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Clinical efficacy of hyaluronic acid in the regenerative treatment of periodontal intrabony defects: integrative review

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ABSTRACT

Introduction: The regeneration of periodontal intrabony defects represents a relevant clinical challenge due to their anatomical complexity and the unpredictability of regenerative outcomes. Hyaluronic acid, a key component of the extracellular matrix, has been proposed as an adjunctive agent in periodontal regenerative therapies.
Objectives: To critically analyze the available scientific evidence on the clinical and radiographic efficacy of hyaluronic acid in the regenerative treatment of periodontal intrabony defects.
Methodology: An integrative literature review was conducted using the PubMed, Web of Science, Cochrane Library, and B-On databases, including studies published between 2018 and 2025. The search strategy combined MeSH terms and the keywords related to hyaluronic acid and periodontal regeneration following PRISMA guidelines; 11 studies were included.
Results: The use of hyaluronic acid, particularly as an adjunctive agent, is associated with significant improvements in clinical periodontal parameters, clinical attachment level gain and probing pocket depth reduction, as well as radiographic evidence of bone fill in specific contexts. When combined with open flap debridement, hyaluronic acid demonstrated additional clinical benefits, particularly in the short term. In minimally invasive approaches and when compared with enamel matrix derivatives, a positive effect was mainly observed during the early healing phases, without sustained differences in the medium term.
Conclusion: Hyaluronic acid appears to be a promising adjunctive therapeutic option in the regenerative treatment of periodontal intrabony defects, contributing to improvements in clinical parameters and to the optimization of early healing.

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RESUMO

Introdução: O medo e a ansiedade dentária são condições altamente prevalentes que comprometem a assiduidade, a cooperação do paciente e os resultados clínicos. Intervenções não farmacológicas, como a aromaterapia, têm sido propostas como estratégias adjuvantes na redução da ansiedade em contexto de medicina dentária.
Objetivos: Avaliar o efeito da inalação de óleo essencial de lavanda (*Lavandula angustifolia*) na ansiedade dentária e em parâmetros fisiológicos em contexto clínico.
Metodologia: Foi conduzido um estudo de caso único (N-of-1) com desenho cruzado (tipo ABBA). Um participante foi submetido a quatro sessões clínicas sob condições alternadas de lavanda (2%) e placebo. A ansiedade foi avaliada através do *State-Trait Anxiety Inventory* (STAI-Y1 e STAI-Y2) e da *Modified Dental Anxiety Scale*. Os parâmetros fisiológicos (pressão arterial, frequência cardíaca e saturação de oxigénio) foram registados antes e após cada sessão. Os dados foram analisados de forma descritiva.
Resultados: Observou-se uma redução da ansiedade de estado (STAI-Y1) em todas as sessões, independentemente da condição. As medidas do STAI-Y1 evidenciaram uma diminuição consistente, enquanto a *Modified Dental Anxiety Scale* apresentou variabilidade e foi interpretada de forma exploratória. Os parâmetros fisiológicos não demonstraram diferenças consistentes ou clinicamente relevantes entre as condições.
Conclusões: A aromaterapia com lavanda poderá contribuir para a redução da ansiedade dentária percebida; contudo, a melhoria observada também na condição placebo sugere um efeito contextual relevante. Estes resultados reforçam a necessidade de estudos controlados, com maior dimensão amostral, para clarificar a eficácia clínica específica da aromaterapia em medicina dentária.

Introduction

Periodontitis is a chronic inflammatory disease of multifactorial origin that develops from untreated gingivitis (a reversible condition) and is characterized by progressive destruction of the tooth-supporting tissues, including the periodontal ligament, root cementum, and alveolar bone.[1,2] Disease progression may involve either horizontal or vertical (angular) bone loss. Horizontal bone loss is characterized by a uniform resorption of the alveolar crest, which remains parallel to the line connecting the cemento-enamel junctions (CEJ) of adjacent teeth, whereas vertical bone loss can lead to the formation of periodontal infrabony defects, in which the base of the defect is located apical to the adjacent residual alveolar crest. Unlike horizontal bone loss, these defects exhibit a complex three-dimensional configuration, characterized by the presence of one or more residual bony walls surrounding the root surface,[3] and therefore represent a significant clinical challenge due to their anatomical complexity and the high risk of progressive clinical attachment loss and eventual tooth loss.

