Original Article

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Dentistry Section

Emergency Clinical Treatment Protocols for Alleviating Pain in Patients with Symptomatic Irreversible Pulpitis of Permanent Teeth: Systematic Review and Meta-analysis

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ABSTRACT

Introduction: Symptomatic Irreversible Pulpitis (SIP) is a frequent cause of dental emergencies, often presenting with severe and persistent pain. Multiple emergency treatment options have been suggested, but the relative effectiveness of these approaches remains uncertain.

Aim: To evaluate the effectiveness of various emergency clinical treatment protocols in reducing pain among patients with SIP in permanent teeth.

Materials and Methods: A comprehensive literature search was conducted using Medical Subject Headings (MeSH) terms and Boolean operators across databases including PubMed, Medline, ClinicalKey, ProQuest, and EBSCOhost. Grey literature sources were also searched for English-language articles published up to August 31,2023. Following PRISMA guidelines, 19 Randomised Controlled Trials (RCTs) were selected based on inclusion and exclusion criteria, and the review was registered with the International Prospective Register of Systematic Reviews (PROSPERO).

Results: Preoperatively, pharmacological strategies such as Non steroidal Anti-inflammatory Drugs (NSAIDs) and Novafen enhanced anaesthesia effectiveness and reduced baseline pain. Intraoperatively, pulpotomy–often with Calcium-enriched Mixture (CEM) or Mineral Trioxide Aggregate (MTA)–consistently relieved pain and was favoured for its simplicity. Occlusal reduction showed mixed results, with some studies reporting benefit. Adjuncts like cryotherapy, laser, and acupuncture demonstrated variable but promising outcomes. meta-analysis indicated that occlusal reduction significantly decreases pain at 12 hours (SMD=-0.32), and cryotherapy irrigation during root canal treatment leads to reduced postoperative discomfort (SMD-1.10), with Calcium Hydroxide {$Ca(OH)_2$} pulpotomy showing substantial pain reduction (SMD-3.27).

Conclusion: This review underscores the efficacy of diverse preoperative, intraoperative and postoperative strategies, in managing endodontic pain in permanent teeth, with pulpectomy and full pulpotomy offering the most consistent pain reduction. Incorporating these evidence-based interventions into clinical practice can enhance patient outcomes and optimise pain management in endodontic emergencies.

Keywords: Acupuncture, Calcium hydroxide, Cryotherapy, Dental occlusion, Emergency treatment, Endodontic emergencies, Pain management, Pulpectomy, Pulpitis, Pulpotomy

INTRODUCTION

Endodontic pain is defined as an unpleasant sensation of varying intensity, often posing a significant challenge due to its impact on patients' quality of life and treatment complexity [1]. Effective management of endodontic pain is critical throughout the preoperative, intraoperative, and postoperative stages of care, requiring a multifaceted approach to ensure optimal outcomes [2]. Dental anxiety and apprehension, often rooted in past experiences of odontogenic pain, are exacerbated by inconsistencies in achieving adequate pain relief [3]. Managing endodontic pain is particularly complex due to its multifactorial aetiology [4], including patient anxiety, pulpal condition, pre-existing pain, and periapical tissue manipulation, necessitating tailored strategies for effective pain control [5].

Emergency endodontic care commonly addresses SIP, which is defined as a clinical condition in which the dental pulp is inflamed and incapable of returning to its normal state [6]. It is typically characterised by persistent, intense pain exacerbated by thermal stimuli [7]. Aetiological factors such as deep caries, extensive restorations, or fractures exposing pulpal tissues often lead to irreversible pulpitis [8,9]. The diagnosis is established primarily through patient history and sensibility tests, including spontaneous or lingering pain to thermal stimuli and exaggerated responses to cold that persist after stimulus removal, in the absence of periapical radiographic changes [6]. However, diagnosis can be challenging, particularly when pain upon tooth compression is absent, necessitating reliance on thermal testing and thorough patient history [9]. A comprehensive approach to emergency pain management involves accurate diagnosis, pharmacological interventions, and timely procedures [10].

Analgesics, anti-inflammatory medications, and local anaesthetics are pivotal in providing immediate relief, while antibiotics and drainage procedures are utilised in cases of infection or abscess formation [11]. In cases where endodontic debridement is not feasible, potent analgesics, including opioids, may be employed as temporising measures until definitive treatment is possible [12]. Liposomal bupivacaine, a novel option for prolonged soft-tissue anaesthesia, holds promise in pain management [13]. Nerve blocks remain essential for operative pain management, but their efficacy may be influenced by anatomical and patient-specific factors [14]. Adjunctive strategies, such as acupuncture, cold applications, and laser phototherapy, offer alternative approaches to optimise outcomes, particularly when conventional methods are inadequate [15-17].

Techniques such as pulpotomy, pulpectomy, and root canal therapy are central to managing endodontic pain and preserving dental function. Pulpotomy involves the removal of infected pulp tissue while preserving the vitality of the root canal pulp to promote dentin formation and maintain tooth integrity [18]. Pulpectomy,

indicated in extensive infections, entails the complete removal of pulp tissue and is often the most effective emergency treatment for irreversible pulpitis [19]. Biocompatible materials like MTA reduce postoperative pain due to their antibacterial properties and cytokine-inducing effects [20]. Intracanal medications, such as $Ca(OH)_2$, enhance pain management through antimicrobial and tissue-altering properties [21].

