Review Article

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Effect of intracanal cryotherapy on postendodontic pain: a systematic review and meta-analysis of randomized controlled trials

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This systematic review aimed to qualitatively and quantitatively evaluate the effectiveness of cryotherapy in the reduction of postendodontic pain. The review question was, "What will be the success rate of cryotherapy technique among human patients with postendodontic pain?”. The review protocol was framed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. Six studies were included in the review, and quantification of five studies was performed through a meta-analysis. In the forest plot representation of the studies comparing the control and cryotherapy groups in terms of the success rate in the management of postendodontic pain, the combined risk ratio (RR) was 0.80 (95% CI: 0.56 to 1.13) with a P value of 0.20. Based on the quantitative analysis, it can be suggested that intracanal cryotherapy does not play a significant role in reducing postendodontic pain.

Keywords: Cryotherapy; Endodontic Treatment; Postendodontic Pain; Randomized Controlled Trials.

INTRODUCTION

Routine dental check-ups are rare reasons for visiting a dentist. More often, it is the presence of pain that leads to an unscheduled visit to the dentist. Among all dental procedures, endodontic procedures are most commonly linked to significant postoperative pain as compared to other clinical procedures [1]. The most probable reasons for the occurrence of this pain are mechanical, chemical, and/or microbiological injuries to the tissues around the root of the tooth receiving root canal treatment (RCT) [2-5]. Such periapical injuries often lead to an inflammatory response known as “endodontic flare up” [6]. Pain during and after endodontic treatment leads to distress to both the patient and the clinician and is often considered a standard of the clinician's skills [7]. The common factors affecting post-RCT pain include inadequate instrumentation of the canal system, extrusion of the irrigating solution, or the intracanal medicament. This post-treatment pain can be avoided by carefully carrying out each step of the RCT, such as working length determination, proper cleaning and shaping of the canal, optimum use of irrigants, and disocclusion of the tooth. Various other strategized protocols have been employed to decrease the pain incidence, including occlusal reductions, different mechanical techniques during glide path applications [8-11], and pharmacological means, such

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Table 1. Combination of keywords for database search strategy

Database	Keywords combination	n
PubMed	["Cryotherapy" (MeSH) OR "Cryotherapy" (All fields) OR "Cold therapy" (All fields) AND "postoperative pain"(MeSH) OR "postoperative pain"(All fields) OR "postendodontic pain (All fields) OR "endodontics"(MeSH) OR "endodontics" (All fields)]	1246
EbscoHost	["Cryotherapy" (MeSH) OR "Cryotherapy" (All fields) OR "Cold therapy" (All fields) AND "postoperative pain"(MeSH) OR "postoperative pain"(All fields) OR "post endodontic pain (All fields) OR "endodontics"(MeSH) OR "endodontics" (All fields)]	39
Scopus	["Cryotherapy" (MeSH) OR "Cryotherapy" (All fields) OR "Cold therapy" (All fields) AND "postoperative pain"(MeSH) OR "postoperative pain"(All fields) OR "post endodontic pain (All fields) OR "endodontics"(MeSH) OR "endodontics" (All fields)]	840

as long-acting anesthetic injections, antihistamines, non-steroidal anti-inflammatory drugs (NSAIDs), salicylic acid, acetaminophen, combinations of ibuprofen and acetaminophen, narcotic analgesics, combinations of narcotic analgesics and salicylic acid, and steroidal anti-inflammatory drugs [12,13]. A majority of these management strategies target inflammation by using analgesics such as NSAIDS. Active research about newer methods to decrease tissue trauma and inflammation is ongoing. Cryotherapy has gained popularity in recent times as a technique to reduce post-procedural pain. It is also known as cryosurgery and cryoablation if it is used instead of surgical procedures. In dentistry, cryotherapy has an established role in decreasing pain after periodontal surgeries, extractions, and implant surgeries [14]. It reduces the adherence of leukocytes to the capillary walls, subsequently reducing the number of migrating cells to the injured tissues and thus diminishing endothelial dysfunction, thereby reducing inflammation [14]. The initial physiological response of the tissue to cryotherapy is a local temperature drop that diminishes cell metabolism; hence, less oxygen is utilized. Furthermore, vasoconstriction occurs, which reduces blood flow and limits the inflammatory damage [15]. Additionally, it also affects peripheral nerve endings by reducing the activation threshold of the nociceptors in the tissues and the speed of pain impulse conduction. Cryotherapy produces a local anesthetic-like effect by lowering the conduction velocity of pain signals [16]. The role of cryotherapy in endodontics in the form of irrigating solutions has not been extensively documented. It can be used for inflamed periradicular tissues by intracanal irrigation with a cold solution after instrumentation of the root canal system. The aim of this systematic review and meta-analysis was to qualitatively and quantitatively evaluate the effectiveness of cryotherapy in reducing postendodontic pain with the help of randomized controlled trials.

