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ORIGINAL ARTICLE

Effectiveness of Intracanal Cryotherapy on Postoperative Pain in Teeth with Symptomatic Apical Periodontitis.

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abstract… Objective: To assess the impact of intracanal cryotherapy in patients with pulp necrosis and symptomatic apical periodontitis at 12, 24, and 72 hours after single-visit root canal therapy using cold saline (2.5°c) as a final irrigant. **Study Design:** Randomized Clinical Trial. **Setting:** Operative Dentistry & Endodontics, Institute of Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. **Period:** May to October 2025. **Methods:** Group a (intracanal cryotherapy: 20 ml of 2.5°c normal saline) and group b (control: 20 ml of room-temperature saline) were randomly assigned 1:1 to 196 systemically healthy adults (aged 18–60 years) with pulp necrosis and symptomatic apical periodontitis. every tooth received a single-visit root canal treatment. visual analog scale (vas) was used to measure postoperative pain at 12, 24, and 72 hours. the chi-square test ($p < 0.05$), general linear model, and mann-whitney u test were used to evaluate between-group differences. **Results:** All 196 participants completed the study. the groups were comparable at baseline for age and sex ($p > 0.05$). no significant between-group differences in pain scores were observed at 12 hours (5.07 ± 0.646 vs. 5.01 ± 0.634; $p = 0.668$) or 24 hours (3.97 ± 1.000 vs. 3.99 ± 1.108; $p = 0.749$). at 72 hours, the cryotherapy group demonstrated significantly lower mean pain scores than the control group (1.31 ± 1.304 vs. 2.08 ± 1.843; $p = 0.008$), with a significantly greater proportion achieving no or mild pain (vas 0–3: 89.8% vs. 70.4%; $\chi^2 = 10.371$, $p = 0.001$). male participants and anterior teeth in the cryotherapy group demonstrated greater analgesic benefit at 72 hours. no adverse events were recorded in either group. **Conclusion:** Intracanal cryotherapy using 20 ml of 2.5°c saline significantly reduced postoperative pain intensity and improved clinical success rates at 72 hours compared with room-temperature saline in patients with symptomatic apical periodontitis.

key words: Cryotherapy, Intracanal Irrigation, Postoperative Pain, Randomized Clinical Trial, Root Canal Treatment, Symptomatic Apical Periodontitis.

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INTRODUCTION

One of the most common procedures in clinical dentistry is root canal therapy (RCT), which is the most effective non-surgical method of treating pulpal and periradicular disease. With reported incidence ranging from roughly 15% to 40% within the first 24 to 72 hours after treatment, postoperative pain is still one of the most common and clinically challenging complications following RCT, despite significant advancements. The majority of pain is mild to moderate in intensity.[1]

The conventional approach to managing post-endodontic pain relies principally on pharmacological adjuncts. Whilst effective in the short term, these agents carry a recognized burden of systemic adverse effects that limit their use in elderly patients, those with comorbidities, and individuals on polypharmacy regimens.[2]encompassing a wide range of pharmacological and non-pharmacological approaches. Through an extensive exploration of 20 distinct parts, the review discusses traditional analgesics, antibiotics, the use of corticosteroids, and the role of novel treatments such as platelet-rich fibrin (PRF This has generated considerable clinical interest in non-pharmacological, procedure-integrated adjuncts that can modulate periapical inflammation and reduce postoperative pain without systemic exposure.

Cryotherapy, which involves the application of cold to tissues for therapeutic purposes, has shown promise as a supplementary method for pain management in dentistry.[5]

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Cryotherapy, initially utilized in various medical disciplines to reduce inflammation and enhance recovery, has garnered attention in endodontics for its potential to regulate inflammatory responses.[6]ice packs were applied in the buccal vestibule of the mandibular first permanent molar for 5 min. Endodontic procedures started after 20 min for efficiently anesthetized teeth. The intraoperative pain intensity was measured using the visual analogue scale (VAS Cryotherapy presents a viable approach to alleviate post-endodontic pain through mechanisms such as vasoconstriction, decreased neural conduction velocity, and reduced release of inflammatory mediators.[7]