Previous research on endodontic pain management has evolved into a multimodal approach combining behavioural, pharmacological, and procedural strategies [2-4,10,11]. Key behavioural methods include effective communication and distraction techniques to alleviate dental anxiety, often rooted in childhood. Pharmacologically, non opioid analgesics like acetaminophen and NSAIDs, such as ibuprofen, remain the primary options for postoperative pain relief. Opioids are reserved for severe cases due to addiction risks, while corticosteroids can help reduce inflammation and pain. Advancements in local anaesthesia, including intraosseous and intraligamentary injections, enhance pain control, particularly in SIP. Procedural techniques such as incision and drainage and cryotherapy also provide immediate pain relief. Occlusal reduction has been effective in managing post endodontic pain, especially after the third day [4]. Future research aims to explore innovative therapies targeting pain pathways, including GABAergic signalling for modulation in inflamed dental tissues and acupuncture for postoperative relief. Emerging techniques such as Low level Laser Therapy (LLLT) and computational approaches targeting inflammatory mediators show promise but require further clinical validation [22]. Overall, these strategies point toward a future focused on non invasive and targeted solutions in endodontic pain management.

The goal of emergency endodontic pain management is to promptly alleviate discomfort, control inflammation and infection, and establish a foundation for definitive treatment. However, despite advancements in pain management strategies, gaps persist in understanding optimal approaches. The present systematic review critically evaluates current evidence on emergency pain management in endodontics, synthesising recent literature and meta-analyses to inform evidence-based clinical practice. By addressing these challenges, authors aim to enhance the quality of care and improve patient outcomes in endodontic treatment.

MATERIALS AND METHODS

This systematic review and meta-analysis were conducted over six months, from March 2023 to August 2023, culminating in data extraction and meta-analysis of eligible studies as per the criteria laid down by the Preferred Reporting Items for Systematic Review 2020 (PRISMA 2020) [23]. The study is registered at PROSPERO under registration code CRD42023450423. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023450423

Research Question

The present review focuses on emergency treatment protocols for alleviating pain in patients with SIP in permanent teeth, which is characterised by rapid progression and severe pain. [Table/Fig-1] presents the outcomes in a PICOS (Population, Intervention, Comparison, Outcome, Study design) format.

PICO	Outcomes
Population	Patients with Symptomatic Irreversible Pulpitis (SIP)
Intervention	Different emergency treatment protocols to alleviate dental pain.
Control	Traditional methods/placebo
Outcome	Change in mean pain scores for different treatments from baseline

[Table/Fig-1]: It shows the PICO question formulated for the study.

Focused Review Question

Is there a difference in pain reduction among different emergency clinical treatment protocols in the management of patients with SIP in permanent teeth?

Literature Search

The search strategy was designed according to the PICOS framework and aimed to identify RCTs evaluating emergency pain management interventions for SIP in permanent teeth from database inception to August 31, 2023. Two reviewers (RM and SM) independently screened the titles and abstracts for eligibility, and disagreements were resolved through discussion with a third reviewer (AP). The search targeted studies involving adult patients (≥18 years) with clinically diagnosed SIP reporting moderate to severe pain.

Eligibility criteria: Eligible interventions included acupuncture, cryotherapy, pharmacological analgesics, occlusal reduction, pulpotomy, pulpectomy, root canal treatment, and anaesthesia-related techniques. Only RCTs published in English up to 31 August 2023, with full-text availability, were included. Studies were excluded if they involved primary teeth, necrotic pulp or periapical pathology, asymptomatic or reversible pulpitis, non RCT designs (observational studies, case series, case reports, reviews), or in-vitro/animal studies, as well as those without usable outcome data. Electronic databases searched included PubMed, Medline, Directory of Open Access Journals (DOAJ), Grey Literature, ProQuest, EBSCOhost, ClinicalKey, and Google Scholar. A combination of controlled vocabulary (MeSH terms) and free-text keywords was used, as detailed in [Table/Fig-2].

Strategy	Number of items searched
(((symptomatic(All Fields) AND irreversible(All Fields) AND ("pulpitis"(MeSH Terms) OR "pulpitis"(All Fields))) OR ((irreversible(All Fields) AND ("pulpitis"(MeSH Terms) OR "pulpitis"(All Fields))) AND ("pain"(MeSH Terms) OR "pain"(All Fields)))) AND (((((((("emergency treatment"(MeSH Terms) OR ("emergency"(All Fields) AND "treatment"(All Fields)) OR "emergency treatment"(All Fields)) AND protocol(All Fields)) OR (("emergencies"(MeSH Terms) OR "emergencies"(All Fields) OR "emergency"(All Fields)) AND ("pain"(MeSH Terms) OR "pain"(All Fields)) AND relief(All Fields))) OR ("cryotherapy"(MeSH Terms) OR "cryotherapy"(All Fields))) OR ("acupuncture therapy"(MeSH Terms) OR ("acupuncture"(All Fields) AND "therapy"(All Fields)) OR "acupuncture therapy"(All Fields))) OR ("analgesics"(All Fields) OR "analgesics"(MeSH Terms) OR "analgesics"(All Fields))) OR ("pulpotomy"(MeSH Terms) OR "pulpotomy"(All Fields))) OR ("pulpectomy"(MeSH Terms) OR "pulpectomy"(All Fields))) OR ("anaesthesia"(All Fields) OR "anaesthesia"(MeSH Terms) OR "anaesthesia"(All Fields)))) AND (("randomised controlled trial"(All Fields) OR "randomised controlled trials as topic"(MeSH Terms) OR "randomised controlled trials"(All Fields) OR "randomised controlled trials"(All Fields)) OR ("randomised controlled trial"(All Fields))OR "randomised controlled trials as topic"(MeSH Terms) OR "randomised clinical trials"(All Fields) OR "randomised clinical trials"(All Fields)))	11095

