



Influence of vehicle for calcium hydroxide on postoperative pain: a scoping review

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This review aims to identify the influence of the vehicle and its concentration used to carry calcium hydroxide (Ca(OH)₂) medicament on postoperative pain.

The protocol for this review was registered in the open science framework (Registration DOI-10.17605/OSF.IO/4Y8A9) and followed the guidelines provided by the Joanna Briggs Institute. Reporting was based on the preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews (PRISMA-ScR). Literature screening and searches were performed on PubMed/Medline, Scopus, and EBSCO hosts. Furthermore, additional records were manually analyzed using various sources. The selected studies were published in English and included the use of any vehicle adjunct to Ca(OH)₂ to evaluate postoperative pain using qualitative and quantitative pain assessment tools. Descriptive analysis was conducted to review the study design, vehicle elements, and their effects.

A preliminary search yielded 7584 studies, of which 10 were included. According to the data collected, the most commonly used Ca(OH)₂ vehicles were chlorhexidine (CHX), normal saline, and camphorated paramonochlorophenol/glycerine (CPMC/glycerine), which had a significant effect on postoperative pain. Among the included studies, six evaluated the effect of CHX as a vehicle. It was observed that a higher concentration of the vehicle (2%) showed a favorable response in reducing postoperative pain.

A majority of studies have validated a positive consequence of using a vehicle on postoperative pain. Although higher vehicle concentrations were found to alter postoperative pain levels, the data were insufficient to draw a firm conclusion. Our scoping review indicates that further clinical studies should focus on using different vehicles at various concentrations and application times to check for feasible and safe exposure in addition to providing pain relief.

Keywords: Calcium Hydroxide; Postoperative Pain; Vehicle.



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INTRODUCTION

Pain and swelling are common symptoms of underlying diseases associated with an offending tooth. Endodontic treatment attempts to reverse the disease process, thereby eliminating associated signs and symptoms. Pain

management is an important prerequisite for a successful endodontic treatment.

Various factors play a role in regulating pain during or after endodontic procedures. Preoperative pain has been proven to be a prognostic factor for postoperative pain and flare-up [1,2]. Furthermore, persistent microbial infection, pulpal necrosis, and inter-appointment factors

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such as inadequate preparation, over-instrumentation, and extrusion of hard tissue debris also contribute to the occurrence of pain or flareups [3–7]. Acute periradicular inflammation caused by endotoxins and enzymes produced by microorganisms in periapical tissues is the most common cause of postoperative pain [8,9]. Optimum instrumentation of the canal, adequate irrigation, and placement of intracanal medication aid in the management of inter-appointment pain [3,10].

Ca(OH)₂ is commonly used as an intracanal medicament. However, certain microorganisms, such as *E. faecalis* [11–13] and *Candida albicans* [14], are resistant to Ca(OH)₂. Microbial load in the canal is a major contributing factor to postoperative pain. Therefore, attempts have been made to improve the efficacy of Ca(OH)₂ by using a variety of vehicles that allow Ca(OH)₂ dissociation and to increase the antimicrobial capacity of the paste [15].

The alkalinity of Ca(OH)₂ imparts its antimicrobial properties. It is also said to have a tissue-altering effect, reducing intracanal microbial load, having the ability to alter the bacterial cell wall, and denaturing the toxins traded by bacteria. Ca(OH)₂ has been proposed to have pain-relieving properties due to its antimicrobial and tissue-altering effects. Furthermore, it plays a role in controlling inflammatory processes and inducing repairs [16]. However, this may not occur as a result of the dentin-buffering effect, which allows microbial proliferation [17], or the resistance of canal microbiota to Ca(OH)₂ concerning the inability of Ca(OH)₂ to penetrate deep into dentinal tubules [11,18].

The vehicle used as adjunct to Ca(OH)₂ determines its work properties and aids ionic dissociation by changing its velocity, causing the paste to be solubilized at different rates by periapical tissues and from within the root canal [19]. Various vehicles such as glycol, saline, L.A., and water have been used to test the efficacy of the medicament in reducing the microbial load and inflammatory process, thereby reducing pain [20]. Generally, three types of vehicles are used for Ca(OH)₂ paste preparation: viscous, aqueous, and oily [21]. Aqueous vehicles contain

water-soluble substances, such as saline, water, dental anesthetics, and Ringer's solution. When the paste comes into direct contact with tissues and tissue fluids, these substances promote a high degree of solubility [21].

