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Effects of Intracanal Medicaments on Postoperative Pain: A Comparative Study of Calcium Hydroxide, Triple Antibiotic Paste, and Chlorhexidine

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Abstract

Introduction: Postoperative pain is a common concern following endodontic treatment and may be influenced by intracanal medication. This study compared postoperative pain associated with calcium hydroxide ($Ca(OH)_2$), triple antibiotic paste (TAP), 2% chlorhexidine (CHX), and saline.

Materials and methods: This prospective study included 120 patients (30 per group). The patients received $Ca(OH)_2$, TAP, 2% CHX, or saline as intracanal medicaments during routine endodontic treatment. Pain intensity was recorded using a visual analog scale (VAS) preoperatively and at 6, 12, 24, 48, 72 hours, and 7 days postoperatively. Between-group differences were assessed using the Kruskal-Wallis test, followed by Bonferroni-adjusted Mann-Whitney U tests. Within-group changes were assessed using the Wilcoxon signed-rank test.

Results: Baseline pain was comparable between the groups (median, 7.0; $p = 0.936$). Significant between-group differences were observed at all postoperative intervals ($p < 0.001$). At six hours, the median VAS scores for $Ca(OH)_2$, TAP, 2% CHX, and saline were 5.0, 4.0, 5.0, and 6.0, respectively. At 24 hours, the scores were 3.0, 2.0, 3.0, and 5.0, while at 7 days, they were 0.0, 0.0, 0.0, and 2.0. The effect size increased from $\varepsilon^2 = 0.208$ at six hours to 0.509 at seven days. TAP showed less pain than calcium hydroxide and 2% CHX from 24 hours onward.

Conclusion: Postoperative pain decreased in all groups, with lower pain scores observed in the $Ca(OH)_2$, TAP, and 2% CHX groups than in the saline comparison group. TAP was associated with the lowest pain scores, while $Ca(OH)_2$ and CHX showed comparable outcomes. These findings suggest that the choice of intracanal medicament may influence postoperative pain; however, the results should be interpreted in light of the observational study design and the limited antimicrobial role of saline as a comparison condition.

Categories: Dentistry
Keywords: calcium hydroxide, chlorhexidine, endodontics, postoperative pain, root canal therapy

Introduction

Postoperative pain is a common clinical concern following endodontic treatment and may negatively affect patient comfort, satisfaction, and perception of treatment [1]. Although root canal treatment is primarily directed toward the elimination of microbial infection and prevention of reinfection, instrumentation and chemical procedures may induce transient inflammatory responses in the periapical tissues [2]. The extrusion of microorganisms, infected debris, or irrigating and medicament materials beyond the apical foramen may further contribute to postoperative discomfort [3]. Therefore, effective intracanal disinfection while minimizing postoperative inflammatory responses remains an important consideration in endodontic treatments.

Intracanal medicaments are commonly used to reduce the microbial load within the root canal system and to control persistent infections during treatment [4]. Calcium hydroxide ($Ca(OH)_2$) has traditionally been used because of its high alkalinity and antimicrobial activity [5]. Triple antibiotic paste (TAP), consisting of a combination of antibiotics, has also been investigated for its ability to target a broad spectrum of endodontic microorganisms [6]. Chlorhexidine (CHX), particularly at 2% concentration, possesses substantial antimicrobial activity and substantivity and has therefore been used as an intracanal antimicrobial agent [7]. In contrast, saline provides a relatively inert comparison condition and allows the

assessment of pain outcomes in the absence of a specific antimicrobial medication.

Shahnawaz et al. [8] reported that triple antibiotic paste produced the greatest reduction in *Enterococcus faecalis* counts, followed by 2% CHX gel and $Ca(OH)_2$, whereas saline showed substantially less microbial reduction. These findings provide a rationale for further clinical evaluation of these medicaments with respect to postoperative pain and patient-centered outcomes. Despite the widespread use of intracanal medicaments, the differences in their effects on postoperative pain remain clinically relevant.

A comparative evaluation of commonly used medicaments at multiple postoperative intervals may help clarify their relative effects on the temporal pattern and magnitude of pain following endodontic treatment. Therefore, this study aimed to compare postoperative pain following the use of $Ca(OH)_2$, TAP, 2% CHX, and saline as intracanal medications. The objectives were to evaluate and compare pain intensity among the four groups at 6, 12, 24, 48, and 72 hours and 7 days after treatment and to assess the change in pain from the preoperative level to 7 days within each treatment group.

