AIP and/or pulp necrosis with or without CAP were obturated with AH Plus and ADseal (Meta Biomed, Cheongju-si, South Korea) epoxy-resin-based sealers and CeraSeal (Meta Biomed) and EndoSeal TCS calcium silicate-based sealers in a study. The participants were recalled at 1-week, 1-month, and 3-month intervals. The findings revealed no significant difference between sealers in terms of postobturation pain [25]. The results are similar to our study at 1-week and 1-month outcomes.

The presence of preoperative pain has the potential to induce postobturation pain, which can affect the results. Therefore, the patients without pain were selected in this prospective randomised clinical trial. The age range was

restricted to minimise individual differences. Due to the possibility of complications and the increased procedure time in molar teeth, single-rooted and single-canaled teeth were preferred. The teeth with CAP were exclusively included. To avoid any clinician-related differences, the entire endodontic procedure was carried out by a single operator. As it was not possible to blind the operator during the procedure, only the patients were blinded. The working length was confirmed by both digital radiography and apex locater device. If the apex locator provided inconsistent measurements, the radiograph image was relied upon instead. All shaping, irrigation, and obturation procedures were carefully performed to ensure as much standardisation as possible. Care was taken to avoid overinstrumentation so as not to cause any additional postobturation pain. The use of ultrasonic irrigation activation was preferred to minimise residual pulp in vital cases and the bacterial load in nonvital cases and to provide a more effective assessment of postoperative pain. Considering the irrigant extrusion, the ultrasonic tip (NSK, Nakanishi Inc., Japan) was placed shorter than the working length and was used at moderate power. Root canal enlargement and obturation were performed according to the root canal diameter. Postoperative pain was assessed at six time points (6 h, 24 h, 48 h, 72 h, 7 d and 30 d). Although most pain studies include 7 d of follow-up, it is worth noting that patients may experience pain again in the future due to the possibility of persistent infection. Therefore, a 30-d pain follow-up was incorporated into this study, considering the possibility of pain reports exceeding 7 d. Researches have focused more on short-term postoperative pain rather than persistent pain, although the latter has a greater cumulative effect. This is because short-term pain is typically more intense and occurs at a higher frequency. Additionally, conducting studies with longer follow-up periods presents technical and financial obstacles. Despite the difficulty in follow-up, postobturation pain studies with follow-ups of 30 d and longer have been reported in the literature [5, 25].

As in the present study, the lack of an objective method and subjective data collection and analgesic use masking perceived pain are the main limitations of pain studies. Additionally, the splint-mouth design was not an appropriate methodology due to the application of four different root canal sealers in this study. Within the limitations, the highest score was recorded at 6 h after obturation in all groups because of the initial inflammatory response in periapical tissues. Overall, the bioceramic-based root canal sealers presented lower mean values than AH Plus, but the difference was not statistically significant. After 24 h, pain reduced in all groups, and a moderate or higher pain was not reported. After 72 h, no pain was reported, and the 30 d results were similar to the 72 h results. An ultrasonic/sonic technique may be recommended as an additional protocol to improve pain control [26]. A systematic review and meta-analysis by Chalub et al. [27] reported less postobturation pain with the use of ultrasonic activation. The use of ultrasound activation in this study may have been effective in reporting reasonable levels of pain throughout the study. The results of cytotoxicity studies have indicated that epoxy resin-based sealers release toxic monomers and can increase oxidative stress, which could be related to the release of reactive oxygen species that provoke pain via tissue inflammation [28]. MTA-Bioseal and MTA-Fillapex contain salicylate resin [29]. Therefore, they have the potential to exhibit similar properties to epoxy resin based sealers. In this study, there was no difference between vital and nonvital cases for NeoSealer Flo and GuttaFlow Bioseal root canal sealers in the first 48 h and other time periods, but there was a difference for MTA Bioseal and AH Plus root canal sealers. This difference may be due to the fact that the toxic monomers released by the resin content of the sealers cause more reactions in healthy periodontium. The methodological variability between studies may result in similar or different levels of postoperative pain between vital and nonvital cases.

A number of studies have examined gender differences in pain perception. While the results are inconclusive, the majority of studies indicate that females exhibit heightened sensitivity to pain [30]. Al Negrish and Habahbeh reported an incidence of post-endodontic pain in women (6%) and men (3%) [31]. Sayeed et al. indicated a higher incidence in women (7.4%) than men (1.8%) [32]. Ali et al. found that the incidence of postoperative pain was higher in women (2.81 ± 2.83) than men (2.02 ± 2.50) [2]. Another study supporting the above studies found that women received 2.3 times more analgesics than men [9]. The results of these studies are compatible with our findings. Additionally, females have been shown to be more sensitive to pain in a number of experimental pain models, including electrical, thermal, mechanical or chemical stimuli, as well as more advanced, clinically relevant pain models [30]. These results may help explain why the female participants in our study required a greater quantity of analgesics within the initial 24-hour period than the male participants did.

According to the results, hypothesis $H_0$1 was accepted, $H_0$2 was partially accepted as the difference was found in the first 48 h in vital and non-vital cases. $H_0$3 was rejected because more analgesics were used in vital cases than in nonvital cases in all groups.

Conclusions

The sealers used did not cause persistent pain in any patients over 30 d and reduced pain within a few days. Pulp status affected the frequency of pain and analgesic

intake within the first 24 h, but did not increase the pain level. The results support the idea that the bioceramic-based sealers tested in our study can be used safely in clinical practice in terms of postobturation pain. Further prospective clinical trials are recommended to focus on long-term follow-up of postobturation pain in various pulpal, periapical diseases and retreatment cases with novel bioceramic-based sealers to fill the information gap in this area.

Author contributions

Design of the work; A.T., A.E., acquisition; S.D.B., interpretation of data; A.T., drafted the work; A.T., S.D.B., revised; A.T., D.H., S.D.B. All the authors have read and approved the final version of the manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved and numbered (01.06.2023-07/06) by the Ethical Committee of the University of Kirikkale. and was registered under the protocol ID NCT06515756 (https://clinicaltrials.gov/) according to the CONSORT statement of the updated guidelines for reporting randomized clinical trials. Informed consent was taken from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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