[Table/Fig-2]: It depicts the MeSH/Emtree terms and text words used in the literature search.

A detailed search strategy is given in [Table/Fig-3].

History — Download history | Clear history

Search	Add to builder	Query	Items found	Time
#7	Add	Search (((((symptomatic irreversible pulpitis) AND irreversible pulpitis) OR dental pain)) AND ((((((emergency protocols) OR analgesics) OR cryotherapy) OR pulpotomy) OR pulpectomy) OR anaesthesia) OR acupuncture) OR occlusal reduction)) AND ((randomized controlled trials) OR randomized clinical trial)	11095	05:50:07
#6	Add	Search ((symptomatic irreversible pulpitis) AND irreversible pulpitis) OR dental pain	103820	05:49:53
#5	Add	Search (((((symptomatic irreversible pulpitis) AND irreversible pulpitis) OR pain)) AND ((((((emergency protocols) OR analgesics) OR cryotherapy) OR pulpotomy) OR pulpectomy) OR anaesthesia) OR acupuncture) OR occlusal reduction))) AND ((randomized controlled trials) OR randomized clinical trial)	97869	05:48:08
#4	Add	Search (randomized controlled trials) OR randomized clinical trial	875467	05:35:15
#3	Add	Search ((((symptomatic irreversible pulpitis) AND irreversible pulpitis) OR pain)) AND ((((((emergency protocols) OR analgesics) OR cryotherapy) OR pulpotomy) OR pulpectomy) OR anaesthesia) OR acupuncture) OR occlusal reduction)	340844	05:34:51
#2	Add	Search ((((((emergency protocols) OR analgesics) OR cryotherapy) OR pulpotomy) OR pulpectomy) OR anaesthesia) OR acupuncture) OR occlusal reduction	891370	05:34:44
#1	Add	Search ((symptomatic irreversible pulpitis) AND irreversible pulpitis) OR pain	1417167	05:31:10

[Table/Fig-3]: Search strategy employed for the systematic review.

Data Extraction

Two independent reviewers (RM and SM) identified the records through the databases. Duplicates were removed via the

EndNote™ reference manager. The title and abstract of each study were reviewed and critically assessed by two independent reviewers (RM and SM). The following study characteristics were extracted from each included article: author and year of publication, patient demographics (including age and gender), total number of participants, pulpal diagnosis, type and nature of pain, emergency treatment protocol employed and study conclusions. The data were independently conducted by two reviewers (RM and SM), with disagreements resolved by discussion with a third reviewer (AP). Data regarding the included studies were also extracted using a predefined protocol and entered into a structured form in Microsoft Office Excel 2007 (Microsoft Corporation, Redmond, WA, USA). The Revised Cochrane Risk of Bias Tool for Randomised Trials (RoB 2) tool [24,25] was utilised for quality assessment of RCT, evaluating the Risk of Bias (RoB) at the study level across seven domains. Meta-analysis was performed on six studies with comparable outcomes at the same follow-up intervals, using Review Manager version 5.4 developed by Cochrane.

Quality Assessment of Selected Studies

The methodological quality of the included RCTs was assessed using the Cochrane RoB tool implemented through Review Manager (RevMan) version 5.4.1 [24]. This tool evaluates potential sources of bias across seven key domains: random sequence generation and allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), completeness of outcome data (attrition bias), and selective outcome reporting (reporting bias), other bias [25]. Each domain was independently evaluated by two reviewers (RM, SM) and judgments were recorded as "Yes" (indicating low risk), "No" (high risk), "Unclear," or "Not applicable." Discrepancies in assessment were resolved through discussion, with involvement of a third reviewer (AP) when necessary. Based on these evaluations, each study was categorised as having an overall RoB rated as low, some concern, or high. A moderate RoB was assigned when one or more domains were marked as "unclear" but none as high-risk.