Viscous vehicles are also water-soluble substances, such as glycerine, polyethylene glycol, and propylene glycol, which release Ca²⁺ and OH⁻ ions at a relatively slow pace for a prolonged period. Compared to aqueous vehicles, they have lower solubility. [21].

Oily vehicles or non-water-soluble substances, such as olive oil, silicone oil, camphor, and metacresyl acetate, promote lowest solubility and diffusion of the paste within the tissues [21].

The pain threshold of each individual determines the pain perception. This parameter was used to weigh the intensity of pain, indicating the significance of several pain assessment tools. These pain assessment tools can be broadly classified into unidimensional and multi-dimensional tools [22,23]. The studies included in this review used various pain assessment tools such as the visual analog scale (VAS), numeric rating scale (NRS), Heft-Parker Visual Analog Scale (HP VAS), universal pain assessment tool, and verbal rating scale, leading to heterogeneity in the data.

Scoping reviews offer an extremely vital tool that can help analyze the range of available evidence and provide scope for further research. To the best of our knowledge, there is very little and inconsistent literature on the effect of Ca(OH)₂ vehicles on postoperative pain.

Hence, the underlying objective was to highlight, through a scoping review, whether the vehicle carrying Ca(OH)₂ affects postoperative pain levels.

METHODS

The protocol of this study was registered in the Open Science Framework (Registration DOI: 10.17605/OSF.IO/4Y8A9) and met the Joana Briggs Institute criteria [24]. In addition, this scoping review was based on PRISMA-ScR [25].

1. Inclusion Criteria

The selected studies were published in English and included the use of any vehicle adjunct to $\text{Ca}(\text{OH})_2$ to evaluate postoperative pain with the help of qualitative and quantitative pain assessment tools. The studies included both primary root canal treatments and secondary root canal treatments (retreatment cases).

2. Search

The literature search and screening were conducted on PubMed/Medline, Scopus, and EBSCO hosts, and additional records were analyzed manually through various sources, including gray literature, until June 2021. The following search methodology was designed based on MeSH terms. ([CALCIUM HYDROXIDE] OR [INTRA CANAL MEDICAMENT] OR [INTRA CANAL MEDICATION] OR [MEDICAMENT] OR [VEHICLE OR SALINE OR PEG] AND ([POST OPERATIVE PAIN] OR [INTER APPOINTMENT PAIN] OR [FLARE UP] OR [ENDODONTIC FLARE UPS] OR [ENDODONTIC PAIN])

3. Screening

The search was performed using the Zotero software. All potentially relevant studies were selected for full scrutiny, including those that met the inclusion criteria. Two researchers (K.A. and A.G.) independently assessed the full-text papers for duplicity. Any discord regarding the suitability of the studies involved was handled by debate and accord by a third reviewer (V.A.). Only articles that met all the criteria were incorporated. Discussions were done to address discrepancies in screening titles, abstracts, and full-text publications.

4. Data extraction, analysis, and alignment:

Data extraction and alignment were performed in accordance with the guidelines of Peter et al. [24]. According to these guidelines, data must be arranged in the form of graphics or tables. A standardized form was

used to extract the data. The study design, characteristics of the vehicles employed, pain evaluation method, and several other aspects were addressed in the descriptive analysis. Table 1 presents the characteristics of the studies included.

RESULTS

The preliminary search yielded a total of 7584 likely related records from all databases, and five articles were found by manual search. After the removal of duplicates and full-text screening, ten studies were selected (nine randomized clinical trials and one clinical study). Fig. 1 shows the screening process in accordance with the PRISMA ScR. Table 2 presents the results of the included studies.

Among the studies included in this scoping review, there was strong evidence that the vehicle used can change the work characteristics of the $\text{Ca}(\text{OH})_2$ paste.

Six studies [15,26–30] evaluated the effect of CHX, an aqueous vehicle, on postoperative pain in comparison to other vehicles such as saline, CPMC/glycerine paste (oily vehicle), and dexamethasone; of these, three studies indicated lower postoperative pain with the use of CHX (2%) as a vehicle. Two other studies indicated otherwise [15,28], probably due to the lower concentration of CHX. One study [29] indicated higher postoperative pain in the CHX (2%) group than in the dexamethasone group.

A recent study compared the effects of chitosan (natural polysaccharide) and metapex (silicone oil-based vehicle containing iodoform) to $\text{Ca}(\text{OH})_2$ paste—a polyethylene glycol paste (viscous) as a vehicle and found that it reduced postoperative pain to some extent, indicating its potential for use as a vehicle to aid in pain management [31].