Materials And Methods

Study design and setting

This prospective study was conducted in the Department of Conservative Dentistry and Endodontics, RKDF Dental College and Research Centre, Bhopal, Madhya Pradesh, India, from July to December 2022. The study was conducted as part of routine clinical endodontic procedures performed in the department, and the investigator prospectively assessed the postoperative pain following root canal treatment. Ethical approval (RKDF/DC/2022/SS-042) was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants before inclusion.

Participants and eligibility criteria

Adult patients presenting to the Department of Conservative Dentistry and Endodontics who required nonsurgical root canal treatment were screened consecutively for eligibility during the study period. Patients meeting the predefined inclusion criteria and none of the exclusion criteria were considered for inclusion. Eligible participants were enrolled prospectively, and postoperative pain was assessed at the predefined follow-up intervals. The final study sample comprised 120 participants, with 30 participants in each of the four medicament groups. The eligibility criteria are summarized in Table *1*.

Inclusion criteria	Exclusion criteria
Adult patients aged ≥18 years	Patients below 18 years of age
Presented to the department and required routine nonsurgical root canal treatment	Unable to understand the VAS
The involved tooth was restorable	The involved tooth was non-restorable
Clinical diagnosis of symptomatic irreversible pulpitis or pulp necrosis associated with symptomatic apical periodontitis	Clinical diagnosis other than symptomatic irreversible pulpitis or pulp necrosis with symptomatic apical periodontitis
Diagnosis is established based on presenting symptoms, clinical examination, pulp sensibility findings, percussion and palpation responses, and appropriate preoperative radiographic assessment	Diagnosis could not be reliably established due to inadequate clinical or radiographic information
Able to understand the VAS	Unable to reliably communicate or quantify pain intensity
Able to comply with scheduled postoperative assessments	Incomplete pain records or missing assessments at predefined postoperative time points

TABLE 1: Inclusion and exclusion criteria

VAS: visual analog scale.

Clinical procedure

After a diagnosis was established from the presenting symptoms, clinical examination, pulp sensibility testing, percussion and palpation findings, and preoperative radiographs [9], all endodontic procedures were performed by a single experienced endodontist with more than five years of clinical experience. A standardized two-visit non-surgical root canal treatment protocol was followed for all participants. Local

anesthesia was administered according to the tooth involved, followed by rubber dam isolation. The operative field was disinfected, and caries and unsupported tooth structures were removed before preparation of the access cavity. Canal orifices were identified and negotiated with stainless steel K-files (Dentsply Maillefer, Ballaigues, Switzerland). Working length was determined using an electronic apex locator (Dentaport ZX; J. Morita Corp., Kyoto, Japan) and subsequently verified using a periapical radiograph.

The canals were prepared using ProTaper Universal nickel-titanium rotary instruments (Dentsply Maillefer, Ballaigues, Switzerland) in a crown-down technique to a final apical size of ProTaper F3 (size 30, 0.09 taper) or F4 (size 40, 0.06 taper) as indicated by canal anatomy and apical gauging. Throughout instrumentation, approximately 15-20 mL of 3% sodium hypochlorite was used per canal, delivered in frequent aliquots (~2 mL after each instrument) via a 30-gauge side-vented irrigation needle placed 1-2 mm short of the established working length without binding. No additional irrigant activation (ultrasonic, sonic, or laser) was performed; irrigation was accomplished by conventional syringe delivery with gentle apical-coronal motion. Following completion of biomechanical preparation, the canals were irrigated with 17% EDTA for three minutes, followed by a final rinse with 5 mL sterile saline.

Patients were categorized according to the intracanal medication used during routine clinical treatment: Group I, $Ca(OH)_2$; Group II, TAP; Group III, 2% CHX; and Group IV, saline, with 30 patients in each group. The investigator did not determine or modify the choice of medication for study purposes; the medication routinely used during treatment was recorded prospectively. For Group I, $Ca(OH)_2$ paste (Ultracal XS; Ultradent Products Inc., South Jordan, UT, USA) was introduced into the prepared root canal using a size 25 Lentulo spiral (Dentsply Maillefer, Ballaigues, Switzerland), positioned approximately 2 mm short of the established working length. The canal was filled uniformly with medication without intentional extrusion beyond the apical foramen.

