



# The role of cryotherapy in the reduction of postoperative pain in patients with irreversible pulpitis and/or apical periodontitis: A randomized controlled clinical study

**Hemal Patel, Sonali Kapoor, Ankit Arora, Purnil Shah, Hardik Rana**

*Department of Conservative Dentistry and Endodontics, Manubhai Patel Dental College and Hospital, Gujarat, India*

**Purpose:** To compare and assess the efficacy of cryotherapy in reducing postoperative pain after bio-mechanical preparation in irreversible pulpitis and/or apical periodontitis in single-rooted teeth.

**Methods:** A total of eighty patients presenting with single-rooted teeth exhibiting irreversible pulpitis and/or apical periodontitis were subjected to a randomized allocation into two groups of 40 each. Irrigation was done using 5% sodium hypochlorite along with a heated plugger to warm it at 90°C for 5 seconds in all 80 teeth. Group 1 underwent final irrigation utilizing normal saline at room temperature. Group 2 received final irrigation using normal saline refrigerated between 2-5°C. Pain levels were assessed and recorded before the procedure and at 24 and 48-hour time intervals.

**Results:** No statistically significant differences were found in VAS pain scores between Group 1 and Group 2 at the 24-hour mark. Conversely, at the 48-hour mark, a significant statistical difference was observed in the VAS pain scores between Group 1 and Group 2. Group 1 exhibited a higher mean VAS score compared to Group 2.

**Conclusion:** Based on the constraints inherent in this study, it can be inferred that employing cryotherapy with the use of cold saline at 2°C to 5°C as a final irrigant leads to a reduction in postoperative pain at 48 hours.

**Keywords:** Cryotherapy; normal saline; permanent tooth; warm sodium hypochlorite.

## Introduction

During endodontic clinical practice, there are many instances when patients report postoperative pain in teeth that were asymptomatic before the initiation of root canal therapy. Managing such patients is challenging. (1) Reasons for the pain can include the movement of microorganisms and toxins into the periapical region (2,3). There are many strategies to control this pain, and one of the re-

cent inclusions is cryotherapy, which involves cold therapy that extracts heat from the area of application (4).

Physical, biological, and clinical evidence suggests that cryotherapy reduces hemorrhage, edema, inflammation, and the excitation velocity of nerve signals, hence it leads to a reduction in pain and spasm (5). The analgesic effect of cryotherapy is due to the combination of slower propagation of neural pain signals and decreased release

Cite this article as: Patel H, Kapoor S, Arora A, Shah P, Rana H. The role of cryotherapy in the reduction of postoperative pain in patients with irreversible pulpitis and/or apical periodontitis: A randomized controlled clinical study. Turk Endod J 2024;9:39–46.

Correspondence: Sonali Kapoor. Manubhai Patel Dental College and Hospital, Gujarat, India  
Tel: +91 982 – 532 30 57 e-mail: docsonali@gmail.com

Submitted: November 1, 2023 Revised: January 2, 2024 Accepted: January 23, 2024 Published: May 00, 2024

©2024 Turkish Endodontic Society



of chemical pain mediators, which also triggers a decrease in metabolism by more than 50%, allowing better oxygen flow to the injured tissues (6).

The utilization of cryotherapy in the context of endodontic treatment has increasingly gained prominence. The present study was designed and implemented with the aim of evaluating the efficacy of cryotherapy in diminishing postoperative pain subsequent to biomechanical preparation in individuals with irreversible pulpitis and/or apical periodontitis in single-rooted teeth. There are two groups in the study. In Group 1 (control group), the final irrigation procedure was performed using normal saline at room temperature, and in Group 2 (experimental group), the final irrigation procedure was performed using normal saline at a cold temperature range of 2 to 5°C.

The null hypothesis was formulated stating that there will not be any notable difference in the reduction of postoperative pain between the two groups of patients undergoing root canal treatment for irreversible pulpitis and/or apical periodontitis in single-rooted teeth.

### Objectives:

To determine the reduction in post-operative pain after final irrigation using normal saline at room temperature.