A recent study by Arslan et al. evaluated the effect of lidocaine HCl, an aqueous vehicle (20 mg/mL lidocaine HCl with 0.0125 mg/mL epinephrine) in comparison to normal saline (0.9%), and showed a

Table 1. Characteristics of included studies

No	Title	Author journal	Country	Study type	Inclusion criteria	Intervention group	Intervention time	Placement method
1	Incidence of postoperative pain after intracanal procedure based on antimicrobial strategy	Siqueira, et al. JOE 2002 [8]	Brazil	Clinical study	Necrotic pulp or need for retreatment	(CPMC)/ glycerine paste	Inter appointment	Endodontic files
2	Calcium hydroxide as intra canal medication: Effect on Posttreatment pain	Walton, et al. JOE 2003 [46]		Randomised	Vital or necrotic pulps with or without peri apical pathosis	Group 1- Calcium hydroxide + methylcellulose 2.5% Group 2- Cotton pellet	Inter appointment	Delivered by syringe, compacted by paper points
3	Postoperative pain following the use of two different intracanal medications	Gama, et al. Clin Oral Invest 2008 [15]	Brazil	Randomised	Treatment and Re-treatment cases and presence/absence of apical periodontitis	G I- CHX gel (0.12%); GI-I-Ca(OH) ₂ /CPMC/ glycerinepaste	Inter appointment	lentulospirals
4	Intracanal Medications versus Placebo in Reducing Postoperative Endodontic pain- A Double-Blind Randomized Clinical Trial Blind Randomized Clinical Trial	Singh, et al. Braz Dent J 2013 [26]	India	Randomized; double blind	Pulpal necrosis, acute apical periodontitis	Group I: calcium hydroxide paste prepared with 2% chlorhexidine gel in equal parts (w/w), Group II: 2% chlorhexidine gel (Endogel, Itapetininga, SP, Brazil), Group III: commercial calcium hydroxide paste (Calcipulpe, Septodont, France) and Group IV: no dressing (control).	Inter appointment	lentulospirals
5	Comparison of Inter Appointment Pain Between Calcium Hydroxide Mixed With 2% Chlorhexidine and Calcium Hydroxide Mixed With Normal Saline; A Randomized Controlled Trail	Khattak, et al. JKCD 2014 [27]	Pakistan	Randomized Lottery method	irreversible pulpitis or periapical periodontitis	Group 1 -calcium hydroxide mixed with 2% Chlorhexidine Group 2- calcium hydroxide mixed with 0.9% normal saline	Inter appointment	lentulospirals
6	Incidence of postoperative pain after use of calcium hydroxide mixed with normal saline or 0.2% chlorhexidine digluconate as intracanal medicament in the treatment of apical periodontitis	Menakaya, et al. Saudi Dental J [28]	Nigeria	randomized (balloting).	apical periodontitis	Group A was the control group and comprised teeth treated with obturation calcium hydroxide mixed with normal saline intracanal medicament. Group B was the experimental group and comprised teeth treated with calcium hydroxide mixed with 0.2% chlorhexidine digluconate intracanal medicament.	Post obturation	lentulospirals
7	Comparative evaluation of post-operative pain with different calcium hydroxide formulations when used as intracanal medicament in root canal treatment- In vivo study	Thakur, et al. IP Indian Journal of Conservative and Endodontics [31]	India	Random (method not given)	Vital teeth; Presence of sinus tract; irreversible pulpitis, with or without apical Periodontitis; periapical resorption.; No previous root canal intervention; Tooth mobility within 0 to 1 degree	Group 1: Calcium hydroxide paste (Ivoclar) Group 2: Calcium hydroxide paste with iodoform (Metapex) Group 3: Calcium hydroxide points (Hygenic) Group 4: Calcium hydroxide paste using chitosan (0.2%) as vehicle Group 5: Control group containing dry sterile cotton.	Inter appointment	Not mentioned
8	The Effect of Different Combinations of Calcium Hydroxide as Intra-Canal Medicament on Endodontic Pain: A Randomized Clinical Trial Study	Ghanbarzadegan, et al. Iranian Endodontic Journal 2019 [29]	IRAN	Randomized triple blind (random no tables)	necrotic molar or permanent premolar with closed apex, lack of any kind of resorption	G1- -Ca(OH) ₂ + Saline G2-Ca(OH) ₂ + 2%Chx G3—Ca(OH) ₂ + Dexamethasone	Inter appointment	lentulospirals
9	Effect of combination of Calcium Hydroxide and Chlorhexidine Gel 2% as Intra Canal medication on Post Operative Pain and Bacterial Endotoxin in Necrotic teeth	Alarbeed, et al. Acta Scientific Dental Sciences 2019 [30]	Egypt	Randomized; single blind	Necroted single rooted teeth with apical periodontitis	G1- -Ca(OH) ₂ + 2%CHXgel G2- -Ca(OH) ₂ paste G3- no med	Inter appointment	
10	Effect of calcium hydroxide mixed with lidocaine hydrochloride on postoperative pain in teeth with irreversible pulpitis and symptomatic apical periodontitis: a preliminary randomized controlled prospective clinical trial	Arslan, et al. Clin oral Invest 2020 [32]	Germany	Randomized triple blind	mandibular molar teeth that were diagnosed with irreversible pulpitis (prolonged pain to cold test) and symptomatic apical periodontitis (percussion pain)	G1- -Ca(OH) ₂ + 0.9%saline G2- -Ca(OH) ₂ + lidocaineHCl	Inter appointment	Lentulospiral