Data Analysis

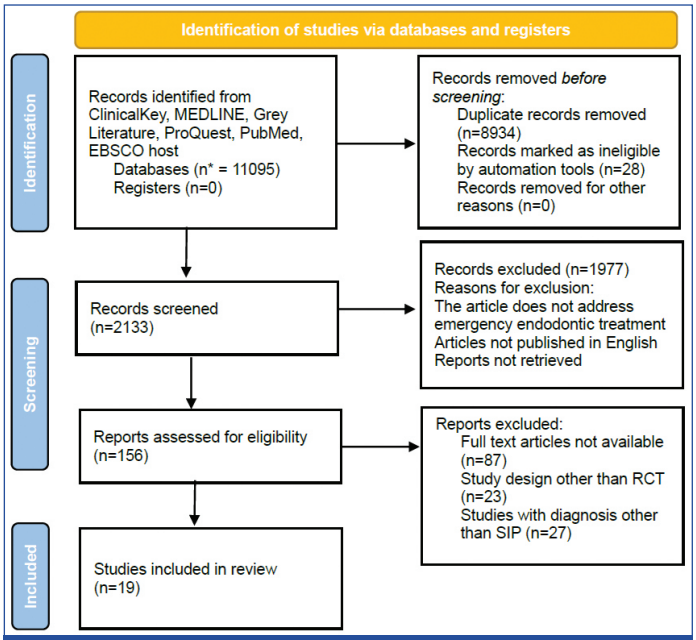
Quantitative data from eligible RCTs were analysed using Review Manager (RevMan) version 5.4.1. For continuous outcomes such as postoperative pain scores, the SMD and corresponding 95% Confidence Intervals (CIs) were calculated to assess effect sizes across different interventions. A random-effects model was applied due to the anticipated clinical and methodological heterogeneity among the included studies. Heterogeneity was assessed using the I^2 statistic, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. A p-value of <0.05 was considered statistically significant for effect estimates. Subgroup analyses were conducted where sufficient data were available.

RESULTS

Study characteristics: The initial search identified 11,095 titles. After screening, 19 studies were included in the qualitative synthesis for data extraction and quality assessment [Table/Fig-4] [16,17,19,20,26-40]. Overall, 2573 patients were included in this review with a diagnosis of SIP in permanent teeth.

Quality Assessment of Included Articles [Table/Fig-5] [16,17,19,20,26-40]

The following emergency protocols were used in these studies: Seven studies compared root canal treatment and pulpotomy



[Table/Fig-4]:Identification of studies via databases. [16,17,19,20,26-40]

Author names/ Year of study	Place of study	Sample size (Intervention Group/Control Group)	Emergency protocol used	Conclusions
Asgary S and Eghbal MJ 2010 [35]	Tehran	407, 202/205	1.Single visit root canal treatment 2.CEM pulpotomy	Pulpotomy treatment with CEM cement thus had better pain-reducing effects than One visit root canal treatment in irreversible pulpitis cases.
Fullmer S et al., 2014 [26]	Ohio	100, 50/50	1. Acetaminophen /hydrocodone 2. Placebo	A combination dose of 1000 mg acetaminophen/10 mg hydrocodone given 60 minutes before the administration of the Inferior Alveolar Nerve Block (IANB) did not result in a statistically significant increase in anaesthetic efficacy.
Bane K et al., 2015 [27]	France	94, 47/47 at 6 months: 43/41	1. Pulpotomy 2. Intraosseous methylprednisolone injection	Methyl prednisolone injection for acute pulpitis relieved pain by a minimally invasive pharmacologic approach more effectively than by the reference pulpotomy and conserves scarce dental resources.
Bultema K et al., 2016 [36]	Ohio	95, 47/48	1. Liposomal bupivacaine 2. 0.5% bupivacaine	Although liposomal bupivacaine had some effect on soft-tissue anaesthesia, it did not reduce pain to manageable clinical levels.
Ramalho KM et al., 2016 [17]	Brazil	60, 15/15/15/15	1. Laser irradiation at 2 points for 4 seconds, 2. Laser irradiation at 2 points for 40 seconds 3. Sham laser application 4. No treatment	No benefit of LPT in SIP as there was no difference in comparison to placebo
Zaman H and Ahmed SS 2016 [37]	Pakistan	250, 125/125	1. Occlusal reduction 2. No occlusal reduction	Occlusal reduction helps in reducing post-instrumentation pain
Murugesan H et al., 2017 [28]	India	157, 53/52/52	1. Acupuncture + placebo 2. Sham acupuncture + placebo 3. Acupuncture + ibuprofen	Classical acupuncture is a safer and more effective alternative to analgesics for management of pain.

