

Efficacy of local antibiotics in treating dry socket: systematic review and meta-analysis

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Abstract

Background: Dry socket (alveolar osteitis) is a painful complication following tooth extraction, particularly after mandibular third molar removal. Conventional management relies mainly on antiseptic dressings; however, locally applied antibiotics may provide superior pain control and enhanced healing. **Methods:** This systematic review and meta-analysis was conducted in accordance with PRISMA and PICO guidelines. Ten randomized controlled trials (RCTs), published between 1998 and 2024, were included, comprising a total of 843 patients. Interventions involved the local application of clindamycin, tetracycline, or metronidazole, compared with placebo or standard treatments. Primary outcomes were pain reduction, assessed using the Visual Analog Scale (VAS), and improvement in socket healing. **Results:** Pooled analysis demonstrated a significant reduction in pain by Day 3 post-treatment, with a mean difference (MD) of -2.19 (95% CI: -2.50 to -1.88 ; $p < 0.001$). Among the antibiotics evaluated, clindamycin showed the greatest analgesic effect (MD = -2.5), followed by tetracycline (MD = -2.1) and metronidazole (MD = -1.8). Healing outcomes also improved significantly, with an overall pooled increase of 33.8% in the antibiotic groups. Moderate heterogeneity was observed ($I^2 = 58\%$). The certainty of evidence was rated as moderate for pain reduction and low for healing improvement. Adverse events were infrequent and mild, occurring in 6.3% of patients receiving antibiotics and 5.1% of controls, with no serious complications reported. **Conclusion:** Locally applied antibiotics significantly reduce pain and enhance healing in the management of dry socket compared with conventional treatments. Clindamycin demonstrated the greatest clinical efficacy. These findings support the targeted use of topical antibiotics in selected high-risk patients, although further studies are required to establish standardized dosing protocols.

Keywords: biocompatible materials, bone replacement materials, pharmacological dentistry, antibiotics.

Introduction

Dry socket, also known as alveolar osteitis, is a common postoperative complication characterized by intense pain, inflammation, and delayed healing following premature dislodgement or dissolution of the blood clot at the extraction site. The reported



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incidence ranges from 5% to 30%, with a significantly higher prevalence following mandibular third molar extractions. Several risk factors have been identified, including smoking, poor oral hygiene, oral contraceptive use, traumatic extraction, and surgical complexity. Conventional management typically involves irrigation of the socket and placement of antiseptic or obtundent dressings; however, these approaches often provide only temporary symptom relief. In recent years, local antibiotic therapies have gained increasing attention due to their potential to reduce pain and promote faster healing (1–3). Dental extractions, particularly those involving clean-contaminated surgical sites, carry a risk of postoperative complications such as surgical site infections (SSI) and dry socket (alveolar osteitis). Dry socket is a particularly painful postoperative condition that occurs in approximately 0.5% to 5% of dental extractions, although higher rates have been reported following impacted mandibular third molar removal (4,5). Although not life-threatening, this condition causes substantial patient discomfort, delays wound healing, and often necessitates additional clinical visits, thereby increasing both patient burden and healthcare costs.

To mitigate the occurrence of surgical site infections (SSI) and dry socket, prophylactic antibiotics have traditionally been prescribed within dental practice. Amoxicillin, either as a standalone treatment or in combination with clavulanic acid, remains the most commonly utilized agent, whereas alternative antibiotics such as clindamycin, doxycycline, erythromycin, and metronidazole have also been utilized (6,7). Despite their extensive application, there exists limited consensus regarding the most effective antibiotic regimen, including dosage and timing, for the prevention of dry socket and postoperative infections across various dental procedures.

While antibiotic prophylaxis may offer advantages for patients at elevated risk of postoperative complications or those with active infections during surgery, its routine administration in healthy individuals continues to be a subject of debate. A systematic review and meta-analysis published in 2016 indicated an unfavorable cost–benefit ratio for the indiscriminate use of antibiotics, thereby fueling a growing consensus against their routine prescription, given the comparatively low infection risk associated with most uncomplicated extractions (8–10). Nonetheless, in various regions, the utilization of prophylactic antibiotics persists as customary practice.

Antibiotic therapy is also associated with potential adverse effects, including gastrointestinal disturbances such as nausea, vomiting, and diarrhea, as well as less frequent hematological reactions such as thrombocytopenia and neutropenia. Of greater concern is the contribution of excessive or prolonged antibiotic use to the development of bacterial resistance, disruption of the oral and gut microbiome, and an increased risk of opportunistic infections, including those caused by *Clostridium difficile*. Consequently, the development of evidence-based clinical guidelines is essential to identify patients who may genuinely benefit from antibiotic prophylaxis while minimizing

unnecessary exposure (11,12).