To determine the reduction in post-operative pain after final irrigation using normal saline at 2-5°C.

To compare postoperative pain reduction between the two groups.

### PICO Framework:-

P (Problem):- Presence of Post-operative Pain after initiation of root canal therapy.

I (Intervention):- Using Cryotherapy with normal saline at 2- 5°C as final irrigant.

C (Control):- Final irrigation with normal saline at room temperature.

O (Outcome):- Outcome assessment done with visual analogue scale.

### Materials and Methods

In order to calculate the sample size, several parameters were considered. From the pool of patients receiving endodontic treatment at the Department of Conservative Dentistry and Endodontics, a total of 80 individuals diagnosed with irreversible pulpitis and/or apical periodontitis were carefully chosen. To estimate the reduction in post-operative pain in VAS at 24 and 48 hours between two groups as a mean difference of 1.2 with a standard deviation of 1.9 at 95% confidence and 80% power, specific calculations were

made. Prior to commencing the research, approval was obtained from the Institutional Ethical Committee, ensuring compliance with ethical guidelines. Detailed explanations of the procedure were provided to the patients, and informed consent was acquired. Randomization in both groups was done by the odd-even method.

The selection criteria employed for patient inclusion were as follows:

#### Inclusion Criteria:

Age group above 18 years.

Patients suffering from irreversible pulpitis and/or apical periodontitis.

Single-rooted tooth.

Tooth with mature apex.

#### Exclusion Criteria:

Patient with any systemic disease.

Patient with swelling.

Severely damaged tooth.

Tooth previously undergone root canal treatment.

Patients who have taken analgesics during the past 24 hours.

Patient with absence of opposing teeth.

Tooth with immature apex.

Presence of any defect in the root: caries, restoration, root resorption, fractures, craze lines, extreme root curvatures.

Eligible patients (n = 80) were randomized into two groups: control (n = 40): final irrigation with normal saline at room temperature, and experimental (n = 40): final irrigation with normal saline at 2-5°C. Preoperative pain assessment was performed using a patient questionnaire, and pain was measured on the Heft-Parker Visual Analog Scale.

The root canal treatment procedure was started by administering local anesthesia (LA) lignocaine with adrenaline 1:80,000 (Lignox 2% A, Indoco Remedies Ltd, Mumbai, India) in a single-rooted tooth in both groups 1 and 2. After checking the effect of local anesthesia, rubber dam isolation was performed. Straight-line access cavity preparation was done using an Endo access (Dentsply Sirona, Dentsply Maillefer, Ballaigues, Switzerland) bur and Endo-Z (Dentsply Sirona, Dentsply Maillefer, Ballaigues, Switzerland) bur at high speed under air-water spray. Subsequently, coronal pre-flaring of canal orifices and working length determination was done with a Root ZX mini apex locator (Root ZX mini J Morita Corp, Japan) and it was confirmed with an IOPA radiograph. Biomechanical preparation was completed using hand K files (Mani, India) in

a crown-down technique. Irrigation of the root canal was performed by a 5 ml side-vented, 30 gauge syringe, and 5% sodium hypochlorite was warmed at 90°C using a heated plugger, the Fast Pack device (Orikam Neoendo, Punjab), for 5 seconds in both groups. The final irrigation was performed with normal saline at room temperature and using cold saline at 2 to 5°C for the control and experimental groups, respectively. After that, no intracanal medicament was used, and the access cavity was temporized with Cavit (3M, Mumbai, India).

### Follow-Up and Post-Operative Pain Analysis

Patients were recalled for follow-up on days 1 and 2 to check the postoperative pain. Postoperative pain was analyzed using the Heft-Parker Visual Analog Scale and a patient questionnaire that included the duration, nature, and quality of pain, and the number of medications the patient required to relieve the pain or any other complaints related to the same tooth. A medication of 650 mg of paracetamol was prescribed as an escape route if the pain was unbearable. Preoperative and postoperative pain assessments were performed, and a patient questionnaire was provided to patients in English as well as the local language (Gujarati), or it was translated verbally. The patient was assessed clinically to check for intraoral complications, and a percussion test was performed to check the periapical status.