Periodontal regeneration is one of the main goals of contemporary periodontal therapy, aiming not only to control infection and inflammation but also to restore the structural and functional integrity of lost periodontal tissues.[2,4] Over the past decades, several regenerative approaches have been proposed, including surgical and minimally invasive techniques (MIST/MINST), the use of biomaterials, bone grafts, guided tissue regeneration (GTR) membranes, enamel matrix derivatives (EMD), and platelet concentrates (PRP, PRF, A-PRF).[5-7] Despite substantial advances, clinical outcomes remain variable and depend on multiple factors, such as systemic diseases—which have a bidirectional relationship with periodontal disease—the morphology of the defect, the surgical technique employed (preferably MIST/MINST), and the biological characteristics of the material used.[8,9]

In this context, the investigation of new biomaterials with bioactive properties has gained increasing relevance. Hyaluronic acid (HA) is a glycosaminoglycan naturally present in the extracellular matrix of various tissues, including periodontal connective tissue, and is recognized for its fundamental role in tissue homeostasis and its ability to modulate wound-healing processes.[10,11] HA exhibits anti-inflammatory, angiogenic, and viscoelastic properties and promotes cell migration and proliferation, enhancing the activity of fibroblasts, osteoblasts, and endothelial cells through activation of CD44 receptors. In addition, studies have shown its role in modulating inflammation and stimulating cementoblasts and periodontal ligament cells, thereby contributing to tissue reorganization and clot stability during the early healing phase.[12] These characteristics have generated growing interest in its application in periodontology, particularly as an adjunctive agent in regenerative procedures.

In recent years, several clinical studies have evaluated the use of HA, either alone or in combination with other regenerative approaches, in the treatment of periodontal intrabony defects.[13-19] However, the reported outcomes show considerable heterogeneity in terms of clinical protocols,

concentrations used, surgical techniques, and evaluation parameters, making an integrated analysis of the available evidence necessary. Therefore, the present integrative review aims to analyze and synthesize the scientific literature regarding the clinical and radiographic effectiveness of HA in the regenerative treatment of periodontal intrabony defects, identifying possible clinical benefits, potential advantages, limitations in clinical practice, and gaps in current knowledge that justify its consideration and potential integration into routine regenerative protocols, thereby contributing to a better understanding of its therapeutic role.

Methodology

Study design

An integrative literature review was conducted with the aim of collecting, analyzing, and synthesizing relevant scientific evidence on the use of hyaluronic acid (HA) in the regenerative treatment of periodontal intrabony defects.

Search strategy

The literature search was performed in major health sciences databases, including PubMed, Web of Science, B-On, and the Cochrane Library. The search strategy used combinations of the following keywords: "hyaluronic acid", "intrabony defects", "periodontal regeneration", and "periodontal intrabony defect", including both free terms and MeSH-controlled terms, combined using the Boolean operator "AND" as follows: In PubMed, the search strategy was structured using MeSH descriptors combined with Boolean operators: ("hyaluronic acid") AND ("intrabony defect") AND ("periodontal regeneration"), yielding 15 results. In Web of Science, the search strategy was structured using MeSH descriptors combined with Boolean operators: ("hyaluronic acid") AND ("intrabony defect") AND ("periodontal regeneration"), yielding 19 results.

In B-On, the search strategy was structured using MeSH descriptors combined with Boolean operators: ("hyaluronic acid") AND ("periodontal intrabony defect"), yielding 20 results. In the Cochrane Library, the search strategy was structured using MeSH descriptors combined with Boolean operators: ("hyaluronic acid") AND ("periodontal intrabony defect"), yielding 22 results.