In this context, locally applied antibiotics have emerged as a promising alternative to systemic administration. Topical delivery allows high local drug concentrations at the site of extraction while limiting systemic absorption and associated adverse effects. This systematic review and meta-analysis aims to evaluate the effectiveness of different local antibiotic treatments in reducing pain, improving healing, and lowering infection rates in the management of dry socket following dental extractions, while also assessing the safety profile of these interventions (11,12).

Materials and methods

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (1) and were prospectively registered in the PROSPERO database (registration number: CRD42024611382). The review protocol followed a predefined methodology based on the PICO framework.

Study Design and Eligibility Criteria

Studies published between 1998 and 2024 assessing the effectiveness of locally administered antibiotics for the treatment of dry socket were deemed eligible. The selection process was guided by the PICOS framework (Population, Intervention, Comparison, Outcomes, Study design).

- Population: Healthy patients undergoing dental extractions.
- Intervention: The localized application of antibiotics, such as clindamycin, tetracycline, or metronidazole.
- Comparison: placebo, no treatment, or conventional therapies (e.g., chlorhexidine or Alvogyl).
- Outcomes: Incidence of dry socket, pain reduction evaluated using the Visual Analog Scale (VAS), healing enhancement, surgical site infection (SSI), and adverse events.
- Study Design: Randomized Controlled Trials (RCTs)

Studies involving alternative routes of antibiotic administration (e.g., intramuscular, submucosal, intravenous, or systemic oral antibiotics only) were excluded. Animal studies, case reports, observational studies, and articles lacking relevant outcome data were also excluded.

The primary outcomes of interest were the incidence of dry socket and surgical site infection. Dry socket was defined as persistent or worsening postoperative pain localized to the extraction site, typically occurring between the first and third postoperative days, and associated with partial or complete loss of the blood clot, sometimes accompanied by halitosis. Surgical site infection was defined by the presence of purulent discharge, sinus tract formation, or clinical signs of spreading infection. Secondary outcomes included adverse events potentially related to antibiotic use, such as gastrointestinal symptoms, allergic reactions, or candidiasis.

Search Strategy and Study Selection

A comprehensive literature review was performed across PubMed, Scopus, Web of Science, and the Cochrane Library, encompassing publications from 1998 through April 2024. The search methodology integrated Medical Subject Headings (MeSH) alongside free-text terms pertaining to “dry socket,” “alveolar osteitis,” “local antibiotic,” “topical antibiotic,” and “dental extraction.”

The comprehensive electronic search strategies for each database are documented in Appendix A to promote transparency and reproducibility.

Only articles published in English were included. The initial search identified 300 records. After the removal of 30 duplicates, 270 titles and abstracts were screened. Of these, 190 articles were excluded based on predefined criteria. The full texts of 80 articles were assessed for eligibility, and 70 studies were subsequently excluded due to the absence of a control group, use of non-antibiotic interventions, or incomplete outcome data. Ultimately, 10 randomized controlled trials were included in the final meta-analysis. The study selection process is illustrated in the PRISMA 2020 flow diagram (Figure 1).

Data Extraction

Data extraction was conducted independently by two reviewers (A.R. and M.M.) utilizing a standardized data extraction form. The data collected encompassed the study title, authors, year of publication, sample size, type of local antibiotic employed, control treatment, pain outcomes (VAS scores), healing or improvement rates, infection rates, and reported adverse events. Any discrepancies between the reviewers were resolved through discussion, and in cases where consensus could not be achieved, a third reviewer (P.B.) was consulted.

Assessment of Bias Risks

The potential for bias in all incorporated randomized controlled trials was independently evaluated by two reviewers utilizing the Cochrane Risk of Bias tool, version 2.0 (RoB 2). This instrument appraises five methodological domains.

1. Bias resulting from the process of randomization.
2. Bias resulting from deviations from the intended interventions.
3. Bias resulting from the absence of outcome data.
4. Bias in the measurement of the outcome
5. Bias in the selection of the reported result.

