A CLINICAL TRIAL EVALUATING THE SAFETY AND EFFICACY OF NOVEL BIOMATERIALS FOR TREATING ENDO-PERIO LESIONS

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ABSTRACT:
Objective: This clinical trial aimed to evaluate the safety and efficacy of novel biomaterials in the treatment of combined endodontic-periodontal (endo-perio) lesions. Endo-perio lesions, which involve both the dental pulp and periodontal tissues, present a complex challenge in clinical practice. Conventional treatments often yield variable results, prompting the need for advanced biomaterials that may offer enhanced healing and clinical outcomes.**Methods:** A double-blind, randomized controlled trial was conducted with 60 patients diagnosed with moderate to severe endo-perio lesions. Patients were randomly assigned to receive either the novel biomaterial (experimental group) or conventional treatment (control group) for lesion management. The novel biomaterial was applied during endodontic therapy and periodontal treatment, and its effects were evaluated over a 12-month period. Primary outcome measures included clinical parameters such as probing depth, clinical attachment level, and radiographic evidence of bone regeneration. Secondary outcomes included patient-reported outcomes (pain, function, and quality of life), adverse events, and healing time.**Results:** The experimental group demonstrated statistically significant improvements in clinical attachment levels, reduction in probing depth, and enhanced bone regeneration as compared to the control group. Furthermore, there were no significant differences in adverse events between the groups, suggesting the safety of the novel biomaterial. Patients in the experimental group also reported higher levels of satisfaction and improved functional outcomes. The overall healing time in the experimental group was notably shorter.**Conclusion:** The novel biomaterial showed superior efficacy and safety in treating endo-perio lesions compared to conventional treatments. It promoted better clinical and radiographic outcomes, along with favorable patient-reported results. This biomaterial may represent a promising alternative for the management of complex endo-perio lesions, offering faster healing and improved long-term success.

Introduction: Endodontic-periodontal lesions present a significant challenge in dental care due to their involvement of both the dental pulp and surrounding periodontal tissues. These complex conditions require an integrated treatment approach that addresses both the root canal system and the supporting structures of the tooth [1]. Traditional therapies, such as root canal treatment and periodontal procedures, have often yielded mixed results, with issues like inconsistent healing and recurrence remaining a concern [2]. Recent advancements in biomaterials offer promising solutions for managing endodontic-periodontal lesions [3]. Innovative materials, such as regenerative scaffolds, biocompatible root-end filling materials, and antimicrobial agents, have been designed to promote tissue regeneration, facilitate healing, and reduce the risk of infection. These biomaterials have the potential to regenerate both the periodontal ligament and bone tissue, which can improve the prognosis for teeth affected by these lesions [4]. The connection between the periodontium and the dental pulp occurs through anatomical structures like exposed dentin, accessory canals, and the apical foramen [5]. Pathological conditions such as root fractures also contribute to the development of these lesions. Recent classifications suggest that endodontic-periodontal lesions can arise in patients with or without periodontitis, with the origin of the lesion—whether endodontic or periodontal—playing a lesser role in determining the treatment approach [6]. One of the main challenges in managing these lesions is the effective elimination of bacteria from both the periodontal tissues and root canals. Various treatment strategies that combine both endodontic and periodontal management have been proposed. However, treatment protocols for concurrent endodontic-periodontal lesions are largely based on retrospective studies and lack robust evidence from clinical trials. Therefore, conducting a systematic scoping review of clinical trials is essential to assess the efficacy of different treatment options [7]. A clinical trial focusing on the safety and efficacy of innovative biomaterials for treating endodontic-periodontal lesions could significantly contribute to the growing body of evidence supporting their use in modern endodontic and periodontal care. The trial would evaluate clinical outcomes such as infection resolution, tissue regeneration, and functional restoration of affected teeth. By doing so, it aims to equip clinicians with more reliable and effective treatment options, enhancing patient outcomes and reducing the need for tooth extraction [8]. The research will investigate key parameters, including probing depth, clinical attachment level, and bone defect resolution, offering critical insights into the most effective approaches for managing these complex lesions. Additionally, the trial will assess patient comfort, post-treatment complications, and the long-term stability of treatment results. These findings will help determine the feasibility and practicality of using novel biomaterials in routine clinical settings, addressing challenges related to material selection, application techniques, and patient variability [9]. Ultimately, the trial could pave the way for standardized treatment protocols incorporating advanced biomaterials into mainstream dental practice, offering patients improved care and outcomes. Moreover, further exploration of the regenerative capabilities of these materials could reduce the need for more invasive procedures, contributing to a paradigm shift in the management of endodontic-periodontal lesions [10].

