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The effect of cryotreated sodium hypochlorite irrigation at different concentrations on postoperative pain in mandibular first molars with symptomatic irreversible pulpitis: a randomized controlled clinical trial

Kübra Gürler[1] and Koray Yilmaz[1*]

Abstract

Background The purpose of this study was to evaluate the effects of cryotreated 2.5% and 5% sodium hypochlorite (NaOCl) on postoperative pain during endodontic treatment procedures in mandibular first molars with symptomatic irreversible pulpitis.

Methods One hundred and thirty two patients with permanent mandibular first molars diagnosed with symptomatic irreversible pulpitis were included in the study. The teeth were randomly divided into four groups: the normal 2.5% NaOCl group ($n=33$), the cryotreated 2.5% NaOCl group ($n=33$), the normal 5% NaOCl group ($n=33$) and the cryotreated 5% NaOCl group ($n=33$). In the normal NaOCl groups, the root canals were irrigated with NaOCl solution at 25 °C at all stages of the root canal treatment. In the cryotreated NaOCl groups, the root canals were irrigated with NaOCl solution at 2 °C at all stages of the root canal treatment. The participants were asked to rate the intensity of their postoperative pain via a Visual Analog Scale (VAS) at 6 h, 12 h, 24 h, 48 h, and 72 h. The data were analyzed using the Shapiro-Wilk, Levene's, Kruskal Wallis H and the Chi-square test.

Results The basic demographic data, preoperative pain values and analgesic intake of the four study groups were similar. Postoperative pain levels at 6 h were significantly lower in the cryotreated 2.5% NaOCl group than in all the other groups ($p<.05$). Postoperative pain levels at 12 h were statistically similar between the cryotreated 2.5% NaOCl group and the cryotreated 5% NaOCl group ($p>.05$) and significantly lower than those in the other two groups ($p<.05$).

Conclusions Using cryotreated NaOCl irrigation at different concentrations during root canal treatment procedures in mandibular first molars with symptomatic irreversible pulpitis effectively reduced postoperative pain.

Trial registration This study was registered at ClinicalTrials.gov (NCT06820996) on 11 February 2025.

Keywords Cryotherapy, Irreversible pulpitis, Postoperative pain, Root canal treatment, Sodium hypochlorite

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Background

Pain management during and after endodontic treatment is a significant concern for both patients and clinicians [1]. The incidence of postoperative pain, characterized as a feeling of discomfort after root canal treatment, has been estimated to vary from 3% to 58% [2, 3]. The state of pulpal and periradicular tissues, preoperative pain and the presence of periapical radiolucency are the most significant factors affecting postoperative pain [4–6]. Periapical tissue inflammation is one of the most prominent causes of postoperative pain. The development of postoperative pain may also be associated with mechanical and chemical irritation of periapical tissue and microorganisms [2]. Common factors that contribute to postoperative pain include inadequate shaping and cleaning of the root canal system, the extrusion of irrigation solution apically, intracanal medicament or debris, hyperocclusion, missing of root canals, and persistent periapical pathology [6, 7]. Establishing and maintaining the working length throughout the treatment, properly cleaning and shaping the canal, and diligently adhering to effective irrigation solutions can largely prevent this condition. Treatment options such as analgesics, corticosteroids, occlusal reduction, low-level laser therapy, local anesthesia, preoperative antihistamine administration, various root canal instrumentation techniques, and root canal filling techniques have been explored in the literature to alleviate postoperative pain [6–11].

Recently, cryotherapy has emerged as a popular technique to reduce postoperative pain. Cryotherapy is derived from the Greek word "cryos", meaning "cold" [12]. Clinical and physiological evidence has demonstrated that applying cold in various modalities can effectively reduce musculoskeletal pain, muscle spasms, and connective tissue tension by reducing peripheral nerve conduction velocity, local inflammation, bleeding, and edema [13]. The Van't Hoff law states that cryotherapy induces vasoconstriction, slows cellular metabolism, limits biochemical reactions, and inhibits neural receptors in the skin and subcutaneous tissues [14]. This, in turn, delays the speed of pain signals, causing a local anesthetic-like effect [15]. Cryotherapy has also been used in dentistry for postoperative pain control after intraoral surgical procedures [16, 17]. The efficacy of cold saline in the final irrigation after root canal preparation to reduce postoperative pain in endodontics has been investigated in various studies in the literature [18, 19].