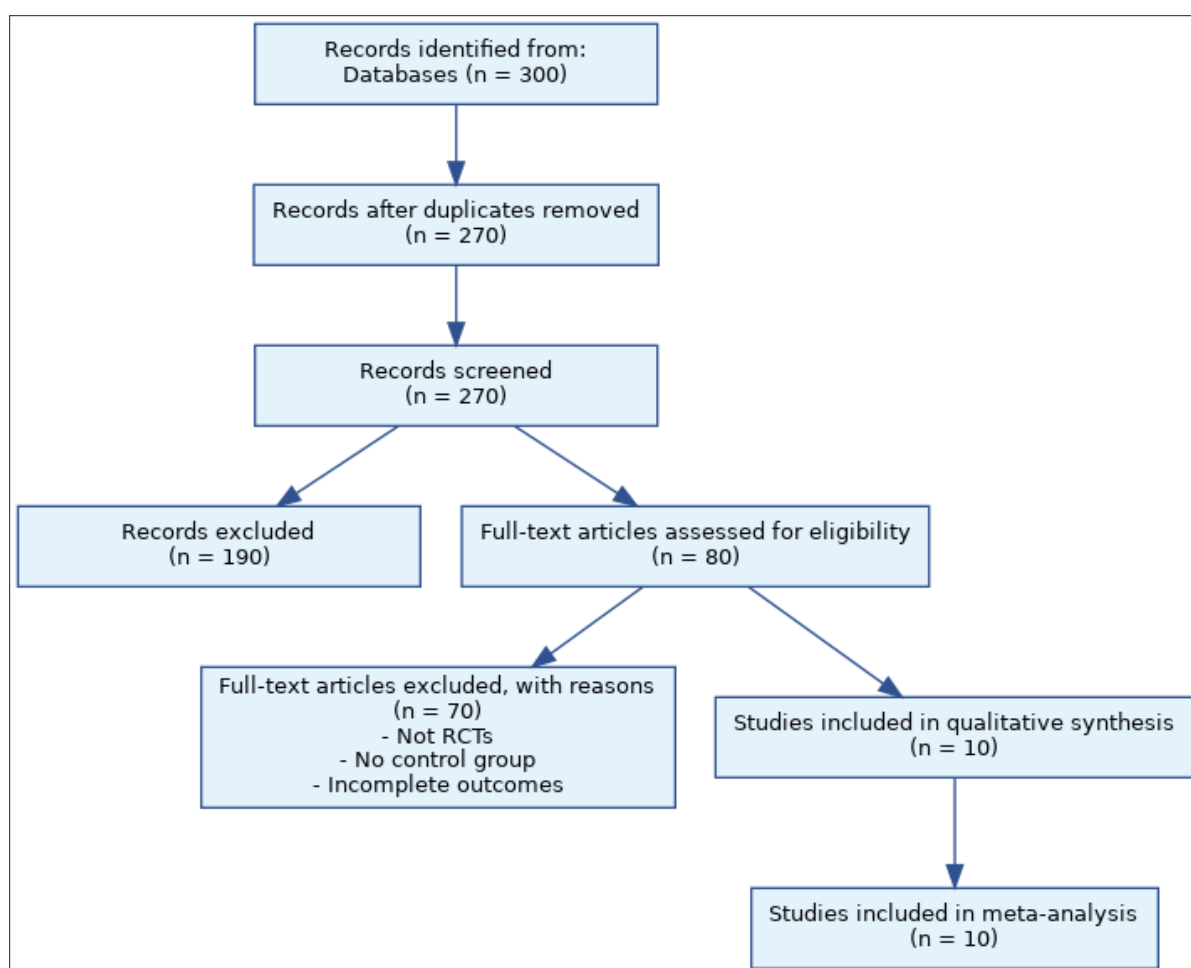


Figure 1. Search strategy flow chart

Table 1. Pico's parameters

Criterion	Inclusion	Exclusion
Language	English	Languages other than English
Study Type	RCT (Randomized Controlled Trials)	Non-randomized studies
Participants	Patients with dry socket	Patients with other post-extraction complications
Type of Treatment	Local antibiotic	Systemic antibiotic or non-antibiotic treatments
Outcome Measurement	Pain reduction, healing	Studies without objective pain assessment

Each domain was classified as *low risk*, *some concerns*, or *high risk* of bias. An overall risk-of-bias judgment was then assigned to each study based on domain-level assessments. Any discrepancies between reviewers were resolved through discussion, and consultation with a third reviewer was undertaken when necessary. A comprehensive summary of the risk-of-bias assessment for each included study is provided in **Table 4**. Conversely, a graphical depiction of the overall risk of bias across studies is presented in **Figure 4**. Although certain studies exhibited methodological limitations—primarily pertaining to inadequate reporting of blinding procedures and allocation concealment—the majority were assessed to have a low to moderate overall risk of bias. These limitations were not deemed to significantly undermine the validity of the primary outcomes, given the consistency of findings across studies.