In Group II, TAP was prepared from ciprofloxacin, metronidazole, and minocycline in a 1:1:1 ratio. Ciprofloxacin (500 mg; Ranbaxy Laboratories Ltd., Mumbai, India), metronidazole (400 mg; J.B. Chemicals & Pharmaceuticals Ltd., Mumbai, India), and minocycline (Minoz 100 mg; Ranbaxy Laboratories Ltd.) were pulverized under aseptic conditions and mixed in equal proportions by weight. Antibiotic powder was combined with sterile 0.9% saline to obtain a homogeneous paste of intracanal consistency. The prepared TAP was introduced into the canal using a size 25 Lentulo spiral (Dentsply Maillefer, Ballaigues, Switzerland), maintaining the delivery instrument at approximately 2 mm short of the working length.

For Group III, 2% CHX gel (Gluco-Chex 2%; Cerkamed, Stalowa Wola, Poland) was placed into the prepared canal using a syringe with an intracanal delivery tip. The medicament was gradually introduced to ensure adequate filling of the canal while avoiding apical extrusion. For Group IV, sterile 0.9% saline was introduced into the prepared canal using the same general intracanal delivery approach and served as the comparison condition. After placement of the assigned medication, excess material was removed from the pulp chamber, and a sterile cotton pellet was placed over the canal orifices. The access cavity was temporarily sealed with reinforced zinc oxide-eugenol restorative material (IRM; Dentsply Sirona, Charlotte, NC, USA) to prevent coronal leakage and contamination during the interappointment period.

The intracanal medicaments were left in place for seven days. Patients returned for the second visit at seven days, when the medicament was removed and the canals were obturated. At the second appointment, the temporary restoration was removed, and the intracanal medicament was eliminated by copious irrigation with sterile saline and gentle canal instrumentation. The canals were subsequently dried with sterile paper points and obturated with gutta-percha cones and an epoxy resin-based sealer using a standardized obturation technique. The access cavity was restored using a routine restorative protocol. The same experienced endodontist performed all the clinical procedures to minimize operator-related variability.

Assessment of postoperative pain

Pain intensity was assessed using a 10-cm VAS, a validated patient-reported measure of pain intensity. The scale consisted of a horizontal 10-cm line anchored at 0, representing “no pain,” and 10, representing “worst pain imaginable.” VAS was selected because it provides a continuous measure of perceived pain intensity and has been widely used for the assessment of acute and postoperative pain [10]. Scores were recorded to one decimal place, with higher values indicating greater pain intensity.

Before the initiation of treatment and prior to the administration of local anesthesia, each patient was instructed by the investigator on how to use the VAS. Patients were asked to place a mark on the line corresponding to the intensity of the pain they experienced at that particular time. The distance in millimeters from the 0-mm endpoint to the patient's mark was recorded as the VAS score, with higher values indicating greater pain intensity. Patients were instructed to use the same scale and method of assessment at every subsequent time point and to base each assessment on their pain at that specific time rather than recalling the maximum pain experienced during the preceding interval.

Preoperative pain was recorded immediately prior to treatment. Postoperative pain was assessed 6, 12, 24,

48, and 72 hours and 7 days after treatment. A standardized pain diary containing the VAS was provided to each participant, and the patients were instructed to record their pain at each predefined assessment time. Where required, participants were contacted at scheduled assessment intervals to minimize missing observations and ensure completion of the pain diary. Similar VAS-based pain diaries with assessments at 6, 12, 24, 48, and 72 hours, and 7 days have been used in clinical studies of postoperative endodontic pain.

Analgesic use was recorded because postoperative analgesics can modify reported pain intensity. Patients were instructed to document any analgesic taken during follow-up, including the name, dose, and time, in the pain diary, together with the corresponding VAS assessment. They were advised not to take an analgesic without recording it. Analgesic consumption was then considered when interpreting the postoperative pain scores. No participant was excluded because of analgesic use. VAS assessment and postoperative follow-up were standardized across all four groups.

Sample size calculation

The sample size was calculated using G*Power version 3.1.9.7 (Heinrich Heine University Düsseldorf, Düsseldorf, Germany) for a one-way analysis of variance comparing four groups. Based on a previous study reporting an effect size of Cohen's f = 0.34 for pain reduction with intracanal medicaments [11], with 80% power ($1-\beta = 0.80$) and a 5% alpha error ($\alpha = 0.05$), the analysis yielded a total of 100 patients (25 per group) across four groups. Allowing for an anticipated 20% loss to follow-up, the target was increased to 120 patients, with 30 participants in each group.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (Released 2011; IBM Corp., Armonk, NY, USA). Normality was assessed with the Shapiro-Wilk test. Because the continuous variables were not normally distributed, they were summarized as median and interquartile range (IQR). Categorical variables were summarized as frequencies and percentages. Postoperative VAS scores were compared between groups with the Kruskal-Wallis H test, followed by Bonferroni-adjusted Mann-Whitney U tests for pairwise comparisons. The change from preoperative pain to the seven-day score within each group was assessed with the Wilcoxon signed-rank test. Categorical variables were compared with the chi-square test. Effect sizes were reported as epsilon-squared (ε^2) for the Kruskal-Wallis tests and as r for the pairwise and within-group tests. Statistical significance was set at $p < 0.05$.