METHODS

1. Protocol and Registration

The protocol of the systemic review was framed using the PRISMA checklist. The prepared protocol was registered on the International Prospective Register of Ongoing Systematic Reviews (PROSPERO) with the acknowledgement registration number CRD-183893.

2. PICO question

The review question was formulated using the PICO framework of a systematic review defining population, intervention, comparison, and outcome. The formulated question was "What will be the success of cryotherapy technique among human patients on postendodontic pain?".

3. Search process and selection of studies

A comprehensive literature search was performed using the following databases: Medline/PubMed, Scopus, and Ebsco host, along with manual search. Search was performed using a combination of keywords and the Boolean operators "AND" and "OR" (Table 1). The

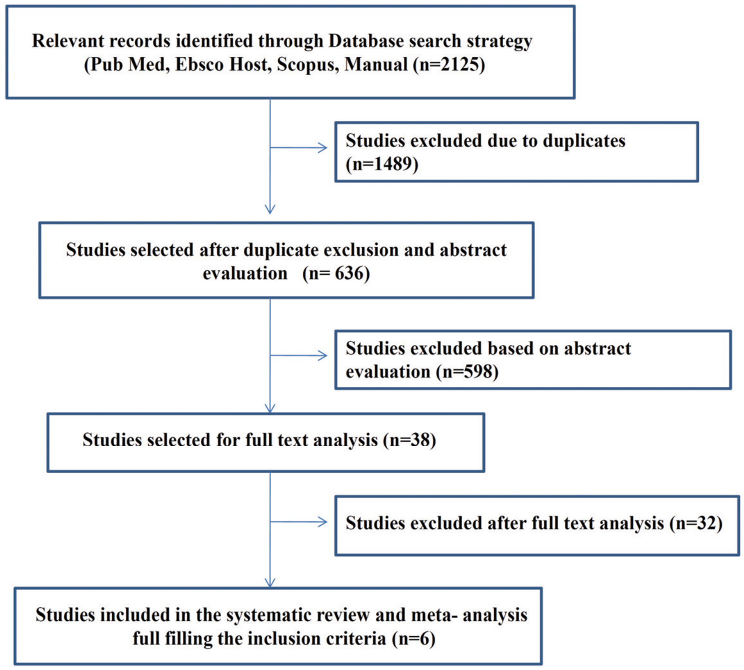

Fig. 1. PRISMA flowchart

collected data were manually searched for identification and exclusion of duplicates.

4. Inclusion and exclusion criteria

Three investigators studied the titles and abstracts of all the articles that were identified through electronic and manual database searches. Articles that did not meet the inclusion criteria were excluded. All remaining articles were obtained and screened independently by three reviewers to reach a consensus. A criterion for the inclusion of studies was established:

1. All studies published from 1960 to May 2020
2. Clinical studies published in the English language
3. Adult human patients undergoing non-surgical RCT
4. Any vital and/or non-vital teeth of the maxillary or mandibular arch undergoing non-surgical RCT
5. All studies should be randomized trials having both control and experimental group

Exclusion Criteria included:

1. Re-treatment cases
2. Presence of any systemic disease or allergic reaction
3. Studies reporting the effect of any medication on postendodontic pain
4. Studies on pediatric patients
5. Studies involving severe periodontal diseases
6. Patients with immature apices or root resorption
7. Pregnant patients
8. Studies involving procedural errors or mishaps during root canal treatment
9. Studies involving teeth having roots with severe curvature

5. Quality assessment and data extraction

From the total database search, the relevant articles were manually searched and the bibliographies of relevant papers and review articles were also screened to extract the exact relevant data. Finally, the data were framed in the form of a PRISMA flowchart (Fig. 1).

Two examiners extracted the data and analyzed each individual study using the following parameters: author (year)/ country, journal, language, age group, total patient size, sex, tooth type, sample size, groups involved, case selection, number of visits and the days after obturation, pain evaluation scale, and statistical results. Any disagreements between the two authors were resolved by a third author. The risk of bias assessment was performed using