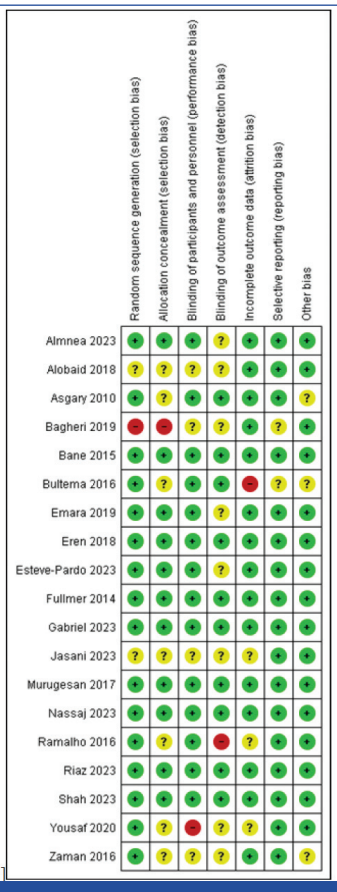
Alobaid AS and Amal A 2018 [38]	Saudi Arabia	51	1. CaOH (Pulpdent (Watertown, MA, USA)) 2. Without CaOH	Complete pulp extirpation followed by cotton pellet of Ca(OH)2 reduced post-endodontic pain more than the control group but not significantly.
Eren B et al., 2018 [29]	Turkey	66, 22/22/22	1. Partial pulpectomy 2. Pulpotomy 3. Total pulpectomy	Pulpotomy, partial pulpectomy, and total pulpectomy are equally effective in symptom relief, but pulpotomy is often preferred for its simplicity, quick symptom relief, and reduced procedure time.
Bagheri M et al., 2019 [20]	USA	45, 15/15/15	1. Pulpotomy + white MTA soaked cotton pellet 2. Pulpotomy + dexamethasone soaked cotton pellet	Pulpotomy procedures can reduce pain related irreversible pulpitis. Pulpotomy with MTA soaked cotton pellet significantly reduces pain intensity.
Emara RS et al., 2019 [40]	Egypt	308, 154/154	1. Occlusal reduction 2. No occlusal reduction	The occlusal reduction was effective in reducing the intensity of postoperative pain 12h and 24h after root canal instrumentation in the first visit.
Yousaf A et al., 2020 [39]	Pakistan	262, 131/131	1. Occlusal reduction of 2 mm 2. No occlusal reduction	Occlusal reduction has no significant impact on postoperative pain.
Raed D et al., 2023 [30]	Saudi Arabia	100, 50/50	1. Occlusal reduction 2. No occlusal reduction	No statistically significant difference in postoperative discomfort. In the occlusion-eased group, the pattern of postoperative pain did indicate a steady reduction
Esteve-Pardo G et al., 2023 [19]	Spain	80, 40/40	1. Pulpotomy 2. Pulpectomy	Pulpectomy and pulpotomy effectively eliminate pain and achieve high levels of patient satisfaction. The patient's perceptions of the duration and discomfort of the two treatments were similar.
Jasani P et al., 2023 [16]	India	60, 30/30	1. Cold saline (cryotherapy, temperature of 2.5 °C.) 2. Normal saline	Cryotherapy resulted in significantly less postoperative pain compared to room temperature normal saline irrigation.
De Grado GF et al., 2023 [31]	France	78, 30/48	1. Pulpotomy + articaine 2. Pulotomy + eugenol	Pulpotomy effectively relieves pain with either articaine or eugenol, with eugenol preferred as the pulp dressing
Nassaj AE et al., 2023 [32]	Iran	120, 30/30/30/30	1. Novafen tablet 2. Mefenemic acid 250 mg 3. Celecoxib 200 mg 4. Ibuprofen 600 mgdiclofenac	Both Ibuprofen and Novafen can serve as the analgesics of choice for pain relief.
Riaz M et al., 2023 [33]	Pakistan	120, 30/30/30/30	1. Diclofenac 2. Piroxicam 3. Tramadol 4. Control	Preoperative analgesics significantly increase the effectiveness of Inferior Alveolar Nerve Block (IANB).
Shah VR et al., 2023 [34]	India	120, 60/60	1. Cold saline (cryotherapy) 10 mL 2.5 °C 2. Normal saline	Final irrigation with 2.5°C cold saline can result in a significant reduction in postoperative pain as compared to that of normal saline after single-visit endodontics in single-rooted teeth.

[Table/Fig-5]: Characteristic details of the included individual studies [16,17,19,20,26-40].

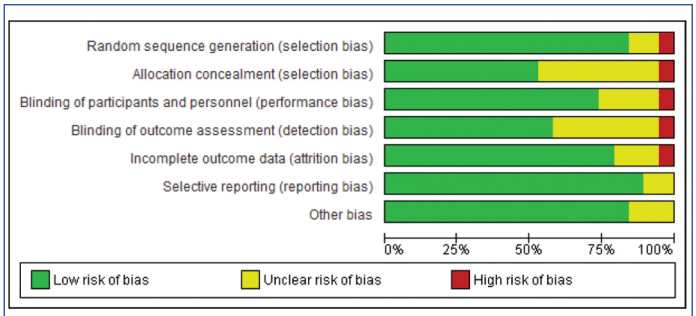
procedures [19,20,27,29,31,35,38]. One study used Ca(OH)2 as an intracanal medicament [38], while the other used CEM cement in pulpotomy [35]. The root canal treatment and pulpotomy effectively relieved symptoms, with pulpotomy preferred for its time efficiency and comparable efficacy. Use of $Ca(OH)_2$ and CEM in pulpotomy showed greater pain reduction than the control groups. Eugenol was more effective than articaine as a pulpotomy dressing, further reducing pain scores [31]. Both pulpotomy and pulpectomy were found to be similarly effective for the emergency treatment of SIP [19]. Four studies assessed the effect of occlusal reduction [30,37,39,40]. Occlusal reduction was found to be effective in reducing the intensity of postoperative pain, however, two studies [30,39] showed no significant effect. Two studies [16,34] assessed the effect of cryotherapy. In both studies, cold saline was used for final irrigation. The application of cryotherapy resulted in significantly less postoperative pain compared to normal room temperature saline irrigation in both studies. One study evaluated the effect of acupuncture as compared to the use of analgesics [28]. Classical acupuncture was found to be a safer and more effective alternative to analgesics. Four studies evaluated the effect of different analgesics such as diclofenac, acetaminophen, mefenamic acid, piroxicam, tramadol, ibuprofen, liposomal bupivacaine, novafen, and celecoxib [26,32,33,36]. The use of analgesics had provided better anaesthetic success. One study evaluated the effect of laser on pain reduction but no significant benefits were seen [17].

