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Research Article

Effect of Intracanal Cryotherapy on Postoperative Pain in Molar Teeth with Symptomatic Irreversible Pulpitis and Apical Periodontitis: A Randomized Clinical Trial

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Abstract

Aim: The aim of the present study was to evaluate the effect of cryotherapy using cold saline irrigation as a final irrigant on postoperative pain in molar teeth with symptomatic irreversible pulpitis and apical periodontitis

Methods: A total of 30 patients with symptomatic irreversible pulpitis and apical periodontitis in their mandibular first molars, were included in the study. After completion of biomechanical preparation using Mpro Rotary system in a single visit and irrigation with 2.5% sodium hypochlorite for cleaning and shaping. Patients were randomly assigned into two groups (n = 15). In(group A), final irrigation was done using 15 ml cold saline (2.5°C) for 6 mins at three successive times. The solution was stored in refrigerator until use and then its temperature was checked using digital thermometer. In(group B), final irrigation was done using 15 ml room temperature saline for 6 mins. In both groups irrigation procedures were done using 27-gauge side-vented needle fit to a 5ml disposable plastic syringe placed 2-3 mm away from apex without binding. Pain was recorded postoperatively after 6, 12, 24, 48 and 72 hours by Numerical Rating Scale (NRS). Patients were given an analgesic (Ibuprofen 200 mg) in case of severe pain. All demographic data. NRS scores and number of analgesics taken were collected from the patients and statistically analyzed by chi-square test and Mann-whitney U test.

Results: Results showed a statistically significant decrease in postoperative pain in the cryotherapy group compared to the control group at each time interval, also cryotherapy reduced postoperative analgesic intake at all tested intervals ($p < 0.05$).

Conclusions: Cryotherapy aids in reducing postoperative pain in both magnitude and time span, also it had satisfactory effect on reduction of post-operative analgesic intake. The use of cryotherapy is a simple, cost-effective, and non-toxic option for postoperative pain control in single visit root canal treatment.

Keywords: Cryotherapy; Irreversible Pulpitis; Postoperative Pain; Single Visit RCT; Symptomatic Apical Periodontitis

Abbreviations

NRS: Numerical Rating Scale; NaOCl: Sodium Hypochlorite; EDTA: Ethylenediaminetetraacetic Acid; RCT: Root Canal Treatment; ASA: American Society of Anesthesiologists.

Introduction

The main rationale of endodontic treatment is to eliminate microorganisms from the infected root canal system by an adequate chemo mechanical debridement followed by a three dimensional obturation to achieve a hermetic seal to provide a conducive environment for periradicular healing. However, even with the utmost care in performing root canal therapy, some patients experience pain or flare ups following the treatment. This post-endodontic pain is an unpleasant, common sensation encountered in a clinical scenario which may affect the quality of patient-doctor relationship [1]. The incidence of this post endodontic pain (PEP) was reported to range from 3-58% [2].

The common factors influencing the occurrence of pain after RCT include the condition of pulp and periradicular tissue, preoperative pain, the presence of periapical radiolucency, insufficient instrumentation, irrigant, intracanal dressing, apical debris extrusion, hyperocclusion, missed canals and apical patency during root canal preparation [3]. Postendodontic pain most often occurs during the first 24 to 48 hours after obturation, and generally recedes in a few hours [4] although it occasionally persists for several days [5].

Several strategies have been developed for postoperative pain management in addition to following all conventional safely measures during treatment as prescribing prophylactic analgesics and corticosteroids, administering long lasting anaesthesia, occlusal reduction [6,7]. Optimum use and judicious selection of irrigant [8], and use of magnifying devices, such as dental loupes and endodontic microscopes.

A possible strategy for reduction of post-operative endodontic pain is cryotherapy which is a relatively new form of treatment in which the body is briefly exposed to very cold temperatures in order to promote healing and other therapeutic results. The basic technique of cryotherapy stresses rapid cooling slow thawing and repetition of freezing process to minimize tissue destruction.

