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Research Article

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Comparative Effectiveness of Local Antimicrobial Strategies for Peri-implantitis: A Network Meta-analysis

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Abstract

The study conducted a network meta-analysis to compare local antimicrobial strategies used as adjuncts to nonsurgical peri-implantitis therapy, including chlorhexidine, minocycline, doxycycline, and photodynamic therapy. Twenty-three controlled trials involving 1,248 implants with a minimum follow-up of 6 months were included based on systematic searches of MEDLINE, Embase, and the Cochrane Library. Primary outcomes were changes in probing pocket depth (PPD) and bleeding on probing (BOP), while secondary outcomes included radiographic bone fill and disease resolution rate. A random-effects network model was applied, and consistency was assessed using node-splitting. At 12 months, adjunctive local antibiotics achieved the greatest PPD reduction (−1.4 mm, 95% CI −1.9 to −0.9) compared with debridement alone, followed by chlorhexidine (−0.9 mm, 95% CI −1.3 to −0.5) and photodynamic therapy (−0.8 mm, 95% CI −1.2 to −0.4). However, none of the adjunctive approaches consistently improved radiographic bone levels across studies. SUCRA rankings indicated that minocycline microspheres had the highest probability of clinical superiority, although heterogeneity in defect morphology and debridement protocols limited definitive conclusions. Overall, local antimicrobials provide modest improvements in clinical parameters, while long-term disease control remains primarily dependent on adequate mechanical access and supportive maintenance.

Keywords: peri-implant disease, local antimicrobials, network meta-analysis, minocycline, photodynamic therapy

1. Introduction

Peri-implantitis is an inflammatory disease affecting the soft and hard tissues around dental implants and is now a common cause of late implant complications [1]. The condition is marked by bleeding on probing, increased probing pocket depth, suppuration, and progressive marginal bone loss, which may eventually lead to implant failure. With the growing use of dental implants, peri-implantitis has become an important clinical problem. Current clinical guidelines recommend non-surgical debridement as the first-line treatment, while surgical therapy is advised when

inflammation persists or when peri-implant defects are advanced [2]. These recommendations emphasize the need for effective adjunctive measures that can improve infection control while keeping treatment simple and localized. Mechanical debridement is the foundation of non-surgical peri-implantitis therapy. Clinical studies consistently show that mechanical instrumentation can reduce probing depth and bleeding on probing. However, complete disease resolution is difficult to achieve. Many studies report only limited improvement in soft-tissue inflammation and little or no radiographic bone gain, even when non-surgical treatment is repeated during maintenance care [3,4]. These limitations are more pronounced in sites with deep baseline pockets or complex defect shapes. As a result, clinicians often add local antimicrobial agents after mechanical debridement to enhance biofilm control without exposing patients to systemic antibiotics.

Chlorhexidine (CHX) is one of the most widely used local antiseptics in peri-implant care. Studies in peri-implant mucositis and peri-implantitis show that CHX gels, chips, or submucosal irrigation can reduce plaque and bleeding in the short term when combined with mechanical therapy [5]. However, the additional reduction in probing depth is usually small. Importantly, the only recent meta-analysis specifically evaluating chlorhexidine as an adjunct to non-surgical peri-implantitis therapy reported a statistically significant but clinically modest benefit, together with marked heterogeneity and limited long-term evidence [6]. These findings suggest that CHX may be useful, but its relative effectiveness compared with other local antimicrobials remains unclear. Local antibiotic delivery systems, such as minocycline microspheres and doxycycline gels, have also been widely studied. Several controlled trials indicate that these agents can further reduce probing depth and bleeding when used after mechanical debridement, particularly in mild to moderate peri-implantitis [7]. However, treatment effects vary across studies, and the benefits often depend on defect type, application frequency, and follow-up duration. In addition, concerns about antimicrobial resistance, patient acceptance, and cost limit the routine use of local antibiotics in all cases.