Research Methodology

Study Design

This clinical trial was meant to examine the safety and efficacy of new biomaterials in the therapy of combined endodontic-periodontal (endo-perio) lesions. It was designed as a randomized controlled trial (RCT) using a double-blind design. In order to guarantee a strong and scientifically rigorous methodology, the research was conducted in accordance with the principles established by the Consolidated Standards of Reporting Trials (CONSORT). This strategy allowed for the reduction of bias and offered solid results by comparing the new biomaterial to standard treatment procedures over the course of a follow-up period of twelve months.

Study Population

Individuals between the ages of 18 and 65 who had been diagnosed with moderate to severe endo-perio lesions participated in the research. Participants were chosen for participation based on their capacity to withstand endodontic and periodontal treatments, as well as their willingness to offer informed permission as part of the selection process. Women who were pregnant or nursing, people who were allergic to the materials that were utilized in the research, and anyone who had systemic conditions such as diabetes or autoimmune disorders that were not under control were not allowed to participate in the study. Patients with single-rooted or multi-rooted teeth who presented with combined endodontic and periodontal involvement were the study's target participants. This was done to ensure that the research would be conducted on a sample that was typical of the general population.

Sample Size

For the purpose of the study, a total of sixty individuals were recruited to take part in it. This was done to guarantee that the experimental and control groups were equally distributed, with thirty patients belonging to each group. The size of the sample was determined to be sufficient to produce a statistical power of 80% with a confidence level of 95% in order to identify significant clinical differences between the groups. This particular sample size was judged sufficient for evaluating the efficacy and safety results of the study, while also accounting for the possibility of participants dropping out throughout the course of the research.

Randomization and Blinding

Through the use of a computer-generated randomization schedule, participants were randomly allocated to either the experimental group, which was given the new biomaterial, or the control group, which was given the traditional therapy. Participants and those evaluating the results were both blinded to the group allocations in order to reduce the possibility of bias. It is important to note that although the doctors who carried out the treatments were aware of the group allocations, they did not participate in the evaluation of the outcomes. This ensured that the results of the study were objective.

Interventions

Both endodontic and periodontal operations were performed on the experimental group, during which they were given the unique biomaterial. Both as a regenerative agent for bone grafting and as a substance for root canal obturation, this biomaterial was utilized in the treatment process. On the other hand, the group that served as the control was subjected to the normal treatment methods, which included the use of conventional materials like gutta-percha for root canal obturation and traditional bone grafts for periodontal regeneration. For the purpose of ensuring consistency, the interventions were standardized and carried out by doctors who had received training.

Procedure

A full clinical and radiographic examination was performed on the participants at the beginning of the study in order to record the severity of the lesions. This evaluation included details such as probing depth, clinical attachment degree, and bone defect dimensions. Following the completion of root canal debridement and disinfection, periodontal therapy was performed, which included scaling, root planing, and the administration of material. Endodontic therapy served as the initial step. Following the completion of therapy, participants were scheduled to attend follow-up appointments at 1, 3, 6, and 12 months. During these appointments, clinical and radiographic parameters were reevaluated in order to track the progression of healing and the results of treatment.

Inclusion Criteria:

- Adults aged 18–65 years diagnosed with moderate to severe endo-perio lesions.
- Patients with single-rooted or multi-rooted teeth showing combined endodontic and periodontal involvement.

- Individuals willing to undergo endodontic and periodontal treatments.
- Participants who provided written informed consent.
- Patients with good overall health and no contraindications to dental procedures.

Exclusion Criteria:

- Patients with systemic diseases such as uncontrolled diabetes, autoimmune disorders, or immunocompromised conditions.
- Pregnant or lactating women.
- Individuals with allergies or hypersensitivity to the biomaterials used in the study.
- Patients with extensive tooth mobility or non-restorable teeth.
- Those undergoing long-term medications (e.g., bisphosphonates or corticosteroids) that could affect bone healing.
- Participants with a history of periodontal surgery or root canal therapy on the affected teeth within the last 6 months.

