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USE OF PRF AND OZONE THERAPY FOR BONE REGENERATION IN APICAL PERIODONTITIS DEFECTS WITHOUT THE USE OF GRAFTING MATERIAL: 3 CASE REPORTS WITH UP TO 4-YEAR FOLLOW-UP

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ABSTRACT

The regeneration of periapical defects remains a significant challenge in dentistry, necessitating innovative therapeutic approaches to restore bone and periodontal integrity. This article explores the combined use of Platelet-Rich Fibrin (PRF) and ozone therapy as an alternative to traditional grafting methods. PRF, derived from the patient's blood, is rich in growth factors like TGF-β, PDGF, EGF, and VEGF, which promote bone regeneration and tissue healing. Ozone therapy, known for its antimicrobial and anti-inflammatory properties, complements PRF by reducing bacterial load and modulating inflammation, further enhancing the regenerative process. This study reports three cases where PRF and ozone therapy were used to treat periapical defects without grafting material, showing promising results. Over a four-year follow-up period, the patients exhibited complete or near-complete healing of bone defects, as evidenced by computed tomography scans. The synergy between PRF and ozone therapy accelerates recovery, reduces treatment times, and improves overall outcomes, making it a viable, less invasive alternative for patients with periapical lesions.

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INTRODUCTION

The regeneration of periapical defects represents a significant challenge in dentistry, requiring innovative and effective therapeutic approaches to restore bone and periodontal integrity. Platelet-rich Fibrin (PRF) has emerged as a promising alternative in this context, due to its exceptional biological properties, including growth factors that stimulate tissue regeneration and healing of bone defects (Dohan *et al*, 2006). PRF is obtained through a simple process of centrifugation of the patient's blood, which concentrates platelets, fibrin, and other components essential for healing, such as leukocytes and growth factors, forming a gel that can be applied directly to the injured area (Choukroun *et al*, 2006). These growth factors, such as Epidermal Growth Factor (EGF), Transforming Growth Factor Beta (TGF-β), Platelet-Derived Growth Factor (PDGF), and Vascular Endothelial Growth Factor (VEGF), play a crucial role in modulating the bone repair and regeneration process (Dohan *et al*, 2006; Choukroun*et al*, 2006; Marx, 2004, Kawase *et al*, 2016). These growth factors present in PRFcan induce cell proliferation, stimulate angiogenesis, and promote cell differentiation, processes that are fundamental for bone regeneration (Choukroun *et al*, 2006; Marx, 2004; Kawase *et al*, 2016; Singh *et al*, 2020). TGF-β, for example, is known to promote the differentiation of mesenchymal cells into osteoblasts, favoring the formation of new bone. PDGF, in turn, acts on the chemotaxis of fibroblasts and endothelial cells to increase the synthesis of extracellular matrix, which contributes to effective tissue repair. VEGF is essential for new blood vessels, providing the irrigation necessary to sustain bone growth and the recovery of surrounding tissues. The presence of these substances in PRF contributes to an environment favorable to regeneration, accelerating healing and improving the body's response to treatment (Dohan *et al*, 2006; Choukroun *et al*, 2006; Marx, 2004). In addition to PRF, ozone therapy has been investigated as an adjunct therapy in periapical defects. Ozone, with its antimicrobial and anti-inflammatory properties, has shown a potential to complement the regenerative effects of PRF (Ahmed *et al* 2021). It reduces the bacterial load in the affected area, minimizing the risk of postoperative infections, and modulating the inflammatory response, creating a more favorable environment for regeneration. PRF with ozone can improve bone healing and soft tissue recovery, reduce treatment times, and increase

the success rates of endodontic and periodontal procedures (Ahmed *et al* 2021; Alkahtani *et al*, 2020). Recent studies suggest that the association between PRF and ozone therapy offers a synergistic approach to periapical defects, enhancing therapeutic results (Indhuja *et al*, 2016). The use of PRF to provide the growth factors necessary for bone regeneration, together with the action of ozone to control infections and reduce inflammation, offers an innovative perspective in clinical practice. This combination could be a significant step towards more effective and less invasive treatments for patients and promote faster recovery and better long-term results (Dioguardi*et al*, 2017; Adabi *et al*, 2020). This article aims to report 3cases where the use of PRFand ozone therapy were used to aid in the regeneration of periapical defects without grafting material and their4-year follow-up.