Recent studies demonstrate the efficacy of intracanal cryotherapy with cold saline irrigation in root canal therapy. However, several specific methodological limitations recur across the existing literature and constrain the generalizability of prior findings. Many published trials have enrolled patients with heterogeneous pulpal and periapical diagnoses, including teeth with vital pulps or normal periapical status, in which the inflammatory substrate for cryotherapy's effect may be absent or attenuated This method utilizes the anti-inflammatory and analgesic properties of cold to alleviate pain and discomfort post-treatment. Despite its potential, the evidence supporting cryotherapy in endodontics is limited and requires further investigation through well-designed clinical trials.[8]

In patients with pulp necrosis and symptomatic apical periodontitis undergoing a single-visit root canal procedure, this study assessed the effectiveness of cold saline irrigation in lowering postoperative pain. To improve knowledge of intracanal cryotherapy and its effects on endodontic patient outcomes, the study sought to assess pain levels at various postoperative intervals.

METHODS

At the Department of Operative Dentistry and Endodontics, Institute of Dentistry, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Pakistan, a parallel-group, randomized clinical trial with a 1:1 allocation ratio was carried out. The study was conducted from May to October 2025, a period of six months.

Before participating enrollment, the LUMHS Research Ethics Committee reviewed and formally approved the study protocol (Approval No. LUMHS/REC/-721). The Declaration of Helsinki's ethical guidelines were strictly adhered to during the study. Before any study-related procedures were carried out, each participant provided written informed consent. This was supplemented by a standard verbal explanation of the study's objectives, methods, risks, and the right to withdraw at any time without repercussions.

Inclusion criteria were systemically healthy adults aged 18–60 years of either sex, a diagnosis of pulp necrosis, confirmed by a negative response to both cold (ROEKO Endo-Frost by Coltene Group) and electric pulp testing, a diagnosis of symptomatic apical periodontitis (SAP), confirmed by a positive response to percussion and periapical radiographic evidence of periradicular changes, moderate to severe preoperative pain, corresponding to a Visual Analog Scale (VAS) score of 4–10 and single- or multi-rooted teeth requiring primary root canal treatment.

Exclusion criteria were teeth requiring endodontic retreatment, a documented history of chronic analgesic or anti-inflammatory medication use, complex root canal anatomy identified on pre-operative radiographs, including calcified canals, open apices, or untraceable canal paths, radiographic evidence of internal or external root resorption, and systemic conditions including diabetes mellitus, hypertension, and pregnancy or lactation.

The required sample size was calculated a priori using OpenEpi software (Version 3.01, www.openepi.com), applying the module for randomized clinical trials. The calculation was based on the proportions reported by Keskin et al[9], in which 85.88% of patients in the cryotherapy group and 68.23% in the control group were free of significant postoperative pain. With a two-sided significance level of 5% (α = 0.05), a statistical power of 80% (β = 0.20), and a 1:1 allocation ratio, the minimum required sample size was calculated to be 196 participants in total (98 per group).

The 196 eligible participants were allocated to one

of two groups in equal numbers (n = 98 per group) using simple randomization. A randomization list was generated prior to the study by an independent researcher not involved in participant enrolment or treatment delivery, using a lottery method. Allocation was concealed using sequentially numbered, opaque, sealed envelopes prepared by the same independent researcher. Each envelope was opened immediately prior to the final irrigation step by the treating operator to prevent foreknowledge from influencing earlier stages of treatment.
Participants were blinded to group allocation throughout the study; both the cold and room-temperature saline solutions were delivered using identical syringes and needles, and participants were not informed of which solution they received. The statistician responsible for data analysis was also blinded to group allocation, with groups coded as Group A and Group B until analysis was complete. The treating operator could not be blinded owing to the observable temperature difference between the two irrigation solutions.