Various irrigation solutions that are effective for organic and inorganic tissues are used during root canal treatment. Sodium hypochlorite (NaOCl) is the most commonly used irrigation solution. It has antibacterial and physicochemical properties [20] and is unique in dissolving organic tissues [21]. NaOCl irrigation combined with mechanical instrumentation has been consistently shown to substantially reduce the microorganism load in root canals [22]. There have been several attempts to increase the antimicrobial efficacy of NaOCl in the root canal system, such as changing its concentration, increasing the contact time with the dentin walls of the root canal, increasing the total volume of irrigation, increasing its temperature, and using manual or mechanical activation methods [3, 23]. These methods to increase the efficacy of NaOCl can also result in heightened toxic effects on periapical tissues owing to the tissue-irritating properties of the solution. This extrusion into the periapical region increases postoperative pain, especially in teeth with open apices and necrotic pulps [21, 24]. Therefore, instead of using high concentrations of NaOCl, which could increase its toxic effects, safer means, such as increasing its temperature and using it in large volumes, may increase its efficacy [21, 25].

Nevertheless, in certain clinical situations, the use of higher concentrations cannot be entirely avoided due to their superior tissue dissolution and antimicrobial effects. Despite concerns regarding cytotoxicity, higher NaOCl concentrations (≥ 5%) remain common in clinical practice because they provide superior tissue dissolution and broader antimicrobial action, which is particularly advantageous in molars with complex anatomy. Balancing efficacy with safety is essential, and evaluating whether temperature reduction can allow the use of higher concentrations without increasing pain is clinically relevant.

Several clinical trials have examined the use of cryotreated NaOCl as a final rinse [26–28], and evidence from these studies, along with findings on cold saline irrigation [19, 29], consistently indicates that cooling the final irrigant significantly reduces postoperative pain. However, no randomized clinical trial has evaluated the effect of using cryotreated NaOCl at different concentrations throughout the entire chemomechanical preparation. Our study fills this gap by applying cryotreated NaOCl continuously during instrumentation, not just at the final rinse stage, enabling a more comprehensive evaluation of its effect on pain reduction.

This randomized clinical trial investigated the effects of cryotreated 2.5% and 5% NaOCl on postoperative pain during endodontic treatment procedures in mandibular first molars with symptomatic irreversible pulpitis. The null hypothesis of this study is that cryotreated NaOCl, regardless of concentration, does not significantly influence postoperative pain compared with normal NaOCl at room temperature.

Methods

This study was a single-blind, randomized controlled clinical trial. This randomized controlled trial was conducted and reported in accordance with the CONSORT 2010 guidelines. This study received ethical approval

from the Cukurova University Faculty of Medicine Clinical Research Ethics Committee (meeting no: 153, decision no: 30, date: March 07, 2025). The study protocol was registered with ClinicalTrials.gov (NCT06820996) on 11 February 2025. Patients were recruited consecutively from individuals who presented to the Department of Endodontics, Cukurova University Faculty of Dentistry, with spontaneous or prolonged pain consistent with symptomatic irreversible pulpitis between March 2025 and July 2025. All patients were screened for eligibility according to the inclusion and exclusion criteria, and those meeting the criteria were invited to participate in the study.

Sample size calculation

The sample size was based on a previous study using G*Power version 3.1.9.2 (Franz Faul; Universitat Kiel, Germany) with a power of 80%, an α error of 5%, and an effect size of 0.5 [30]. The minimum sample size was calculated to be 120 patients (n = 30). Further estimations, taking into consideration 10% dropouts, suggested a total adjusted sample size of 132 patients (n = 33). Written informed consent was obtained from all participants involved in the study.

Inclusion criteria

- Systemically healthy patients classified as ASA I or ASA II (American Society of Anesthesiologists Physical Status Classification).
- Mandibular first molars with a confirmed diagnosis of symptomatic irreversible pulpitis, established by the presence of spontaneous or prolonged pain, a positive response to cold and electric pulp testing, and a preoperative Visual Analog Scale (VAS, 0–10) score ≥ 4.
- Teeth without radiographic periapical radiolucency.
- Patients who had not taken analgesics or antibiotics in the last 24 h before the procedure were included in the study.

Exclusion criteria

- Mandibular first molars showed a negative response to cold and electric pulp tests.
- Mandibular first molars in poor periodontal condition (pocket depth > 4 mm).
- Mandibular first molars identified radiographically or after the endodontic access cavity as having 4 or more root canals.

Group randomization

Randomization was achieved with four block sizes to ensure equal distribution between groups using an online computer-generated block randomization technique (www.randomizer.org). Allocation concealment was maintained by using sequentially numbered, opaque, sealed envelopes prepared by an independent researcher who was not involved in patient recruitment or treatment. The envelopes were opened only after the patient met the inclusion criteria and consented to participate, thereby minimizing selection bias.

Patients were randomly assigned to four groups:

1) Normal 2.5% NaOCl group.
2) Cryotreated 2.5% NaOCl group.
3) Normal 5% NaOCl group.
4) Cryotreated 5% NaOCl group.

Root canal treatment procedures

The preoperative VAS scores of the patients were recorded before the endodontic procedures. A single operator (K.Y.) performed all the root canal treatment procedures under magnification (3× loop) and illumination. All treatments were completed in a single visit to avoid the potential confounding effect of interappointment medicament placement on postoperative pain, ensure protocol standardization, and align with the current clinical preference for single-visit endodontics in teeth with vital pulp and no periapical pathology [3].