CASE REPORTS

Case #1: Patient A.T.M.G., female, 47 years old, non-smoker, in good health, went to a private practice back in February 2020 with a complaint of a small fistula in the region of the #12 element and discomfort when chewing in that area (Fig 1). At the computed tomographic exam, a small periapical defect on #12 was evident (Fig 2). The endodontic treatment seemed to be well performed, 12 years ago. The treatment plan, which the patient agreed with, was to do a periapical surgery to remove the apex of the root, retrograde obturation with Mineral Trioxide Aggregate (MTA), and fill the gap with FRP to aid bone regeneration. Two days before the procedure the patient started to take 875mg of Amoxicillin twice a day and will continue for 7 days. Before initiating the surgery, blood was collected to produce the PRF plug and membranes.

Figure 1. Initial buccal view

Figure 2. Initial computed tomography

The patient was anesthetized with 4% Articaine with epinephrine 1: 00,000 (DFL – Rio de Janeiro, RJ, Brazil), administered by the infiltrative technique in the region to be operated. The Ozone therapy was included at this moment to stimulate either soft or hard tissues before surgery, consisting of gas applications (MedPlus Dental, Philozon- BalneárioCamboriu/Brazil) of 5mcg/ml, 1 ml per point, and 3 points per teeth, on the buccal mucosa (Fig 3).After this, a linear incision was made on the mucogingival junction, with two vertical releases, with a 15c blade (Fig 4). A mucoperiosteal flap was raised and the lesion was accessed (Fig 5).

Figure 3. Gas ozone application in the region

Figure 4. Buccal view of the incisions

Fig. 5. Full flap raised

A 701 bur was used to remove the apex of #12, perform the osteotomy, and a curette aided to remove any lefts of the lesion around the apex. The cavity was filled with saline solution and gas ozone was bubbled into, it to help periapical disinfection (Fig 6). Then the retrograde obturation with MTA was done by an endodontist (Fig 7). After this phase, the PRF plug was inserted into the cavity, and gently accommodated (Fig 8), and a Polydioxanone (PDO) membrane (Plenum Bioengenharia, Jundiaí, SP, Brazil) was used to cover the lesion and isolate the bone defect from the mucosa (Fig 9). Above the PDO membrane, a PRFmembrane was also used before the closure of the flap (Fig 10). At last, more gas ozone was infiltrated in the region, as done in the beginning (Fig 11). 600mg Ibuprofen twice a day was prescribed for pain control. Sutures were removed after 10 days. The patient returned after 4 years for control of the procedure (Fig 12) and did another computed tomography (Fig 13), where we could note the complete repair of the lesion and the mucosa.