All treatments were delivered by a single trained operator following a standardized protocol. Local anesthesia was administered using 2% lidocaine with 1:100,000 epinephrine, and operative field isolation was achieved with a rubber dam. Conventional endodontic access cavities were prepared with a round bur in a high-speed handpiece. A glide path was established using a size 10 K-file, and working length was determined with an electronic apex locator (Wispex by BOMEDENT) and confirmed with a periapical radiograph. Chemo-mechanical preparation was performed using nickel-titanium rotary instruments in a crown-down sequence, with continuous irrigation using 3% sodium hypochlorite (NaOCl) delivered via a 5 mL syringe and a 31-gauge side-vented needle to the working length. A final rinse with 17% ethylenediaminetetraacetic acid (EDTA) solution was administered for one minute to remove the smear layer, after which canals were dried with sterile paper points.

Participants randomized to Group A received a final irrigation with 20 mL of sterile normal saline chilled to 2.5°C (±0.5°C). The solution was stored in a refrigerator until immediately prior to use and its temperature was verified with a calibrated digital thermometer at the chairside before delivery. The cold saline was delivered to the full working length using a 31-gauge side-vented needle via a 5 mL syringe, in four successive 5 mL syringes over a total irrigation period of five minutes.

Participants randomized to Group B received a final irrigation with 20 mL of sterile normal saline maintained at standard room temperature (21–25°C). The volume, delivery instrument, and duration were identical to those used in Group A to ensure procedural equivalence.

Following completion of final irrigation in both groups, root canals were obturated with gutta-percha using the cold lateral condensation technique. Coronal access cavities were permanently restored with direct composite resin in the same visit.

The primary outcome was postoperative pain intensity, assessed using a standard 100 mm horizontal Visual Analog Scale (VAS), anchored at 0 mm ("no pain") and 100 mm ("worst imaginable pain"), recorded at three postoperative intervals: 12, 24, and 72 hours. Participants were instructed by a blinded research assistant in the use of the VAS prior to discharge and were contacted by telephone at each time point to record their scores. For the purposes of categorical analysis, continuous VAS scores were dichotomized into two clinically meaningful categories: no pain or mild pain (0–3) and moderate to severe pain (4–10). No rescue analgesia was prescribed; participants were instructed to report spontaneous use of any analgesics, which was recorded as a secondary outcome.

All data were entered and analyzed using SPSS Statistics software (Version 22.0; IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD); categorical variables are presented as frequencies and percentages. The normality of continuous data was assessed using the Shapiro–Wilk test. As VAS pain scores were not normally distributed, between-group differences in continuous pain scores at each time point were analyzed using the Mann–Whitney U test. Temporal progression of mean pain scores across both groups over the four measurement

points (pre-operative, 12 h, 24 h, 72 h) was assessed using a General Linear Model (GLM) for repeated measures. Between-group differences in dichotomized pain outcomes were analyzed using the chi-square test. Potential confounding variables including patient age, sex, tooth type, and pre-operative VAS score were controlled through a pre-specified stratification strategy. A p-value of less than 0.05 was considered statistically significant for all tests

RESULTS

A total of 196 participants fulfilled the eligibility criteria and were enrolled in the study, with 98 allocated to Group A (intracanal cryotherapy) and 98 to Group B (room-temperature saline control). All enrolled participants completed the study and were included in the final analysis; there were no withdrawals, drop-outs, or protocol deviations.

The cohort comprised 119 males (60.7%) and 77 females (39.3%), with a mean age of 33.32 years (SD = 11.98; range 18–59 years). The involved teeth included 63 anterior teeth (32.1%) and 133 posterior teeth (67.9%). Baseline comparability between the two groups was assessed for all demographic and clinical variables. The groups were well matched for age (Group A: 32.71 ± 12.07 years; Group B: 33.92 ± 11.92 years; p = 0.483) and sex distribution (Group A: 60 males, 38 females; Group B: 59 males, 39 females; $\chi^2 = 0.000$, p = 1.000). However, a statistically significant difference in tooth type distribution was observed between the two groups ($\chi^2 = 4.585$, p = 0.032), with Group B containing a higher proportion of posterior teeth (Group A: 39 anterior, 59 posteriors; Group B: 24 anterior, 74 posterior); this imbalance was accounted for in subsequent stratified analyses.

