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BRIEF COMMUNICATION

Local application of 1 % alendronate gel as an adjunct in periodontal therapy

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ABSTRACT

Introduction: periodontitis is a chronic inflammatory disease that causes bone and tooth loss, requiring innovative adjunctive therapies.
Objective: to evaluate the efficacy of 1 % alendronate gel applied locally as a complement in periodontal therapy.
Methods: a systematic review of the scientific literature was conducted across multiple databases, using a keyword algorithm and Boolean operators to identify relevant sources. selected studies, after rigorous inclusion and exclusion criteria, were critically assessed for timeliness, methodological quality, and thematic relevance, and integrated into the final synthesis.
Results: reviewed studies show that topical 1 % alendronate reduces periodontal probing depth, improves clinical attachment level, and promotes bone regeneration. Clinical trials demonstrated greater efficacy in non-smokers, while meta-analyses confirmed additional benefits compared to conventional therapies. In animal models, the gel significantly enhanced bone regeneration in furcation defects. However, concerns remain about long-term safety, particularly the risk of mandibular osteonecrosis associated with systemic bisphosphonate use.
Conclusions: 1 % alendronate gel represents a promising strategy in periodontology, improving clinical and radiographic parameters. Nevertheless, longer controlled studies are needed to validate its safety and efficacy, enabling standardized clinical protocols for its application.

Keywords: Alendronato; Periodoncia; Regeneración Ósea; Inflamación.

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INTRODUCTION

Periodontitis is a progressive microbial disease that causes destruction of tooth-supporting tissues due to the host's inflammatory and immune responses. For many years, the standard approach to preventing and treating periodontal diseases has been mechanical therapy, supplemented when necessary by surgical intervention. Researchers have sought to develop a treatment modality that modifies the host response to interfere with the destructive mechanisms of the disease and thereby influence its pathological outcome.[1]

The host response acts as a protective mechanism but also contributes to tissue damage and alveolar bone resorption, leading to disruption of periodontal ligament fibers. To counteract this, researchers developed a host-modulating therapy that alters the host response to disrupt the destructive pathways of periodontal disease. [1] This has generated interest in host modulation therapy, which reduces bone resorption by modifying the host response. Among the agents investigated, bisphosphonates stand out as potent inhibitors of bone resorption and are used in the treatment of metabolic bone diseases such as Paget's disease and osteoporosis. It has been proposed that bisphosphonates, by suppressing bone resorption, may protect against alveolar bone loss in periodontitis.[2] Alendronate, in particular, is an effective inhibitor of bone resorption, and its efficacy has been demonstrated in both animal and human studies. Moreover, given that periodontitis is more prevalent and treatment-resistant in smokers, alendronate could represent a significant advancement in these cases.[3]

The role of bisphosphonates (BPs) in periodontitis treatment has been studied in animal models to assess their ability to delay bone loss around teeth affected by the disease. BPs have shown significant potential to reduce bone loss when administered systemically. Furthermore, their local use in conjunction with scaling and root planing (SRP) resulted in decreased bone loss and improved mineral density. [4]

Alendronate (ALN) is an aminobisphosphonate that inhibits bone tissue resorption. Both in humans and animal models, systemic ALN use has been shown to reduce alveolar bone resorption and improve bone density. However, previous reports have linked systemic ALN use to medication-related osteonecrosis of the jaw (MRONJ), suggesting that its use in periodontitis treatment should be approached cautiously. As an alternative, local ALN administration has been proposed to avoid these adverse effects. [4,5]

Local application of 1 % ALN gel as an adjunct to SRP for the treatment of chronic and aggressive periodontitis, as well as Grade II furcation defects, has demonstrated reduced probing depth (PD), improved bone fill, and increased clinical attachment level (CAL). These positive outcomes suggest this approach could represent a new direction in periodontal regeneration.[6]

In this context, the present study aims to scientifically evaluate—through a review of clinical and experimental studies—the efficacy and safety of local 1 % alendronate gel as an adjunctive periodontal therapy.

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METHODS

A systematic review was conducted following PRISMA 2020 guidelines to evaluate the efficacy of 1 % alendronate gel as an adjunct in periodontal therapy. The search period spanned from 2019 to 2024, focusing on recent clinical and experimental studies.

Information sources included PubMed, SciELO, Scopus, and Google Scholar, as well as gray literature and secondary references. Articles in English, Spanish, and Portuguese were considered.

The search strategy employed Boolean strings such as (((bisphosphonates) AND (periodontitis)) AND (alendronate)) AND (periodontal therapy), along with MeSH terms: "bisphosphonates," "periodontitis," "alendronate," and "periodontal therapy."

Inclusion criteria were: articles published within the last five years, with full-text access, and directly related to the research topic. Excluded were duplicates, thesis works, non-scientific reports, commercial studies, and articles lacking clinical relevance.