Inclusion criteria

Studies were included if they met the following criteria: article types comprising systematic reviews, meta-analyses, clinical case reports, randomized controlled clinical trials, prospective cohort studies, and longitudinal observational studies; human studies; articles written in Portuguese or English; and publications between 2018 and 2025.

Exclusion criteria

The following were excluded: in vitro studies; animal (in vivo) studies; studies not involving intrabony defects or therapies unrelated to HA; and any studies not fulfilling the inclusion criteria.

Study selection process

Study selection was performed in several stages. Initially, records were identified through database searches. After removal of duplicates, titles and abstracts were screened according to the predefined inclusion and exclusion criteria. Potentially eligible articles were then assessed in full text to determine final eligibility. The process of identification, screening, eligibility, and inclusion of studies was summarized in a flowchart prepared in accordance with PRISMA 2020 recommendations, adapted to the context of an integrative review, and guided by the PICO strategy (Population, Intervention, Comparison, Outcome). In total, eleven studies were included in this integrative review (Figure 1).

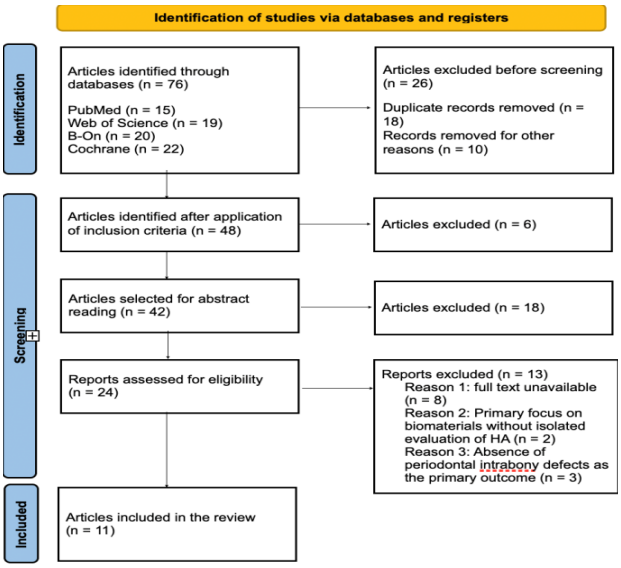

Figure 1. PRISMA flowchart.

Results

A total of 11 studies were included in the final analysis. Mamajiwala et al. reported a randomized, double-blind, split-mouth clinical trial (20 patients) comparing 0.8% hyaluronic acid (HA) gel as an adjunct to open flap debridement (OFD) with OFD plus placebo in intrabony defects over 12 months.[15] After 12 months, both groups showed significant clinical improvement relative to baseline, with superior outcomes in the HA group. Mean CAL gain was 5.1 ±0.74 mm at test sites versus 3.9 ±0.9 mm at control sites ($p = 0.008$), and mean PD reduction was 5.4 ±1.09 mm versus 4.1 ±0.58 mm, respectively ($p = 0.006$). Mean GR increase was lower in the HA group (0.5 ±0.60 mm) than in the control group (1.1 ±0.81 mm; $p = 0.04$), indicating greater soft-tissue stability at HA-treated sites. Radiographically, mean DF was significantly higher in the test group (5.67 ±2.01 mm) than in controls (4.49 ±1.78 mm;