Mean preoperative VAS pain scores were comparable between the two groups (Group A: 7.81 ± 0.845; Group B: 7.64 ± 0.944; overall mean 7.72 ± 0.90; range 6–9; p = 0.236), confirming successful baseline equivalence with respect to pain severity

Postoperative VAS pain scores declined progressively across all three time points in both groups. Overall mean scores across the entire cohort were 5.04 ± 0.64 (range 4–7) at 12 hours, 3.98 ± 1.05 (range 1–6) at 24 hours, and 1.69 ± 1.64 (range 0–6) at 72 hours.

Between-group comparisons using the Mann–Whitney U test revealed no statistically significant differences in pain scores at 12 hours (Group A: 5.07 ± 0.646 vs. Group B: 5.01 ± 0.634; p = 0.668) or at 24 hours (Group A: 3.97 ± 1.000 vs. Group B: 3.99 ± 1.108; p = 0.749). However, at 72 hours, the cryotherapy group demonstrated a significantly lower mean pain score compared with the control group (1.31 ± 1.304 vs. 2.08 ± 1.843; p = 0.008), indicating a clinically meaningful and statistically significant analgesic benefit emerging at this later time point. The mean pain scores and between-group comparisons at all time points are summarized in Table-I.

When VAS scores were dichotomized into clinically meaningful categories (no or mild pain: 0–3; moderate-to-severe pain: 4–10), at 12 hours all participants in both groups reported moderate-to-severe pain (100% in both groups; p = 1.000), reflecting the expected acute postoperative response. At 24 hours, no significant inter-group difference was observed in the proportion of patients achieving mild or no pain (Group A: 26/98, 26.5%; Group B: 29/98, 29.6%; $\chi^2 = 0.101$, p = 0.751). By 72 hours, however, a significantly greater proportion of participants in the cryotherapy group reported no or mild pain compared with the control group (Group A: 88/98, 89.8%; Group B: 69/98, 70.4%; $\chi^2 = 10.371$, p = 0.001), confirming the superior long-term analgesic effectiveness of intracanal cryotherapy.

Sex-stratified analysis revealed that female participants reported consistently higher pain scores than males across both groups and all time points. Within the cryotherapy group, female participants reported higher pain at 12 hours (5.18 ± 0.834 vs. 5.00 ± 0.487; p = 0.308) and at 24 hours (4.29 ± 0.867 vs. 3.77 ± 1.031; p = 0.036). The most striking sex-related difference in the cryotherapy group emerged at 72 hours, where male participants reported substantially lower pain scores than females (0.85 ± 1.102 vs. 2.03 ± 1.284; $p < 0.001$), indicating that males derived a significantly greater benefit from cryotherapy at this time point. In the

control group, sex-related differences in pain did not reach statistical significance at 12 or 24 hours ($p = 0.249$ and $p = 0.101$, respectively), although females reported higher scores at 72 hours (2.46 ± 2.175 vs. 1.83 ± 1.555; $p = 0.007$). Complete sex-stratified data are presented in Table-II.

Stratification by tooth type revealed that, within the cryotherapy group, posterior teeth were associated with significantly higher postoperative pain compared with anterior teeth at 24 hours (4.25 ± 0.921 vs. 3.54 ± 0.969; $p = 0.001$) and at 72 hours (1.78 ± 1.365 vs. 0.59 ± 0.785; $\chi^2 = 5.628$, $p = 0.018$). No significant difference between anterior and posterior teeth was detected at 12 hours in the cryotherapy group ($p = 0.700$), nor at the preoperative baseline ($p = 0.078$). Within the control group, tooth type did not significantly influence postoperative pain at any time point ($p > 0.05$ at all intervals), suggesting that the tooth-type effect is specific to the cryotherapy intervention. These findings are detailed in Table-III.

No procedure-related adverse events were recorded in either group throughout the study period. No participant reported any adverse reaction attributable to the irrigation solution, and no episodes of flare-up requiring emergency management were documented.

DISCUSSION

This single-blind randomized clinical trial evaluated the effect of a standardized intracanal cryotherapy protocol on postoperative pain following single-visit root canal treatment in teeth with necrotic pulps and symptomatic apical periodontitis. The principal finding was a statistically significant reduction in postoperative pain in the cryotherapy group at 72 hours, with no significant between-group differences at 12 or 24 hours. Correspondingly, a significantly greater proportion of participants in the cryotherapy group achieved no or mild pain by 72 hours.