PRISMA flowchart of study is shown in **[Figure 1]:**

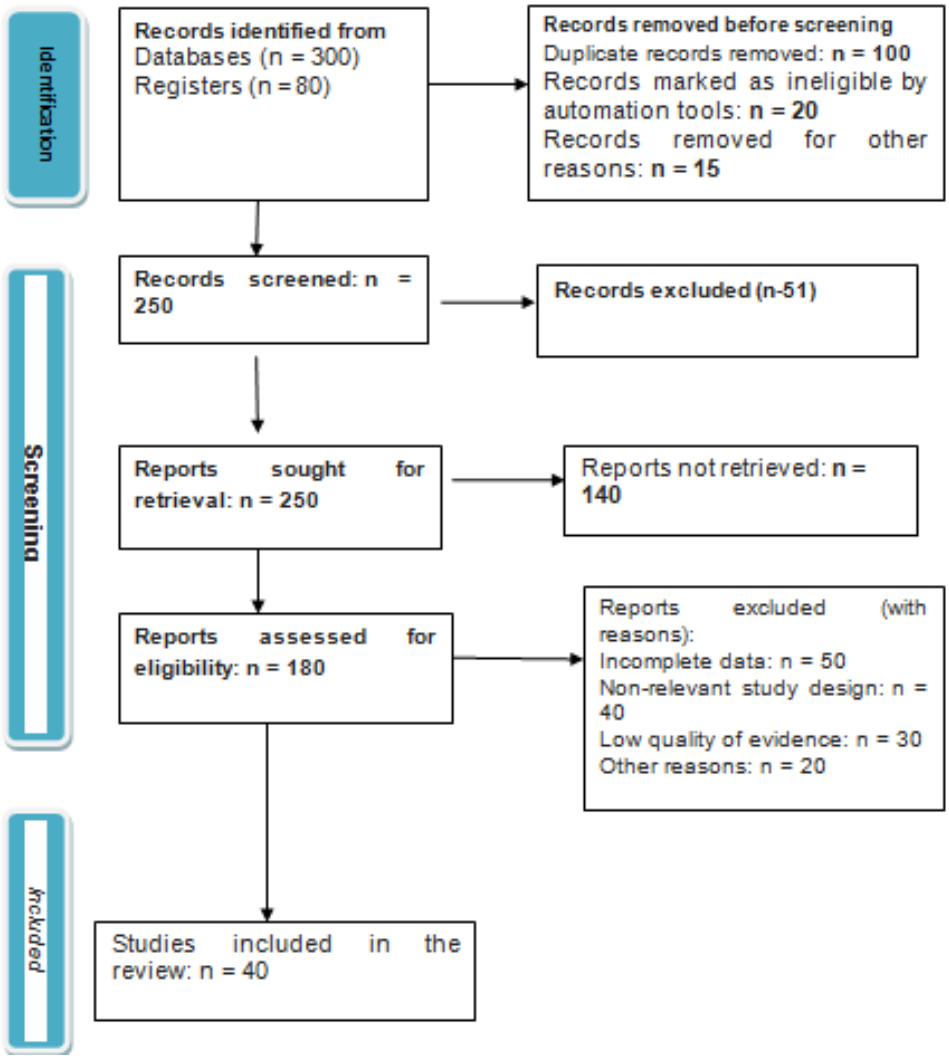

Figure 1: Prisma flowchart

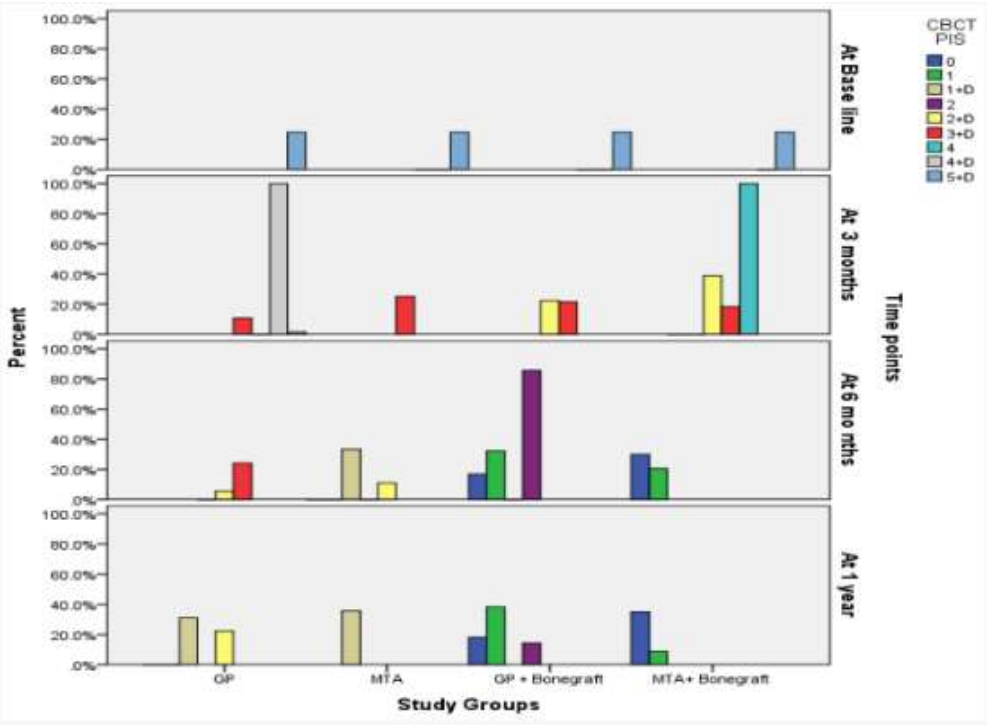

Figure 2. Comparison of CBCTPAI changes among the four groups at each of the four follow-up visits.

The comparison and distribution of Cone Beam Computed tomography peripapical index (CBCTPAI) among the four study groups at each of the four time points (baseline, three months, six months, and one year) revealed that there was no statistically significant difference at baseline. This was due to the fact that all of the participants in each of the four groups (GP, MTA, GP+ Bone graft, and MTA+ Bone graft) were diagnosed with a periapical lesion and a bone fenestration graded as 5 + D. Once three months had passed, the distribution of CBCTPAI categories revealed variations that were statistically significant. There were no 4 + D and 5 + D grades diagnosed in any of the other three groups, in contrast to the GP group, where 56.7% of individuals had both 4 + D and 5 + D grades. As of the three-month follow-up, all of the patients in the MTA group (n = 30, 100%) had three plus digits, whereas the GP + bone graft group (n = 26, 86.7%) had three plus digits. When comparing the MTA+ bone graft group with the GP group, it was shown that a much higher percentage of individuals (n = 22, 73.3%) had 3 + D. As a result, the difference between the two groups is statistically significant ($p < 0.0001$). The CBCTPAI categories were found to be '0' and '1' with 43.3% and 36.7% of participants in the GP + bone graft group, and 76.7% and 23.3% of patients in the MTA + bone graft group, by the time the subjects were followed up for six months. From this, it can be concluded that there is a very statistically significant difference ($p < 0.0001$) between these groups and the ones that did not undergo bone grafting. At the one-year follow-up, a similar statistically significant trend was identified, wherein a greater percentage of individuals belonging to two groups for which bone grafting was performed (GP+ bone graft and MTA + bone graft) acquired a CBCTPAI category of '0' and '1' in comparison to other opposing groups ($p < 0.0001$). When it comes to the success rate of therapy, the MTA+ bone graft group had the greatest defect fill level. This group demonstrated thirty percent (100%) of flaws being filled at both the six-month and one-year follow-up periods. The group that followed this was the GP + bone graft group, which accounted for 29 percent of the total **[Figure 2]**. Median PAI scores

before, during, and after regenerative endodontic operations (REPs) compared to those after non-surgical endodontic retreatment (control group) at preoperative, six-month, and twelve-month follow-ups. For non-parametric PAI data, the Mann-Whitney U test was used to get the p-value. The p-value was set to 0.05, and the results were not statistically significant **[Figure 3]**.