Table 2. Post-operative pain assessment

Author / Journal Year of publication	Grouping	6 h	12 h	24 h	48 h	72 h	5 days	7 days
Al-Nahlawi T et al J Contemp Dent Pract. 2016 [24]	Group 1 Control	56.3	53.6	53.6	45.84	-	-	38.52
	Group 2 EndoVac (room temperature)	44.7	47.4	47.40	40.16			39.98
	Group 3 Cryotherapy	13.0	13.0	13.0	28.0			35.50
Gundogdu EC et al J Endod. 2018 [23]	Control	-	-	77.76 ± 19.53	-	57.24 ± 24.72	40.81 ± 28.95	34.24 ± 28.07
	Intracanal Cryotherapy			38.18 ± 19.19		18.82 ± 22.53	8.45 ± 12.58	0.82 ± 2.92
	Intra-oral Cryotherapy			22.00 ± 26.95		12.10 ± 22.52	3.14 ± 8.55	0.33 ± 1.53
	Extra-oral Cryotherapy			32.25 ± 31.30		16.05 ± 18.33	3.80 ± 6.83	1.05 ± 2.46
Vera J et al J Endod 2018 [21]	Control	3.53 ± 1.9	-	2.02 ± 1.5	0.49 ± 0.8	-	-	-
	Cryotherapy	1.59 ± 1.9		0.46 ± 1.5	0.25 ± 0.7			
Vieyra JP et al Niger J Clin Pract. 2019 [20]	Group-A Cryotherapy 4°	-	-	0.66 ± 0.83	0.25 ± 0.43	0.04 ± 0.82	-	-
	Group-B Cryotherapy 2.5°			0.88 ± 0.97	0.26 ± 0.60	0.05 ± 0.97		
	Group-C Control			0.58 ± 0.82	0.23 ± 0.44	0.02 ± 0.83		
Alharthi AA et al Saudi Dental Journal 2019 [22]	Group-1 Cryotherapy	0.79 ± 1.37	-	0.43 ± 0.76	0.07 ± 0.27	-	-	-
	Group-1 Room temp. irrigation	1.15 ± 1.66		0.79 ± 1.37	0.14 ± 0.54			
	Group-3 Control	3.71 ± 2.99		3.00 ± 3.11	2.43 ± 2.94			

the checklist given by the Joanna Briggs Institute Critical Appraisal Checklist for Randomized Control Trial [17]. For applying the risk of bias, 12 criteria were used. Two evaluators independently applied the risk of bias for all studies, followed by a discussion of each point. Any disagreement was resolved by a third examiner to reach a final consensus.

6. Outcomes

Success was defined as no or mild pain according to patient-reported pain scores, e.g., visual analog scale (VAS) [18], after RCT [19-21]. The other way was the evaluation and comparison of mean VAS scores of the control and cryotherapy groups to evaluate the improvement in pain level [20-24] (Table 2).

RESULTS

The total number of relevant articles identified through the search strategy, through electronic and manual searches, was 2125. Duplicate articles were excluded from the analyses. After excluding duplicates, 636 articles were screened for abstract evaluation. Considering the strict inclusion and exclusion criteria, only six articles were included in the systematic review. Of these, five studies were included in the meta-analysis. Thirty-two articles were excluded after full-text reading.

Table 3. Study characteristics

Author	Year of publication, Journal, language	Sample	Type of study and teeth involved	Groups	Case selection	No. Of visits and day of obturation after RCT	Pain scale	Outcome
Keskin et al. [19]	2017 Aust Endod J	170 patients Males = 68 Females = 102 Age- 19 to 63 y 85 patients per group	Randomized Clinical Trial maxillary or mandibular tooth	Two groups Control group- final irrigation with 5 ml saline at room temperature for 5 min. Cryotherapy group- final irrigation with 5 ml saline at 2.5°C temperature for 5 min	Asymptomatic irreversible pulpitis OR Symptomatic irreversible pulpitis OR Symptomatic apical periodontitis	Single visit Obturation done on same day as canal preparation	100 mm VAS	Significantly lower pain in cryotherapy group after 24 h (P < 0.05) significant 48 h (P < 0.05) significant
Vera et al. [21]	2018 J Endod	186 patients Males = 69 Females = 117 Age- not specified 93 in each group	Randomized Clinical Trial - single canal tooth	Two groups Control group- final irrigation with 20 ml saline at room temperature using a microcannula with Endovac negative pressure system for 5 min Cryotherapy Group-final irrigation with 20 ml cold saline at 2.5°C temperature using a cold (2.5°) microcannula attached with Endovac negative pressure system for 5 min	Necrotic pulp and Symptomatic apical periodontitis	Two visits Obturation done after 7 days of the first visit	100 mm VAS	Significantly lower pain in cryotherapy group after 6 h- (P < 0.05) significant 24 h (P < 0.05) significant 72 h (P < 0.05) significant
Al-Nahlawi et al. [24]	2016, J Contemp Dent Pract	75 patients Age- 20 to 46 y 25 patients in each group	Randomized Clinical Trial -single rooted single canal tooth	Three groups Group-1-(control) no additional irrigation was given Group-2-20 ml saline with EndoVac negative irrigation system at room temperature for 5 min Group-3- 20 ml of saline at 2-4°C temperature with EndoVac negative irrigation system for 5 min	Vital teeth with irreversible pulpitis	Single visit Same day obturation	100 mm VAS	Significantly lower pain in cold saline irrigation group compared to control group and room temperature irrigation group After 6 h (P < 0.001) significant 12 h (P < 0.001) significant 24 h (P < 0.001) significant 48 h (P = 0.001) significant 1 week (P = 0.230) not significant
Vieyra et al. [20]	2019 Niger J Clin Pract.	240 pts Females = 129 Males = 111 Aged 18 to 65 y 80 patients in each group	Randomized Clinical Trial maxillary and mandibular teeth	Three groups Group-A-final irrigation with 5 ml of cold (4°), 17% EDTA followed by 10 ml of cold (4°) saline with EndoVac system for 1 min room temperature Group-B-final irrigation with 5 ml of cold (2.5°), 17% EDTA followed by 10 ml of cold (2.5°) saline with EndoVac system for 1 min Group-C-(control) final irrigation with 5 ml of (room temp.), 17% EDTA followed by 10 ml of cold (room temperature), saline with EndoVac system for 1 min	Intentional RCT for Prosthodontic work	Single visit Obturation done on the same day	100 mm VAS	Significantly lower pain in cold irrigation group A and B compared to control group C After 24 h (P < 0.05) significant 48 h (P < 0.05) significant 72 h (P < 0.05) significant