Ca(OH)₂, calcium hydroxide; CHX, chlorhexidine; CPMC, camphorated paramonochlorophenol; G, group; HCl, hydrochloric acid.

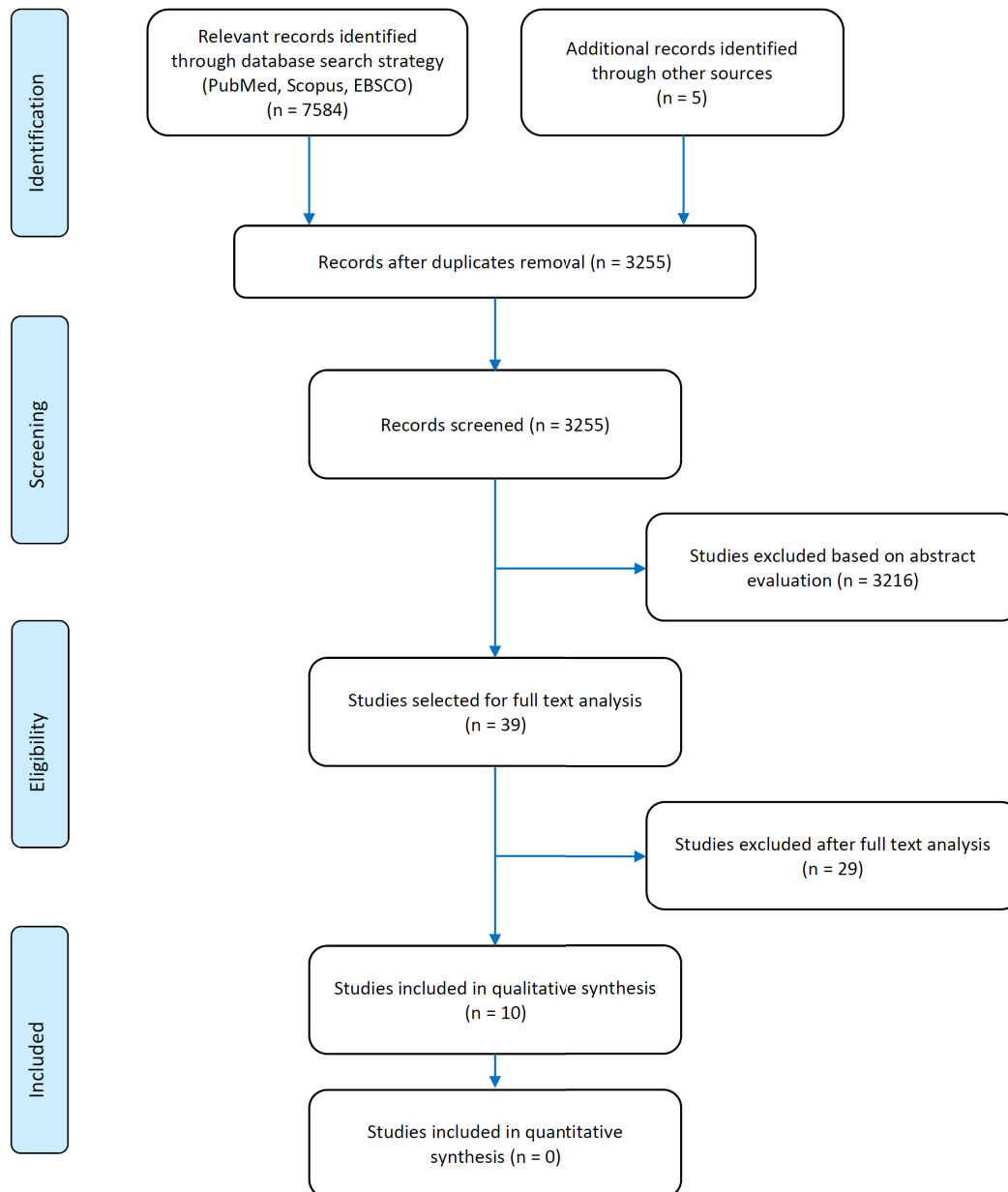


Fig. 1. A flowchart of screening of studies according to the extension for scoping review

significant difference ($P < 0.05$) in both groups, indicating that lidocaine is very effective as a vehicle for reducing postoperative pain [32].

The pain perception of each individual is based on their pain threshold, which is used as a benchmark to compare pain severity, emphasizing the need for diverse pain assessment tools.

Four studies [26,27,31,32] used the VAS, one study [29] used the HP VAS, and another [30] used the NRS. One study [28] used the universal pain assessment tool,

whereas three studies [4,8,15] used the verbal rating scale.

DISCUSSION

This scoping review is the first to synthesize information on the influence of a variety of vehicles used in adjunct with $\text{Ca}(\text{OH})_2$ and the effect of their concentration on postoperative pain.

The need to conduct this scoping review is attributed

Table 2. Results of included studies

No	Study	Outcome accessed and tool	Medicament	Time period	Results
1.	Siqueira, et al. JOE 2002 [8]	Post operative pain (none, mild, moderate and severe)	Ca(OH) ₂ /CPMC/glycerinepastein GI-treatment cases, GI-retreatment cases	1 Week	No statistically significant difference at any time period
2.	Walton, et al. JOE 2003 [46]	Post operative pain (none, mild, moderate and severe)	G I-Ca(OH) ₂ +methylcellulose solution (2.5%) GII-Cotton pellete	Upto 48 h (4h, 24h, 48h)	No statistically significant difference at any time period
3.	Gama, et al. Clin Oral Invest 2008 [15]	Post operative pain (none, mild, moderate and severe)	G I- CHX gel (0.12%); GII-I-Ca(OH) ₂ /CPMC/glycerine paste	1 Week	No statistically significant difference