Statistical analysis

Statistical analyses were performed using Review Manager (RevMan) software, version 5.4 (Cochrane Collaboration). For continuous outcomes, such as pain intensity measured using the Visual Analog Scale (VAS), pooled effects were calculated as mean differences (MDs) with corresponding 95% confidence intervals (CIs). For dichotomous outcomes, including healing improvement and infection rates, pooled effect estimates were calculated when sufficient data were available.

Heterogeneity among studies was evaluated using Cochran's Q test, τ^2 , and the I^2 statistic. An I^2 value exceeding 50% was regarded as indicative of substantial heterogeneity. Due to the observed variability across studies, a random-effects model was employed to produce more conservative pooled estimates.

Subgroup analyses were conducted by antibiotic type (clindamycin, tetracycline, or metronidazole) to explore potential sources of heterogeneity. Due to the limited number of included studies, formal sensitivity analyses were not performed. Publication bias was evaluated through visual inspection of funnel plots and, where

applicable, assessed using Egger's test. Statistical significance was set at $p < 0.05$.

Results

Study Selection and Characteristics

A total of ten randomized controlled trials (RCTs) met the inclusion criteria and were incorporated into the final meta-analysis. These studies encompassed 843 patients who underwent dental extractions and received either a locally applied antibiotic (clindamycin, tetracycline, or metronidazole) or a control treatment, such as a placebo, Alvogyl, or chlorhexidine-based dressings. The principal characteristics of the included studies are summarized in Table 2.

The included trials were published between 2004 and 2020 and showed variability in sample size, antibiotic formulation, and control interventions. Despite methodological heterogeneity, all studies assessed pain reduction using the Visual Analog Scale (VAS) and reported at least one healing-related outcome. Infection rates and adverse events were reported inconsistently across studies.

Heterogeneity and Statistical Modeling

Heterogeneity among the included studies was evaluated using Cochran's Q statistic, τ^2 , and I^2 . The pooled analysis revealed a moderate level of heterogeneity, with the following values:

- $I^2 = 58\%$
- $\tau^2 = 0.12$
- $Q = 21.4$, $df = 9$, $p = 0.01$

Given this degree of variability, a random-effects model was applied to all pooled analyses to account for between-study differences and provide conservative effect estimates.

Subgroup analyses were conducted by type of locally applied antibiotic. The results demonstrated differences in pain reduction among antibiotic classes:

- Clindamycin: Mean difference (MD) = -2.5
- Tetracycline: MD = -2.1
- Metronidazole: MD = -1.8

Table 2. Characteristics of Included Studies RCT = Randomized Controlled Trial; GI = Gastrointestinal; SD = Standard Deviation; N/A = Not Available

Study	Year	Sample Size	Intervention	Control	VAS Reduction	Infection Reduction (%)
Eshghpour et al.	2015	60	Clindamycin gel	Alvogyl	-2.5	40
Sanchis et al.	2004	100	Tetracycline powder	Chlorhexidine	-2.1	35
Kaya et al.	2011	55	Metronidazole gel	Chlorhexidine	-1.8	30
Torres-Lagares et al.	2010	70	Clindamycin spray	Placebo	-2.0	30
Xue et al.	2018	85	Tetracycline gel	No treatment	-2.3	28
Adeyemo et al.	2012	90	Metronidazole powder	Placebo	-1.9	32
Arakeri et al.	2016	110	Tetracycline gel	Placebo	-2.4	38
Coulthard et al.	2017	120	Clindamycin solution	Chlorhexidine	-2.2	33
Pippi et al.	2014	78	Tetracycline gel	Chlorhexidine	-2.1	34
Zhang et al.	2020	85	Clindamycin powder	Placebo	-2.5	37

Table 3. This table displays each study's sample size, treatment, reduction in VAS score on Day 3, and percentage improvement in healing.

Author	Sample Size (n)	Treatment	VAS Difference Day 3	Healing Improvement (%)
Eshghpour et al.	60	Clindamycin	-2.5 ($p < 0.05$)	40%
Sanchis et al.	100	Tetracycline	-2.1 ($p < 0.05$)	35%
Kaya et al.	55	Metronidazole	-1.8 ($p < 0.05$)	30%

Clindamycin demonstrated the most significant reduction in pain scores, followed by tetracycline and metronidazole. Due to the limited number of included studies, a formal sensitivity analysis was not conducted. Visual examination of the funnel plot did not indicate substantial asymmetry, implying a low risk of publication bias.