p = 0.03), whereas DR was higher in the HA group (3.93 ± 2.79 mm vs. 3.18 ±1.53 mm) but without statistical significance. Overall, 65% of test sites achieved a CAL gain > 4 mm compared with 40% of control sites, and 85% of defects in the HA group showed defect fill > 4 mm versus 70% in the control group. Pilloni et al. evaluated the outcomes of regenerative surgery for intrabony defects using a single-flap approach (SFA) combined with either cross-linked HA (test) or enamel matrix derivative (EMD) (control) in a randomized clinical trial with 24-month follow-up. At 24 months, both groups demonstrated statistically significant clinical improvements compared with baseline (p < 0.001). Mean CAL gain was 2.19 ±1.11 mm in the HA group and 2.94 ±1.12 mm in the EMD group, with no statistically significant difference between groups (p = 0.067). In contrast, PD reduction was significantly greater in the EMD group (4.5 ±0.97 mm) than in the HA group (3.31 ±0.70 mm; p = 0.001). In the HA group, 87.5% of defects exhibited CAL gains ≤ 3 mm, whereas in the EMD group 37.5% of sites achieved CAL gains ≥ 4 mm. Regarding residual PD, 93.75% of EMD-treated sites showed final PD between 2–3 mm, while most HA-treated sites had residual PD between 4–5 mm. REC increased in both groups, without statistically significant intergroup differences.[16] Božić et al. reported an uncontrolled case series assessing a combined regenerative approach for deep intrabony defects (stage III-IV patients) with using cross-linked HA in conjunction with deproteinized porcine bone xenograft and papilla preservation techniques. At baseline, mean PPD was 7.89 ±1.60 mm and mean CAL was 8.72 ±1.82 mm. After 6 months, a statistically significant PPD reduction of 4.54 ± 1.65 mm was observed (p < 0.001), resulting in a mean residual PPD of 3.35 ±0.72 mm. Mean CAL gain was 3.65 ± 1.67 mm (p < 0.001), accompanied by a mean increase in REC of 0.89 ±0.59 mm (p < 0.001). In terms of CAL distribution, 44.4% of sites showed gains of 2–3 mm, 11.1% showed gains of 4 mm, and 40.7% exhibited gains ≥ 5 mm. With respect to pocket resolution, 51.9% of sites presented residual PPD ≤ 3 mm, 40.7% had PPD of 4 mm, and only 7.4% had PPD of 5 mm. Using a cut-off of PPD ≤ 4 mm, overall pocket closure was achieved in 92.6% of sites. Radiographically, although no standardized quantitative measurements were performed, the authors reported evident defect fill at 6 months based on the clinical cases presented.[18] Rodríguez-Aranda et al. performed a systematic review, conducted according to PRISMA guidelines, to assess clinical and radiographic outcomes of hyaluronic acid (HA), used alone or in combination with other regenerative therapies, in the surgical treatment of periodontal intrabony defects. Across all HA-treated groups, statistically significant improvements in clinical attachment level (CAL) gain and PD reduction were reported after 6–12 months of follow-up. In several studies, mean CAL gain in HA test groups ranged approximately between 2.6 mm and 4.5 mm, depending on the therapeutic combination used (HA alone, HA + open flap debridement, HA + membranes, or HA + grafts). PD reduction was also clinically relevant, with decreases in the order of 3–4 mm in some trials.