4.	Singh, et al. Braz Dent J 2013 [26]	Post operative pain; Visual Analogue Scale (VAS)	G I-Ca(OH) ₂ + CHX(2%); GII-CHXgel(2%); GIII-Ca(OH) ₂ paste; G-IV Control (no dressing)	4h, 24h, 48h, 72h, 96h	Groups I and II were significantly more effective in reducing the postoperative pain values than Groups III and IV (P < 0.05)
5.	Khattak, et al, JKCD, 2014 [27]	Post operative pain; VAS	G I-Ca(OH) ₂ + CHX(2%); GII-Ca(OH) ₂ + 0.9% Normal Saline	6h, 12h, 24h, 48h	Group I was significantly more effective in reducing post operative pain in comparison to Group III and IV (P = 0.001)
6.	Menakaya, et al. JCDP 2015 [28]	Post operative pain; Universal pain assessment tool	G I-Ca(OH) ₂ + 0.9% Normal Saline; GII-Ca(OH) ₂ + CHX digluconate (0.2%)	1 day, 1 week, 1, 3, 6 months	Incidence of post operative pain was lower in group 1 (not statistically significant)
7.	Ghanbarzadegan, et al. Iranian Endodon J 2019. [29]	Post operative pain; Heft Parker VAS (HP VAS)	G I-Ca(OH) ₂ + 0.9% Normal Saline; GII-Ca(OH) ₂ + CHX(2%); GIII-Ca(OH) ₂ + Dexamethasone (8 mg / 2 ml)	4h, 24h, 48h, 72h, 96h	Significant difference (P < 0.05) was found in terms of mean pain at 24,48 and 72 hours between GI and GIII. GIII was more effective in reducing pain
8.	Alarbeed, et al. Acta Scientific Dental Sciences 2019 [30]	Post operative pain; Numeric Rating Scale (NRS)	G I-Ca(OH) ₂ + CHX(2%); GII-Ca(OH) ₂ paste; GIII-cotton pellet (placebo)	4h, 24h, 48h, 14 days	G I showed lower post operative pain than G II and G III (P < 0.001) at 24h, 48h and 14 days
9.	Thakur, et al. IP Indian Journal of Conservative and Endodontics; 2020 [31]	Post operative pain; VAS	G I- Ca(OH) ₂ paste; GII-Ca(OH) ₂ + Iodoform; GIII-Ca(OH) ₂ points; GIV-Ca(OH) ₂ + Chitosan(0.2%) GV-Cotton pellete	12h, 24h, 48h	The medicament causing least post operative pain were GI> G III> G IV> G II (P < 0.05)
10.	Arslan, et al. Clin Oral Invest 2020 [32]	Post operative pain; VAS	G I-Ca(OH) ₂ + 0.9% Saline; G II-Ca(OH) ₂ + 20 mg/ml Lidocaine HCl with epi (0.0125 mg/ml)	Everyday for a week	G II resulted in less pain in comparison to G I (P < 0.05)