Results

A total of 120 patients were included in the study, with 30 patients in each group. No participant in any group reported using a rescue analgesic during the seven-day follow-up. The baseline demographic and clinical characteristics were comparable among the four groups. Median age ranged from 31.0 to 34.0 years ($p = 0.743$), while sex distribution ($p = 0.958$), tooth type ($p = 0.996$), preoperative pain scores ($p = 0.936$), and pulp/periapical diagnosis ($p = 0.990$) showed no significant between-group differences. The median preoperative VAS score was 7.0 in all groups (Table *2*).

Characteristic		Group I, $Ca(OH)_2$ (n = 30)	Group II, TAP (n = 30)	Group III, 2% CHX (n = 30)	Group IV, saline (n = 30)	Test statistic	p-value
Age (years)	Median (IQR)	32.5 (26-41)	34.0 (27-42)	31.0 (25-40)	33.5 (28-43)	H = 1.24	0.743
Sex, n (%)	Male	14 (46.7%)	13 (43.3%)	15 (50.0%)	14 (46.7%)	χ^2 = 0.31	0.958
	Female	16 (53.3%)	17 (56.7%)	15 (50.0%)	16 (53.3%)		
Tooth type, n (%)	Maxillary anterior	8 (26.7%)	7 (23.3%)	8 (26.7%)	7 (23.3%)	χ^2 = 1.87	0.996
	Maxillary posterior	6 (20.0%)	7 (23.3%)	6 (20.0%)	7 (23.3%)		
	Mandibular anterior	7 (23.3%)	8 (26.7%)	7 (23.3%)	8 (26.7%)		
	Mandibular posterior	9 (30.0%)	8 (26.7%)	9 (30.0%)	8 (26.7%)		
Preoperative pain (VAS)	Median (IQR)	7.0 (6-8)	7.0 (6-8)	7.0 (5-8)	7.0 (6-8)	H = 0.42	0.936
Pulp/periapical diagnosis, n (%)	Symptomatic irreversible pulpitis	12 (40.0%)	11 (36.7%)	12 (40.0%)	11 (36.7%)	χ^2 = 0.87	0.990
	Necrotic pulp with symptomatic apical periodontitis	18 (60.0%)	19 (63.3%)	18 (60.0%)	19 (63.3%)		

TABLE 2: Baseline characteristics of the study participants according to intracanal medicament group

Data are presented as median and interquartile range (IQR) for continuous variables and n (%) for categorical variables. Continuous variables were compared using the Kruskal-Wallis H test, and categorical variables were compared using the chi-square test. $p < 0.05$ was considered statistically significant.

$Ca(OH)_2$: calcium hydroxide, TAP: triple antibiotic paste, CHX: chlorhexidine.

Postoperative pain scores differed significantly among the four groups at 6, 12, 24, 48, and 72 hours and at 7 days (all $p < 0.001$). At six hours, the median VAS scores were 5.0, 4.0, 5.0, and 6.0 in the $Ca(OH)_2$, TAP, 2% CHX, and saline groups, respectively. At 24 hours, the corresponding scores were 3.0, 2.0, 3.0, and 5.0, which decreased further at 72 hours to 1.0, 0.0, 1.0, and 3.0, respectively. At day 7, the median VAS scores were 0.0, 0.0, 0.0, and 2.0, respectively. The between-group effect size increased from $\varepsilon^2 = 0.208$ at six hours to $\varepsilon^2 = 0.509$ at seven days (Table *3*).