Gundogduet et al. [23]	2018 J Endod	100 patients Aged- >18 y 25 patients in each group	Randomized Clinical Trial maxillary and mandibular molar teeth	Four groups Control group- after irrigation with NaOCl and EDTA, final irrigation done with 20 ml saline at room temperature for 5 min Intracanal cryotherapy-after irrigation with NaOCl and EDTA, final irrigation done with 20 ml cold saline (2.5°C) for 5 min Intra-oral cryotherapy- After final irrigation done with 20 ml saline at room temp. for 5 min, as in the control group, small ice packs covered with sterile gauze placed inside the mouth for 30 min Extra-oral cryotherapy- After final irrigation done with 20 ml saline at room temp. for 5 min, as in the control group, small ice packs covered with wrapped with 2 layers of paper towel placed extra-orally on the cheek surface for 30 min	Symptomatic apical periodontitis with vital pulp	Single visit Obturation on the same day	100 mm VAS	All the cryotherapy groups shows significantly low postoperative pain ($P < 0.05$) than control group at 1^{st}day ($P < 0.01$) significant 3^{rd}day- ($P < 0.05$) significant 5^{th}day- ($P < 0.05$) significant 7^{th}day- ($P < 0.05$) significant
Alharthi et al. [22]	2019 Saudi Dent J	105 patients Aged-18 to 50 years 35 patients per group	Randomized controlled trial single rooted teeth	Three groups Group 1- (cryotherapy) after BMP, final irrigation done with 10 ml cold (1.5°-2.5°C) saline for 5 min Group-2- (room temperature) after BMP, final irrigation done with 10 ml saline (room temp) for 5 min Group-3- (control group) after BMP no more irrigation was given.	Cases requiring RCT	Single visit Obturation on the same day	100 mm VAS	Significantly low postoperative pain in cryotherapy and room temperature irrigation group compared to control group but no significant difference in cryotherapy group and room temp. saline group after 6 h ($P = 0.006$) significant 24 h ($P = 0.001$) significant 48 h ($P = 0.001$) significant

1. Study characteristics

Six clinical studies, Keskin et al. (2016), Vera et al. (2018), Alharthi et al. (2019), Al-Nahlawi et al. (2016), Vieyra et al. (2019), and Gundogdu et al. (2018) [19-24], reporting the success of cryotherapy technique in the control of postendodontic pain, were included in the final analysis. The individual characteristics of each study are described in Table 3.

2. Meta-analysis

The meta-analysis was performed using RevMan 5.3 software. Data from five studies were analyzed. The data were extracted and divided into two groups based on the characteristics of the effect size. Three studies [19-21] evaluated the success rates, and the effect size was dichotomous/binary in nature. For each included study, random risk ratios were calculated using the Mantel-Haenszel method. The analysis involved studies comparing the control and cryotherapy groups in terms