The statistical analysis was performed by entering the data into a Microsoft Excel sheet and using SPSS software version STATA/IC-13.

Descriptive statistics were calculated as the mean, standard deviation (SD), and confidence interval (CI).

Comparison of postoperative pain to baseline data (preoperative pain) in individual groups was performed by independent t tests.

Comparison between postoperative pain reductions after 24 hours was performed by paired t tests.

Comparison of preoperative and postoperative pain reduction was performed by paired t tests.

## Results

A total of 80 patients who met the eligibility criteria were enrolled in the study. They were randomized into two groups (n = 40) who received the allocated intervention. There were no patients lost during follow-up at 24 and 48 hours. Therefore, a total of 80 patients, with 40 patients in each group, were assessed.

Statistically, no significant difference was present in the VAS score of pain between Group 1 (Control Group) and Group 2 (Experimental Group) in the preoperative time period and at 24 hours. In Group 1 (Control Group), the mean VAS score was higher than that in Group 2 (Experimental Group), indicating a statistically significant difference in the VAS score of pain between Group 1 (Control Group) and Group 2 (Experimental Group) at 48 hours. (Table 1)

In Group 1 (Control Group), the majority of the study subjects (50%) had severe pain, while in Group 2 (Experimental Group), the majority (42.5%) had mild pain in the preoperative time period. A statistically significant difference was present in the nature of pain between Group 1 (Control Group) and Group 2 (Experimental Group) in the preoperative time period. Statistically, no significant difference was present in the nature of pain between Group 1 (Control Group) and Group 2 (Experimental Group) at 24 hours. In Group 1 (Control Group), 40 percent of study subjects had no pain, while in Group 2 (Experimental Group), 72.5 percent of study subjects had no pain at 48 hours. A statistically significant difference was present in the nature of pain between Group 1 (Control Group) and Group 2 (Experimental Group) at 48 hours. (Table 2) (Fig. 1-3)

Statistically, no significant difference was present in the quality of pain between Group 1 (Control Group) and Group 2 (Experimental Group) in the preoperative time period and at 24 hours. In Group 1 (Control Group), the majority of the study subjects (52.5%) had dull pain, while in Group 2 (Experimental Group), the majority (72.5%)

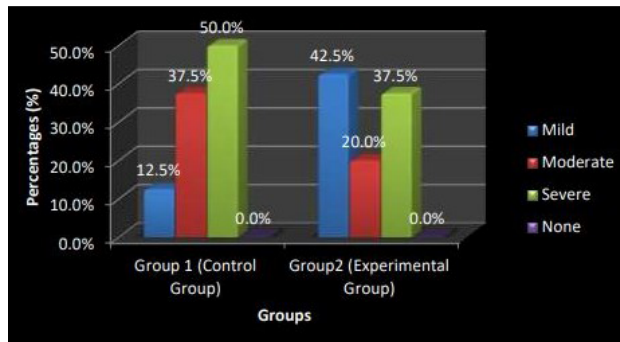
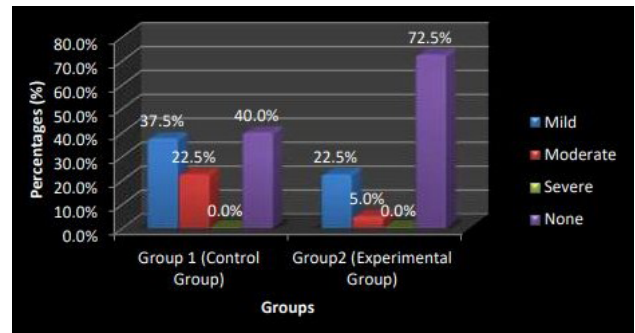
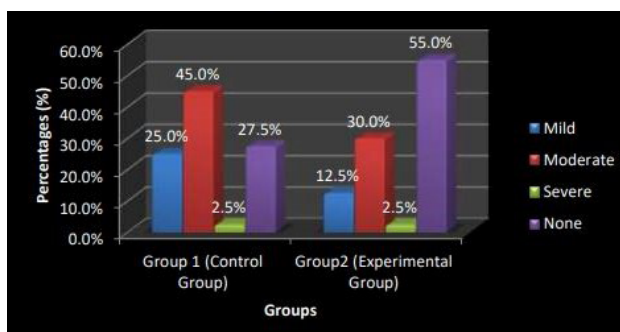
**Table 1.** Pain on VAS score between groups