Time interval	Group I, $Ca(OH)_2$ (n = 30)	Group II, TAP (n = 30)	Group III, 2% CHX (n = 30)	Group IV, saline (n = 30)	Kruskal-Wallis H	p-value	Effect size (ε^2)
Preoperative VAS, median (IQR)	7.0 (6-8)	7.0 (6-8)	7.0 (5-8)	7.0 (6-8)	0.42	0.936	0.005
6 hours, median (IQR)	5.0 (4-6)	4.0 (3-5)	5.0 (4-6)	6.0 (5-7)	18.74	<0.001*	0.208
12 hours, median (IQR)	4.0 (3-5)	3.0 (2-4)	4.0 (3-5)	5.5 (4-7)	24.31	<0.001*	0.270
24 hours, median (IQR)	3.0 (2-4)	2.0 (1-3)	3.0 (2-4)	5.0 (4-6)	31.56	<0.001*	0.351
48 hours, median (IQR)	2.0 (1-3)	1.0 (0-2)	2.0 (1-3)	4.0 (3-5)	38.92	<0.001*	0.432
72 hours, median (IQR)	1.0 (0-2)	0.0 (0-1)	1.0 (0-2)	3.0 (2-4)	42.17	<0.001*	0.468
7 days, median (IQR)	0.0 (0-1)	0.0 (0-0)	0.0 (0-1)	2.0 (1-3)	45.83	<0.001*	0.509

TABLE 3: Postoperative pain intensity according to intracanal medicament group during the follow-up period

Data are presented as median (interquartile range). Between-group comparisons at each assessment time were performed using the Kruskal-Wallis H test. Epsilon-squared (ε^2) was reported as the effect-size measure for the Kruskal-Wallis test.

*p < 0.05 was considered statistically significant.

VAS: visual analog scale, $Ca(OH)_2$: calcium hydroxide, TAP: triple antibiotic paste, CHX: chlorhexidine.

Pairwise analysis showed significantly lower pain scores in each medication group than in the saline group at all postoperative time points ($p < 0.05$). TAP also showed significantly lower pain scores than $Ca(OH)_2$ and 2% CHX from 24 hours onward ($p = 0.038$ and $p = 0.021$ at 24 hours and $p = 0.004$ and $p = 0.002$ at 7 days, respectively). No significant differences were observed between $Ca(OH)_2$ and 2% CHX at any time point (all $p > 0.05$) (Table 4).

Time	Comparison	U statistic	p-value (adjusted)	Effect size (r)
6 hours	Group I vs. Group IV	312.5	0.042*	0.37
	Group II vs. Group IV	198.0	<0.001*	0.58
	Group III vs. Group IV	345.0	0.048*	0.33
	Group I vs. Group II	378.0	0.186	0.18
	Group I vs. Group III	442.5	0.892	0.03
	Group II vs. Group III	356.0	0.098	0.21
12 hours	Group I vs. Group IV	285.0	0.018*	0.41
	Group II vs. Group IV	162.0	<0.001*	0.64
	Group III vs. Group IV	318.0	0.036*	0.36
	Group I vs. Group II	342.0	0.072	0.23
	Group I vs. Group III	438.0	0.845	0.04
	Group II vs. Group III	324.0	0.048*	0.27
	Group I vs. Group IV	246.0	0.006*	0.47
	Group II vs. Group IV	118.5	<0.001*	0.73

24 hours	Group III vs. Group IV	276.0	0.014*	0.42
	Group I vs. Group II	312.0	0.038*	0.28
	Group I vs. Group III	435.0	0.812	0.04
	Group II vs. Group III	288.0	0.021*	0.33
48 hours	Group I vs. Group IV	198.0	<0.001*	0.56
	Group II vs. Group IV	84.0	<0.001*	0.82
	Group III vs. Group IV	234.0	0.004*	0.48
	Group I vs. Group II	276.0	0.014*	0.35
	Group I vs. Group III	428.0	0.762	0.05
	Group II vs. Group III	252.0	0.007*	0.40
72 hours	Group I vs. Group IV	162.0	<0.001*	0.62
	Group II vs. Group IV	66.0	<0.001*	0.87
	Group III vs. Group IV	198.0	<0.001*	0.55
	Group I vs. Group II	246.0	0.006*	0.40
	Group I vs. Group III	420.0	0.698	0.06
	Group II vs. Group III	228.0	0.004*	0.44
7 days	Group I vs. Group IV	138.0	<0.001*	0.67
	Group II vs. Group IV	48.0	<0.001*	0.91
	Group III vs. Group IV	174.0	<0.001*	0.60
	Group I vs. Group II	228.0	0.004*	0.44
	Group I vs. Group III	408.0	0.612	0.07
	Group II vs. Group III	210.0	0.002*	0.48

TABLE 4: Pairwise comparisons of postoperative pain intensity (VAS scores) between intracanal medicament groups

Pairwise comparisons were performed using the Mann-Whitney U test with Bonferroni adjustment for multiple comparisons. The effect size was expressed as r, *p < 0.05; after adjustment, it was considered statistically significant.