TABLE-I

Mean postoperative pain scores (VAS) ± standard deviation for Group A (cryotherapy) and Group B (control) at each assessment time point, with between-group comparisons

Variable	Group A (Cryotherapy) Mean ± SD	Group B (Control) Mean ± SD	Total Mean ± SD	P-Value*
Preoperative Pain	7.81 ± 0.845	7.64 ± 0.944	7.72 ± 0.898	0.236
Pain at 12 Hours	5.07 ± 0.646	5.01 ± 0.634	5.04 ± 0.639	0.668
Pain at 24 Hours	3.97 ± 1.000	3.99 ± 1.108	3.98 ± 1.052	0.749
Pain at 72 Hours	1.31 ± 1.304	2.08 ± 1.843	1.69 ± 1.639	0.008†

*Mann–Whitney U test. †Statistically significant ($p < 0.05$).

TABLE-II

Comparison of mean pain scores (± standard deviation) between male and female participants in the cryotherapy and control groups at all assessment time points

Variable	Group	Male Mean ± SD	Female Mean ± SD	Chi²	P-Value
Preoperative Pain	Cryotherapy	7.83 ± 0.905	7.76 ± 0.751	—	0.525
	Control	7.69 ± 0.951	7.56 ± 0.940	—	0.576
Pain at 12 Hours	Cryotherapy	5.00 ± 0.487	5.18 ± 0.834	—	0.308
	Control	4.95 ± 0.729	5.10 ± 0.447	—	0.249
Pain at 24 Hours	Cryotherapy	3.77 ± 1.031	4.29 ± 0.867	2.829	0.093
	Control	3.83 ± 1.191	4.23 ± 0.931	3.338	0.068
Pain at 72 Hours	Cryotherapy	0.85 ± 1.102	2.03 ± 1.284	3.226	< 0.001†
	Control	1.83 ± 1.555	2.46 ± 2.175	7.259	0.007†

Chi-square values reported for dichotomized VAS scores. Mann–Whitney U test used for continuous comparisons. — indicates chi-square not calculable (no variation in category). †Statistically significant ($p < 0.05$).

TABLE-III

Comparison of mean pain scores (± standard deviation) between anterior and posterior teeth in the cryotherapy and control groups at all assessment time points. Anterior n = 39 (cryotherapy), 24 (control); Posterior n = 59 (cryotherapy), 74 (control)

Group	Time Point	Anterior (n = 39 / 24) Mean ± SD	Posterior (n = 59 / 74) Mean ± SD	Chi^2	p-value
Cryotherapy	Preoperative Pain	7.62 ± 0.907	7.93 ± 0.785	—	0.078
	Pain at 12 Hours	5.08 ± 0.422	5.07 ± 0.763	—	0.700
	Pain at 24 Hours	3.54 ± 0.969	4.25 ± 0.921	3.769	0.052
	Pain at 72 Hours	0.59 ± 0.785	1.78 ± 1.365	5.628	0.018†
Control	Preoperative Pain	7.75 ± 0.897	7.61 ± 0.963	—	0.639
	Pain at 12 Hours	5.21 ± 0.779	4.95 ± 0.571	—	0.077
	Pain at 24 Hours	4.00 ± 0.978	3.99 ± 1.153	0.042	0.838
	Pain at 72 Hours	1.88 ± 1.484	2.15 ± 1.949	0.096	0.757

Chi-square test applied to dichotomized VAS scores. Mann–Whitney U test used for continuous comparisons. — indicates chi-square not calculable (no variation in category). †Statistically significant ($p < 0.05$).

These findings confirm that intracanal cryotherapy exerts a clinically meaningful and statistically significant analgesic effect in this patient population, with the benefit becoming most pronounced at the later postoperative interval.