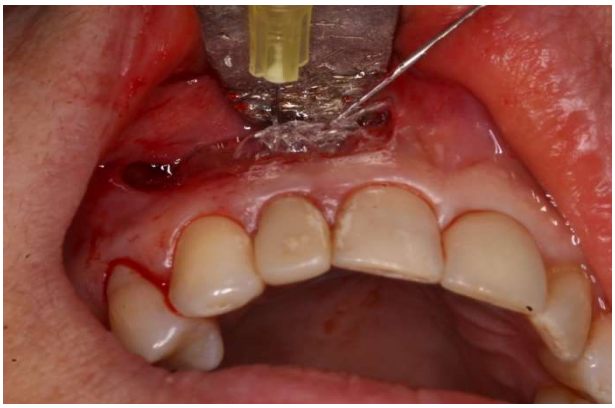

Figure 6. Periapical disinfection with ozone gas

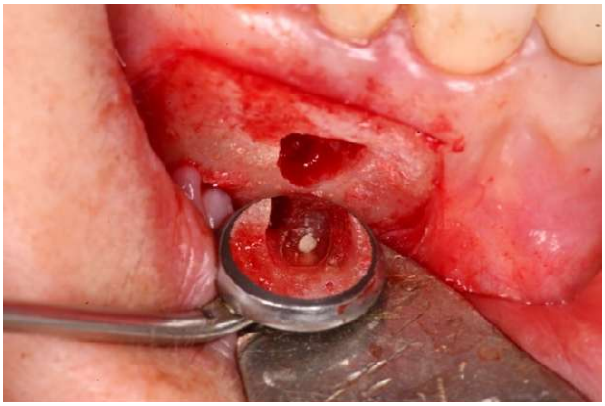

Figure 7. Retrograde obturation with MTA before bone regeneration

Fig. 8. PRFplug insertion into the cavity

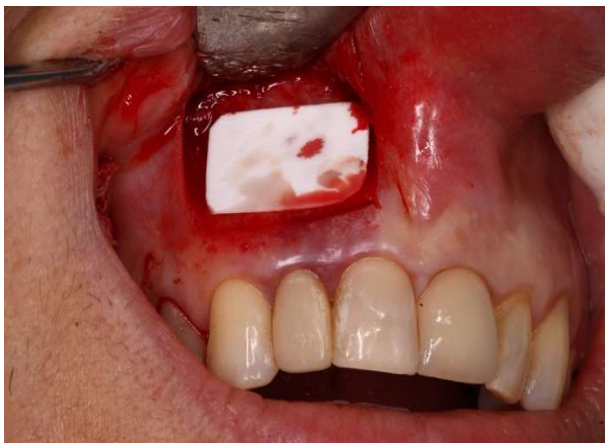

Figure 9. PDO membrane placed over the PRFplug in the cavity

Figure 10. PRF membrane placed over the PDO membrane

Figure 11. Immediate post-operative application of gas ozone

Figure 12. 4-year buccal view follow-up

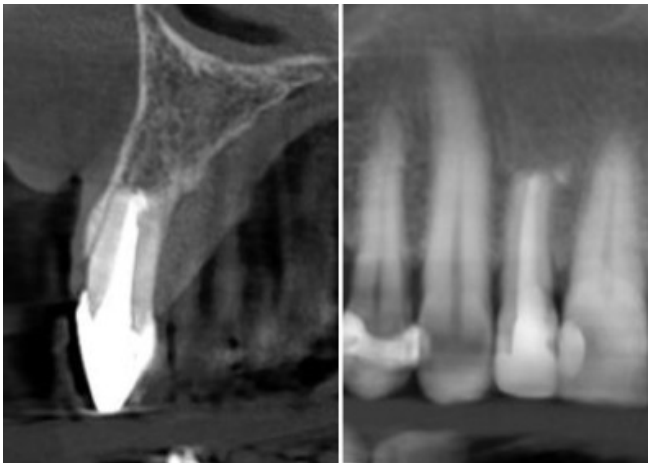

Figure 13. 4-year computed tomography follow-up

Case #2: C.G.V., female, 56 years, non-smoker, searched for a periodontist in July 2019 with similar symptoms as case#1 (Fig 14). She had a history of trauma when she was young, that led to endodontic treatment in tooth #11. The initial computed tomography showed periapical lesions in this tooth (Fig 15). The treatment plan and procedures were just as shown in Case #1. After 4 years the patient returned for control of the lesions, and we could see an almost total regeneration of the periapical lesion (Fig 16).