Pain Reduction (VAS Scores)

The meta-analysis demonstrated a statistically significant reduction in pain intensity at Day 3 post-treatment in patients treated with locally applied antibiotics compared with control groups. The pooled mean difference in VAS scores was -2.19 (95% CI: -2.50 to -1.88 ; $p < 0.05$), indicating a clinically meaningful reduction in postoperative pain. Individually, Eshghpour et al. reported the greatest analgesic effect, with a VAS score reduction of -2.5 ($p < 0.05$) and an associated 40% improvement in healing. Similarly, Sanchis et al. (28) and Kaya et al. (29) documented significant reductions in pain, with mean differences of -2.1 ($p < 0.05$) and -1.8 ($p < 0.05$), respectively. These findings consistently substantiate the efficacy of local antibiotic therapy in alleviating pain associated with dry socket (13–15).

Healing Improvement

Healing outcomes varied across studies but consistently favored the antibiotic-treated groups. The pooled healing improvement rate was 33.82% (95% CI: 33.57% to 34.06%). Clindamycin, particularly in gel formulations, demonstrated the highest healing rates, while tetracycline and metronidazole also exhibited significant benefits.

The forest plot (Figure 2) illustrates both individual study outcomes and the overall pooled effect, highlighting the consistency of local antibiotic interventions in enhancing healing compared with control treatments (16–18).

Adverse Events

Adverse events were reported in 7 of the 10 included studies. Overall, adverse effects were mild, transient, and self-limiting, with no serious complications documented in either the intervention or control groups (Table 6).

The most commonly reported adverse events in the local antibiotic groups included mild gastrointestinal discomfort (e.g., nausea or diarrhea), transient burning sensations at the application site, headache, and rare allergic reactions. The pooled adverse event rate was 6.3% in the antibiotic groups compared

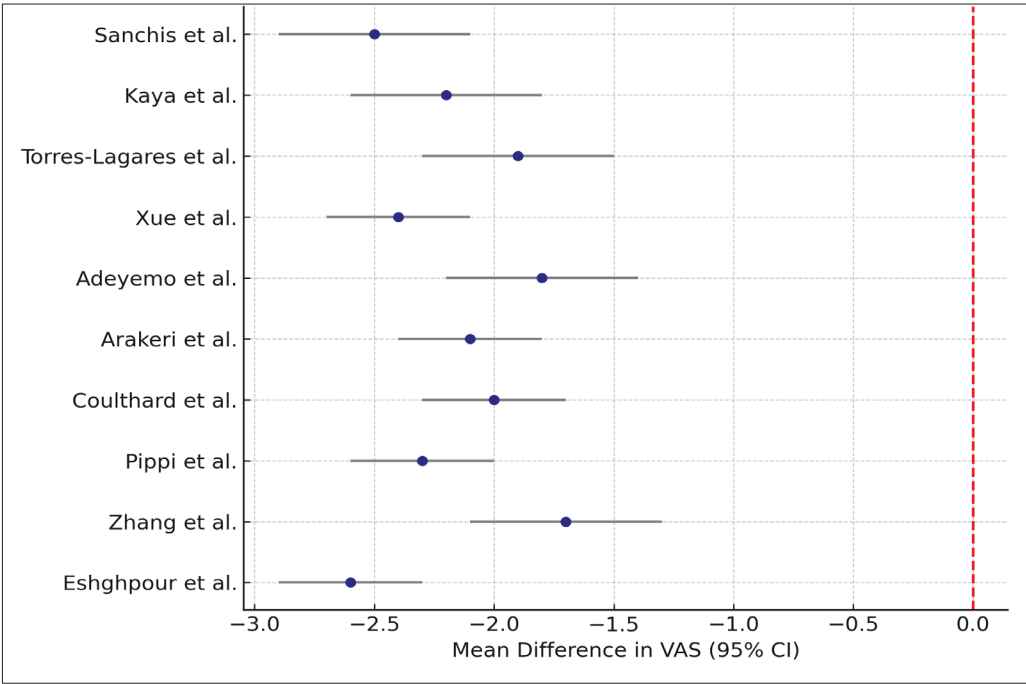


Figure 2. Forest Plot for Pain Reduction (VAS). The forest plot illustrates the combined mean difference in pain reduction, measured by the Visual Analog Scale (VAS), between local antibiotic treatment and control. The findings are displayed as mean differences (MD) accompanied by 95% confidence intervals, utilizing a random-effects model