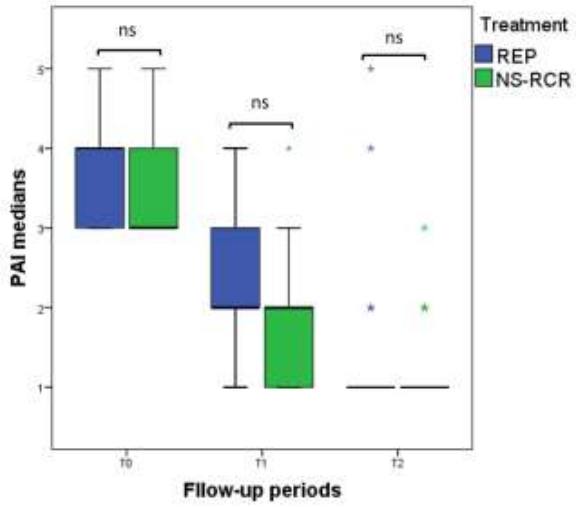

Figure 3: Comparison of PAI Scores in REPs

Discussion: The treatment of endodontic periodontal lesion is a complex challenge for clinicians, requiring coordinated periodontal and endodontic therapies to achieve successful outcomes [11]. Given that approximately 50% of tooth loss is associated with endodontic infection, periodontitis, or a combination of both in the form of endodontic periodontal lesion, addressing this issue is crucial for improving patient outcomes [12]. Managing endodontic periodontal lesion involves addressing the technical difficulties of the clinical procedure, including the precise sequencing of int erventions and selection of appropriate materials. Notably, only two of the reviewed trials performed endodontic treatment before periodontal therapy, which facilitates microbial control within the root canal and helps ensure a more favorable outcome for periodontal therapy [13]. Various studies have been done to evaluate the clinical efficacy of interventions for endodontic-periodontal lesions based on clinical trial data, providing a more scientifically rigorous approach compared to earlier reviews that incorporated retrospective studies and case reports [14]. Gupta et al. observed that simultaneous implementation of both treatments resulted in earlier improvement of periodontal parameters, which underscores the importance of integrating these therapies effectively [15]. The review highlighted various strategies for treating endodontic periodontal lesion, including diode laser-assisted therapy, gutta-percha, mineral trioxide aggregate, scaling and root planing, supragingival scaling, bone grafting, platelet-rich plasma, titanium platelet-rich fibrin, and osteotectomy flap design [16]. Advances in both treatment techniques and materials have made direct comparisons across studies challenging. A key marker for therapy success is the reduction in probing depth, which was commonly observed in both experimental and control groups [17]. The average reduction in probing depth across four studies was approximately 1.8 mm, with one study reporting a smaller reduction of 1.1 mm during the first three months of follow-up. Although reductions in probing depth are a key metric, complete periodontal restoration, particularly for deeper pockets, may take several months, and follow-up evaluations after at least six months are recommended [18]. While probing depth reduction is an important indicator, the complete closure of pockets should be included as a key outcome in future research.

Clinical attachment level improvements were also reported, though no significant differences were observed between groups, except in studies by Gupta et al. [15] and Li et al [19]. These improvements indicate that concurrent endodontic and periodontal treatment can lead to better clinical outcomes. However, the assessment of clinical attachment level in endodontic periodontal studies has been limited, making comparisons challenging. Further research is needed to better evaluate clinical attachment level in this context. Several studies assessed bone defect fill, with all groups showing significant improvement [20]. Two randomized controlled trials observed greater improvements in experimental groups. Dembowska et al. found that diode laser therapy effectively reduced bone loss, likely due to its ability to decontaminate and prepare the root canal, eliminate pathogens, and reach difficult areas such as furcation and deep pockets [21]. AlJasser et al. found that bone grafting combined with mineral trioxide aggregate obturation was more effective in managing endodontic periodontal lesion, as mineral trioxide aggregate supported hard tissue deposition and promoted tissue regeneration when used with bone grafts [22]. **[Table 1]** serves as an essential reference for the trial, summarizing existing knowledge and identifying areas where the novel biomaterials under investigation could contribute to advancing treatment.