The relevant teeth were anesthetized with articaine hydrochloride (Ultracain D-S; Sanofi, Paris, France) and 4% 1:100,000 adrenaline and were isolated with a rubber dam. Caries tissues were removed and an endodontic access cavity was prepared under water cooling with diamond round and fissure burs. The working length of the teeth was determined using a #10 K-type hand file and an electronic apex locator (VDW Gold; VDW, Munich, Germany), and periapical radiographs were taken to verify the working length. The mesial canals were prepared with the Reciproc Blue R25 file (25/0.08) (VDW, Munich, Germany), and the distal canals were prepared with the Reciproc Blue R40 file (40/0.06) (VDW, Munich, Germany).

In all groups, a total of 63 millilitres (mL) of irrigant solution was delivered per tooth in 5 mL aliquots as follows: 10 mL after access preparation and working length determination, 20 mL during Reciproc single-file instrumentation (four intermediate irrigation points), and 33 mL during the standardized final irrigation protocol (per canal: 5 mL NaOCl, 2 mL saline, 2 mL 17% EDTA, 2 mL saline). The temperature was monitored with a digital thermometer throughout the procedure.

All irrigation protocols from the access cavity preparation to the root canal filling were performed as follows:

1) Normal 2.5% NaOCl group (n = 33): Forty-five mL of 2.5% NaOCl were placed in a glass container at

room temperature (25 °C) and monitored with a digital thermometer to ensure that the temperature remained constant at 25 °C. The root canals were irrigated with a total of 10 mL of 2.5% NaOCl (Wizard; Rehber Kimya) at 25 °C during root canal preparation. The procedure was completed by applying 5 mL of 25 °C 2.5% NaOCl, 2 mL of saline, 2 mL of 17% ethylenediaminetetraacetic acid (EDTA) (EndoSolution; PPH Cerkamed) and 2 mL of saline for each root canal, respectively, as the final irrigation solution.

2) Cryotreated 2.5% NaOCl group ($n = 33$): Forty-five mL of 2.5% NaOCl cooled to 2 °C in the refrigerator was placed in 2.5 mL syringes. The syringes were placed inside a special storage box to maintain the temperature during use. The box was packed with ice, and a temperature of 2 °C was confirmed with a digital thermometer. The root canals were irrigated with 10 mL of 2.5% NaOCl at 2 °C during root canal preparation. The procedure was completed by administering 5 mL of 2.5% NaOCl at 2 °C, 2 mL of saline, 2 mL of 17% EDTA, and 2 mL of saline for each root canal, respectively, as the final irrigation solution.
3) Normal 5% NaOCl group ($n = 33$): The same irrigation protocol described for Group 1 was applied, with the only difference being the use of 5% NaOCl at 25 °C.
4) Cryotreated 5% NaOCl group ($n = 33$): The same protocol described for Group 3 was followed; however, the 5% NaOCl was cooled to 2 °C prior to use and maintained at this temperature throughout the procedure by placing the syringes inside a special storage box.

The root canals were dried with paper points (President Dental) and then filled with gutta percha (President Dental) and AH Plus root canal sealer (Dentsply Maillefer, Ballaigues, Switzerland) using the cold lateral condensation technique.

The cold lateral condensation technique was intentionally selected to ensure standardization and reproducibility across all cases. Although the Reciproc R25 and R40 instruments create relatively large apical preparations (0.08 and 0.06 tapers, respectively), cold lateral condensation remains a widely accepted, reliable, and reproducible obturation method in both clinical and research settings. This technique allows consistent control of the obturation length, minimizes technique sensitivity, and facilitates comparability with previous studies investigating postoperative pain after single-visit root canal treatment. Modified warm techniques may provide denser fills but introduce additional variables such as heat application and operator dependence, which could confound postoperative pain outcomes.

The teeth were permanently restored with composite resins (Clearfil Majesty Posterior, Kuraray Medical Inc., Tokyo, Japan). Each participant, irrespective of group allocation, was prescribed ibuprofen 100 mg, to be taken as needed every 6 h for up to 72 h (maximum 400 mg/day). Participants were instructed to use analgesics only if needed and to indicate yes/no use within 72 h on a medication log.

Postoperative evaluation

An investigator who was blinded to the study conditions performed the postoperative pain observations. All participants were provided with a questionnaire based on the VAS, which described their pain and analgesic intake at 6, 12, 24, 48, 48, and 72 h, and patients were asked to complete the questionnaire. Patients were invited for clinical controls, and VAS scores were recorded 72 h after treatment.