It reduces the local blood flow by vasoconstriction and therefore reduces local inflammatory reaction, swelling, and oedema, It also slows the conduction of nerve signals, potentially reducing pain transmission [9].

Some studies have demonstrated that cryotherapy minimizes secondary hypoxic injury through the reduction of cellular metabolism and injury area [10].

Cryotherapy has been used for pain relief in sports injuries, runner's knee, pain and swelling after a hip or knee replacement, to treat pain or swelling under a cast or a splint, and lower back pain [11]. In dentistry, cryotherapy has been used after intra-oral surgical procedures, such periodontal surgery, extractions, and implant placement, and was found to be effective in reducing swelling and pain [12]. Recently it has been introduced as a posttreatment pain reliefing method in endodontics.

Subjects and Methods

Study design and Sample size calculation

The design of this study was a parallel, double-blinded, randomized clinical trial that was approved by the institutional review boards/ethical committees (IRBs/ECs) of the Faculty of Dentistry, Cairo University. The study was registered at www.clinicaltrials.gov (NCT03716635). The sample size was determined using a previous study by [13] in which the outcome variable was postoperative pain assessed by Numeric Rating Scale. The sample was divided into 2 groups. A total sample size of 16 cases (8 cases per group) was sufficient to detect an effect size of 1.6245, a power of 80% and a significance level of 5%.This number was increased to 22 cases (11 cases in each group) to account for the necessity to use non parametric test. Further increase to 30 cases (15 cases each group) to compensate for possible losses during follow up. Sample size was calculated using G*Power program (University of Düsseldorf, Düsseldorf, Germany).

Eligibility criteria

The patients were recruited from the outpatient clinic of the Department of Endodontics. The inclusion criteria for patient selection were as follow: age (20-40 years), healthy patients (ASA I, II). Diagnosed with Symptomatic irreversible pulpitis and apical periodontitis in mandibular first molar teeth with sharp pain to cold pulp tester (ethychloride spray) compared to contralateral which lingers after removal of stimulus with no or slight widening in the periodontal ligament (PDL).

Patients exclusion criteria included those who are allergic to anaesthetics or drugs used in the study, pregnant or nursing females, those having hemostatic disorders or using anticoagulant therapy during the last month and those consuming analgesics or corticosteroids during the last 12 hours before treatment.

Randomization

After the explanation of the treatment procedure, all the included patients signed a printed informed consent that explains the involved procedures and the possible risks. They were randomly divided into two equal groups of 30 patients, where the random sequence was generated by the Center of Evidence-Based Dentistry, Faculty of Dentistry, Cairo University using computer software, (http://www.random.org/). Based on this number the patient was then allocated to either (Group A) or (Group B) and the table was kept with the assistant supervisor. Following applying local anaesthesia, access cavity preparation and biomechanical preparation, the operator contacted the assistant supervisor and used the irrigation protocol assigned to that patient. The assistant supervisor was the one who generated the random sequence and assigned the participants to either group.

Procedural steps

After the preoperative pain for each patient was recorded using the Numeric Rating scale (NRS), local anaesthesia was done by using 1.8 ml of 2% Mepivacaine HCl with 1: 100,000 epinephrine (Alexandria Co. for Pharmaceuticals, Alexandria, Egypt) through an inferior alveolar nerve block. Intra-pulpal injection was the supplemental anesthesia of choice when needed. Rubber dam was placed to isolate the tooth and an access cavity was performed with a high-speed handpiece using round bur and Endo-Z bur (Dentsply Maillefer, Ballaigues, Switzerland).

The canals were explored with #10 or #15 K-type hand files (MANI, INC. Industrial Park, Utsunomiya, Tochigi, Japan) in a watch-winding motion. The working length (WL) was measured by an apex locator (Root ZX, J. Morita, USA) and then confirmed radiographically.