	Group 1 (control group)		Group 2 (experimental group)		p value
	Mean	SD	Mean	SD	
Preoperative					
VAS	109.30	42.17	90.53	45.82	>0.05**
24 hours					
VAS	55.80	44.10	40.23	49.18	>0.05**
48 hours					
VAS	36.10	34.97	19.40	34.26	≤0.05*

Level of significance  $p \leq 0.05$ , \*Significant, \*\*Non Significant.

**Table 2.** Nature of pairwise distribution between groups

	Group 1 (control group)		Group 2 (experimental group)	
	Number	Percentages	Number	Percentages
Preoperative				
Mild	5	12.5	17	42.5
Moderate	15	37.5	8	20
Severe	20	50	15	37.5
None	0	0	0	0
Total	40	100	40	100
24 Hours				
Mild	10	25	5	12.5
Moderate	18	45	12	30
Severe	1	2.5	1	2.5
None	11	27.5	22	55
Total	40	100	40	100
48 Hours				
Mild	15	37.5	9	22.5
Moderate	9	22.5	2	5
Severe	0	0	0	0
None	16	40	29	72.5
Total	40	100	40	100

**Fig. 1.** Depicting nature of pain wise distribution between groups pre-operatively.**Fig. 3.** Depicting nature of pain wise distribution between groups at 48 hours.**Fig. 2.** Depicting nature of pain wise distribution between groups at 24 hours.

had no pain at 48 hours. A statistically significant difference was present in the quality of pain between Group 1 (Control Group) and Group 2 (Experimental Group) at 48 hours. (Table 3)

Statistically, no significant difference was present in relieving pain between Group 1 (Control Group) and Group 2 (Experimental Group) in the preoperative time period and at 24 hours. In Group 1 (Control Group), the majority of the study subjects (60%) had self-relieved pain, while in Group 2 (Experimental Group), the majority (72.5%) had no pain at 48 hours. A statistically significant difference was present in relieving pain between Group 1 (Control Group) and Group 2 (Experimental Group) at 48 hours. (Table 4)

## Discussion

Endodontic pain that occurs during and after treatment creates an apprehensive condition for patients. Understanding the exact cause of pain is sometimes the most difficult task for clinicians. There can be many reasons for

**Table 3.** Quality of pain wise distribution between groups

	Group 1 (control group)		Group 2 (experimental group)	
	Number	Percentages	Number	Percentages
Preoperative				
Throbbing	13	32.5	13	32.5
Dull	21	52.5	16	40
Sharp	1	2.5	6	15
Constant	4	10	4	10
None	1	2.5	1	2.5
Total	40	100	40	100
24 Hours				
Throbbing	3	7.5	0	0
Dull	23	57.5	17	42.5
Sharp	1	2.5	0	0
Constant	1	2.5	1	2.5
None	12	30	22	55
Total	40	100	40	100
48 Hours				
Throbbing	4	10	0	0
Dull	21	52.5	11	27.5
Sharp	1	2.5	0	0
Constant	0	0	0	0
None	14	35	29	72.5
Total	40	100	40	100

**Table 4.** Relieved of pain wise distribution between groups

	Group 1 (control group)		Group 2 (experimental group)	
	Number	Percentages	Number	Percentages
Preoperative				
Self	15	37.5	19	47.5
Medication	25	62.5	21	52.5
Pain absent	0	0	0	0
Total	40	100	40	100
24 hours				
Self	27	67.5	19	47.5
Medication	2	5	2	5
Pain absent	11	27.5	19	47.5
Total	40	100	40	100
48 hours				
Self	24	60	11	27.5
Medication	2	5	0	0
Pain absent	14	35	29	72.5
Total	40	100	40	100

the pain, such as mechanical, chemical, and microbiological (7). One of the most common causes of postoperative pain and failure of endodontic treatment is persistent microorganisms after endodontic procedures. It was previously reported in ex vivo studies that there are intact

untouched areas present after mechanical instrumentation; hence, an advanced irrigation approach is required to control the microorganisms from a complex root canal system (8).