Statistical analysis

SPSS 26.0 software was used for statistical analysis of the obtained data (IBM Corp, Amork, NY). The pain scores data were not normally distributed according to the Shapiro-Wilk test. The homogeneity of the data was assessed with Levene's test. Kruskal Wallis H test was performed to compare the age and pain score among the four groups and a Chi-square test was applied to assess the associations between gender and analgesic intake. Pain values at different hours (6 h, 12 h, 24 h, 48 h and 72 h) for each group were analyzed using Friedman test. The level of significance was set at $p < .05$.

Results

Overall, 150 patients were evaluated for eligibility for the study. The study included 132 patients who met the inclusion criteria and accepted treatment. The study included 68 female and 64 male systemically healthy patients aged 18–65 years with symptomatic irreversible pulpitis. No patients were lost to follow-up in any group (Fig. 1).

There were no statistically significant differences in basic demographic data (mean age or gender) (Table 1) or preoperative pain values among the four study groups ($p > .05$) (Table 2).

Postoperative pain levels at 6 h were significantly lower in the cryotreated 2.5% NaOCl group than in all the other groups ($p < .05$). Postoperative pain levels at 12 h were statistically similar between the cryotreated 2.5% NaOCl group and the cryotreated 5% NaOCl group ($p > .05$) and were significantly lower than those in the other two groups ($p < .05$). At 24 h, the pain scores in both the 5% NaOCl groups (normal and cryotreated) were significantly lower than those in the normal 2.5% NaOCl group

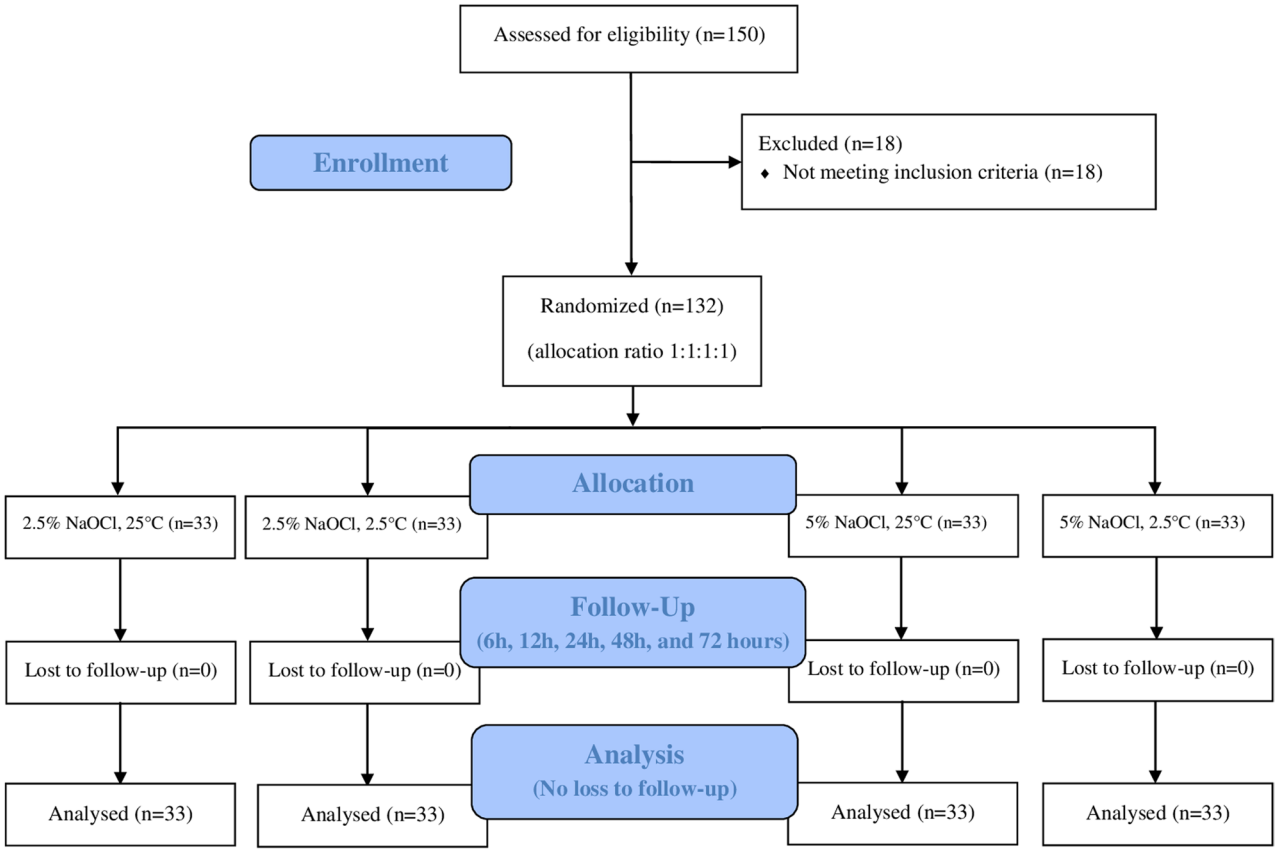


Fig. 1 CONSORT flowchart showing the progress of participants throughout the trial. A total of 132 patients were assessed for eligibility and randomly allocated to four groups (allocation ratio 1:1:1:1). No participants were excluded after randomization, and all patients completed the study with no loss to follow-up

