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INPLASY

Comparative Efficacy of Different Intracanal Medications in Multiple-Visit Root Canal Treatment: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 July 2025 and was last updated on 1 July 2025.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis aimed to evaluate and compare the effectiveness of different intracanal medications in reducing postoperative pain and improving clinical outcomes in multiple-visit root canal treatment.

Condition being studied Root canal therapy is the main treatment modality for dental pulp and periapical diseases, aiming to remove infected or necrotic pulp tissue, aiming to remove infected or necrotic pulp tissue and perform a tight root-canal filling to promote healing[1; 2]. However, in clinical practice, due to the complex anatomical structure of the root canal system and the potential presence of residual microorganisms, a single-visit treatment may fail to achieve complete healing of periapical lesions, leading to persistent symptoms[3]. Some patients may still experience postoperative pain, swelling, or persistent periapical inflammation[4]. Irreversible pulpitis generally necessitates chemomechanical debridement of vital tissue, whereas symptomatic apical periodontitis targets eradication of established biofilm within the necrotic canal system; these distinctions drive the choice of medicament and visit protocol. Therefore, multi-visit root canal therapy is frequently employed, especially in cases with acute inflammation or complicated infections. In this approach, specific medicaments are placed inside the canal and the tooth is temporarily sealed after the first visit, and then further treatment is performed on subsequent visits[5]. It is anticipated that the antibacterial, anti-inflammatory, and tissue-regenerative properties of the intracanal medicaments will help improve success rates and patient comfort[6; 7].

METHODS

Participant or population N/A.

Intervention N/A.

Comparator N/A.

Study designs to be included Randomized controlled trials (RCTs) or quasi-RCTs.

Eligibility criteria Randomized controlled trials (RCTs) or quasi-RCTs that compare different intracanal medicaments (or medicament vs. control) and their impact on postoperative pain, healing rates, or other related outcomes.
Participants aged 18 years and above, diagnosed with irreversible pulpitis or acute/chronic apical periodontitis requiring multiple visits; cases with only vital pulp therapy are not included.
At least one group received a specific intracanal medicament (e.g., Ca(OH)_2, CHX, TAP, etc.) and was compared to a control or another medicament group.
The primary outcome was postoperative pain (scoring), with secondary outcomes including periodontal healing parameters (e.g., BOP, CAL, PD) or other relevant clinical and radiographic indicators.
Only human RCTs were included; the language was limited to English and Chinese; animal, in vitro and retrospective studies were excluded.

Information sources A systematic search was conducted in the following databases: Web of Science (WoS); PubMed; China National Knowledge Infrastructure (CNKI)
The search covered literature up to February 1, 2025. To ensure comprehensiveness, we also manually checked reference lists of relevant articles and reviews to identify any additional potential studies. The search was limited to English and Chinese, with no restriction on publication year.

Main outcome(s) Based on the predefined search strategy, we retrieved 538 Chinese-language articles from CNKI, 2,216 English-language articles from PubMed, and 718 from Web of Science, for a combined total of 3,472. After removing duplicates, automated exclusions, and other irrelevant items, 2,574 articles remained for title and abstract screening. Subsequently, 2,530 were excluded due to not meeting the inclusion criteria (incorrect research direction or design), leaving 44 articles for full-text review and assessment. Among these, 5 were excluded because the full text was unavailable, leaving 39 articles for rigorous evaluation. After another round of screening, 32 did not meet the quality or content requirements, resulting in 7 studies included in this systematic review (Figure 1).

Quality assessment / Risk of bias analysis Two reviewers independently applied the Cochrane risk-of-bias tool (RoB 2.0 or RoB 1.0, depending on the requirement during the writing process) for each included study, evaluating:
Random sequence generation
Allocation concealment
Blinding of participants and personnel
Blinding of outcome assessment
Incomplete outcome data
Selective reporting
Other possible sources of bias
Each domain was rated as “low risk,” “unclear risk,” or “high risk” according to the Cochrane Handbook. Any disagreements were resolved through discussion or by a third reviewer.

Strategy of data synthesis In accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, we provide a detailed description of our literature search strategy, inclusion and exclusion criteria, quality assessment methods, and statistical analysis procedures[11].
To comprehensively capture relevant studies comparing different intracanal medications, our search strategy explicitly included multiple commonly used substances such as calcium hydroxide, chlorhexidine, triple antibiotic paste (TAP), double antibiotic paste (DAP), dexamethasone, and lidocaine. This inclusive approach ensured that all relevant randomized controlled trials evaluating various medicaments were systematically identified for comparison.

Subgroup analysis Primary Analysis: For continuous variables such as pain scores, if the studies provided mean ± standard deviation (Mean ± SD), the mean difference (MD) or standardized mean difference (SMD) was used as the effect size. For dichotomous outcomes such as healing rate or complications, we used risk ratios (RR) or odds ratios (OR).
Heterogeneity Assessment: We used the Q test and the I2statistic to assess heterogeneity across studies. If I^2 ≥ 50%, suggesting moderate-to-high heterogeneity, a random-effects model was applied. When heterogeneity was very high, we considered subgroup analyses or sensitivity analyses.Primary Analysis: For continuous variables such as pain scores, if the studies provided mean ± standard deviation (Mean ± SD), the mean difference (MD) or standardized mean difference (SMD) was used as the effect size. For dichotomous outcomes such as healing rate or complications, we used risk ratios (RR) or odds ratios (OR).
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applied. When heterogeneity was very high, we considered subgroup analyses or sensitivity analyses.
Subgroup and Sensitivity Analyses: If sufficient data were available, subgroup analyses were conducted based on follow-up intervals (e.g., 24 h, 48 h, 72 h) and type of intracanal medicament, aiming to explore potential sources of heterogeneity. Sensitivity analyses were performed by excluding studies with high risk of bias or very small sample sizes to observe changes in pooled estimates.
Publication Bias: We used funnel plots and Egger's regression test to assess publication bias quantitatively.
All statistical analyses were performed using R software (version 4.1.4; R Foundation for Statistical Computing, Vienna, Austria) with the meta (version 6.0-0) and metafor (version 3.8-1) packages. A two-sided $p < 0.05$ was considered significant. Results were visualized via forest plots, summarizing the effect size and corresponding 95% confidence intervals for each included study.

Sensitivity analysis Subgroup and Sensitivity Analyses: If sufficient data were available, subgroup analyses were conducted based on follow-up intervals (e.g., 24 h, 48 h, 72 h) and type of intracanal medicament, aiming to explore potential sources of heterogeneity. Sensitivity analyses were performed by excluding studies with high risk of bias or very small sample sizes to observe changes in pooled estimates.
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Country(ies) involved China.

Keywords Multiple-visit root canal treatment; Intracanal medicament; Postoperative pain; Calcium hydroxide; Chlorhexidine; Triple antibiotic paste.

Contributions of each author
Author 1 - Qinfen Shen.
Author 2 - Meijia Shao.
Author 3 - Wenqin Shen.

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