The selection process initially identified 284 articles. After removing 73 duplicates and applying relevance filters, 92 were excluded for analyzing adverse effects, 62 for addressing other specialties, 27 for lacking significant contribution, 13 for focusing on osteonecrosis, and 10 for inaccessibility. Ultimately, 7 studies were included in the synthesis. The process was illustrated using a PRISMA flow diagram.

Data extraction and analysis were performed using an Excel matrix, collecting variables such as author, year, study type, sample, intervention, and main results. A qualitative synthesis was conducted, and where appropriate, a meta-analysis compared alendronate efficacy versus placebo or conventional therapies. Initial keyword searches ("bisphosphonates," "periodontitis," "alendronate," "periodontal disease," "bone regeneration," "periodontal therapy") yielded 284 articles. After title screening, 73 duplicates were removed. Abstract screening excluded 92 studies on long-term bisphosphonate adverse effects, 62 on other specialties, 27 for insufficient relevance, 13 on osteonecrosis, 7 commercial reports, and 3 non-scientific articles, leaving 7 scientific studies for analysis (Figure 1).

Table *1*. Search results by database and query.

Database	Search String	Results
PubMed	(((bisphosphonates) AND (periodontitis)) AND (alendronate)) AND (periodontal therapy)	174
Google Scholar	(((bisphosphonates) AND (periodontitis)) AND (alendronate)) AND (periodontal therapy)	67
Scopus	(((bisphosphonates) AND (periodontitis)) AND (alendronate)) AND (periodontal therapy)	43
Total		

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Fig. 1 PRISMA 2020 flow diagram for article selection.

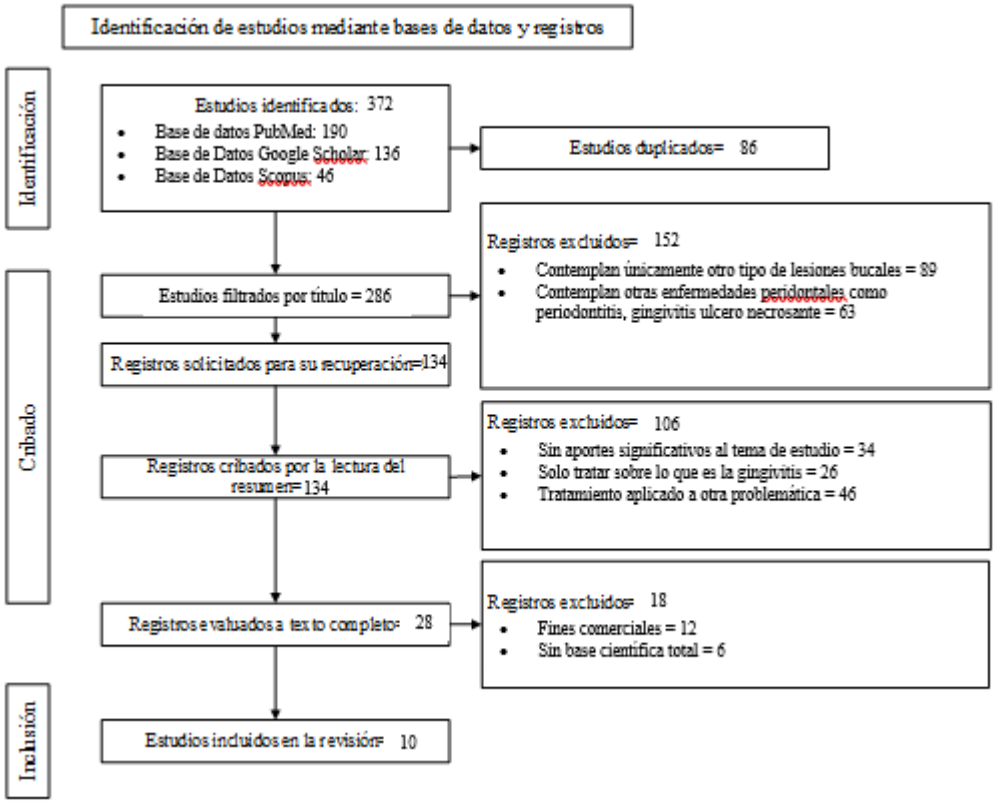

Table 2. Types of Investigations.