All teeth in both groups were instrumented by a crown-down preparation technique using nickel–titanium rotary instruments mpro with X smart plus motor(Dentsply Maillefer, Ballaigues, Switzerland. preparation starts by using orifice opener file #18(.09) 3mm shorter than W.L followed by #20 file (.04) till full W.L and was finished with file #25 (.06). Each file was introduced inside the canal using EDTA gel. Canals were then irrigated with 3 ml 2.5% sodium hypochlorite solution between each two successive instruments. After competition of biomechanical preparation final flush was done as follows :

- **Experimental group (cryo group):** Final irrigation was done using 15 ml cold saline (2.5°C) for 6 mins at a three successive times. The solution was stored in refrigerator until use and then its temperature is checked using digital thermometer.
- **Control group (saline group):** Final irrigation was done using 15 ml room tempreture saline for 6 mins.

In both groups irrigation procedures were done using a 27 gauge side-vented needle fit to a 5ml disposable plastic syringe placed 2-3 mm away from apex in the canal space without binding.

All canals were dried with paper points. The canals were then obturated with the modified single cone technique and Ad Seal resin-based root canal sealer (Meta Biomed Co. Ltd, Korea). The treatment was concluded by sealing the access cavity with a temporary filling (Meta Biomed Co. Ltd, Korea).

Ibuprofen (200mg) was prescribed to be administered in case of emergency. The patients were asked to fill the NRS at 6, 12, 24, 48 and 72 hrs after the treatment and number of analgesics taken.

Statistical analysis

Statistical analysis was performed with IBM® (IBM Corporations, NY, USA) SPSS® (SPSS, Inc., an IBM Company) (Statistics Version 20 for Windows). Continuous data were tested for normality using Shapiro Wilk and Kolmogrov Smirnov tests. Mean and standard deviation values were used for data presentation and Mann – Whitney U test was used for comparison between the two groups. Categorical data were presented as frequencies and percentages and Chi-square test was used for comparison between the two groups. The significance level was set $P \leq 0.05$.

Study outcome

The outcome of the study was postoperative pain intensity which was measured using an 11-point NRS where the endpoints are the extremes of no pain and worst pain. Pain intensity was assigned into one of four pain categories: none (0); mild (1-3); moderate (4-6); and severe (7-10).

As for the secondary outcome was number and frequency of analgesic tablets taken by the patient after endodontic treatment at 6.12. 24. 48 and 72 hrs after root canal treatment.

Results

A total of 30 patients were enrolled in this study and randomly divided into 2 groups (n = 15). The flow of participants is represented in consort flow diagram (Figure 1). Only one patient was lost during follow-up.

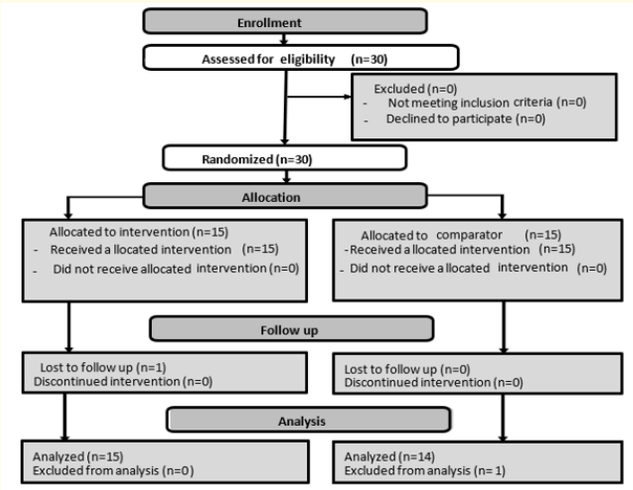

Figure 1: CONSORT Flow diagram of the trial design.

Baseline data

No statistically significant differences were found between the groups in terms of baseline data (age, sex and preoperative pain score) ($P > 0.05$) (Table 1).