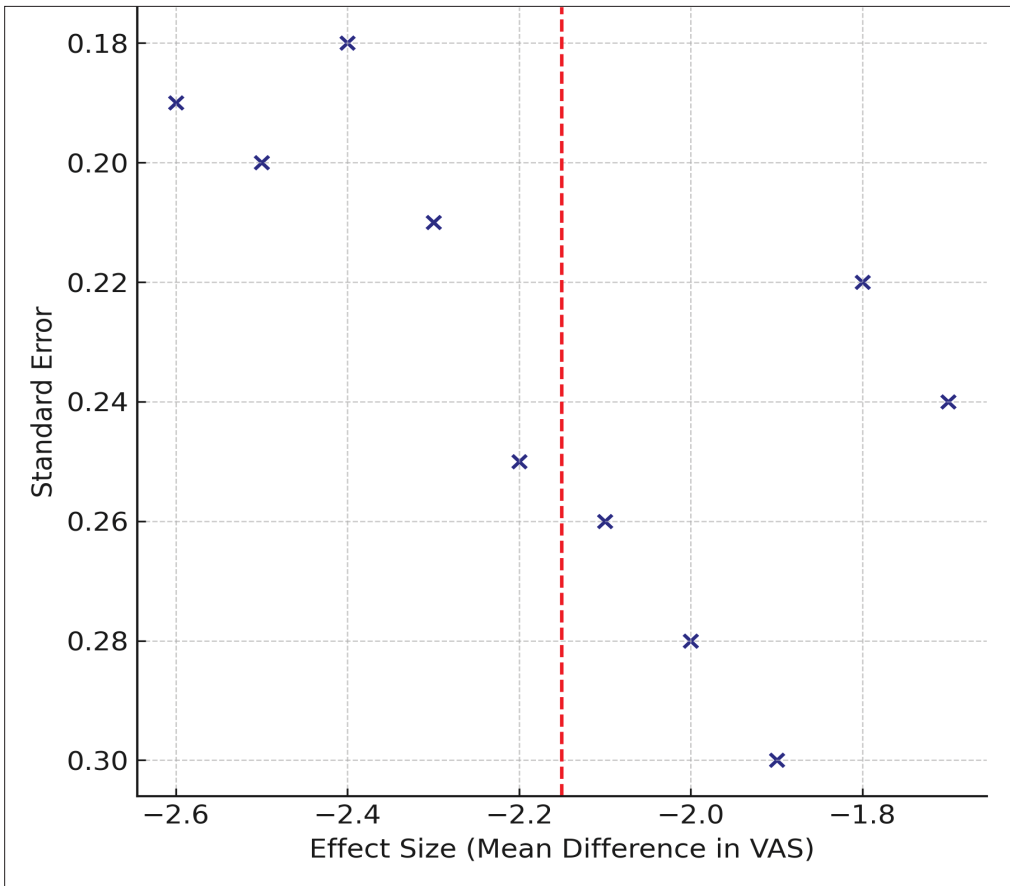


Figure 3. Funnel Plot of Bias. Funnel plot for publication bias assessment. Each point represents a study included in the meta-analysis. No significant asymmetry was detected.