Table 1 Distribution of patients by age (mean ± SD) and gender across normal 2.5% NaOCl at room temperature, cryotreated 2.5% NaOCl, normal 5% NaOCl at room temperature and cryotreated 5% NaOCl groups. Statistical tests: age - Kruskal–Wallis H; gender - χ^2 test. Values are mean ± SD or n (%)

Study Groups	2.5% NaOCl, 25 °C (*n* = 33)	2.5% NaOCl, 2.5 °C (*n* = 33)	5% NaOCl, 25 °C (*n* = 33)	5% NaOCl, 2.5 °C (*n* = 33)	Total (*n* = 132)	*p* Value
Mean age (mean ± SD)	39.33 ± 15.08	38.7 ± 16.18	39.33 ± 15.08	38.7 ± 16.18	39.01 ± 15.44	0.992
Gender						
Female	17(51.5)	15(45.5)	19(57.6)	17(51.5)	68(51.5)	0.808
Male	16(48.5)	18(54.5)	14(42.4)	16(48.5)	64(48.5)	

($p < .05$). The cryotreated 2.5% NaOCl group presented intermediate pain levels that did not differ significantly from those of either the normal 2.5% or the 5% NaOCl groups ($p > .05$). Postoperative pain levels at 48 and 72 h were statistically similar in all four study groups ($p > .05$) (Table 2). Postoperative pain levels at 6 and 12 h were significantly different across the study groups ($p < .05$), whereas postoperative pain levels at 24 and 48 h and postoperative pain levels at the 48 and 72 h were similar ($p > .05$) (Table 2) (Fig. 2). There was no statistically significant difference in analgesic intake among the groups ($p > .05$) (Table 3).

Discussion

This randomized controlled clinical trial aimed to evaluate the effect of cryotreated sodium hypochlorite (NaOCl) at two different concentrations (2.5% and 5%) on postoperative pain in mandibular first molars with symptomatic irreversible pulpitis. The null hypothesis that cryotreated NaOCl, regardless of concentration, does not significantly influence postoperative pain compared with normal NaOCl at room temperature was rejected. Compared with the normal 2.5% and 5% NaOCl groups, the cryotreated NaOCl groups -particularly the cryotreated 2.5% group during the first 12 h- showed significantly

Table 2 Mean (± standard deviation) / Median (minimum-maximum) preoperative pain score values and postoperative pain score values at 6 h,12 h, 24 h, 48 h and 72 h (VAS) in the four groups. Between-group: Kruskal–Wallis H test. Within-group across time: Friedman test. Superscripts A–B indicate between-group differences at a given time point ($p < .05$); a–e indicate within-group change over time ($p < .05$)

	2.5% NaOCl, 25 °C	2.5% NaOCl, 2.5 °C	5% NaOCl, 25 °C	5% NaOCl, 2.5 °C	*p* Value
	mean ± SD / median(min-max)	mean ± SD / median(min-max)	mean ± SD / median(min-max)	mean ± SD / median(min-max)	
Pre-op Pain	6.13 ± 1.16 / 6 (4–8)^{Aa}	6.06 ± 0.94 / 6 (5–8)^{Aa}	5.8 ± 0.99 / 6 (4–8)^{Aa}	5.6 ± 0.88 / 6 (4–7)^{Aa}	0.289
6. hours	2.13 ± 1.38 / 2 (1–5)^{Ab}	1.13 ± 1.04 / 1 (0–4)^{Bb}	2.53 ± 1.33 / 2 (1–5)^{Ab}	1.93 ± 1.14 / 2 (0–4)^{Ab}	< 0,001
12. hours	1.6 ± 0.62 / 2 (1–3)^{Ac}	0.8 ± 0.66 / 1 (0–2)^{Bc}	1.4 ± 0.96 / 1 (0–3)^{Ac}	0.73 ± 0.44 / 1 (0–1)^{Bc}	< 0,001
24. hours	1 ± 0.90 / 1 (0–3)^{Ad}	0.46 ± 0.5 / 0 (0–1)^{ABd}	0.4 ± 0.62 / 0 (0–2)^{Bd}	0.33 ± 0.47 / 0 (0–1)^{Bd}	0.005
48. hours	0.13 ± 0.34 / 0 (0–1)^{Ad}	0.2 ± 0.4 / 0 (0–1)^{Ad}	0.2 ± 0.4 / 0 (0–1)^{Ad}	0.13 ± 0.34 / 0 (0–1)^{Ad}	0.813
72. hours	0.13 ± 0.34 / 0 (0–1)^{Ade}	0 ± 0 / 0 (0–0)^{Ade}	0.13 ± 0.34 / 0 (0–1)^{Ade}	0.06 ± 0.25 / 0 (0–1)^{Ade}	0.19
p Value	< 0,001				