	Group A (cryo) (n = 15)	Group B (saline) (n = 15)	P-value*
Age (Years) Mean ± Std. Dev	30.2 (5,9)	31.1 (5.1)	0.505
Gender [n (%)]			
Males	2 (13.3%)	4 (26.7%)	0.361
Females	13(86.7%)	11 (73.3%)	
Preoperative pain score (NRS) Mean ± std. Dev	8.3(0.6)	7.9(0.6)	0.079

Table 1: Mean, standard deviation (Std. Dev), frequencies (n), percentages and results of Mann-Whitney test and Chi-square test for comparisons of baseline data in the two groups.

*Significant at P-value ≤ 0.05.

Outcome data

There was a statistically significant difference between the two groups in the terms of the intensity of postoperative pain at all tested interval (6, 12, 24, 48 and 72 hours postoperatively) (Table 2) (Figure 2). Also There was a statistically significant reduction in the incidence of pain in cryo group in relation to control group at all tested time intervals except at 6 and 72 hrs (Figure 3). As for comparing changes in pain scores with time in both groups revealed a significant reduction in pain intensity between preoperative and all postoperative pain scores in both groups (Figure 4). Also there was a statistically significant reduction in the frequency and quantity of analgesic intake postoperatively being less in cryo group than in control group (Table 3).

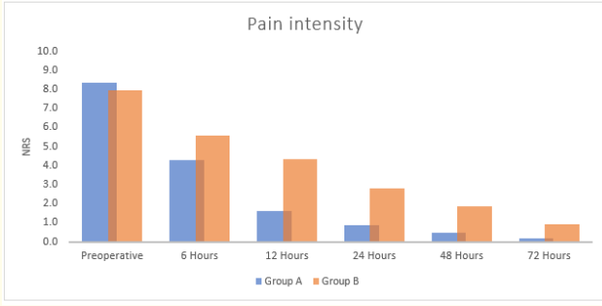

Figure 2: Bar chart representing the mean NRS scores at different observation periods postoperatively in the two groups.

Interval	Mean ± Std. Dev		P-value
	Group (A) cryo	Group (B) Saline	
6 hours postoperatively	4.3 ± 1.9	5.6 ± 2.0	0.044
12 hours postoperatively	1.6 ± 1.6	4.3 ± 2.3	0.002
24 hours postoperatively	0.9 ± 1.2	2.8 ± 1.8	0.002
48 hours postoperatively	0.47 ± 0.9	1.9 ± 1.8	0.008
72 hours postoperatively	0.2 ± 0.4	0.9 ± 1.3	0.041

Table 2: Mean, standard deviation values and the results of Mann-Whitney U test for comparison of NRS scores at different observation periods between the two groups.

*Significant at P-value ≤ 0.05.

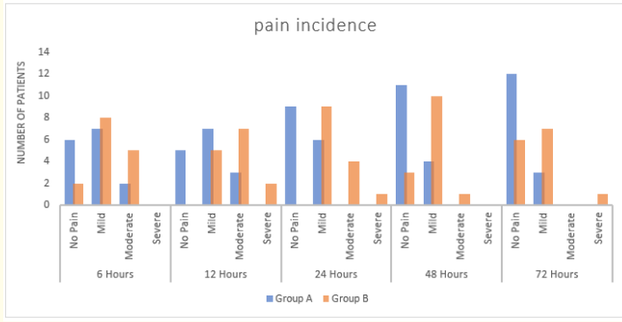

Figure 3: Bar chart representing incidence of pain categories at different observation periods postoperatively in the two groups.

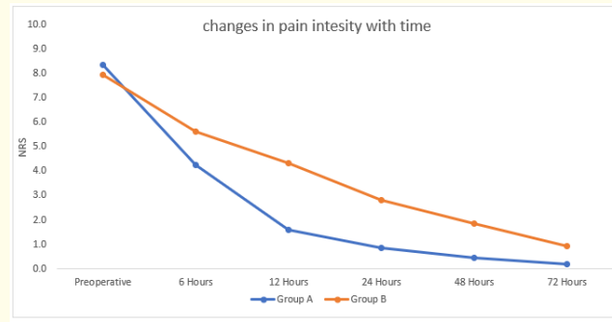

Figure 4: Line chart representing the changes in pain intensity with time in both groups.