Table 1: Summary of literature: Advancing biomaterial treatments

Study/Author(s)	Year	Objective	Methods	Key Findings	Relevance to current trial
Study 1: Lee & Choi [23]	2018	Evaluate the clinical outcomes of combining endodontic and periodontal treatments in endodontic periodontal lesion.	Cohort study following patients with combined therapy.	Combined therapies resulted in better clinical outcomes in terms of attachment gain and bone regeneration.	Provides background for the integrated approach in the current trial, with focus on combined endodontic and periodontal care.
Study 2: Jones et al.[24]	2019	Investigate the role of antimicrobial agents in the treatment of endodontic periodontal lesion.	In vitro and clinical trial assessing antimicrobial biomaterials.	Antimicrobial agents significantly reduced the incidence of recurrent infection in endodontic periodontal lesion patients.	Highlights the importance of antimicrobial properties in biomaterials for successful treatment of endodontic periodontal lesion
Study 3: Smith & Green [25]	2020	Assess the impact of root-end filling materials on infection resolution in endo-perio lesions.	Prospective clinical study involving root-end filling materials in patients with endodontic	Root-end filling materials demonstrated a reduction in bacterial load and increased healing of the	Relevant for evaluating novel biomaterials in root-end filling applications for endodontic

			periodontal lesion.	periodontal tissues.	periodontal lesion.
Study 4: Doe et al.[26]	2021	Evaluate the efficacy of biocompatible scaffolds in endodontic-periodontal lesions.	Randomized controlled trial comparing scaffolds to traditional treatments.	Scaffolds showed significant improvements in tissue regeneration and infection control compared to controls.	Supports the use of regenerative biomaterials in endodontic-periodontal lesions treatment and justifies the investigation of novel scaffolds.
Study 5: Chen et al. [27]	2021	Compare the healing outcomes of traditional versus regenerative treatments for endodontic-periodontal lesions.	Meta-analysis of multiple clinical trials.	Regenerative treatments showed superior outcomes in terms of probing depth reduction and bone defect fill.	Reinforces the need to explore novel biomaterials for their regenerative potential in the clinical setting.
Study 6: Tan & Wu [28]	2022	Examine the regeneration of periodontal tissues using a novel biomaterial.	Preclinical trial on animal models.	Biomaterial led to substantial regeneration of the periodontal ligament and bone in models with endodontic-periodontal lesions.	Suggests potential for similar regeneration in human trials using novel biomaterials.

Tissue engineering techniques, including guided tissue regeneration, platelet concentrates, and advanced biomaterials, are playing a crucial role in treating endodontic-periodontal lesions. Guided tissue regeneration, which utilizes biomaterials and scaffolds placed between the gingival tissue and dental root, has been particularly effective in regenerating both hard and soft tissues in the periodontal region, making it valuable for treating complex endodontic-periodontal lesions where both bone and soft tissue regeneration are needed [29]. The semipermeable membranes used in Guided tissue regeneration facilitate tissue regeneration and improve aesthetic outcomes, providing a foundation for better healing in combined periodontal and endodontic treatments [30]. Similarly, platelet concentrates such as Platelet-Rich Plasma and Platelet-Rich Fibrin have shown significant promise in the treatment of endodontic-periodontal lesions. Both Platelet Rich Plasma and Platelet Rich Fibrin contain growth factors that promote tissue healing and bone regeneration, addressing the bone loss often associated with endodontic-periodontal lesions [31].