Group I: calcium hydroxide, $Ca(OH)_2$; Group II: triple antibiotic paste, TAP; Group III: 2% chlorhexidine, CHX; Group IV: saline.

VAS: visual analog scale.

Within-group analysis demonstrated a significant reduction in pain from baseline to seven days in all the groups ($p < 0.001$). The median reduction was -7.0 in the TAP group ($Z = -4.82$, $r = 0.88$), -6.0 in both the $Ca(OH)_2$ ($Z = -4.78$, $r = 0.87$) and 2% CHX groups ($Z = -4.75$, $r = 0.87$), and -5.0 in the saline group ($Z = -4.62$, $r = 0.84$) (Table 5).

Group	Preoperative, median (IQR)	7-day, median (IQR)	Median difference (IQR)	Wilcoxon Z	p-value	Effect size (r)
Group I, $Ca(OH)_2$	7.0 (6-8)	0.0 (0-1)	-6.0 (-7 to -5)	-4.78	<0.001*	0.87
Group II, TAP	7.0 (6-8)	0.0 (0-0)	-7.0 (-7 to -6)	-4.82	<0.001*	0.88
Group III, 2% CHX	7.0 (5-8)	0.0 (0-1)	-6.0 (-7 to -5)	-4.75	<0.001*	0.87
Group IV, saline	7.0 (6-8)	2.0 (1-3)	-5.0 (-6 to -4)	-4.62	<0.001*	0.84

TABLE 5: Within-group changes in pain intensity (VAS scores) from preoperative assessment to seven days

Data are presented as median (interquartile range); within-group changes were assessed using the Wilcoxon signed-rank test. The effect size was expressed as r. *p < 0.05 was considered statistically significant.

VAS: visual analog scale, $Ca(OH)_2$: calcium hydroxide, TAP: triple antibiotic paste, CHX: chlorhexidine.

Discussion

This study evaluated postoperative pain following endodontic treatment in patients receiving $Ca(OH)_2$, TAP, 2% CHX, or saline as intracanal medicaments. The four groups were comparable with respect to age, sex, tooth type, preoperative pain, and pulpal/periapical diagnosis, providing a relatively consistent baseline for the interpretation of postoperative pain outcomes. A significant reduction in postoperative pain was observed across all groups during the follow-up period, although the extent of pain reduction varied according to the intracanal medications used. TAP was associated with a more favorable postoperative pain pattern, whereas saline was associated with greater residual discomfort. The progressively wider between-group differences over time suggested that the choice of intracanal medication may influence the course of postoperative pain. These findings are consistent with previous clinical evidence indicating that intracanal medicaments may contribute to reducing postoperative endodontic pain, particularly in teeth with pulpal necrosis and apical periodontitis [12].

Lower pain scores associated with TAP may be related to its broad-spectrum antimicrobial activity. TAP combines antibiotics with complementary antimicrobial spectra, potentially reducing residual intracanal microorganisms and their inflammatory products after chemomechanical preparation [6]. As postoperative pain is partly influenced by persistent microbial irritation and inflammatory mediators within the periapical tissues, more effective microbial suppression may contribute to an earlier reduction in pain [13]. Previous clinical studies have similarly reported lower postoperative pain with TAP than with calcium hydroxide, particularly during the early postoperative period [11,14]. However, the use of antibiotic-containing intracanal medicaments should be considered judiciously because antimicrobial stewardship and the potential for antibiotic resistance remain clinically relevant.

$Ca(OH)_2$ also produced substantial pain reduction, with the median VAS decreasing from 7.0 preoperatively to 0.0 at seven days. Its effect may be explained by its high alkalinity and antimicrobial activity as well as its ability to influence bacterial endotoxins and the inflammatory environment within the root canal [5]. A systematic review and meta-analysis found that $Ca(OH)_2$ reduced postoperative pain compared to no intracanal medication at 24 hours, whereas CHX and some combination medicaments demonstrated greater pain reduction at later intervals [15]. A previous study reported no significant difference in the reduction of postoperative pain between double antibiotic paste and $Ca(OH)_2$ [16]. Another study concluded that $Ca(OH)_2$ alone may have a limited influence on postoperative pain, although its effectiveness may improve when combined with other agents, such as dexamethasone [17]. The present findings therefore support $Ca(OH)_2$ as an effective intracanal medicament for reducing postoperative pain but also indicate that its analgesic effect may not be equivalent to that of TAP at later follow-up points.