Risk of Bias (RoB)

Eleven studies showed low RoB [19,26-34,40], one study [35] showed moderate risk, and seven studies [16,17,20,36-39] showed high RoB [Table/Fig-6,7].



[Table/Fig-6]: Risk of Bias (RoB) assessment of the included studies [16,17,19,20,26-34,36-40].



[Table/Fig-7]: Summary of the overall Risk of Bias (RoB) assessment.

Meta-analysis

A meta-analysis was conducted on six studies, with the extracted data presented in [Table/Fig-8] 16,34,35,37,38,40].

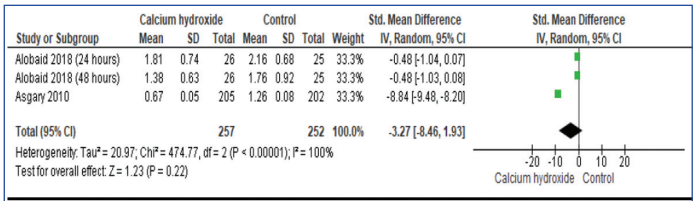
Two studies assessed postoperative pain in a total of 257 participants treated with $Ca(OH)_2$ pulpotomy compared to 252 in control groups [34,37]. The pooled SMD was -3.27 (95% CI: -8.46 to 1.93); however, as the confidence in interval crossed zero, the result was not statistically significant despite high heterogeneity (I^2 = 100%). [Table/Fig-9] [35,38].

Two studies on occlusal reduction subgroup analysis across various follow-up intervals yielded an overall SMD of -0.57 (-1.18, 0.05), suggesting a non significant reduction in pain [37,40]. Among the follow-up intervals, only the 12-hour mark showed significant pain reduction (SMD -0.32, 95% CI: -0.55, -0.10) [Table/Fig-10] [37,40].

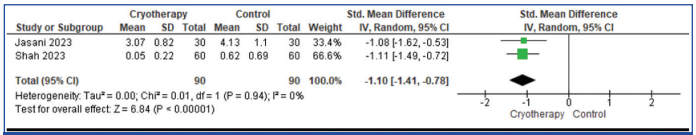
In protocols involving cryotherapy, two studies analysed postoperative pain across 180 participants [16,34]. The pooled SMD was -1.10 (-1.41, -0.780, indicating a statistically significant pain reduction in the cryotherapy group (p-value<0.05), further supporting its efficacy in managing postoperative pain [Table/Fig-11][16,34].

Author names/ Year of study	Sample size	Emergency protocol used	Follow-up	Post-op pain
Asgary S and Eghbal MJ 2010 [35]	407, 202/205	1. Single visit root canal treatment	7 days, 1,2,5 years	day 7: 1.26+-0.08
		2. $Ca(OH)_2$ pulpotomy		day 7: 0.67+-0.05
		3. Placebo		day 7: 59.0+-44
Alobaid AS and Amal A 2018 [38]	51, 26/25	1. $Ca(OH)_2$ {Pulpdent (Watertown, MA, USA)}	24,48 hours	24 h: 1.81+-.74 48 h: 1.38+-0.63
		2. Without $Ca(OH)_2$		24 h: 2.16+-0.68 48 h: 1.76+-0.92
Zaman H and Ahmed SS 2016 [37]	250, 125/125	Occlusal reduction on functional and non-functional cusps	6 days	Day 6:2.6+-0.7
		No occlusal reduction		Day 6:4.4+-0.97
Emara RS et al., 2019 [40]	154/154	1. Occlusal reduction	6,12,24,48 hours	6 h:3.14+-2.62 12 h:1.84+-2.18 24 h:1.55+-2.12 48 h:0.95+-1.71
		2. No occlusal reduction		6 h:3.56+-2.86 12 h:2.64+-2.72 24 h:2.03+-2.17 48 h:1.06+-1.9
Jasani P et al., 2023 [16]	60, 30/30	1. Cold saline (cryotherapy, temperature of 2.5 °C.)	6,12,24,48 hours	6 h:3.07+-0.82
		2. Normal saline		6 h:4.13+-1.10
Shah VR et al., 2023 [34]	120, 60/60	1. Cold saline (cryotherapy) 10ml 2.5 degree C	24,48 hours	24 h:0.40+-0.62 48 h:0.05+-0.22
		2. Normal saline		24 h:1.16+-0.81 48 h: 0.62+-0.69