Author	Study Type	Sample	Intervention	Results	Conclusions
Kajimoto N et al. [8]	Experimental	96 rats randomized into 4 groups: 1) NT (no treatment); 2) SRP; 3) SRP/PLA (placebo gel); 4) SRP/ALN (1% ALN gel)	PLA and ALN gels inserted into periodontal pockets using 1 mL syringe and insulin needle	SRP/ALN showed greater bone fill than SRP/PLA at all timepoints and greater than SRP at 15–30 days	Local 1% ALN gel as SRP adjunct improved bone regeneration in furcation defects in experimental periodontitis rat model
Sheokand V et al. [9]	Randomized clinical trial	60 infrabony pockets in chronic periodontitis patients aged 30–50 years (smokers vs. non-smokers)	0.1 mL alendronate or placebo gel applied after root planing	Alendronate more effective than placebo; better outcomes in non-smokers	Alendronate sites showed greater improvement; non-smokers had significant radiographic alveolar crest height gain and defect fill

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Arena C et al. (10)	Systematic review with meta-analysis	408 patients (207 test, 209 control sites)	RCTs with >6 months follow-up	Topical alendronate in phase II therapy significantly improved PD and CAL	Local alendronate offers benefits in phase II periodontal therapy, though long-term studies are needed
Alwithanani N (11)	Systematic review	EMBASE, Medline, PubMed, Scopus databases	7 studies: 4 topical, 3 oral alendronate as SRP adjunct	SRP + bisphosphonates significantly reduced PD, increased CAL, and filled bone defects vs. SRP alone	Bisphosphonate adjunct appears effective, but practical viability is questionable due to MRONJ risk and short follow-up
Muniz F et al.(12)	Systematic review with meta-analysis	RCTs using local/systemic BP as periodontal adjunct	Separate meta-analyses for local/systemic BP; mean difference (MD) calculated for PPD and CAL at 6 months	All 1% ALN gel studies showed significant periodontal improvements (3–12 months): reduced PPD/BOP, CAL gain, IBD reduction; 7 studies reported greater PPD reduction with ALN	BP + SRP produces additional clinical effects
Li F (13)	Meta-analysis	Cochrane and PRISMA-compliant	Patients with vertical interproximal bone defects or Class II furcation defects	Primary: IBD depth reduction; Secondary: PPD reduction, VCAL/HCAL gain	1% ALN effective in periodontal bone regeneration; synergistic PRF + 1% ALN yielded better outcomes than PRF alone
Shetty B(14)	Randomized split-mouth trial	40 infrabony defects in 20 chronic periodontitis patients	Single dose of simvastatin (SMV) or ALN gel applied after phase I therapy; clinical/radiographic parameters assessed at baseline, 3, and 6 months	Both sites showed significant PPD, plaque index, and bleeding index reduction, plus CAL gain and bone fill; ALN site showed greater CAL gain and bone fill at 6 months	SMV and ALN gels improve clinical/radiographic parameters in infrabony defects; ALN demonstrated superior bone defect fill

DISCUSSION

Bisphosphonates (BPs) as adjunctive periodontal therapy have been extensively studied, demonstrating efficacy in reducing bone loss and improving clinical parameters. Muniz et al.,(12) found that both local and systemic BP administration resulted in significant improvements in probing pocket depth (PPD) and clinical attachment level (CAL) at six months.

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Reviewed studies included periodontitis patients with bone loss. Li F[13] highlighted the importance of these treatments for individuals with vertical interproximal bone defects or Class II furcation defects. Key findings showed reduced intrabony defect (IBD) depth and percentage reduction, indicating BPs' effectiveness in bone regeneration—consistent with Shetty B. [14]

Administration route—systemic versus local—is a crucial consideration. Muniz et al.,[12] and Li F[13] demonstrated that locally applied alendronate (ALN) gels reduce periodontal pocket depth and enhance bone fill.

Furthermore, a split-mouth study by Kajimoto N, [8] in chronic periodontitis patients found that SMV and ALN gels significantly reduced pocket depth in infrabony defects—a common challenge in periodontal therapy whose effective management leads to improved clinical outcomes, as confirmed by Shetty B. [14]

Kajimoto N et al.,[8] emphasized that combining BPs with scaling and root planing (SRP) yields additional clinical benefits, suggesting combination therapy may be more effective than SRP alone. This is supported by evidence showing alendronate + SRP improves clinical and radiographic parameters.

However, despite favorable findings, further research is needed to determine optimal management strategies and long-term safety profiles of bisphosphonates in periodontal therapy, as noted by Wanikar I et al.,[15] Future studies should address variability in results and ensure long-term follow-up.

CONCLUSIONS

Bisphosphonates have demonstrated efficacy in periodontitis treatment via both local and systemic routes, yielding significant improvements in clinical parameters such as probing depth and clinical attachment level—suggesting their capacity to promote bone regeneration and reduce periodontal destruction. Specifically, alendronate gels show promise in reducing intrabony defects, and when combined with SRP, they enhance benefits over conventional therapy. Nevertheless, outcome variability and long-term safety concerns—particularly regarding MRONJ risk—underscore the need for additional research to establish safe, standardized clinical protocols, thereby optimizing bisphosphonate use in patients with significant bone loss.

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