[12] Ostos-Aguilar et al. carried out a systematic review and meta-analysis to evaluate the clinical efficacy of HA, used alone or in combination with bone substitutes, in the treatment of periodontal intrabony defects. In the OFD + HA versus OFD-alone comparison, the 6-month meta-analysis showed a statistically significant CAL gain in favor of HA, with a mean difference (MD) of +1.00 mm (95% CI: 0.65–1.35 mm). A greater PD reduction was also observed, with an MD of 0.76 mm (95% CI: 0.34–1.17 mm). At 12 months, however, differences were no longer statistically significant for either CAL (MD: 0.29 mm; 95% CI: −1.57–2.15 mm) or PD (MD: 0.82 mm; 95% CI: −0.16–1.80 mm), and heterogeneity was high. In the OFD + HA + bone substitute versus OFD + bone substitute comparison, no statistically significant differences were found in CAL gain at 12 months (MD: 0.57 mm; 95% CI: −0.30–1.43 mm) or PD reduction (MD: 1.05 mm; 95% CI: −0.37–2.47 mm). A significant difference was detected for radiographic bone fill (RBF) at 12 months, favoring the HA group (MD: 0.57 mm; 95% CI: 0.15–0.99 mm). The overall certainty of evidence, graded by GRADE, was rated as low to very low, mainly due to the small number of included studies and methodological heterogeneity.[20] Vela et al. performed a prospective, randomized, single-center clinical trial comparing cross-linked HA (xHyA) with enamel matrix derivative (EMD) in regenerative treatment of intrabony defects over 6 months. At 6 months, mean CAL gain was 3.18 ±1.49 mm in the xHyA group and 2.58 ±1.39 mm in the EMD group; intra-group changes were statistically significant (p < 0.001), with no significant difference between groups (p = 0.132). Mean PPD reduction was 2.00 ±1.46 mm in the test group and 1.96 ±1.42 mm in the control group (p < 0.001 intra-group; p = 0.919 inter-group). REC increased by 1.04 ±1.29 mm and 1.11 ±1.22 mm in the xHyA and EMD groups, respectively. Radiographically, defect depth (BC–BD) decreased from 5.34 ±1.59 mm to 2.67 ±0.82 mm in the test group (mean fill ≈ 2.67 mm) and from 5.22 ±1.48 mm to 2.57 ±0.78 mm in the control group (≈ 2.65 mm), with no significant between-group difference (p = 0.718). Defect width decreased by approximately 1.92 mm in the xHyA group and 1.98 mm in the EMD group (p = 0.789). Both treatments resulted in significant improvements in inflammatory parameters and favorable early wound healing, with no relevant adverse events.17 Kaur et al. investigated the adjunctive use of HA in combination with a bioabsorbable membrane for intrabony defects in a randomized split-mouth clinical trial with 6-month follow-up. Mean PD reduction in the HA group was 2.70 ±0.35 mm at 3 months and 4.15 ±0.53 mm at 6 months, compared with 1.85 ±0.41 mm and 2.85 ±0.47 mm in the control group, respectively (p < 0.001). Mean CAL gain at test sites was 2.75 ±0.54 mm at 3 months and 4.20 ±0.67 mm at 6 months, versus 1.75 ±0.42 mm and 2.85 ±0.47 mm at control sites (p < 0.001). Radiographically, greater bone fill was observed in the HA-treated group (1.17 ±0.17) compared with the non-HA group (0.46 ±0.07), with