	Group A (cryo) (n = 15)	Group B (saline) (n = 15)	P-value*
Analgesic intake [n (%)]			0.035
Yes	6 (40%)	11 (78.6%)	
No	9 (60%)	3 (21.4%)	

Table 3: Frequencies, percentages and results of chi-square test for comparison of analgesic intake in the two groups.

*Significant at P-value ≤ 0.05.

Discussion

Judging an endodontic therapy as successful depends not only on its efficacy and proper completion but also on minimal patient discomfort. Postoperative pain has been related to a number of preoperative factors, including gender, pulpal and periradicular condition, tooth type and severity of preoperative pain as well as intraoperative factors such as improper working length determination, inadequate instrumentation, apical extrusion of irrigation solutions, intra-canal dressing or debris and missed canals [14].

Mandibular first molars were chosen because they are significantly more susceptible to cause intraoperative pain as well as postoperative pain. Postoperative pain was found to be significantly higher in the mandible compared to the maxilla [15,16] because the mandible has a dense trabecular pattern, thus there is reduced blood flow and more localization of infection and inflammation, which might delay healing [15]. In addition, mandibular molar teeth accounted for a higher rate of postoperative emergencies as pain or swelling due to the diversity of their root canal configuration.

Cases with symptomatic irreversible pulpitis and apical periodontitis were selected as a main inclusion criterion. These cases showed significantly lower success rate of IANB and higher incidence of postoperative pain compared to asymptomatic teeth [17] Presence of preoperative pain has been cited as predictive factor in the incidence of postoperative endodontic pain [18].

Root canal preparation was performed by crown-down technique with (Mpro system). Early flaring of the coronal part of the preparation may improve instrument control during preparation of the apical third of the canal and the rotary motion has been shown to direct debris toward the orifice, avoiding its compaction in root canal. In addition, it requires less time than the manual technique.

Root canals were irrigated using 2.5% sodium hypochlorite (NaOCl) between every subsequent instrument as it was proven that the reduction of intracanal microbiota is not any greater when 5.25% NaOCl is used as an irrigant compared to 2.5%.Irrigation was done using a conventional syringe with side vented needle 27 gauge which seemed to have a lowering effect on irrigant extrusion into the periapical space compared to regular needle irrigation [19,20]. Moreover, to achieve a safe irrigation protocol, the needle was not inserted more than 2 mm from the working length, as recommended by previous studies [21,22]. Different from previous studies [13,23,24] negative apical pressure systems as EndoVac was not used because it is not commonly available in all dental clinics.

Pain was recorded using the NRS because it showed higher compliance rates, higher responsiveness, easier to use, better understood by most patients and good applicability relative to other pain scales [25]. In addition, NRS has been commonly used as the outcome measure in different studies evaluating postoperative pain after root canal treatment [13,24,26].

A follow-up period of 72 hours was selected in this study. Similar to previous study [13] comparing the effect of cryotherapy using cold saline irrigation as a final irrigant on postoperative pain, while other studies extended it up to 7 days [13,23,27]. It was stated that 40% post-treatment pain prevalence at 24 hours substantially decreases within the first 2 days [28], therefore a follow-up period of 72 hours was seen to be suitable.

In our study, postoperative analgesics were only prescribed on-demand and not a regular prescription of medication since it would influence the outcome measures of the study. This recommendation is consistent with other reports [13,23,24]. Since the objective was primarily to assess postoperative pain after root canal instrumentation, patients were advised to take analgesics only in the case of severe pain.