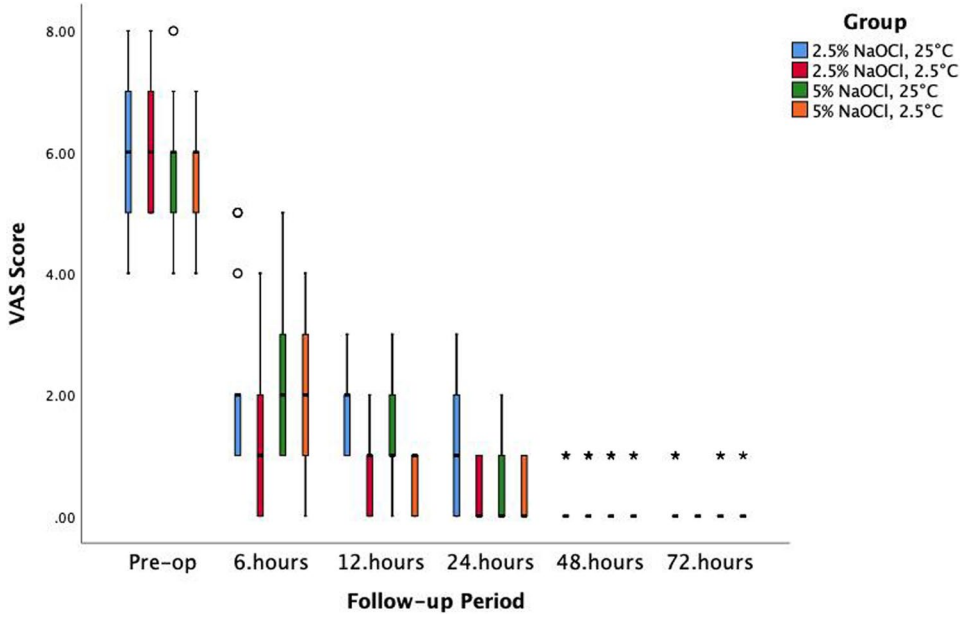


Fig. 2 Box-and-whisker plots of VAS pain scores (0–10) for the four groups at each follow-up period (preoperative, 6 h, 12 h, 24 h, 48 h, and 72 h; $n = 33$ per group). Each box represents the interquartile range (IQR); the horizontal line indicates the median; whiskers extend to the most extreme values within 1.5×IQR, and values beyond whiskers are plotted as circles (outliers). Asterisks (*) denote a statistically significant difference among groups at the corresponding time point ($p < .05$; Kruskal Wallis with Dunn's post-hoc)

Table 3 Frequency and percentage of patients who required analgesics after treatment in each group. Between-group: χ^2 test

	2.5% NaOCl, 25 °C	2.5% NaOCl, 2.5 °C	5% NaOCl, 25 °C	5% NaOCl, 2.5 °C	Total	*p* Value
	(*n* = 33)	(*n* = 33)	(*n* = 33)	(*n* = 33)	(*n* = 132)	
Analgesic intake						
Yes	6 (18.2)	2 (6.1)	6 (18.2)	4 (12.1)	18 (13.6)	0.419
No	27 (81.8)	31 (93.9)	27 (81.8)	29 (87.9)	114 (86.4)	

lower pain scores, and both cryotreated groups maintained lower pain scores at 24 h. Given this outcome, it was essential to control for potential confounding factors that could influence pain perception, ensuring that the observed effects were attributable to the intervention.

To achieve this goal, the study was carefully designed to minimize variables known to affect postoperative pain, such as preoperative pulp status, the presence of periapical pathology, or multiple tooth pain sources. Patients with necrotic pulp, periapical radiolucency, or more than one painful tooth were excluded. Only mandibular first molars with symptomatic irreversible pulpitis and moderate to severe preoperative pain were included. All patients were treated in a single visit to eliminate the potential confounding effect of intracanal medicament placement. Additionally, only teeth with three canals

were selected to ensure a standardized irrigation volume across groups. To further reduce procedural variability, a single-file reciprocating system (Reciproc) was used for canal preparation. The reciprocating motion is associated with reduced apical extrusion of debris compared with some rotary systems, which is an important factor when evaluating postoperative pain [31]. By using a standardized reciprocating system, we ensured homogeneity of canal shaping across patients, allowing the observed pain differences to be attributed primarily to irrigant temperature and concentration rather than to differences in instrumentation technique. This rigorous standardization allowed a more reliable assessment of the relationships among irrigant temperature, concentration, and postoperative pain.