Ca(OH)₂, calcium hydroxide; CHX, chlorhexidine; CPMC, camphorated paramonochlorophenol; G, group; HCl, hydrochloric acid.

to the fact that all studies conducted on these parameters were at different stages of treatment, and the case selection was not concise. There are no strict guidelines for the duration of the medication's use or the volume of vehicle used. There was a certain amount of heterogeneity in the data extracted from all the included studies; hence, the current scoping review was used to identify gaps in the literature and serve as a foundation for future studies that address these gaps.

In 1920, Hermann introduced an alkaline substance in dentistry, Ca(OH)₂, with a pH of approximately 12.5. Ca(OH)₂ has endured the test of time in the bewildering diversity of the materials used in endodontics. Its biological activities are manifested by the dissociation of

Ca²⁺ and OH⁻ ions. Dentinal permeability, as well as the interlinkage between dentine and OH⁻ ions, influences the passage of OH⁻ ions into dentine. [21,33,34] Dentine permeability is mostly determined by tubular anatomy, tubular density, tubule length and diameter, and dentine buffering capacity [35,36]. The antibacterial effect of Ca(OH)₂ is ascribed to its alkalinity. It is also reported to have a tissue-altering effect, ability to lower the intracanal microbial load, modify the bacterial cell wall, and denature bacteria-produced toxins. Because of its antibacterial and tissue-altering characteristics, Ca(OH)₂ has been hypothesized to have pain-relieving properties. It also aids in the regulation of inflammatory processes and induces repair [16].

The antibacterial effect of calcium hydroxide is due to the release of highly oxidizing free radicals. When hydroxyl ions interact with bacteria, they cause phospholipid peroxidation that damages the bacterial cytoplasmic membrane. Hydroxyl ions also harm DNA, thereby preventing replication. Its high pH results in the breakdown of protein ionic bonds, resulting in protein denaturation and inhibition of cellular metabolism [37].

Elevated pH of the medicament inhibits macrophage adherence and lowers matrix metalloproteinase-8 (MMP-8) levels. This reduces inflammation and exudation, further reducing the pain.

However, this may fail to occur as a result of the dentin-buffering effect, which allows microbial proliferation [17] or the resistance offered against $\text{Ca}(\text{OH})_2$ by certain canal microbiota in addition to the ineffectiveness of $\text{Ca}(\text{OH})_2$ to penetrate deep into the dentinal tubules [11,18].

As discussed earlier, three main types of media are used as vehicles for calcium hydroxide—aqueous, viscous, and oily media. There is a great deal of disparity among the use of an optimum medium for $\text{Ca}(\text{OH})_2$ that would aid in diminishing postoperative pain. According to Estrela et al., when calcium hydroxide distilled water (aqueous vehicle) paste was used, the liberation of Ca^{2+} and OH^- ions was faster and more significant, indicating their rapid action in reducing pain [19,38]. Another study by Gomes et al. found that oily vehicles boost the antibacterial properties of $\text{Ca}(\text{OH})_2$ against *E. faecalis* and other microorganisms, showing greater zones of microbial inhibition with oily vehicles than those with aqueous and viscous vehicles [39]. This disparity in the literature provides inconclusive information regarding which vehicles are better suited to aid adequate microbial reduction and pain prevention.

Heling et al. (1992) advocated the use of CHX as a vehicle in an effort to improve the antimicrobial capacity of $\text{Ca}(\text{OH})_2$ pastes because of its activity against the diverse microbiota of gram-positive, gram-negative, aerobic, and facultative anaerobic microorganisms, yeasts, and viruses, as well as its low level of cytotoxicity

to host tissue [40,41]. It is believed to have a bacteriostatic effect at lower concentrations and a bactericidal effect at higher concentrations. The combination of CHX and $\text{Ca}(\text{OH})_2$ has higher microbial activity, which is attributed to its pain-relieving properties [41].