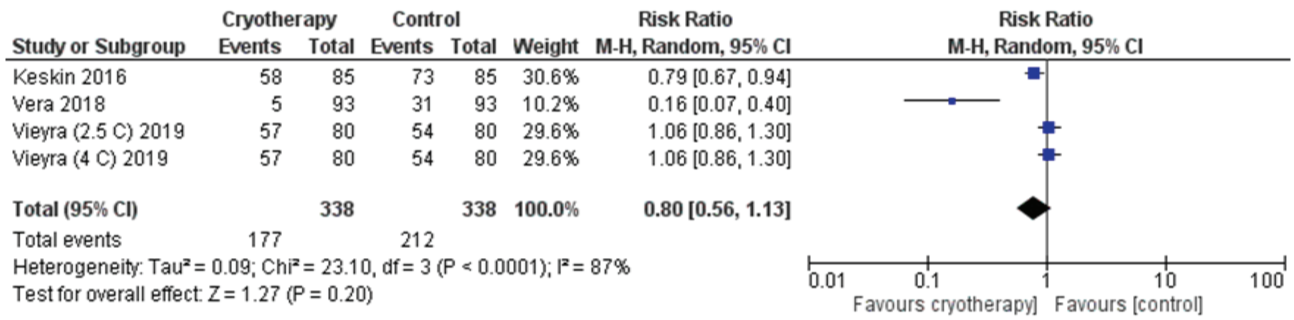

Fig. 2. Forest plot representation of the binary data

of the success rate in the management of postendodontic pain. Figure 2 shows the forest plot representation of the random-effect meta-analysis performed on the studies. The combined risk ratio was 0.80 (95% CI: 0.56, 1.13). The difference was not statistically significant (P = 0.20). There was a high amount of statistical heterogeneity among the included studies (I^2 = 87%, P < 0.05).

The L'Abbe plot was generated to evaluate statistical heterogeneity among studies with a dichotomous effect size (Fig. 3). The risk of success for the cryotherapy group is plotted on the y-axis, and the risk of success of the control group is plotted on the x-axis. The solid diagonal line represents the studies in which the risk of success did not differ between the groups. Studies above this line have a higher risk of success in the cryotherapy group than in the control group. The dashed line shows the estimated effects based on the analysis model. The studies below the solid line along with the dashed line show that the risk of success was higher in the control group than in the cryotherapy group. The scattered studies also showed a high level of heterogeneity among the studies.

The second meta-analysis included four studies that reported continuous data [20-23]. The meta-analysis utilized the mean difference as the effect size. Since the measuring scale was not uniform in different studies, the standardized mean difference was taken as an effect size variable. The calculations involved the division of the mean difference in each study by that study's standard deviation to create an index (standardized mean difference). This index was comparable across the studies.

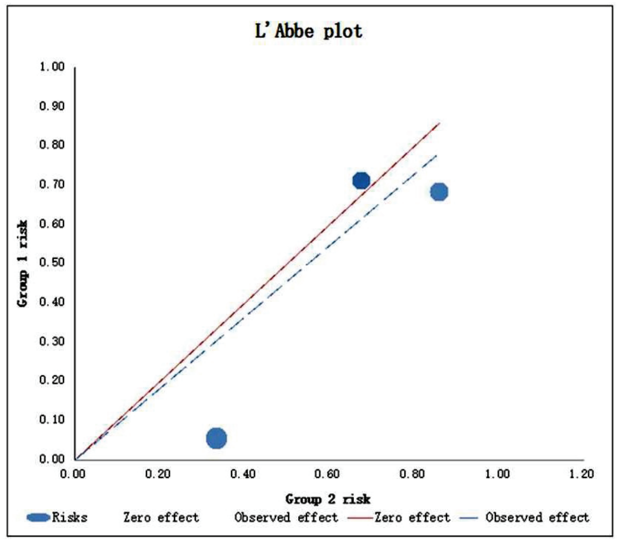

Fig. 3. L'Abbe plot of dichotomous studies

In the present analysis, the standardized mean difference was 0.54 (95% CI: -1.22 to 0.14). The difference was not statistically significant (P = 0.12). There was a high amount of statistical heterogeneity among the included studies (I^2 = 94%, P < 0.05) (Fig. 4).

The heterogeneity in studies reporting continuous data was also evident in the Galbriath plot (Fig. 5). The plot is generated by plotting the result of the division of the effect size by its standard error on the y-axis and the inverse of the standard error on the x-axis. The studies are represented by dots, and a regression line is plotted in the center. Parallel to the regression line, two lines (at twice the standard deviation) create an interval. Most of the dots were expected to lie between the intervals. The Galbriath plot of the included studies showed a high degree of heterogeneity.