The analgesic benefit of intracanal cryotherapy in teeth with symptomatic apical periodontitis has been documented in prior randomized trials. Vera et al.[10] were the first to demonstrate, in a multicenter RCT, that cold saline irrigation significantly reduced both the incidence and intensity of postoperative pain in necrotic teeth with SAP, a finding that provided the clinical rationale for the present investigation. Keskin et al whose data were used for the sample size calculation in the present study, reported a substantially higher proportion of pain-free patients in the cryotherapy group at 24 hours.[9] The present study extends these observations to a later time point, demonstrating that the between-group divergence in pain scores, though absent at 12 and 24 hours, becomes most prominent at 72 hours. This temporal pattern suggests that the anti-inflammatory effects of cryotherapy are not immediate but rather accumulate over time as the periradicular inflammatory response naturally resolves.

The pattern of findings in the present study is broadly consistent with, yet also adds nuance to, the existing meta-analytic evidence. Sadaf et al.[8] and Hespanhol et al.[11] both reported significant pain reduction at 6 and 24 hours in teeth with SAP, but the former found no significant effect beyond 24 hours. More recently, Patel et al in a meta-analysis restricted to SAP, confirmed a significant benefit at 6 hours but noted methodological heterogeneity as a key limitation.[12] The present study, by contrast, identified significant benefit at 72 hours but not at the earlier time points. This discrepancy may be attributable to several factors. First, the present cohort was characterized by high baseline pain severity, which may have attenuated any group differences in the first 24 hours as both groups remained in the moderate-to-severe pain range. Second, the natural resolution of acute postoperative inflammation between 24 and 72 hours may have allowed the anti-inflammatory effect of cryotherapy to become comparatively more evident. Third, the use of a side-vented positive-pressure delivery system rather than the negative-pressure system used in several previous trials may have resulted in subtly different irrigant distribution patterns, potentially affecting the timing of the therapeutic effect.

The biological rationale underpinning the observed analgesic effect is well established. Vera et al. demonstrated in vitro that 2.5°C saline can reduce the external root surface temperature, sustaining this reduction for up to five minutes.[10] This degree of tissue cooling is sufficient to trigger a cascade of physiological responses with direct relevance to pain modulation. The net effect is a dampening of the neurogenic and vascular components of the periapical inflammatory response that are primarily responsible for postoperative pain in SAP. The

progressive divergence in pain scores between the two groups observed from 24 to 72 hours in the present study is consistent with this mechanism, as the cumulative anti-inflammatory effect of the initial cooling intervention may be most discernible after the acute phase of the inflammatory cascade has partially resolved. The absence of a statistically significant difference at 12 hours may reflect the overwhelming dominance of acute mechanical trauma from instrumentation at this early time point, which may mask the more subtle anti-inflammatory benefit of cryotherapy.

When outcomes were analyzed categorically, the superiority of cryotherapy became particularly evident at 72 hours. This difference in clinical success is of practical significance, particularly given that postoperative pain remains one of the most common causes of patient dissatisfaction following root canal treatment and a major driver of unscheduled postoperative visits.[13] The absence of any significant difference in effectiveness at 12 or 24 hours further underscores that intracanal cryotherapy, as delivered in the present protocol, should not be regarded as an acute analgesic but rather as a modality that confers sustained benefit in the later postoperative period.

A noteworthy secondary finding was the significant influence of sex on postoperative pain perception and on the analgesic response to cryotherapy. Female participants reported consistently higher pain scores than males across both groups and all time points, with the largest sex-related difference observed within the cryotherapy group at 72 hours, where males reported substantially lower pain than females. This pattern is consistent with a substantial body of literature demonstrating that women generally exhibit greater pain sensitivity, a lower pain threshold, and reduced pain tolerance compared with men, attributable to complex interactions between gonadal hormones, differences in central and peripheral pain processing pathways, and psychosocial factors.[14] In the context of endodontic pain specifically, female sex has been identified as an independent predictor of higher postoperative pain intensity.[15] The superior analgesic response to cryotherapy observed in male participants may reflect sex-specific differences in peripheral pain modulation or in the degree of neurogenic inflammation within periradicular tissues, though the precise mechanisms remain to be elucidated. These findings suggest that sex should be considered as a stratification variable in future cryotherapy trials and may have implications for individualizing postoperative pain management in endodontic practice.