Sodium hypochlorite (NaOCl) is widely employed as a

primary root canal irrigation solution due to its dual attributes of tissue dissolution and antimicrobial properties. The antibacterial efficacy of root canal irrigants can be enhanced through various means, one of which involves heating sodium hypochlorite. Giardino et al. (9) conducted a study to assess the impact of temperature on the antibacterial activity of sodium hypochlorite, and their findings indicated that heated sodium hypochlorite exhibited improved antimicrobial properties as an irrigating solution. Consequently, in our current study, a fast pack device was utilized to warm the sodium hypochlorite to a temperature of 90°C during the irrigation process of the root canal system in both the control and experimental groups. Notably, to date, no studies have been conducted specifically examining the application of fast pack devices in this context.

A fast pack (Orikam Neoendo, Punjab) is a device used to heat Gutta-percha in the down pack obturation technique. It has a wide temperature range of 90 to 250°C and has five memory programs to customize the temperature and cut-off time as per the material used.

Irrigants are usually carried into the root canal via needles and syringes. In our study, to carry irrigants like normal saline and sodium hypochlorite to the pulp space, 30 gauge side-vented needles (Orikam Neoendo, Punjab) were used. Neo-endo 30 gauge side-vented needles are 25 mm in length and yellow in color, with a rounded tip with one lateral vent and a closed front end. It is an ideal tool for irrigation that prevents the extrusion of irrigation solution into periapical tissue, and sterile needles can be used only once. It eliminates hydraulic pressure and ensures the safe delivery of the solution.

Various factors can contribute to the occurrence of pain during endodontic treatment. These include apical instrumentation, inadvertent extrusion of debris, pre-existing periradicular inflammation, local anesthetic injection, pressure from a rubber dam clamp, and prolonged opening of the oral cavity, intracanal dressing, pretreatment pain, and patient-related factors (5). Moreover, the application of increased mechanical pressure during endodontic procedures has the potential to induce or expedite the movement of these materials into the periapical region, thereby triggering pain sensations (10).

The frequency of post-endodontic pain ranges between 1.4 and 16 percent and sometimes up to 50 percent (11). Various strategies are employed to decrease postoperative pain discomfort in patients. These include pharmaceutical strategies such as using long-acting anesthesia and prescribing medications such as nonsteroidal anti-inflammatory drugs, analgesics like paracetamol, narcotic analgesics, or a combination of both. Nonpharmacologi-

cal strategies include preoperative relaxation approaches, novel techniques for glide-path preparation, occlusal reduction, various strategies for irrigation and biomechanical preparation, or varied kinematics during root canal treatment that minimize the extrusion of debris, which would inhibit pain pathway initiation (12). In pursuit of addressing these challenges, various therapeutic approaches have been implemented, with cryotherapy emerging as one of the recent modalities in this continuum (13). Cryotherapy, rooted in the concept of cold therapy that traces its origins back to ancient Greek practices, involves the extraction of heat from the targeted area rather than the direct application of cold itself. This approach serves to prevent or alleviate the occurrence of pain (2).

The reduction in temperature at the external surface of the root has been observed to impede the generation and release of pain-inducing substances, such as bradykinin, thus minimizing periapical edema (14). Cryotherapy also decreases the adherence of inflammatory cells to the capillary walls within the periapical region, resulting in a diminished presence of such cells in the periapical area. Furthermore, cryotherapy has been found to slow down peripheral nerve conduction (5). By inhibiting neural receptors in the periapical area, cryotherapy attenuates the transmission of pain signals, thereby reducing pain perception. Additionally, cryotherapy induces vasoconstriction and reduces local blood flow, along with a decline in metabolic activity, within the treated area (15).