The preoperative pain level of patients is an essential factor in the cause of postoperative pain in endodontically treated teeth, along with age, gender, pulp condition, materials, and techniques used during root canal treatment [32]. The effects of these variables were minimized in our study, as there was no significant difference in age or gender distribution or baseline preoperative pain score among the four groups. This study used a 10-cm VAS ranging from 0 to 10 to measure preoperative and postoperative pain intensity. All patients were asked to document their preoperative pain levels on a form prior to the procedure, and teeth with VAS scores indicating moderate or severe preoperative pain were included in the study [33].

A systematic review of pain intensity and severity before, during, and after root canal treatment revealed that pain intensity was highest in the first 6 h. The pain intensity decreased to approximately 40% by the end of 24 h and gradually decreased to 11% over 1 week [34]. Therefore, in our study, five time intervals of 6, 12, 24, 48, and 72 h after treatment were chosen to assess pain intensity in patients.

Cryotherapy reduces the temperature on the outer surface of the root, limiting inflammatory reactions, the release of pain-producing substances, and swelling in the periapical region. Thus, this method can help reduce postoperative pain in the short term [35, 36]. Changes in nerve conduction velocity, inhibition of nociceptors, and decreases in metabolic enzyme activity levels after cryotherapy also reduce pain [37–39]. Studies have reported the use of intracanal cryotherapy for pain reduction after endodontic treatment in recent years. In an in vitro study, Vera et al. demonstrated that flushing root canals with 2.5 °C cold saline solution for 5 min reduced the external root surface temperature by more than 10 °C and maintained this temperature for 4 min, suggesting that this temperature reduction would be sufficient for local anti-inflammatory effects in periradicular tissues [40]. A significant reduction in postoperative pain was also observed compared with the control group in another study in which 2.5 °C cold saline was used as the final irrigation solution in the root canal treatment of symptomatic and asymptomatic maxillary and mandibular teeth [18]. Cryotherapy has also been suggested to reduce postoperative pain by modulating peripheral nerve conduction and lowering the excitability of nociceptors [41]. In our study, we aimed to assess how irrigation with cryotreated NaOCl impacts the level of postoperative pain throughout the entire root canal, drawing on insights from the literature.

Using cryotreated NaOCl in root canal irrigation significantly reduces postoperative pain levels, especially in the early postoperative period [28, 42]. We performed root canal irrigation with NaOCl at different temperatures and concentrations. The rationale for using NaOCl is its excellent organic tissue dissolving properties and antimicrobial activity, making it the most widely used irrigation solution. A previous study revealed that cryotreated NaOCl has more significant antimicrobial activity against *Enterococcus faecalis (E. faecalis)* than does room temperature NaOCl, significantly reducing the number of *E. faecalis* [43]. Another study reported that significantly more free chlorine is released from refrigerated NaOCl than from room temperature and that higher amounts of active chlorine indirectly translate into higher antimicrobial activity [44].

A recent study evaluating the effect of the final irrigation solution temperature of NaOCl on postoperative pain relief in root canal treatment of symptomatic irreversible pulpitis and apical periodontitis teeth revealed that the cold NaOCl group presented lower postoperative pain values than the other groups did at all follow-up intervals [26]. An additional study using cold NaOCl and room temperature NaOCl as the final irrigation solutions demonstrated that the cryotherapy group had significantly lower postoperative pain levels at all time intervals tested and a reduction in analgesic intake at 6 h postoperatively. The NaOCl group treated at 2 °C presented significantly less postoperative pain and analgesic intake than the NaOCl group treated at 25 °C did [28]. Another study evaluated the effects of final irrigation of root canals with NaOCl solution at different temperatures on postoperative pain levels and antimicrobial activity [42]. All of these studies in the literature used cryotreated NaOCl as the final irrigation solution. In our study, cryotreated NaOCl was used throughout the entire root canal procedure, which is different from other studies. The results of the present study indicate that postoperative pain values at 6 h were significantly lower in the cryotreated 2.5% NaOCl group than in the other groups. The cryotreated 2.5% NaOCl and 5% NaOCl groups presented statistically similar postoperative pain values at 12 h, which were significantly lower than those of the other

two groups. This finding aligns with previous studies [26, 28, 42] and supports the hypothesis that the analgesic benefit of cryotreated NaOCl is primarily attributable to its local anti-inflammatory effect on periradicular tissues.