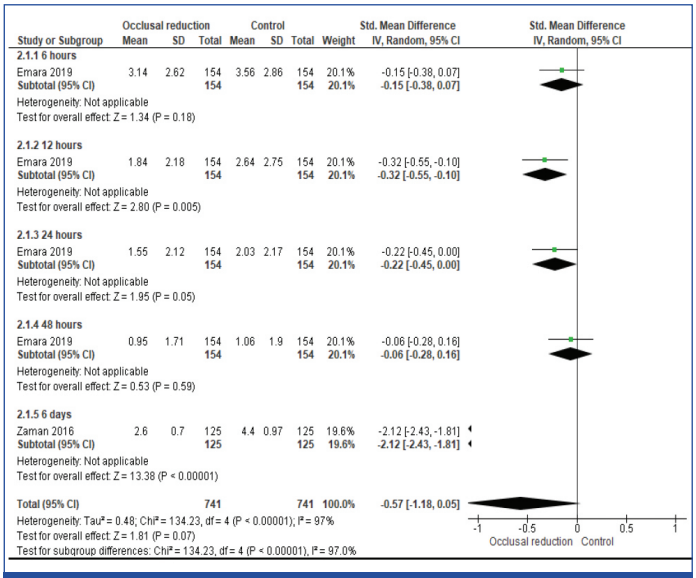
[Table/Fig-8]: Data extraction sheet for the meta-analysis, where pain scores were assessed using the Visual Analogue Scale (VAS) and the Numerical Rating Scale (NRS) [16,34,35,37,38,40].



[Table/Fig-9]: The meta-analysis results for calcium hydroxide [35,38].



[Table/Fig-11]: The meta-analysis results for cryotherapy [16,34].



[Table/Fig-10]: The meta-analysis results for occlusal reduction [37,40].

DISCUSSION

Endodontic emergencies usually present with intense, sharp, or radiating pain, which involves the dental pulp, the innermost tissue containing nerves and blood vessels. Symptoms include lingering discomfort, throbbing pain, thermal sensitivity, gum tenderness, swelling, and, in severe cases, abscess formation with fever and malaise [41]. Pain severity in SIP often exceeds 60 mm on the VAS scale [20]. Prompt dental intervention is essential to prevent complications such as tooth loss and systemic infection.

Endodontic treatment during emergencies aims to provide immediate pain relief. A systematic review is indispensable to consolidate and evaluate existing evidence comprehensively. This review included 19 RCTs assessing the efficacy of various interventions. By analysing and synthesising available studies, such reviews support evidence-based decisions in endodontic emergencies, assess study quality for reliability, and use I^2 to quantify heterogeneity that influences generalisability. In this review, high heterogeneity was noted (I^2 = 100% for postoperative pain after $Ca(OH)_2$ use and 97% for occlusal reduction). A random-effects model was used appropriately to account for both within-study and between-study variability, offering a conservative estimate of treatment effects.

Earlier studies have explored emergency interventions for managing acute dental pain, particularly in SIP [35,36,42-50]. Tomson PL et al., evaluated pulpotomy versus root canal treatment and found similar outcomes in pain relief and clinical success, supporting pulpotomy as less invasive alternative [42]. Another review concluded that antibiotics, offer uncertain benefit and pose potential harm, emphasising the need for definitive treatment [43]. A review on acupuncture showed moderate effectivity in pain and enhancing anaesthesia [44]. A systematic overview [45] on analgesic use identified ibuprofen and acetaminophen combinations as the most effective and safest, while opioids were linked to more adverse effects. Building on this evidence, the present review synthesises findings from RCTs to provide insight into the efficacy and clinical relevance of emergency pain management protocols in endodontics. Among the included studies, the trial by Asgary S and Eghbal MJ demonstrated that $Ca(OH)_2$ exhibits notable antimicrobial and anti-inflammatory properties, effectively reducing pain [35,46]. $Ca(OH)_2$ creates an alkaline environment that is hostile to bacteria, diminishes inflammation, aids in dissolving necrotic tissue, and promotes healing [47,48]. Despite initial pain, $Ca(OH)_2$ significantly reduced postoperative pain, suggesting its efficacy as an intracanal medicament. CEM used for pulpotomy, demonstrated pain relief comparable to that achieved with single-visit RCT in cases of SIP [35]. CEM's effectiveness may result from its ability to modulate neuronal excitability through calcium ion release and extracellular alkalinity, enhancing regenerative and analgesic potential [49]. CEM showed antibacterial properties by dissociating into calcium and hydroxyl ions, which increase pH and calcium concentration [50]. Such mechanisms enhance bacterial inhibition and promote tissue healing. Multicentre trials highlight the need for cost-effective options in regions where extraction is common, and non inferiority trials show pulpotomy to be as effective as root canal treatment with added advantages of lower cost, time, and invasiveness.

Pulpotomy is an effective emergency treatment for SIP, preserving the vitality of pulp while alleviating pain. Compared to pulpectomy, pulpotomy offered immediate pain control [19]. MTA outperformed Dexamethasone (DEX) and dry cotton dressing in relieving postoperative pain [20], attributed to its ability to stimulate cytokine release, promote hard-tissue formation, and preserve pulp integrity without cytotoxic effects [51]. Pulpotomy provides rapid pain relief by alleviating pulpal pressure, reducing inflammation, and severing nociceptive nerves [29]. The role of pulpotomy in managing SIP continues to expand, with recent studies exploring innovative approaches. Eugenol provided greater pain relief than articaine after emergency pulpotomy, especially on days 1, 3, and 7 [31]. Eugenol's efficacy stems from its antibacterial [52], anti-inflammatory [53], antioxidant [54], and analgesic properties [55], Eugenol modulates inflammation and anaesthesia, offering a pharmacological profile [55].