Among the non-steroidal anti-inflammatory drugs, Ibuprofen was selected in previous cryotherapy studies [13,23,24]. It is proved to be effective for treating acute pain and inflammation related to endodontic treatment, rapidly absorbed and metabolized by the liver [29]. Ibuprofen also inhibits COX-1 and COX-2 enzymes, which catalyze the formation of the prostaglandins that mediate the process of inflammation and pain [30].

The baseline characteristics including age, gender and preoperative pain intensity showed no significant difference between the two groups implying successful randomization which assumes similar distribution of factors and minimizing any potential effects of these parameters on the results of the present study.

The results of this study showed significant reduction in postoperative pain in the cryotherapy group compared to the control group at each time interval. This was in harmony with the six clinical studies in the literature that proved that intracanal cryotherapy applications significantly reduce postoperative pain [13,23,24,31,32].

The results of this study also showed an insignificant increase in the percentage of cases that reported some pain relief (showing no to mild pain) in the cryotherapy group compared to the control group at 6 hours followed by a significant increase at 12, 24 till 48 hours. The insignificance increase at 6 hours and 72 hours might be due to the fact that the highest incidence of pain usually takes place at the first 24 hours then declines to negligible levels by time due to resolution of inflammation and reduction of inflammatory meditors that trigger pain after complete RCT as reported by other studies [33]. This also explains the gradual decrease of pain in both groups along the tested intervals but with a significant higher rate of pain reduction in cryo group compared to control group that remained showing a significant decrease of pain through out all tested intervals.

In our study it was also proved that cryotherapy reduced postoperative analgesic intake at all tested intervals which was in agreement with all previous studies [13,24,32,34]. Although this reduction was significant regarding overall number of patients (40% in cryo group, 78.6% in saline group) and number of analgesic tablets intake.

These results could be explained by the fact that 2.5°C saline application reduces the temperature of the root more than 10°C and maintained it for 4 mins, as it was emphasized *in vitro* study by [35]. This root temperature reduction possibly extends to the periapical area causing vasoconstriction and reduces vascular permeability, the action that could have a local anti-inflammatory effect by reducing periradicular tissue exudate leading to decrease edema [11]. Also this reduction in blood flow reduce cellular metabolism causing cells to use less oxygen flow, leading to better oxygen diffusion into damaged tissues [36]. Cryotherapy has been also shown to decelerate peripheral nerve conduction inducing lo-

cal anesthetic effect. As the temperature decreases, the conduction velocity of nerve fibres decreases until it stops completely [37]. Cold application may also induces analgesia by stimulating the release of neuro effective agents such as endorphins. Endorphins bind to opioid receptors, thus inhibiting transmission of impulses to the central nervous system. In addition, cold application might decrease the activation threshold of tissue nociceptors, resulting in a local anesthetic effect that is defined as cold induced neuropraxia [38]. Thus, the analgesic effect of cooling is produced by a combination of a decreased release of chemical mediators of pain and a slower propagation of neural pain signals.

To our knowledge, there is no published research about the time needed for a cryotherapy therapeutic effect on endodontic pain ; it varies depending on the nature of the tissue. It was reported when minimal fat and muscle are present (e.g., when applied to a finger), 3 to 5 minutes of cryotherapy has been recommended. This time is minimal compared with the approximate 20 minutes recommended for areas with more deeply affected tissue like the hip [39]. Cold transmission to the periodontal ligament may also be different in apical and coronal portions of the root because of differences in dentin properties and thickness at both levels. Thicker cervical dentin makes it more difficult to transmit therapeutic effectors to the adjacent tissues. On the other hand, apical dentin being thinner would facilitate more efficient cold transmission [40] inspite of being higher in mineralization.

Conclusion

Cryotherapy aids in reducing postoperative pain in both magnitude and time span, also It had satisfactory effect on reduction of post operative analgesic intake. It is a simple, cost-effective, and non-toxic option for postoperative pain control in single visit root canal treatment.

Conflict of Interest

The authors deny any conflicts of interest in this study.

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