Photodynamic therapy (aPDT) is another local adjunct that aims to reduce bacterial load using light-activated agents. Some clinical trials report greater short-term reductions in bleeding and probing depth with aPDT compared with mechanical debridement alone, especially in patients who cannot use antibiotics [8]. Nevertheless, results differ among studies because of variation in photosensitizers, light sources, and treatment protocols. Recent reviews indicate that evidence for long-term benefit remains limited [9,10]. Several meta-analyses have evaluated adjunctive treatments for peri-implantitis. Pairwise meta-analyses suggest that local and systemic antibiotics may provide additional clinical benefit, but they also raise concerns about side effects and antibiotic resistance [10]. Reviews focusing on non-antibiotic adjuncts, including chlorhexidine and aPDT, generally report small improvements and highlight large differences between studies [11,12]. More recent network meta-analyses attempt to compare multiple treatments, but many combine peri-implant mucositis and peri-implantitis or group different antimicrobials together, which limits direct comparison between specific local agents [13]. Despite these analyses,

important gaps remain. Many studies include small samples and short follow-up periods. Definitions of peri-implantitis are not consistent across trials. Key factors such as defect morphology, implant surface type, and details of mechanical debridement are often poorly reported [14,15]. As a result, clinicians still lack clear evidence on how commonly used local antimicrobial agents compare with each other when applied as adjuncts to standardized non-surgical therapy.

In this study, a network meta-analysis was performed to compare the clinical effectiveness of commonly used local antimicrobial strategies—chlorhexidine, minocycline, doxycycline, and photodynamic therapy—when used as adjuncts to non-surgical peri-implantitis treatment. Controlled clinical studies with a minimum follow-up of six months were included. Outcomes such as probing pocket depth, bleeding on probing, radiographic bone changes, and disease resolution were assessed. By integrating direct and indirect evidence within a single analytical framework, this study provides a comparative evaluation of local antimicrobial adjuncts and aims to support evidence-based treatment selection and future clinical trial design in peri-implantitis management.

2. Materials and Methods

2.1 Study Selection and Sample Characteristics

A structured search was carried out in MEDLINE, Embase, and the Cochrane Library for clinical trials on local antimicrobials used with nonsurgical treatment of peri-implantitis. Trials were included if they enrolled adults with peri-implantitis, had a follow-up period of six months or longer, and reported probing pocket depth (PPD) or bleeding on probing (BOP). Twenty-three trials met these criteria, with a total of 1,248 implants from 982 participants. Most studies included implants with pockets of at least 5 mm, bleeding on probing, and radiographic bone loss. Trials usually excluded patients who had taken antibiotics or antiseptic rinses in the previous months or had uncontrolled systemic disease.

2.2 Treatment Groups and Comparators

This review compared local antimicrobial strategies used in addition to mechanical debridement. Interventions included chlorhexidine preparations, minocycline microspheres, doxycycline gels, and antimicrobial photodynamic therapy. Mechanical debridement alone served as the reference treatment. Some trials used a single application of the antimicrobial agent, while others repeated the application during follow-up. Delivery forms varied and included gels, microspheres, or light-activated products. Each intervention was grouped according to its active ingredient and delivery method to allow direct and indirect comparisons across studies.

2.3 Outcome Measures and Data Reliability

The primary outcomes were changes in PPD and BOP between baseline and the 6–12-month examination. Secondary outcomes were radiographic bone changes and the number of implants that met the definition of disease resolution, which included shallow pockets, no bleeding, and no further bone loss. When studies included several implants per patient, the effect sizes reported by the authors were extracted to avoid counting the same patient more than once. Two reviewers independently collected all outcome data, diagnostic criteria, and study features. Any differences were resolved by discussion. The risk of bias was assessed using the Cochrane tool, focusing on randomization, examiner masking, probing calibration, and follow-up completeness.

2.4 Statistical Analysis and Models

A random-effects network meta-analysis was used to estimate treatment effects. Continuous outcomes were summarized as mean differences. Binary outcomes were analyzed as odds ratios. The continuous-outcome model was written as:

$$Y_i=\mu+\delta_j+u_i+\varepsilon_i,$$

where Y_i is the effect in study i,δj is the treatment effect, u_i is the study-level random effect, and ε_i is the residual error.