The 2% CHX group demonstrated a pattern similar to that of $Ca(OH)_2$, with no significant differences between the two groups at any assessed interval. CHX possesses broad-spectrum antimicrobial activity and substantivity, allowing it to remain active within dentinal structures after application [18]. Its ability to reduce bacterial load and bacterial by-products may explain the reduction in postoperative pain observed in the present study [7]. Previous systematic review has also suggested that CHX, alone or combined with $Ca(OH)_2$, may provide greater pain reduction than $Ca(OH)_2$ alone in some clinical settings [19].

In contrast, the saline group consistently demonstrated the highest postoperative pain score. Nevertheless, pain also decreased substantially within this group, with a median reduction of five points from baseline to seven days. This finding indicates that postoperative pain is multifactorial and cannot be attributed solely to

the choice of intracanal medication. Mechanical instrumentation, irrigation, extrusion of debris or irritants, pre-existing periapical inflammation, and the natural resolution of postoperative inflammatory responses can all influence pain [20]. The present findings, therefore, suggest that intracanal medication may modify postoperative pain rather than being its sole determinant.

From a clinical perspective, these findings indicate that intracanal medicament selection may be relevant when postoperative discomfort is an important treatment consideration, particularly in teeth with necrotic pulp and symptomatic apical periodontitis. $Ca(OH)_2$ and CHX were associated with meaningful pain reduction and may remain practical options, whereas TAP was associated with the lowest postoperative pain scores in this cohort. However, selection should also consider antimicrobial indications, potential adverse effects, antibiotic stewardship, treatment protocol, and underlying pulpal and periapical diagnosis rather than pain control alone.

This study had several limitations. Its prospective observational design and the absence of randomized treatment allocation introduce the possibility of treatment-selection bias and residual confounding; therefore, causal relationships cannot be established. Furthermore, the criteria governing the selection of intracanal medicaments were not systematically documented, limiting the ability to determine whether differences in clinical decision-making influenced group allocation and the observed outcomes. The study was conducted at a single dental institution with a relatively modest sample size, which may limit the generalizability of the findings. Other factors that may influence postoperative pain, including the extent of apical instrumentation, occlusal status, analgesic use, and individual pain perception, were not comprehensively controlled or analyzed. Although operative procedures and pain assessments were standardized, the potential influence of these unmeasured factors cannot be excluded. The follow-up period was limited to seven days, and longer-term clinical outcomes were not assessed. Finally, although the VAS is a validated measure of pain intensity, postoperative pain remains subjective and may vary considerably among individuals. Future studies using clearly defined treatment-selection criteria, adequate control of confounding factors, and randomized allocation are warranted to establish the comparative effects of intracanal medicaments more reliably.

Conclusions

Postoperative pain decreased significantly in all four groups over the seven-day follow-up period. TAP was associated with the lowest pain scores, while $Ca(OH)_2$ and 2% CHX demonstrated comparable outcomes. The saline comparison group exhibited higher postoperative pain scores. These findings suggest an association between the intracanal agent used and postoperative pain; however, the nonrandomized observational design, potential treatment-selection bias, and residual confounding limit causal interpretation. Further studies with clearly defined allocation procedures and standardized treatment protocols are warranted to confirm these findings.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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References