statistically significant differences ($p < 0.001$).[21] Iorio-Siciliano et al. conducted a randomized, parallel, single-blinded clinical trial with 6-month follow-up to assess whether adjunctive cross-linked HA (xHyA) enhances clinical and radiographic outcomes of moderate intrabony defects treated with minimally invasive non-surgical therapy (MINST) compared with MINST alone. At 6 months, both groups showed statistically significant improvements in all clinical parameters except GR. In the test group, mean PD decreased from 6.7 ±1.4 mm to 4.0 ±0.8 mm (mean reduction 2.7 mm), whereas in the control group it decreased from 6.8 ±0.8 mm to 4.2 ±0.8 mm (mean reduction 2.6 mm), with no significant inter-group difference at 6 months ($p > 0.05$). CAL improved from 8.4 ±2.8 mm to 5.5 ±1.9 mm in the test group (mean gain 2.8 mm) and from 8.2 ±1.7 mm to 6.0 ±2.4 mm in the control group (mean gain 1.9 mm), again without significant between-group differences at 6 months. At 3 months, however, PD and CAL improvements were significantly greater in the test group ($p < 0.05$), indicating a faster initial response. Pocket closure (PD ≤ 4 mm without BOP) at 3 months was achieved in 84.2% of test sites compared with 10.5% of control sites ($p < 0.001$); at 6 months, pocket closure rates were 78.9% and 63.1%, respectively, with no significant difference. Radiographically, both groups showed significant improvement in CEJ–BD from baseline to 6 months ($p < 0.05$). Mean DF was higher in the xHyA group (2.1 ±0.9 mm) than in controls (1.4 ±1.1 mm; $p = 0.026$), and RDA increased significantly only in the test group (from 35.8° to 53.9°; $p < 0.001$), although inter-group differences in RDA at 6 months were not significant.[13] Bădărău-Suster et al. presented a narrative review summarizing recent advances in regenerative periodontal therapies, with particular emphasis on biomaterials, biologically active derivatives, and minimally invasive surgical approaches. Across the included studies, application of HA in appropriately selected intrabony defects was generally associated with clinically significant reductions in probing pocket depth (PPD), CAL gain, and radiographic defect fill. Comparative trials between HA and EMD indicated that both biomaterials yielded significant clinical improvements over medium- to long-term follow-up (up to 18–24 months), although statistically significant differences between groups did not always translate into clear clinical advantages.[22] Ezer and Gunpinar carried out a randomized clinical trial to evaluate the effect of adjunctive 0.8% HA gel in minimally invasive non-surgical treatment (MINST) of intrabony defects ≥ 3 mm. At 3 months, PD reduction was significantly greater in the test group (−3.29 ±0.77 mm) than in the control group (−2.57 ±0.96 mm; $p < 0.05$). At 6 months, PD reduction was −3.52 ±0.79 mm in the HA group and −3.89 ±1.76 mm in the control group, with no statistically significant difference. CAL gain at 3 months was also higher in the test group (2.52 ±0.94 mm) compared with the control group (1.47 ±0.77 mm; $p < 0.05$), whereas at 6 months CAL gains were 2.88 ±1.05 mm and 2.42 ±1.30 mm, respectively, without significant between-group differences. Gingival recession increased in both groups but was significantly lower in the test group at both 3 and 6 months ($p < 0.05$), indicating reduced gingival recession with adjunctive HA. Radiographically, both groups demonstrated significant reductions in intrabony defect depth (INFRA) at 6 months ($p < 0.05$ intra-group), with mean INFRA reduction of 0.81 ± 1.03 mm in the HA group and 0.72 ±0.97 mm in the control group, without significant inter-group differences. No significant between-group differences were observed for total defect depth, CEJ–AC, or defect angle.[14] Rodríguez-A et al. conducted a randomized clinical trial with 18-month follow-up to compare cross-linked HA 1.8% with EMD in regenerative treatment of intrabony defects, evaluating both clinical and radiographic outcomes. Both groups showed statistically significant improvements from baseline ($p < 0.001$). At 18 months, mean PD reduction was 3.96 ±1.41 mm in the HA group and 4.38 ±1.50 mm in the EMD group, with no significant difference between treatments. Mean CAL gain was similar in both groups (3.43 ±1.62 mm for HA and 3.50 ±1.81 mm for EMD). In the EMD group, 53.8% of sites exhibited CAL gains of 2–3 mm at 6 months, whereas in the HA group 48.1% of sites showed CAL gains ≥ 4 mm at 18 months. GR increase was greater in the EMD group (0.88 ±0.64 mm at 18 months) than in the HA group (0.53 ±0.53 mm). Radiographically, both groups demonstrated significant reductions in INFRA at 6 months (−2.1 ±1.1 mm in the HA group and −2.0 ±1.4 mm in the EMD group; $p < 0.001$), with progressive increases in regenerated area up to 18 months (18.1 mm^2 for HA and 18.3 mm^2 for EMD). The mean percentage defect fill at 18 months was approximately 79.5% in the HA group and 84.1% in the EMD group, with no statistically significant differences between treatments.[23]