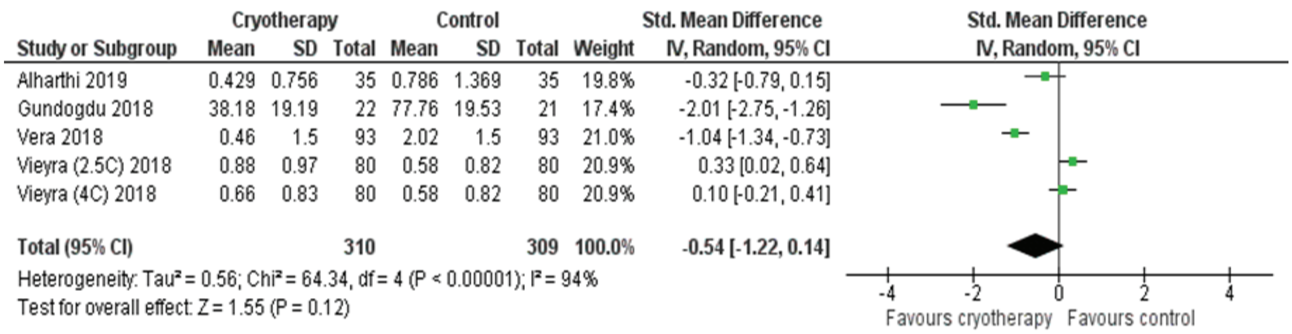

Fig. 4. Forest plot representation of studies with continuous data

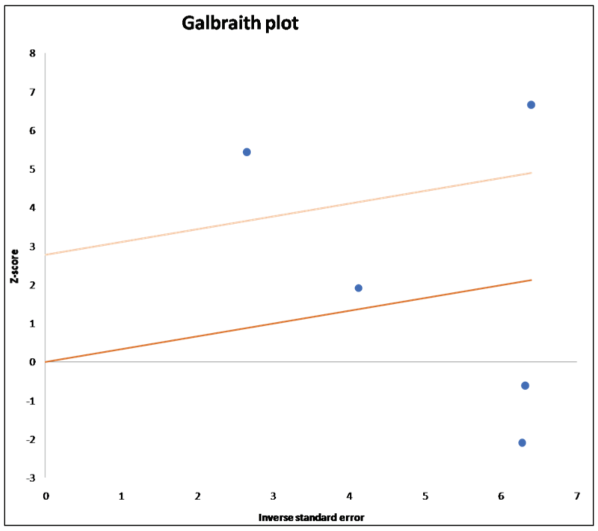

Fig. 5. Galbriath plot of studies with continuous data

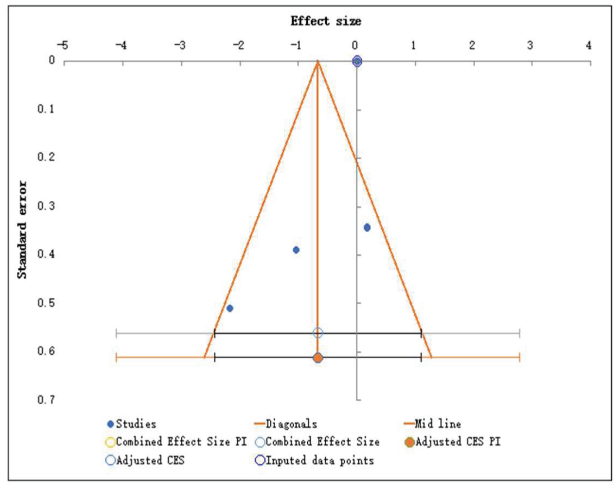

Fig. 6. Funnel plot of dichotomous studies

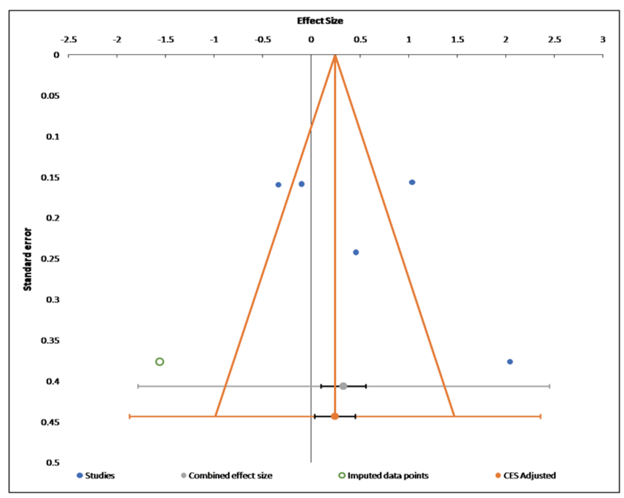

Fig. 7. Funnel plot of studies with continuous data

Funnel plots for studies in both groups were plotted to assess the publication bias (Fig. 6, 7). The funnel plots were visually symmetrical, suggesting a lack of publication bias.

3. Risk of bias

All studies had a low risk of bias [19-24]. For each study, the evidence level was determined according to the guidelines given by the National Services Scotland [25] (Fig. 4). All studies were randomized controlled trials with an evidence level of 1+ (Fig. 8).