Stratification by tooth type revealed that, within the cryotherapy group, posterior teeth were associated with significantly higher postoperative pain scores at 24 and 72 hours compared with anterior teeth. This finding is consistent with prior evidence that molar teeth, by virtue of their greater number of root canals, more complex three-dimensional anatomy, and thicker surrounding alveolar bone, are associated with higher rates and intensities of postoperative pain following root canal treatment.[16] From a cryotherapy-specific perspective, the reduced analgesic benefit in posterior teeth may reflect the diminished thermal transmission efficiency through denser dentinal walls and the greater distance between the intracanal irrigant and the periapical tissues in multi-rooted teeth. Vera et al.[10] noted considerable variation in the degree of cold transmission to the periodontal ligament across different root sections, attributed to differences in dentinal thickness and mineralization. Importantly, no significant association between tooth type and postoperative pain was found in the control group at any time point, indicating that the tooth-type effect identified in the present study is specific to the cryotherapy intervention rather than a general characteristic of postoperative pain in this population.

No adverse events were recorded in either group throughout the study period. This finding is consistent with the prevailing safety profile reported in the cryotherapy literature and supports the characterization of intracanal cryotherapy as a safe adjunctive procedure.[17,18] The theoretical risk of irrigant extrusion and associated periapical complications was mitigated in the present study through the use of a side-vented needle, which minimizes apical extrusion by directing irrigant flow laterally rather than apically. The absence of any postoperative flare-ups or emergency presentations

further reinforces the clinical suitability of this protocol for single-visit treatment in the population studied.

From a clinical standpoint, intracanal cryotherapy possesses several attributes that enhance its practical appeal. It requires no additional equipment beyond a refrigerator and uses a single-use sterile saline that is universally available and inexpensive. Unlike pharmacological adjuncts which carry contraindications in patients with renal impairment, peptic ulcer disease, or hypersensitivity; cryotherapy is free of systemic interactions and adverse effects, making it particularly suitable for elderly patients and those with complex medical histories. The present findings demonstrate a clinically significant reduction in pain intensity in the proportion of patients achieving mild or no pain by 72 hours, support the integration of this five-minute adjunct into routine single-visit endodontic practice, particularly in cases with active periapical inflammation.

Several limitations of the present study warrant acknowledgement. Although participants and the outcome assessor were blinded to group allocation, full double-blinding was not achievable owing to the inherent observability of irrigant temperature by the treating operator. This is a common and widely acknowledged limitation of intracanal cryotherapy trials. Pain was assessed using a unidimensional VAS, which, whilst validated and widely used, does not capture the multidimensional character of the pain experience, including its affective and cognitive components. The study did not record analgesic consumption as a co-primary outcome, limiting the interpretation of the effectiveness data. The significant imbalance in tooth type distribution between the two groups represents a potential confound that ideally would have been addressed through stratified randomization. The present trial was conducted at a single center, which may limit the generalizability of the findings to other clinical settings, patient populations, and operators.