The $\text{Ca}(\text{OH})_2$ /CPMC mixture is an efficient oil-based mixture of the two medications that has a synergistic effect against the polymicrobial root canal flora. Evidence suggests that a combination of $\text{Ca}(\text{OH})_2$ and CPMC has a wider antimicrobial spectrum and kills microorganisms at a faster rate compared with $\text{Ca}(\text{OH})_2$ integrated with inert vehicles such as water, saline, and glycerine [8].

Lidocaine Hydrochloride (HCl) is routinely used as a topical local anesthetic solution [42–44]. When combined with $\text{Ca}(\text{OH})_2$, it acts as an aqueous vehicle for the rapid dissociation of ions, contributing to their antimicrobial properties.

Chitosan is a natural polymer produced by the deacetylation of chitin in the cells of crabs and shrimp. Biocompatibility, biodegradability, bioadhesion, and toxicity to humans are all properties of this substance. It can chelate numerous metal ions in acidic circumstances, as well as a broad antibacterial spectrum, contributing to its success in endodontic treatment. Chitosan's chelating effect aids in the elimination of the inorganic fraction of the smear layer, and when combined with $\text{Ca}(\text{OH})_2$, it extends the duration of action of the medicament [45].

Apexcal is a viscous polyethylene glycol-based paste with calcium hydroxide (29%), bismuth carbonate (22%), and excipients (polyethylene glycol, glycerine, and water) (49%) that maintains a homogeneous consistency during its action.

Walton et al. evaluated post-treatment pain using $\text{Ca}(\text{OH})_2$ - H_2O paste compared to a cotton pellet. Post-treatment pain was assessed for 48 hours as none, mild, moderate, or severe. They concluded that there was no significant difference in post-treatment pain between the two groups at any period or with any diagnosis or symptom [46]. No controls were used for this study.

Among the included studies, six evaluated the effect

of CHX as a vehicle compared with various other vehicles, such as saline, CPMC/glycerine paste (oily vehicle), and dexamethasone. Gama et al. evaluated the incidence of postoperative pain after intracanal dressing with either 0.12% CHX digluconate or a CH/CMPC paste among treatment and retreatment cases, which were further grouped based on the presence/absence of apical periodontitis. The pain intensity was recorded as the level of discomfort experienced by the patient, which was categorized as no pain, mild, moderate, or severe pain. The total sample size was 138, of which 58 were asymptomatic cases in each group. There was no statistically significant difference in the incidence of postoperative pain between the two groups, which could be attributed to the lower concentration of CHX [15].

In their randomized clinical trial, Singh et al. assessed the effect of Ca(OH)_2 paste mixed with CHX gel (2%) and a commercially available calcium hydroxide paste on 68 mandibular molars diagnosed with pulpal necrosis and acute apical periodontitis. Pain was recorded at intervals of 24 h, 48 h, 72 h, and 96 h using VAS. The combination of Ca(OH)_2 and CHX gel significantly reduced postoperative pain. This could be attributed to the synergistic effect of the antimicrobial properties of CHX and Ca(OH)_2 [26].

Khattak et al. (2014) aimed to determine the efficacy of 2% CHX (aqueous vehicle) compared to normal saline, which is also an aqueous vehicle, in 80 subjects. The pain assessment tool used was the VAS, which was assessed at 6, 12, 24, and 48 h. The study reported lower pain levels in the CHX group than in the saline group. The reduction in pain was substantial at 6 h and 24 h. The properties of Ca(OH)_2 are improved by CHX by lowering the endotoxin content in the root canal, which could explain its success [27].

In their randomized control trial in 2015, Menakaya et al. compared the efficacy of Ca(OH)_2 combined with normal saline (aqueous vehicle) and 0.2% chlorhexidine digluconate on postoperative pain. The pain intensity was assessed using the universal pain assessment tools, recorded at intervals of 1 d, 1 week, and 1, 3, and 6 months after obturation. Postoperative pain occurred only

at 1 day and 1-week intervals. The incidence of postoperative pain was higher in the experimental group than in the control group; however, this difference was not statistically significant. The results of this study were inconsistent with those of a previous study by Khattak et al., which could be attributed to the lower concentration of CHX used in this study. The lower concentration of CHX used may have contributed to the lower antimicrobial action of the mixture [28].