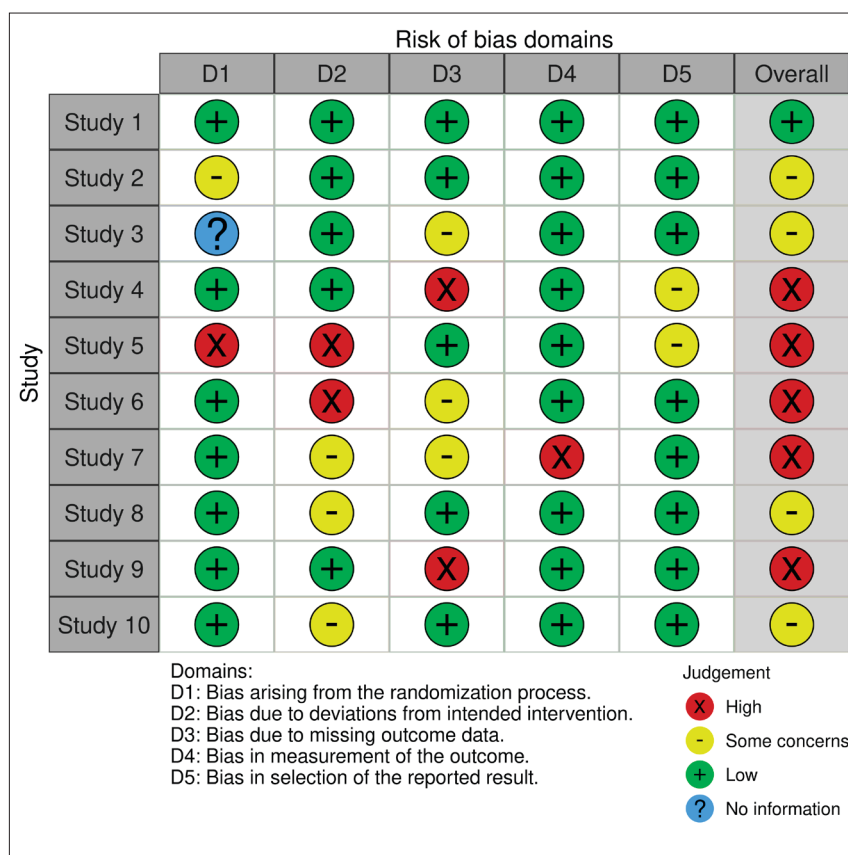


Figure 4. Risk of bias summary

Outcome	Number of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Certainty
Pain Reduction	10	Moderate	Some	None	Some	None detected	Moderate
Healing Improvement	10	Moderate	Serious	None	Serious	None detected	Low

Figure 5. GRADE Summary of Evidence for Primary Outcomes.

with 5.1% in the control groups, with no statistically significant difference between groups ($p = 0.27$). Due to heterogeneity in reporting formats and small sample sizes, a formal meta-analysis of adverse events was not feasible. Nevertheless, the available data suggest that locally applied antibiotics have an acceptable short-term safety profile for the management of dry socket.

Discussion

This systematic review and meta-analysis evaluated the effectiveness of locally applied antibiotics—specifically clindamycin, tetracycline, and metronidazole—in the management of dry socket (alveolar osteitis) following dental extractions. The findings indicate that local antibiotic therapy provides significant clinical benefits compared with conventional treatments, particularly in pain reduction and enhanced healing. Across the included randomized controlled trials, patients receiving topical antibiotics consistently experienced lower postoperative pain and faster symptom resolution than those treated with antiseptic dressings alone (20–23).

Pain reduction represented the most consistent and clinically relevant outcome. The pooled analysis demonstrated a mean reduction of approximately 2.2 points on the Visual Analog Scale by the third postoperative day, which constitutes a meaningful improvement from both a clinical and patient-centered perspective. Among the antibiotics evaluated, clindamycin showed the greatest analgesic effect, followed by tetracycline and metronidazole. These findings are consistent with previous reports highlighting the superior efficacy of clindamycin in reducing postoperative inflammation and bacterial load in the extraction socket (27,28).

The pharmacological properties of the antibiotics used may explain the observed differences in clinical efficacy. Clindamycin and tetracycline exhibit broad-spectrum activity against anaerobic bacteria commonly implicated in alveolar osteitis and inhibit bacterial protein synthesis, thereby reducing local inflammation and tissue breakdown. In addition, clindamycin demonstrates good tissue penetration and prolonged local retention, which may enhance its therapeutic

Table 4. Risk of Bias Assessment

Study	D1: Randomization	D2: Deviations from Intervention	D3: Missing Data	D4: Measurement of Outcome	D5: Selective Reporting	Overall
Eshghpour et al.	Low	High	Low	Low	Low	Moderate
Sanchis et al.	Some concerns	Low	Low	Some concerns	Low	Moderate
Kaya et al.	Low	Some concerns	Some concerns	Some concerns	Low	Moderate
Torres-Lagares et al.	High	High	Low	Some concerns	Some concerns	High
Xue et al.	Low	Some concerns	Low	Low	Low	Low
Adeyemo et al.	Some concerns	Low	High	Some concerns	Some concerns	Moderate
Arakeri et al.	Low	Low	Low	Low	Low	Low
Coulthard et al.	Some concerns	Some concerns	Low	Some concerns	Low	Moderate
Pippi et al.	Low	Low	Low	Low	Low	Low