The literature lacks a consensus on the optimum NaOCl concentration for root canal irrigation [21, 45]. High concentrations of NaOCl have greater organic tissue dissolving properties but also greater cytotoxicity [21, 24, 46]. Therefore, lower concentrations of NaOCl are considered safer to use. NaOCl concentrations ranging from 0.5% to 8% have been used in most studies on postoperative pain [47]. Mostafa et al. demonstrated that irrigation with 1% NaOCl required less analgesia than irrigation with 5.25% NaOCl in mandibular molars with necrotic pulp [48]. Verma et al. reported no significant difference in the incidence or severity of pain due to irrigation with 1% or 5% NaOCl. Nevertheless, there was a lower degree of pain in the 1% NaOCl group [49]. Unlike these two studies, Farzaneh et al. reported that 2.5% NaOCl used in root canal irrigation of teeth with irreversible pulpitis treated in a single visit caused more postoperative pain than did 5.25% NaOCl [50]. The present study used NaOCl at concentrations of 2.5% and 5% at different temperatures for root canal irrigation. Unlike other studies, our study failed to find a significant effect of the NaOCl concentration on early postoperative pain. This study suggests that cryotreated NaOCl irrigation is the main factor that reduces postoperative pain in the early period after endodontic treatment. The use of 5% NaOCl in the present study was based on its superior tissue-dissolving capacity and antimicrobial spectrum, which are particularly important in mandibular molars with complex anatomy. Although concerns about cytotoxicity have been reported, higher concentrations remain widely used in clinical practice to ensure adequate debridement [21, 45, 46]. Our findings suggest that cryotreatment may mitigate the potential proinflammatory effects of higher concentrations by reducing periradicular irritation, thereby allowing clinicians to benefit from the enhanced efficacy of 5% NaOCl without increasing postoperative pain. This finding has important clinical implications, as it supports the safe use of higher concentrations when combined with temperature modulation.

One limitation of the present study is that postoperative pain was assessed only during the first 72 h. Although this period captures the peak pain phase, previous systematic reviews and clinical studies have reported that pain may persist for up to 7 days in a subset of patients [7, 34]. Therefore, our results mainly reflect the early postoperative phase and may not be generalizable to pain patterns beyond the first week. Another limitation is the restriction of the study sample to mandibular first molars with three canals, which may limit the generalizability of the findings to other tooth types or anatomical variations. In addition, the single-blind design constitutes a potential limitation. Although patients were not informed about group allocation, the clear temperature difference between cryotreated and room-temperature solutions could have been perceived by some participants, potentially introducing reporting bias and influencing VAS scores. Nevertheless, the use of a single experienced operator and the strict standardization of procedures likely minimized systematic bias. Finally, the study did not evaluate biological or inflammatory correlates of pain. Objective measurements, such as the quantification of cytokines (e.g., IL-1β and TNF-α) or neuropeptides (e.g., substance P and CGRP) in periapical exudate, could provide additional insight into the biological mechanisms of pain reduction with cryotreated NaOCl. Similarly, future studies may incorporate systemic inflammatory markers or non-invasive thermal imaging to correlate clinical pain scores with biological activity. Another limitation is that the potential influence of cryotreated NaOCl on tissue dissolution efficiency and antimicrobial activity has not been clinically evaluated. Future studies should incorporate standardized methods to quantify tissue dissolution and microbial reduction to comprehensively assess the clinical efficacy of cryotreated NaOCl beyond pain control. Another potential limitation is the standardized prescription of 100 mg ibuprofen to all participants, which could have masked subtle differences in pain perception between groups. Nevertheless, using the same analgesic regimen for all patients minimized variability and allowed a fair comparison of postoperative pain among the groups.

No studies in the literature indicate that the organic tissue dissolution efficiency decreases when the temperature of NaOCl decreases below room temperature. Nevertheless, we consider that the organic tissue dissolution effect of NaOCl may decrease when the temperature is lowered below room temperature. Although our study focused on the effect of cryotreated NaOCl on postoperative pain, new clinical studies are needed to investigate different methods that can tolerate the possible decrease in its tissue dissolving activity.

Conclusions

Using cryotreated NaOCl irrigation at different concentrations during root canal treatment procedures in mandibular first molars with symptomatic irreversible pulpitis effectively reduced postoperative pain.

Abbreviations

NaOCl	Sodium hypochlorite
VAS	Visual Analog Scale
ASA	American Society of Anesthesiologists Physical Status Classification
EDTA	Ethylenediaminetetraacetic acid
E. faecalis	Enterococcus faecalis

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Informed consent statement
Informed consent was obtained from all individual participants included in the study.

Permission to reproduce material from other sources
Not applicable.

Authors' contributions
**Kübra Gürler: ** Investigation, Supervision, Writing – review and edit, **Koray Yilmaz: ** Clinical procedures, Investigation, Methodology, Supervision, Writing – review and edit.

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Data availability
Raw data supporting the findings of this study are available from the corresponding author on request.

Declarations

Ethics approval and consent to participate
This clinical study was carried out under the approval of the Ethics Committee of Cukurova University School of Medicine and in accordance with the principles of Helsinki (version 2008) (meeting no: 153, decision no: 30, date: March 07, 2025). All participants provided written informed consent prior to their inclusion in the study.

Competing interests
The authors declare no competing interests.

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