In a 2019 study, Ghanbarzadegan et al. compared the effects of three different vehicles: CHX (2%), normal saline, and dexamethasone. Pain severity was measured using the HP VAS scale at intervals of 4, 24, 48, 72, and 96 h. At the 4-hour interval, there was no statistically significant difference in mean pain; however, G1 and G3 exhibited a significant difference in mean pain from day 1 to 72 h, which was not statistically significant at 96 h. In comparison to CHX, the combination of Ca(OH)_2 and dexamethasone had a significant short- and medium-term effect on postoperative pain levels [29].

Alarbeed et al. (2019) evaluated the effect of Ca(OH)_2 mixed with CHX gel as a vehicle at a concentration of 2% in comparison to commercially available Ca(OH)_2 pastes with no medication as the control group. Intracanal medication was administered for 14 days, and postoperative pain intensity was recorded at 4h, 24h, 48h, and 14 days. Each group showed an increase in the median pain value from pre-operative to 24 hours post-operative records, followed by a gradual decrease from 48 hours to 14 days postoperatively. The CHX group experienced significantly less postoperative pain than the Ca(OH)_2 paste group, as measured by a numeric rating scale [30].

In all the above studies, there was a great deal of heterogeneity concerning the concentration of the vehicle used, the control group taken, the period for which the pain was evaluated, and the pain assessment tool used. This lacuna in the studies provides an inconclusive result as to which vehicle has better pain-preventive properties.

In a study by Arslan et al., 60 patients with irreversible pulpitis and symptomatic apical periodontitis with preoperative spontaneous pain and percussion pain were

included. The patients were randomly assigned to one of two groups based on the Ca(OH)₂ vehicle: a control group (mixed with saline) and a second group (n = 30) mixed with lidocaine HCl. Postoperative spontaneous pain scores were recorded using a VAS everyday for one week. During days 1 to 4, the Ca(OH)₂ mixed with lidocaine HCl group experienced significantly less pain than the Ca(OH)₂ mixed with saline group (P < 0.05), indicating the efficacy of lidocaine as a suitable vehicle for pain reduction [32]. Lidocaine was used as the vehicle in only one study. The lack of sufficient literature does not provide concrete evidence for the efficacy of a given vehicle. To reach a definitive conclusion, further studies should be conducted by considering lidocaine as a vehicle.

Thakur et al. compared the effects of different formulations of the Ca(OH)₂ medicament on postoperative pain by incorporating several carriers into the Ca(OH)₂ powder. Group 1: Intracanal medicament was calcium hydroxide paste (Ivoclar); Group 2: intracanal medicament Ca(OH)₂ paste with iodoform (Metapex); Group 3: Ca(OH)₂ points (Hygienic) were used as an intracanal medicament; Group 4: Ca(OH)₂ paste with chitosan (0.2%) as a vehicle was used as an intracanal medicament; Group 5 (control group): dry sterile cotton. According to patient records in the VAS scale, the incidence and intensity of preoperative pain and experienced postoperative pain (on the 6th, 12th, 24th, and 48th h) following the first visit to treatment were analyzed [31]. The Ca(OH)₂ points recorded the lowest postoperative pain at the sixth postoperative hour, while the Ca(OH)₂ with iodine (Metapox) points recorded the highest postoperative pain. Ca(OH)₂ paste (Apexcal) caused the least postoperative pain at the 12th, 24th, and 48th postoperative hours.

Chitosan is a relatively new vehicle, and there is insufficient literature to support its effectiveness as a vehicle to reduce post-treatment pain.

The use of pain assessment tools forms a baseline for comparing and analyzing data from various studies. All the studies included in this review showed a great disparity in terms of inclusion criteria, the parameters for

accessing pain, the time for which the medication was left in the canal, and the time intervals at which postoperative pain was checked. There was a great amount of heterogeneity in the methodologies used in these studies, indicating the need to use a standardized pain assessment tool for analyzing the data quantitatively to reach a definite conclusion. With such disparities in pain assessment, a meta-analysis cannot be applied, and it is difficult to reach a definitive conclusion.

This heterogeneity in methodology, case selection, and agents used gives inconclusive results. The majority of studies confirmed a positive effect of the use of various vehicles on postoperative pain; however, the available evidence is considered insufficient to either support or refute the use of various vehicles to aid in lowering postoperative pain. Further randomized controlled trials are required to reach definitive conclusions. Our scoping review indicates that future studies should focus on using different vehicles at various concentrations and application times with definitive inclusion and exclusion criteria to check for viable and safe exposure in addition to providing pain relief.

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