Discussion

Overall, the available evidence suggests that HA, used either alone or as an adjunctive agent, is associated with consistent improvements in clinical parameters, namely clinical attachment level (CAL) gain and probing pocket depth (PPD) reduction, as well as radiographic signs of bone defect fill. However, joint analysis of the studies shows that these benefits are not uniform and are influenced by factors such as the surgical technique, HA formulation, and follow-up period, which underlines the need for a cautious interpretation of the findings.

When the studies comparing HA adjunctive to open flap debridement (OFD) with OFD alone are considered together, a relatively consistent pattern of additional benefit with HA use can be observed. Studies[15,20,21] showed superior improvements in CAL, PPD, and defect fill when HA was used as an adjunct, suggesting that it may potentiate the regenerative effect of conventional surgical approaches. This effect may be related to the capacity of HA to stabilize the blood clot and modulate the inflammatory response, thereby creating a microenvironment more favorable to

regeneration. Nevertheless, as highlighted particularly by the meta-analysis of Ostos-Aguilar et al. (2023), these benefits tend to be more evident in the short term and may diminish over time, raising questions about their long-term stability.

A similar pattern was observed in studies[13,14] involving minimally invasive techniques such as MINST or MIST. Work by Gundogdu Ezer and Gunpinar (2025) and Iorio-Siciliano et al. (2025) demonstrated that HA is associated with more pronounced improvements in the early healing phases, particularly at 3 months, with no statistically significant differences at medium-term follow-up. These data suggest that HA may primarily play a facilitating role in the initial phase of wound healing rather than act as a determinant of the final outcome. From a clinical perspective, this indicates that its benefit may be more related to the quality of early healing than to sustained regenerative gains. In practice, the decision to integrate HA into minimally invasive approaches may therefore be weighed mainly in light of the need to maximize early healing in well-selected defects, rather than in the expectation of marked long-term differences.

With regard to comparisons between HA and enamel matrix derivatives (EMD), the studies[16,17,23] showed overall similar results between the two biomaterials, with no statistically significant differences in most clinical and radiographic parameters assessed. Although some trends favored EMD, particularly in terms of PPD reduction, these differences did not consistently translate into clinically relevant advantages, indicating that HA may represent a viable therapeutic alternative in selected clinical contexts. The availability of an alternative with a favorable biological profile may be particularly relevant in scenarios where biomaterial choice must balance efficacy, cost, and availability. Regarding the use of HA in combination with other biomaterials, such as bone grafts, studies like that of Božić et al. (2021) reported significant clinical improvements, with clinically relevant CAL gains and PPD reductions. However, interpretation of these results should be cautious, as the combined nature of the interventions makes it difficult to determine the specific contribution of HA. The absence of control groups and variability in surgical protocols and graft types limit the robustness of the conclusions, making it challenging to establish clear causal relationships or to distinguish the isolated effect of HA from the overall effect of the combined approach. From this perspective, it seems more appropriate to regard HA as an interesting potential adjunct within such protocols, but still far from being considered an isolated key determinant of success.

From a critical standpoint, the high methodological heterogeneity among the included studies represents an important limitation of this review. Differences in surgical techniques, HA formulations (cross-linked vs. non-cross-linked) and concentrations, as well as in follow-up durations, hinder direct comparison of results. In addition, several studies involve small sample sizes and a moderate risk of bias, reinforcing the need for randomized clinical trials with greater methodological standardization, longer follow-up, and direct comparisons between different HA formulations and other regenerative biomaterials. For future research, it would be particularly relevant to clarify in which defect types, patient profiles, and surgical contexts the clinical benefit of HA is most predictable and clinically meaningful. The currently available evidence should therefore be interpreted with caution, serving more as an indication of the therapeutic potential of HA than as definitive proof of its superiority over other approaches. Accordingly, the use of HA should be considered on a case-by-case basis, integrating individual clinical judgment and patient preferences until more robust data are available to support clearer and more generalizable recommendations.

Conclusion

HA emerges as a promising therapeutic option in the regenerative treatment of periodontal intrabony defects, demonstrating significant clinical benefits, particularly when used as an adjunct to conventional and minimally invasive surgical approaches. Across the included studies, its application was consistently associated with CAL gains, PPD reduction, and, in certain cases, radiographic improvements in bone fill. HA can be regarded as a complementary therapeutic resource in periodontal regeneration, whose clinical value lies mainly in its strategic integration into already well-established approaches, contributing to optimization of the healing microenvironment and potentially increasing the predictability of outcomes in selected intrabony defects.

All data used in this article were obtained from publicly available databases (PubMed, Web of Science, B-On, and the Cochrane Library). No primary data was generated or and all information is available in the original published articles.

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