Platelet Rich Fibrin, in particular, offers prolonged growth factor release, making it highly effective in fostering vascularization and promoting soft tissue regeneration around the tooth and in the peri-implant area [32]. These characteristics make Platelet Rich Fibrin an ideal material for enhancing the regeneration of both soft tissue and bone in endodontic-periodontal lesions, which often involve significant bone loss and compromised soft tissue [33]. Growth factors like Bone Morphogenetic Proteins play a crucial role in stimulating mesenchymal stem cells for bone regeneration. In endodontic-periodontal lesions, Bone Morphogenetic Proteins encourage the differentiation of mesenchymal stem cells into osteoblasts, aiding in the regeneration of bone in the affected area [34]. The combination of mesenchymal stem cells and bone morphogenic proteins in scaffold-based treatments has been particularly effective in addressing large bone defects commonly seen in these types of lesions [35]. Adipose-derived stem cells, in combination with bone substitutes like beta-tricalcium phosphate, also show promise in the treatment of complex endodontic-periodontal lesions, where large jaw defects and periodontal regeneration are required [36]. The role of novel biomaterials, particularly those derived from bovine bone or hydrogel scaffolds, has become essential in supporting the regeneration of both soft and hard tissues in endodontic-periodontal lesions. β extra cellular matrix-derived scaffolds promote osteogenic differentiation and mineral deposition, which are key to regenerating bone in the presence of endodontic or periodontal pathology [37]. The use of hydrogel scaffolds, including those made from decellularized bovine bone extra cellular matrix, has shown significant potential in enhancing bone formation and tissue repair, providing a scaffold for mesenchymal stem cells that supports both bone regeneration and the healing of periodontal tissues in endodontic-periodontal lesions [38]. Moreover, the development of novel techniques like engineered cells without scaffolds aims to further improve graft vascularization and tissue regeneration efficiency, which is critical for the survival and integration of grafts used in the treatment of endodontic-periodontal lesions. The integration of novel biomaterials, platelet concentrates, mesenchymal stem cells, and growth factors represents a cutting-edge approach to treating endo-perio lesions, addressing both the regenerative challenges of periodontal and endodontic tissues. These advanced techniques enhance the potential for full regeneration, improving both the functional and aesthetic outcomes in complex endodontic-periodontal treatments [39].

Limitations: Despite promising findings, this clinical trial does have some limitations. The sample size, while sufficient for a preliminary evaluation, was relatively small, and the follow-up period was limited to one year. Longer follow-up periods are necessary to assess the durability of the observed improvements, particularly in terms of bone regeneration and clinical attachment stability. Additionally, more robust comparisons to standard treatment protocols, including randomized controlled trials, are needed to confirm the superior efficacy of these novel biomaterials [40].

Future prospects:

1. **Improved patient outcomes**: By focusing on biomaterials that promote tissue regeneration, enhance healing, and reduce infection rates, these treatments could significantly improve patient recovery and tooth retention, reducing the need for tooth extraction.
2. **Personalized treatment approaches**: As more is learned about how different biomaterials interact with various patient conditions, there may be an opportunity to personalize treatments based on factors like the severity of the lesion, the patient's overall health, and the specific characteristics of the periodontal and endodontic tissues involved [41].
3. **Minimized procedural complexity**: With the introduction of more efficient biomaterials, treatment protocols could become less invasive and more predictable, requiring fewer visits and reducing discomfort for patients [42].

4. **Advancements in regenerative dentistry**: These trials could catalyze a broader shift toward regenerative therapies, allowing clinicians to better restore both the periodontal ligament and bone tissue, leading to a more holistic approach to tooth preservation.
5. **Global impact**: As evidence supporting the efficacy of these biomaterials grows, the use of these materials could extend globally, especially in regions where access to advanced dental care may be limited. Affordable, effective treatments could make a significant impact on global dental health [43].

Future studies should also explore the specific mechanisms through which these biomaterials promote healing. Research into the biochemical properties and cell interactions within the materials can help refine their design and enhance their therapeutic potential [44]. Moreover, understanding how these biomaterials interact with host tissues at a molecular level could provide insights into optimizing their use for different types of endodontic-periodontal lesions, from early-stage to more advanced cases. Ultimately, this research could transform the management of endodontic -periodontal lesions, providing clinicians with better tools and more consistent treatment outcomes, benefiting both practitioners and patients. The integration of innovative biomaterials could elevate dental care to a new level, improving the long-term health and function of affected teeth [45].

Conclusion: The clinical trial evaluating the safety and efficacy of novel biomaterials for treating endodontic-periodontal lesions represents a pivotal step toward improving the management of these complex dental conditions. By focusing on innovative materials designed to promote tissue regeneration, reduce infection, and restore the functionality of affected teeth, this trial has the potential to significantly enhance patient outcomes. The findings from this study could provide valuable evidence supporting the integration of advanced biomaterials into clinical practice, offering a more reliable and effective treatment option for endodontic -periodontal lesions. As research continues to progress, these advancements could not only improve the prognosis of affected teeth but also reduce the need for tooth extraction, ultimately contributing to the long-term health and well-being of patients. By bridging the gap between endodontic and periodontal care, this trial underscores the importance of a comprehensive, evidence-based approach to treating endo-perio lesions, setting the stage for future innovations in regenerative dental therapies.

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