In our study, various parameters were checked for pain perception. Considering the VAS of pain between groups, in Group 1, the mean VAS was higher than in Group 2 at 48 hours, indicating a statistically significant difference in VAS of pain between Group 1 and Group 2 at that time (Table 1). There was no significant difference in the visual analog scale score of pain between Group 1 and Group 2 at 24 hours, which can be explained by various previous studies which showed that post-endodontic pain usually occurs during the first 24 hours after treatment and generally diminishes after a few hours (16). However, it sometimes persists for several days (17). According to a recent systematic review, the prevalence of pain during the first 24 hours after root canal treatment is 40%, which gradually decreases (18). The occurrence of post-endodontic pain on day 1 would be due to the instrumentation procedure, which can provoke an acute periapical inflammatory response secondary to mechanical, chemical, and/or microbial injury to periradicular tissue (14).

Regarding the nature of pain in our randomized controlled clinical study, most patients had “moderate to severe pain” preoperatively, and there were zero patients with no pain. After the cryotherapy procedure in the control group at



24 hours, 72.5% of study subjects had pain that was moderate in the majority of patients, and in the experimental group, it decreased to 45 percent. There was a statistically significant difference in the nature of pain between groups 1 and 2 at 48 hours (Table 2). This is in accordance with a study performed by Keskin et al. (11), where there was a significant reduction in postoperative pain in the experimental group compared to the control group.

Considering the quality of pain, there was no statistically significant difference between Group 1 and Group 2 pre-operatively and at 24 hours post-operatively. At 48 hours, in Group 1, the majority of subjects (52.5%) were experiencing dull pain, while in Group 2, the majority of subjects (72.5%) were experiencing no pain. There was a statistically significant difference in the quality of pain between Group 1 and Group 2 at 48 hours (Table 3).

As far as pain-relieving factors are concerned, at 48 hours, in Group 1, the majority of study subjects (60%) were experiencing self-relieved pain, while in Group 2, the majority of subjects (72.5%) were experiencing no pain. There was a statistically significant difference in the relief of pain between Group 1 and Group 2 at 48 hours (Table 4).

Sadaf et al. (19) evaluated the effect of intracanal cryotherapy on postoperative pain after root canal therapy in patients with pulpal or periradicular pathosis and concluded that intracanal cryotherapy (i.e., using cold saline irrigation as a final irrigant) significantly reduces the intensity of pain at 6 and 24 hours after root canal therapy. Hespagnol et al. (6) evaluated the effectiveness of final irrigation with cold saline solution after endodontic treatment compared with saline solution at room temperature against postoperative pain following endodontic treatment and concluded that intracanal cryotherapy was effective in reducing postoperative pain after endodontic treatment in teeth with symptomatic apical periodontitis.

## Conclusion

In conclusion, within the constraints of this study, it can be inferred that cryotherapy utilizing cold saline at 2-5°C as a final irrigant following biomechanical preparation in cases of irreversible pulpitis and/or apical periodontitis effectively reduces postoperative pain. A statistically significant difference in the Visual Analogue Scale (VAS) pain score was observed between Group 1 (control group) and Group 2 (experimental group) at the 48-hour mark. However, further investigations are necessary to determine the actual success rate of different irrigating solutions as cryotherapy agents.

The study had several limitations. Firstly, blinding of the clinician was not feasible due to the use of cooled syringes,

which could introduce potential bias. Additionally, maintaining a consistent temperature of the final irrigation, which involved cold saline at 2-5°C, throughout the entire procedure was challenging. Furthermore, the study only included single-rooted teeth, leading to variations in biomechanical preparation among the study subjects.