Disease resolution was analyzed with a logistic model:

$$logit(p_i)=\alpha+\beta_j+u_i.$$

Direct and indirect comparisons were checked for agreement using node-splitting. Treatment ranks were estimated using the surface under the cumulative ranking curve (SUCRA). Sensitivity analyses removed trials with high risk of bias or missing outcome data.

3. Results and Discussion

3.1 Changes in probing depth and bleeding

Across all included trials, local antimicrobials used with nonsurgical debridement produced greater reductions in probing pocket depth (PPD) than debridement alone. Local antibiotics showed the largest decrease in PPD at about 12 months (−1.4 mm, 95% CI −1.9 to −0.9). Chlorhexidine (CHX) and photodynamic therapy (PDT) also improved PPD but to a smaller degree (−0.9 mm and −0.8 mm, respectively). These pooled estimates are shown in Fig. 1. This pattern agrees with earlier studies in which tetracycline-based agents produced deeper pocket reduction than antiseptics or light-based therapies during nonsurgical peri-implantitis treatment. However, the average gain remained modest [16,17]. CHX and PDT also reduced bleeding on probing (BOP), though the amount of reduction varied between trials. Taken together, these findings indicate that local antimicrobials improve soft-tissue outcomes when added to

debridement, but mechanical access remains the main factor determining the size of the clinical change.

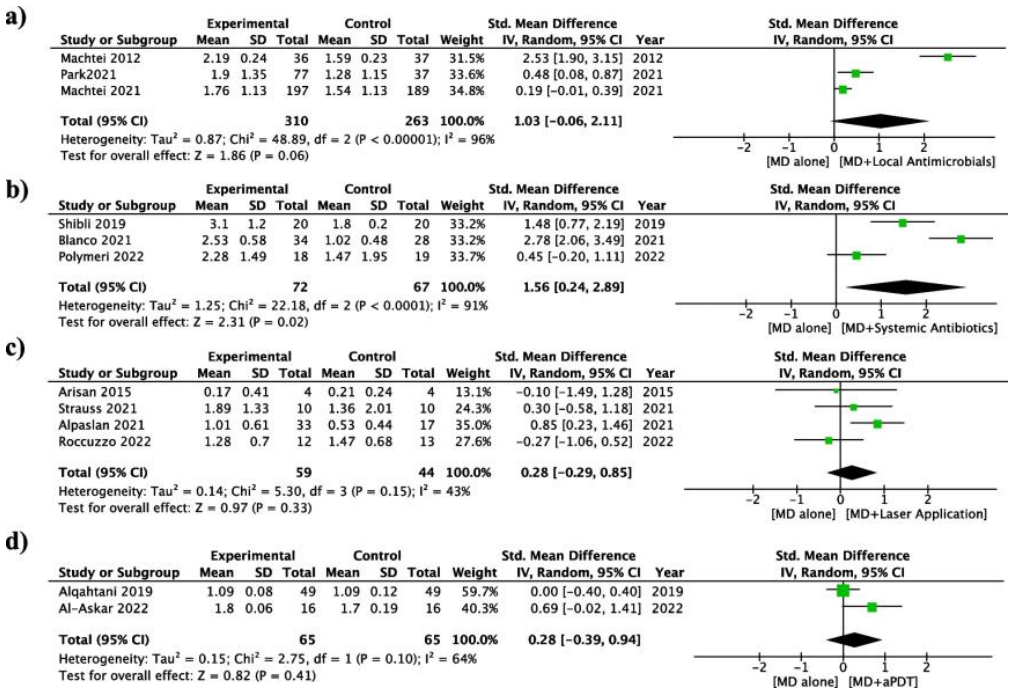


Fig. 1. Mean probing pocket depth values at 12 months for each local antimicrobial treatment and for mechanical debridement alone.

3.2 Bone-level changes and disease resolution

Radiographic bone changes were small in all treatment groups. Local antibiotics, CHX, and PDT showed no clear advantage over debridement alone for bone fill. Most implants demonstrated stable bone levels or only slight gain, and the network estimates were highly variable across studies. This reflects earlier work showing that nonsurgical therapy rarely produces measurable bone regeneration and that bone changes depend more on defect shape and surface accessibility than on the choice of local drug [18,19]. Disease resolution—defined as shallow pockets without bleeding or suppuration and no further bone loss—occurred more often in groups receiving local antimicrobials than in groups treated with debridement alone. Fig. 2 displays the relative probability of resolution for each treatment category. Although resolution rates improved with adjunctive care, a notable portion of sites still showed persistent inflammation. This suggests that both soft-tissue control and long-term stability depend on repeated debridement and regular maintenance rather than on the antimicrobial agent itself [20].