4. Interpretation of studies

Keskin et al. (2016) [19] evaluated the efficacy of cold saline solution as the final irrigant on postoperative pain after a single-visit RCT in 175 vital teeth that were randomly divided into two groups: the control group with room temperature saline irrigation and the cryotherapy group with 2.5°C 0.9% physiological saline solution

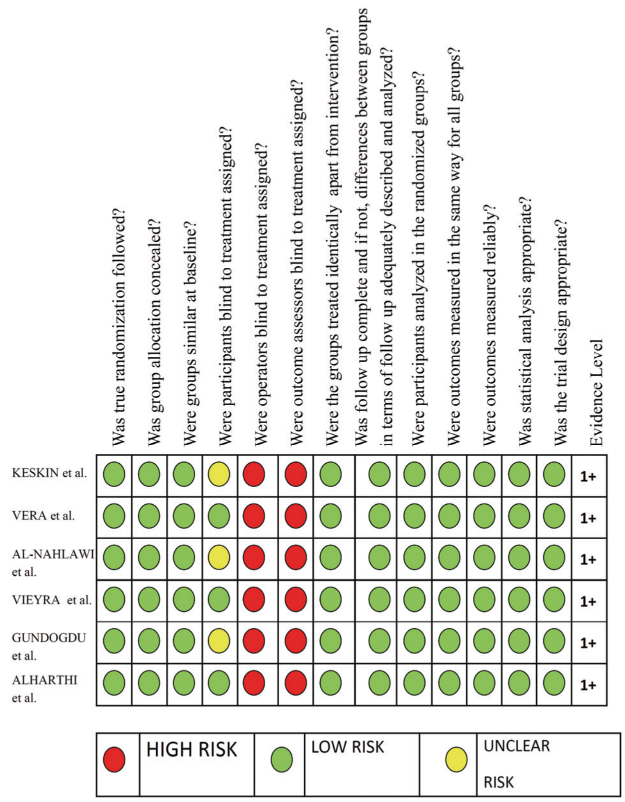

Fig. 8. Evidence level of included studies

irrigation for 5 minutes after completion of canal preparation. Pain was assessed using VAS at 24 and 48 hours after obturation. The results revealed a significant reduction in postendodontic pain levels in the 2.5°C cold saline irrigation group in comparison to the control group ($P < 0.05$).

Vieyra et al. (2019) [20] assessed the reduction in postoperative pain after a single sitting RCT using three different irrigation regimens at different temperatures. A total of 240 patients with vital teeth indicated for conventional RCT were selected for the study, and after root canal preparation, the final irrigation was performed with either 4°C or 2.5°C or room temperature 17% EDTA and 10 mL cold saline solution. Pain assessment was performed using VAS. The observed differences in the degree or duration of pain between the 4°C and 2.5°C groups were not statistically significant ($P > 0.05$). However, the group of patients irrigated with room temperature EDTA showed a significantly higher occurrence of postendodontic pain than the other groups.

Vera et al. (2018) [21] studied the incidence and intensity of postoperative pain after cryotherapy irrigation during root canal treatment of teeth with pulpal necrosis and symptomatic apical periodontitis. A total of 210 single rooted teeth with symptomatic apical periodontitis and a preoperative VAS score > 7, were randomly divided into two groups: the control and cryotherapy experimental group after the completion of canal instrumentation. The final irrigation for the cryotherapy group was with 20 mL of 2.5°C saline solution for 5 minutes using EndoVac and for the control group was room-temperature saline solution. Postoperative pain was assessed at 6, 24, and 72 hours after obturation using VAS. There was a significant difference between the incidence and intensity of postoperative pain between the control and cryotherapy groups ($P < 0.05$).

Alharthi et al. (2019) [22], evaluated the efficacy of cold and room-temperature saline as a final irrigating solution for postoperative pain after endodontic treatment. Vital and non-vital teeth of 105 patients, indicated for RCT, were randomly divided into three groups: The cold saline final irrigation group or cryotherapy group; the room- temperature normal saline final irrigation group; the sodium hypochlorite (NaOCl) irrigation group which was termed as the control group. Postendodontic pain was assessed using the visual analog scale (VAS) at 6, 24, and 48 hours post-treatment. The results showed that the cryotherapy group exhibited the lowest postoperative pain at 6 h, 24 h, and 48 h after obturation. Overall, the control group showed the highest postendodontic pain, but the pain decreased with time in all groups. There was a significant difference in the postendodontic pain values among the three groups ($P < 0.005$).

Gundogdu et al. (2018) [23], evaluated the efficacy of intracanal, intraoral, and extraoral cryotherapy on postoperative pain in molars diagnosed with symptomatic apical periodontitis. One hundred teeth were randomly divided into four groups: control group, intracanal cryotherapy, intra-oral cryotherapy, and extra-oral cryo-therapy. Pain assessment was performed using VAS. Postoperative pain was recorded at 1, 3, 5, and 7 days after endodontic treatment. The cryotherapy groups exhibited significantly less percussion pain and less postoperative pain on all test days ($P < 0.05$).

Al-Nahlawi et al. (2016) [24] evaluated the effect of intracanal cryotherapy, applied using EndoVac, to 75 vital single-rooted teeth during a single-visit RCT. After initiating root canal preparation and irrigation, the teeth were randomly divided into three groups: the first group was the control group with no additional saline irrigation, the second group was irrigated using 20 mL of room temperature saline for 5 minutes via EndoVac, and the third group of patients was irrigated using 20 mL of 2 to 4°C cold saline for 5 minutes using EndoVac. Pain score assessment was performed using VAS at 6, 12, 24, 48 hours, and 7 days after canal obturation. Results revealed that VAS pain values after 6, 12, 24, and 48 hours in the cold saline irrigation group were lower than those of both saline irrigation at room temperature and the control group. The differences were statistically significant ($P < 0.05$).