**Use of AI for Writing Assistance:** Not declared

**Source of Funding:** None declared.

**Conflict of Interest:** None declared.

**Informed consent:** Written informed consent was obtained from patients who participated in this study.

## References

1. Jain A, Davis D, Bahuguna R, et al. A Role of cryotherapy in reducing postoperative pain in patients with irreversible pulpitis; an in-vivo study. *Int J Dent Med Sci* 2018; 2: 43–9.
2. Bleakley C, McDonough S, MacAuley D. The use of ice in the treatment of acute soft-tissue injury: a systematic review of randomized controlled trials. *Am J Sports Med* 2004; 32: 251–61. [[CrossRef](#)]
3. Bazaid DS, Kenawi LM. The effect of intracanal cryotherapy in reducing postoperative pain in patients with irreversible pulpitis: a randomized control trial. *Int J Health Sci Res* 2018; 8: 83–8.
4. Balasubramanian SK, Vinayachandran D. Cryotherapy. A panacea for post-operative pain following endodontic treatment. *Int J Dent Res Oral Sci* 2017; 2: 10–2.
5. Vera J, Ochoa J, Romero M, et al. Intracanal cryotherapy reduces postoperative pain in teeth with symptomatic apical periodontitis: a randomized multicenter clinical trial. *J Endod* 2018; 44: 4–8. [[CrossRef](#)]
6. Hespagnol FG, Guimaraes LS, Antunes LAA, et al. Effect of intracanal cryotherapy on postoperative pain after endodontic treatment: systematic review with meta-analysis. *Restor Dent Endod* 2022; 47: e30. [[CrossRef](#)]
7. Freire B, Geremia J, Baroni BM, et al. Effects of cryotherapy methods on circulatory, metabolic, inflammatory and neural properties: a systematic review. *Fisioter Mov* 2016; 29: 389–98. [[CrossRef](#)]
8. Sundqvist G, Figdor D, Persson S, et al. Microbiologic analysis of teeth with failed endodontic treatment and the outcome of conservative re-treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998; 85: 86–93.
9. Giardino L, Mohammadi Z, Beltrami R, et al. Influence of temperature on the antibacterial activity of sodium hypochlorite. *Braz Dent J* 2016; 27: 32–6. [[CrossRef](#)]
10. Koc M, Tez M, Yoldaş Ö, et al. Cooling for the reduction of postoperative pain: prospective randomized study. *Hernia* 2006; 10: 184–6. [[CrossRef](#)]

11. Keskin C, Özdemir Ö, Uzun İ, et al. Effect of intracanal cryotherapy on pain after single-visit root canal treatment. *Aust Endod J* 2017; 43: 83–8. [[CrossRef](#)]
12. Gurucharan I, Saravana Karthikeyan B, Mahalaxmi S. Intracanal cryotherapy in endodontics. *Aust Endod J* 2017; 43: 138–9. [[CrossRef](#)]
13. Stanek A, Cholewka A, Wielkoszyński T, et al. Whole-body cryotherapy decreases the levels of inflammatory, oxidative stress, and atherosclerosis plaque markers in male patients with active-phase ankylosing spondylitis in the absence of classical cardiovascular risk factors. *Mediators Inflamm* 2018; 2018: 8592532. [[CrossRef](#)]
14. Hess W. The Anatomy of root canals in the teeth of the permanent dentition. Available at: <https://babel.hathitrust.org/cgi/pt?id=mdp.39015023388500&seq=7>. Accessed Apr 22, 2024.
15. Guerreiro-Tanomaru JM, Loiola LE, Morgental RD, et al. Efficacy of four irrigation needles in cleaning the apical third of root canals. *Braz Dent J* 2013; 24: 21–4.
16. Al-Negrish AR, Hababeh R. Flare up rate related to root canal treatment of asymptomatic pulpally necrotic central incisor teeth in patients attending a military hospital. *J Dent* 2006; 34: 635–40. [[CrossRef](#)]
17. Siqueira JF Jr. Microbial causes of endodontic flare-ups. *Int Endod J* 2003; 36: 453–63. [[CrossRef](#)]
18. Pak JG, White SN. Pain prevalence and severity before, during, and after root canal treatment: a systematic review. *J Endod* 2011; 37: 429–38. [[CrossRef](#)]
19. Sadaf D, Ahmad MZ, Onakpoya IJ. Effectiveness of intracanal cryotherapy in root canal therapy: a systematic review and meta-analysis of randomized clinical trials. *J Endod* 2020; 46: 1811–23. [[CrossRef](#)]