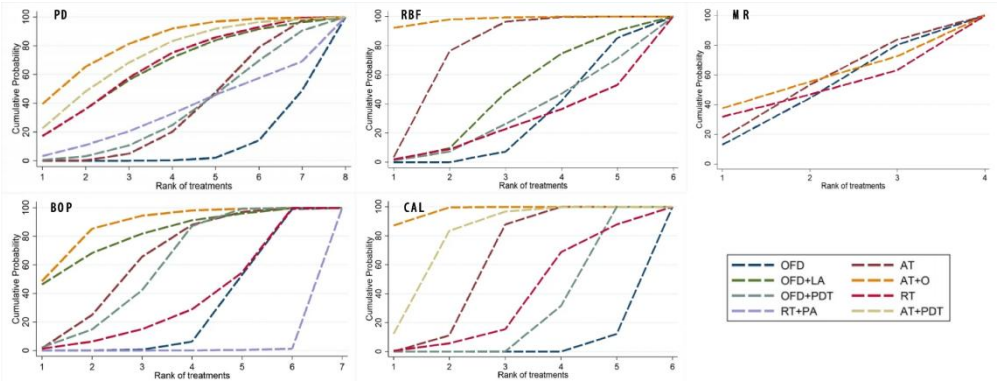


Fig. 2. Disease resolution probabilities at 12 months for the local antimicrobial treatments included in the network analysis.

3.3 Treatment ranking and variability among studies

The network estimated treatment rankings using SUCRA values. Minocycline-based systems had the highest probability of achieving the best PPD reduction. Doxycycline preparations and PDT followed, while CHX showed intermediate probability, and debridement alone ranked lowest. These rankings matched the direction of the pooled clinical outcomes [21]. However, several comparisons were informed by only one or two small trials, which widened confidence intervals. Variations in debridement techniques, defect forms and reapplication schedules also contributed to between-study differences [22]. Such variation has been noted in earlier peri-implantitis reviews and limits the strength of strict ranking conclusions. Local antimicrobials appear useful as adjuncts, but the range of clinical benefit overlaps across agents, and choice of treatment may depend on patient factors, cost, and risk of antibiotic exposure.

3.4 Comparison with previous evidence and clinical implications

The present network meta-analysis supports earlier findings that nonsurgical debridement remains the primary step in peri-implantitis management, and that local antimicrobials provide additional but limited improvement. Local antibiotics produced the largest average gains in PPD and BOP, while CHX and PDT offered smaller but consistent soft-tissue benefits. None of the adjuncts improved bone levels in a predictable way. These outcomes align with recent reports indicating that nonsurgical therapy controls inflammation but rarely regenerates bone [23]. Clinically, local antimicrobials may be useful for improving short-term soft-tissue conditions, stabilizing pockets before surgical treatment, or supporting maintenance when surgical access is not possible. Long-term disease control, however, still depends on effective debridement, plaque control, and follow-up. Future trials with longer follow-up and standardized reporting of defect features are needed to strengthen comparisons between different antimicrobial strategies and to determine which patients benefit the most.

4. Conclusion

This network meta-analysis found that local antimicrobials added to nonsurgical peri-implantitis treatment produced greater reductions in probing depth and bleeding than mechanical debridement alone. Local antibiotics showed the largest average effect, while chlorhexidine and photodynamic therapy gave smaller but steady improvements in soft-tissue conditions. None of the treatments produced consistent bone gain, which suggests that long-term control still depends mainly on adequate debridement and regular maintenance. The study contributes by comparing widely used local treatments within the same model and by providing clearer estimates of their relative effect. However, the included trials differed in defect type, follow-up time, and reporting, which limits the strength of firm conclusions. Longer and better standardized trials are needed to determine which patients and lesion forms respond best to each local antimicrobial approach.

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