1. Di Spirito F, Scelza G, Fornara R, Giordano F, Rosa D, Amato A: Post-operative endodontic pain management: an overview of systematic reviews on post-operatively administered oral medications and integrated evidence-based clinical recommendations. Healthcare (Basel). 2022, 10:760. 10.3390/healthcare10050760
2. Wong J, Manoil D, Näsman P, Belibasakis GN, Neelakantan P: Microbiological aspects of root canal infections and disinfection strategies: an update review on the current knowledge and challenges. Front Oral Health. 2021, 2:672887. 10.3389/froh.2021.672887
3. Tanalp J, Güngör T: Apical extrusion of debris: a literature review of an inherent occurrence during root canal treatment. Int Endod J. 2014, 47:211-21. 10.1111/iej.12137
4. Govindaraju L, Jenarthanan S, Subramanyam D, Ajitha P: Antibacterial activity of various intracanal medicament against Enterococcus faecalis, Streptococcus mutans and Staphylococcus aureus: an in vitro study. J Pharm Bioallied Sci. 2021, 13:S157-61. 10.4103/jpbs.JPBS_623_20
5. Mohammadi Z, Shalavi S, Yazdizadeh M: Antimicrobial activity of calcium hydroxide in endodontics: a review. Chonnam Med J. 2012, 48:133-40. 10.4068/cmj.2012.48.3.133
6. Panchal KG, Virani K, Patel V, Ali Khan A, Pettiwala A, Puranik SS, Joshi S: Triple antibiotic paste: a game changer in endodontics. J Pharm Bioallied Sci. 2024, 16:S1913-5. 10.4103/jpbs.jpbs_1296_23
7. Wassel M, Radwan M, Elghazawy R: Direct and residual antimicrobial effect of 2% chlorhexidine gel, double antibiotic paste and chitosan- chlorhexidine nanoparticles as intracanal medicaments against Enterococcus faecalis and Candida albicans in primary molars: an in-vitro study. BMC Oral Health. 2023, 23:296. 10.1186/s12903-023-02862-x
8. Shahnawaz K, Sarangi P, Satapathy SK, Shinkre R, Raghavendra K, Ahmed S: The effectiveness of different intracanal medicaments in treating apical periodontitis. J Pharm Bioallied Sci. 2025, 17:S2617-9. 10.4103/jpbs.jpbs_980_25
9. Azim AA, Merdad K, Peters OA: Diagnosis consensus among endodontic specialists and general practitioners: an international survey and a proposed modification to the current diagnostic terminology. Int Endod J. 2022, 55:1202-11. 10.1111/iej.13816
10. Huskisson EC: Measurement of pain. Lancet. 1974, 304:1127-31. 10.1016/s0140-6736(74)90884-8
11. Khan AM, Gangoo IK, Ali NA, et al.: The effect of calcium hydroxide, triple antibiotic paste and chlorhexidine on pain in teeth with symptomatic apical periodontitis: a randomised controlled trial. Int J Environ Res Public Health. 2023, 20:10.3390/ijerph20043091
12. Almaslamani MJ, El Mesmari MH, Ismail SM: Effect of intracanal medicament type on postoperative pain - a prospective study. Indian J Dent Res. 2025, 36:284-8. 10.4103/ijdr.ijdr_777_24
13. Al-Ani AM, Ali AH, Koller G: Assessment of bacterial load and post-endodontic pain after one-visit root canal treatment using two types of endodontic access openings: a randomized controlled clinical trial. Dent J (Basel). 2024, 12:88. 10.3390/dj12040088
14. Omaia M, Negm M, Nashaat Y, Nabil N, Othman A: The effect of triple antibiotic paste as an intracanal medicament with an anti-inflammatory agent on post-operative pain of asymptomatic uniradicular necrotic teeth: a double blind randomized clinical trial. F1000Res. 2019, 8:1687. 10.12688/f1000research.19699.3
15. Ahmad MZ, Sadaf D, Merdad KA, Almohaimeed A, Onakpoya IJ: Calcium hydroxide as an intracanal medication for postoperative pain during primary root canal therapy: a systematic review and meta-analysis with trial sequential analysis of randomised controlled trials. J Evid Based Dent Pract. 2022, 22:101680. 10.1016/j.jebdp.2021.101680
16. Samir Abouelenien S, Mohamed Ibrahim S, Gameel Shaker O, Mohamed Ahmed G: Evaluation of postoperative pain in infected root canals after using double antibiotic paste versus calcium hydroxide as intra-canal medication: a randomized controlled trial. F1000Res. 2018, 7:1768. 10.12688/f1000research.16820.1
17. Kochhar R, Bhattacharyya A, Kumari M, Punjabi M: Effect of calcium hydroxide combinations as intracanal medicament for managing post-operative pain in symptomatic apical periodontitis cases: a randomized double blinded study. IP Indian J Conserv Endod. 2025, 10:208-13. 10.18231/j.ijce.12127.1851112270
18. Poppolo Deus F, Ouanounou A: Chlorhexidine in dentistry: pharmacology, uses, and adverse effects . Int Dent J. 2022, 72:269-77. 10.1016/j.identj.2022.01.005
19. Ibrahim AM, Zakhary SY, Amin SA: Calcium hydroxide intracanal medication effects on pain and flare-up: a systematic review and meta-analysis. Restor Dent Endod. 2020, 45:e26. 10.5395/rde.2020.45.e26
20. Sadaf D, Ahmad MZ: Factors associated with postoperative pain in endodontic therapy . Int J Biomed Sci. 2014, 10:243-7.