DISCUSSION

Postoperative pain is an unpleasant and discomforting experience described by patients and reported with a high incidence rate in the range of 3-58% [26]. The most common factors influencing pain occurrence after RCT include improper instrumentation techniques, extrusion of the irrigant, intracanal dressing or apical debris from the apical foramen, hyperocclusion, missed root canal systems, and persistent presence of periapical pathology [13]. Postendodontic pain most often occurs during the first 24 to 48 hours after obturation, and usually recedes in the next few hours, although it can occasionally persist for several days [6]. According to studies by Albashaireh et al., there was no significant difference in the incidence of postendodontic pain between single and multiple-visit root canal treatments [27]. Irrigation is one of the most important steps for successful endodontic treatment. However, according to Bashetty and Hegde, postoperative pain 1-7 days after obturation revealed no association with the type of irrigating solution used [28].

Symptoms associated with pathological conditions such as symptomatic irreversible pulpitis, pulpal necrosis [29], and apical periodontitis can be associated with various attributes, such as changes in periapical pressure, chemical and microbiological inflammatory and pain mediators, and psychological factors [30]. Depending on the severity of these factors, patients tend to seek emergency dental care to manage the pain [31].

The present systematic review and meta-analysis highlight the role of cryotherapy in the reduction of postendodontic pain. Intracanal cryotherapy as an additional step can be easily included and implemented as part of the treatment protocol. It is a more feasible and comfortable option than patients using ice packs after treatment [23].

There is no unanimous decision regarding the optimal dosage for cryotherapy, as it varies depending on the nature of the tissue. When there is minimal fat and muscle [e.g., when applied to a finger], 3 to 5 minutes of cryotherapy has been recommended. In most of the included studies, the time period for intracanal cryotherapy was maintained at 5 minutes. According to Vera et al. in 2015, irrigation of the root canals with a 2.5°C cold saline solution for 5 minutes reduced the external root surface temperature. A similar protocol was employed by various other authors as part of the framework for their respective studies [16].

The use of a negative apical pressure irrigation device has been shown to significantly reduce the incidence of postendodontic pain levels compared to traditional needle irrigation [32]. In 2018, Vera et al. used EndoVac, a negative pressure system, to eliminate the vapor lock effect and ensure continuous delivery of the cold irrigating solution to the apical third of the root canal [21]. Desai et al. and Gondim et al. reported a significant decrease in the periapical inflammatory response by optimally minimizing apical extrusion via the use of EndoVac [32,33].

According to various reports, the VAS scores experienced and reported by patients who underwent single-visit endodontic treatment were low [19,20,22-24]. These results could be attributed to the criteria applied for inclusion of patients, since the teeth with abscess, necrosis, or failed RCT cases were excluded and aseptic protocol was followed to minimize the possibility of inter-appointment flare-ups [19]. In 2018, Vera et al. conducted dual visit endodontic treatment and reported a low mean VAS score. This further demonstrates the lack of variation in postendodontic pain between single and multiple-visit treatments.

Teeth undergoing intentional RCT, for example, for prosthodontic work, may have a lower chance of experiencing postoperative pain compared to cases with irreversible pulpitis and symptomatic apical periodontitis. Microorganisms are associated with the occurrence of postoperative pain after RCT, as pain typically results from acute inflammation of periradicular tissues. Therefore, teeth with irreversible pulpitis and apical periodontitis are at a higher risk of developing post-operative pain [34,35]. Intracanal cryotherapy may be more effective in pain relief for apical periodontitis because of the decrease in inflammation and edema in the apical tissues by low-temperature irrigation methods [36].

The risk of bias assessment of all six included randomized control trials was low with an evidence level of 1+, suggesting their high quality and low publication bias. However, only five studies [19-23] were considered as part of the quantitative analysis. Three studies highlighted the success rate of patients in the form of the number of patients with no or mild pain out of the total number of patients involved in the control and experimental groups. Four studies interpreted the standardized mean difference [20-23]. The combined risk ratios (RRs) of the three studies included in the meta-analysis were 0.80 (95% CI: 0.56 to 1.13) with a P value of 0.20, which is insignificant. In another analysis, the standardized mean difference was 0.54 (95% CI: -1.22 to 0.14) with P value 0.12. Thus, the quantitative results highlighted the less significant role of cryotherapy in controlling postendodontic pain. The limitation of this review is that a small number of studies were included; hence, more reliable clinical studies are encouraged to confirm the effect of cryotherapy on postendodontic pain.

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