CONCLUSION

Intracanal cryotherapy using 20 mL of 2.5°C normal saline delivered over five minutes as a final irrigation adjunct produced a statistically significant reduction in postoperative pain intensity at 72 hours compared with room-temperature saline in patients with pulp necrosis and symptomatic apical periodontitis undergoing single-visit root canal treatment. Sex and tooth type as significant modulators of the cryotherapy response. Anterior teeth were associated with significantly lower postoperative pain compared with posterior teeth.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. AlOmari T, AlThobiti G, AlThobaiti S, AlOufi F, Masuadi E, Jamleh A. **Incidence of postoperative pain after canal shaping by using Reciproc and Twisted File Adaptive systems: A prospective, randomized clinical trial.** Clin Oral Investig. 2020; 24(7):2445-50.
2. Falatah AM, Almalki RS, Al-Qahtani AS, Aljumaah BO, Almihdar WK, Almutairi AS. **Comprehensive strategies in endodontic pain management: An integrative narrative review.** Cureus. 2023; 15(12):e50371.
3. Machado R, Comparin D, Ignácio SA, da Silva Neto UX. **Postoperative pain after endodontic treatment of necrotic teeth with large intentional foraminal enlargement.** Restor Dent Endod. 2021; 46(3):e31.
4. Çiçek E, Koçak MM, Koçak S, Sağlam BC, Türker SA. **Postoperative pain intensity after using different instrumentation techniques: A randomized clinical study.** J Appl Oral Sci Rev FOB. 2017; 25(1):20-26.
5. Parihar AS, Hotchandani K, Sajjanar A, Parakh S, Tiwari H, Bhuyan L. **Prescribing cold: The science and practice of cryotherapy in dental medicine.** J Pharm Bioallied Sci. 2024; 16(Suppl 3):S1935-S1937.
6. Elheeny AAH, Sermani DI, Saliab EA, Turky M. **Cryotherapy and pain intensity during endodontic treatment of mandibular first permanent molars with symptomatic irreversible pulpitis: A randomized controlled trial.** Clin Oral Investig. 2023; 27(8):4585-93.
7. Pérez Serrato CA, Rotemberg Wilf EB. **Aplicación de la crioterapia en endodoncia: su importancia en el control del dolor. Odontoestomatología.** 2024; 26(43):1-13.
8. 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(12):1811-23.e1.
9. Keskin C, Özdemir Ö, Uzun İ, Güler B. **Effect of intracanal cryotherapy on pain after single-visit root canal treatment.** Aust Endod J. 2017; 43(2):83-88.

10. Vera J, Ochoa J, Romero M, Vazquez-Carcano M, Ramos-Gregorio CO, Aguilar RR, et al. **Intracanal cryotherapy reduces postoperative pain in teeth with symptomatic apical periodontitis: A randomized multicenter clinical trial.** Journal of Endodontics. 2018 Jan 1; 44(1):4-8.
11. Hespanhol FG, Guimarães LS, Antunes LAA, Antunes LS. **Effect of intracanal cryotherapy on postoperative pain after endodontic treatment: Systematic review with meta-analysis.** Restor Dent Endod. 2022; 47(3):e30.
12. Patel NK, Doshi P, Dalal SR, Kesharani PR, Shah SS, Kale MH. **Impact of intracanal cryotherapy on postoperative pain in symptomatic apical periodontitis: A systematic review and meta-analysis of randomized clinical trials.** Endodontology. 2025; 37(2):101-09.
13. Suresh N, Nagendrababu V, Koteeswaran V. **Effect of preoperative oral administration of steroids in comparison to an anti-inflammatory drug on postoperative pain following single-visit root canal treatment** – a double-blind, randomized clinical trial. 2021; (September 2020):198-209.
14. Greenspan JD, Craft RM, LeResche L, Arendt-Nielsen L, Berkley KJ, Fillingim RB, et al. **Studying sex and gender differences in pain and analgesia: A consensus report.** Pain. 2007 Nov 1; 132:S26-45.
15. Garcia-Font M, Durán-Sindreu F, Morelló S, Irazusta S, Abella F, Roig M, et al. **Postoperative pain after removal of gutta-percha from root canals in endodontic retreatment using rotary or reciprocating instruments: a prospective clinical study.** Clinical Oral Investigations. 2018 Sep; 22(7):2623-31.
16. AlRahabi MK. **Predictors, prevention, and management of postoperative pain associated with nonsurgical root canal treatment: A systematic review.** J Taibah Univ Med Sci. 2017; 12(5):376-84.
17. Ahmad MZ. **Effects of intracanal cryotherapy on postoperative pain in necrotic teeth with symptomatic apical periodontitis: A randomized controlled clinical trial.** Front Dent Med. 2025; 6:1543383.
18. Almohaimede A, Al-Madi E. **Is intracanal cryotherapy effective in reducing postoperative endodontic pain? An updated systematic review and meta-analysis of randomized clinical trials.** Int J Environ Res Public Health. 2021; 18(22):11750.

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1	**Hareem Qazi:** Study design, editing of manuscript.
2	**Rajesh Kumar:** Data analysis.
3	**Fozia Rajput:** Interpretation of data.
4	**Jeetesh Kumar:** Data collection, manuscript writing.
5	**Feroze Kalhoro:** Data entry.
6	**Mehwish Yaseen:** Revisions.