Pharmacological interventions can achieve pain relief comparable to pulpotomy [27], supporting their use as less invasive options in resource-limited settings. Methylprednisolone highlights the role of medicinal protocols in emergency care, while liposomal bupivacaine showed limited efficacy and high cost, making it impractical for routine pain control [36]. Preoperative acetaminophen/hydrocodone showed limited anaesthetic success, possibly due to opioid metabolism variability and inflammation associated with pulpitis [26]. Comparisons highlight ibuprofen as the most effective, followed by Novafen [32]. The findings support ibuprofen's superiority due to its inhibition of cyclooxygenase [56]. Piroxicam was the most effective preoperative analgesic for improving IANB success, suggesting for managing SIP in mandibular molars [33].

An effective alternative approach is acupuncture, which has been employed for centuries in Chinese medicine [57]. In 1998, the National Institutes of Health (NIH) issued a statement endorsing acupuncture's effectiveness, including postoperative and chemotherapy-induced nausea and vomiting and dental pain [58]. Its mechanisms involve both peripheral and central pathways, including modulation of neurotransmitters and endogenous opioid release [14]. Research demonstrated that acupuncture provides faster pain relief than ibuprofen or sham acupuncture [28]. This makes acupuncture a viable, non invasive option for patients seeking alternatives to pharmacological interventions [59]. Acupuncture's ability to release neurotransmitters like serotonin and beta-endorphins, coupled with its activation of nociceptive inhibitory pathways, provides pain relief [60]. Despite its benefits, patient-specific factors can influence outcomes [61]. Thus, acupuncture's integration into clinical practice warrants further investigation.

Occlusal reduction, involving the mechanical reduction of cusps, has been explored for its role in alleviating postoperative pain. While some studies [39], have shown no significant effect, others [40], indicate its efficacy in reducing pain intensity postoperatively. The different outcomes may be due to variations in methodologies, patient demographics, and treatment protocols [40,62]. Factors such as apical debris extrusion also influence postoperative discomfort [63]. The reduction of functional and non functional cusps mechanically decreases nociceptor sensitisation, providing pain relief [37]. The acceptability of reducing natural tooth structure remains debated, but full occlusal coverage after endodontic treatment is essential to improve longevity and reduce fracture risk.

Cryotherapy has been highlighted as an effective intervention for reducing postoperative pain in endodontic therapy [34]. Cold saline showed pain reduction due to its ability to inhibit the release of pain-producing substances, reduce oedema, and slow peripheral nerve conduction [16]. Thus, Cryotherapy appears promising for improving patient comfort and outcomes, though optimal protocols need further study. Contrary to expectations, Low Power Laser Therapy (LPT) did not alleviate pain in symptomatic irreversible pulpitis (SIP) and showed no benefit compared to placebo [17]. This highlights the need for research into LPT's mechanisms, including its influence on circulation and inflammation, to refine its application in pain management [64].

Meta-analysis of six studies showed $Ca(OH)_2$ pulpotomy produced the greatest pain reduction, though with high heterogeneity [16,34,35,37,38,40]. Cryotherapy also proved effective, while occlusal reduction was overall non significant except at 12 hours. These results highlight the varying impact of interventions and the need to tailor protocols to the clinical context and timing.

Methodological quality was assessed with the Cochrane RoB tool in RevMan 5.4.1. Of the 19 studies, 11[19,26-34,40] showed low risk, one [35] moderate risk, and seven [16,17,20,36-39] high-risk due to issues with randomisation, blinding, or outcome reporting.

Clinically, the findings suggest that less invasive interventions such as pulpotomy and cryotherapy can provide effective and time-efficient pain relief, while pharmacological adjuncts broaden management options. Future studies should adopt standardised protocols, larger multicenter designs, and longer follow-ups to improve generalisability and comparability.

Limitation(s)

At the study level, several included RCTs had small sample sizes, unclear randomisation methods, and inadequate blinding, which may affect internal validity. At the outcome level, pain assessment tools and follow-up intervals varied across studies, reducing comparability and contributing to heterogeneity. At the review level, restricting the search to English-language full-text RCTs may have introduced language and publication bias.

CONCLUSION(S)

In conclusion, the present systematic review comprehensively evaluated a wide range of preoperative, intraoperative, and postoperative interventions aimed at managing pain in endodontic

emergencies in permanent teeth. It highlights several effective strategies, including the use of $Ca(OH)_2$ and CEM for pain relief and healing, as well as pulpotomy procedures with materials like MTA and eugenol, which effectively manage irreversible pulpitis. Pharmacological approaches, including preoperative analgesics like ibuprofen and methylprednisolone, also demonstrated significant improvements in anaesthetic success and pain management. Cryotherapy was found to be a valuable intraoperative technique, offering substantial relief from postoperative pain and swelling. While interventions like occlusal reduction showed mixed results, this review stresses the importance of further research to standardise and validate such techniques. The overall findings underscore the need for well-designed, high-quality studies to refine pain management protocols in endodontics, promoting more effective and individualised patient care.

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