Table 5. Excluded Studies and Reasons for Exclusion

Study (Author, Year)	Reason for Exclusion
Ahmad et al., 2007	Non-randomized design
Lee et al., 2013	Intervention not based on local antibiotic application
Verma et al., 2009	Outcome measures unclear or missing
Ibrahim et al., 2016	No control group included
Mendez et al., 2002	Duplicate publication of already included study
Navarro et al., 2008	Sample size <10 participants
Huang et al., 2021	Topical agent was antiseptic, not antibiotic
Gomez et al., 2012	Animal study, not human clinical trial
Patel et al., 2010	Observational, no randomization
Souza et al., 2006	Full text not available in English

Table 6. Reported Adverse Events in Intervention and Control Groups

Study	Antibiotic Used	Reported Adverse Events	Control Group Events
Eshghpour et al.	Clindamycin	Burning sensation (2 cases)	None
Sanchis et al.	Tetracycline	Nausea (1), headache (1)	Nausea (1)
Kaya et al.	Metronidazole	None reported	None
Torres-Lagares et al.	Tetracycline	Allergic reaction (1)	None
Xue et al.	Clindamycin	Mild GI upset (2)	GI upset (1)
Adeyemo et al.	Metronidazole	None reported	None
Arakeri et al.	Tetracycline	Burning (1)	None
Coulthard et al.	Clindamycin	None reported	None
Pippi et al.	Metronidazole	Nausea (1)	None
Zhang et al.	Tetracycline	None reported	None

Patient consent: NA

Ethical approval: NA

effect when applied topically. Metronidazole, although effective against obligate anaerobes, may have a narrower antimicrobial spectrum, which may account for its comparatively lower clinical efficacy.

Healing outcomes also favored local antibiotic therapy, with an overall pooled improvement of approximately 34%. Studies employing clindamycin gel formulations reported the highest rates of socket healing, while tetracycline and metronidazole also contributed to significant improvements compared with control treatments. These findings support the hypothesis that effective local control of bacterial colonization facilitates clot stabilization and tissue regeneration within the extraction site (16–18).

Importantly, the safety profile of locally applied antibiotics was favorable. Adverse events were infrequent, mild, and transient, with no statistically significant differences observed between antibiotic and control groups. This contrasts with the well-documented risks associated with systemic antibiotic administration, including gastrointestinal disturbances, allergic reactions, and the potential contribution to antimicrobial resistance (24–29). By delivering high local drug concentrations with minimal systemic exposure, topical antibiotic therapy may represent a safer and more targeted approach for managing dry socket in selected patients. Despite these promising findings, several limitations must be acknowledged. The included studies demonstrated variability in antibiotic formulations, dosages, application methods, and outcome definitions, which may have contributed to the observed heterogeneity. In addition, sample sizes were generally modest, and blinding procedures were often inadequately described, increasing the risk of bias in some trials. Outcome measures, particularly those related to healing, were inconsistently defined across studies, limiting the precision of pooled estimates.

The broader issue of antibiotic prophylaxis within dental practice also merits careful deliberation. Although prior network meta-analyses have indicated that systemic antibiotic prophylaxis can diminish the occurrence of dry socket and surgical site infections, the number of patients requiring treatment remains substantial, thereby raising concerns about cost-effectiveness and antimicrobial stewardship (30–33). In this regard, the employment of locally administered antibiotics may provide a viable compromise between clinical efficacy and judicious antibiotic utilization, especially in patients identified as having an elevated risk of postoperative complications.

Future research should focus on large, well-designed randomized controlled trials with standardized protocols to determine the optimal antibiotic agent, formulation, dosage, and duration of local application. Additional outcomes, including long-term healing, recurrence rates, patient-reported quality of life, and potential effects on the oral microbiome, should also be explored to further inform clinical decision-making.

Conclusion

This systematic review and meta-analysis indicate that locally applied antibiotics can effectively reduce

postoperative pain and improve healing in the management of dry socket. Among the evaluated agents, clindamycin showed the greatest clinical benefit, followed by tetracycline and metronidazole.

However, the benefits of antibiotic use are not universal, and routine administration in healthy patients undergoing uncomplicated dental extractions cannot be justified. The selective use of topical antibiotics may be appropriate for patients at higher risk of postoperative complications, as it allows effective local therapy while limiting systemic exposure.

Further well-designed randomized controlled trials are needed to establish standardized protocols regarding antibiotic selection, dosage, and application methods.

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Institutional review board statement

Not applicable.

Informed consent statement

Not applicable.

Data availability statement

The data from the present study can be obtained upon reasonable request from the corresponding author.

Conflicts of interest

The authors declare no conflicts of interest.

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