Figure 14. Initial buccal view

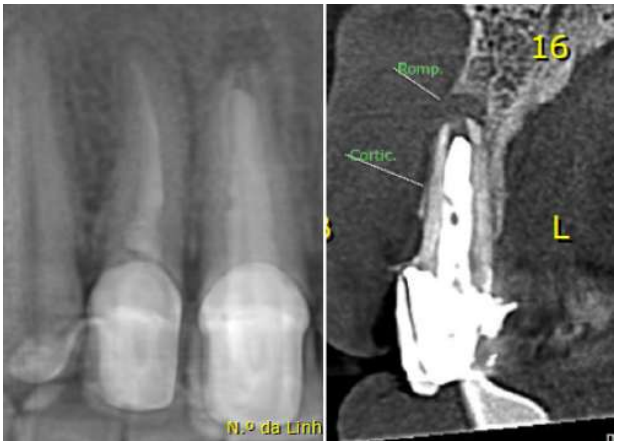

Figure 15. Initial computed tomography of tooth #11

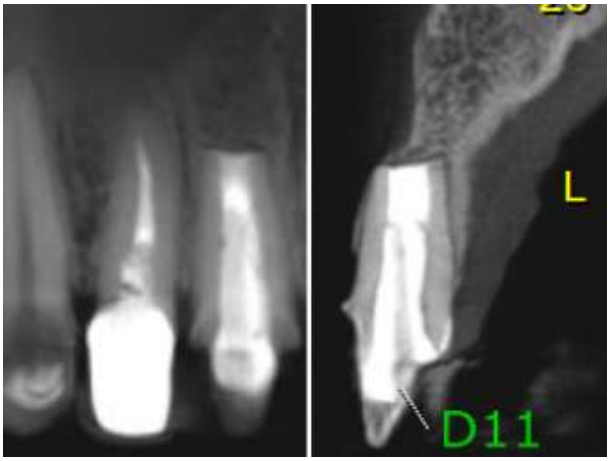

Figure 16. 4-year computed tomography follow-up

Case #3: Patient D.M.C., 32 years, female, non-smoker, and athlete, searched for a periodontist because she was feeling a "strange sensation" when chewing on the left side of her upper maxillae. In the computed tomography exam, we were able to find a huge periapical lesion with great bone resorption from teeth #23 and #24 (Fig 17). Initially,teeth #23 had an endodontic treatment done, and after that, all the surgical procedures were just as cases #1 and #2. After 3 years of follow-up, we could see in the computed tomography exam that the majority of the lesions were replaced by new bone formed, but a very small scar was still present in the periapical region of tooth 23 and the buccal root of tooth 24 (Fig 18). Also, not all alveolar ridge was regenerated around tooth 23, but it was enough to eliminate any symptoms of the patient.

Figure 17. Initial computed tomography of teeth 23 and 24

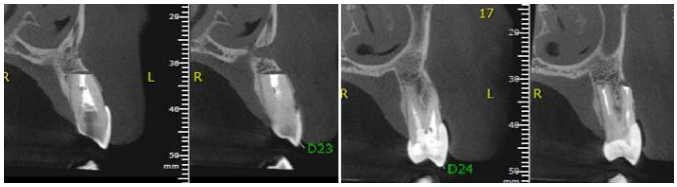

Figure 18. 3 years computed tomography of teeth 23 and 24

DISCUSSION

The treatment of periapical defects, especially those associated with apical periodontitis, has long presented challenges for clinicians, primarily due to the difficulty in regenerating lost bone and tissue without the use of grafting materials. However, the combination of Platelet-Rich Fibrin (PRF) and ozone therapy presents a promising alternative to traditional methods (Al-Maawi *et al*, 2018;Vianna *et al*, 2017). The case reports outlined in this article provide a compelling argument for the efficacy of this combined approach in facilitating bone regeneration and healing in apical periodontitis defects, even without the use of grafting materials.PRF is a biologically rich material derived from the patient's blood, offering a natural source of growth factors that promote tissue healing and regeneration (Dohan *et al*, 2006; Choukroun*et al*, 2006; Al-Maawi *et al*, 2018; Vianna *et al*, 2017). The key growth factors in PRF, such as TGF-β, PDGF, EGF, and VEGF, have been shown to have profound effects on bone regeneration, soft tissue healing, and angiogenesis (Choukroun*et al*, 2006; Kawase *et al*, 2016). This is particularly important in the context of apical periodontitis, where the goal is to restore both bone integrity and function around the affected tooth (Al-Maawi *et al*, 2018; Vianna *et al*, 2017). The results of the case reports demonstrate that PRF when properly prepared and applied provides an optimal biological environment conducive to the healing of bone defects. In the reported cases, the application of PRF directly into the defect site resulted in substantial healing, with long-term follow-up showing complete repair, as evidenced by the computed tomography (CT) scans performed up to four years post-treatment. Ozone therapy, with its antimicrobial and anti-inflammatory properties, plays a crucial adjunctive role in this therapeutic approach. In the context of periapical defects, ozone can help reduce the bacterial load and modulate the inflammatory response, both of which are critical in creating a favorable environment for bone reported to enhance the effectiveness of other regenerative treatments, including PRF (Vianna *et al*, 2017; Oliveira *et al*, 2021). The use of ozone therapy in the reported cases—both as a pre-surgical treatment to stimulate tissue healing and as an intraoperative disinfectant—appears to have contributed positively to the treatment outcomes. The reduction of inflammation and the promotion of tissue healing by ozone may have played a significant role in speeding up recovery times, thus providing patients with a more efficient and comfortable treatment outcome (Franco *et al*, 2020; Candeiro *et al*, 2019). Paraendodontic

surgeries are essential procedures for the treatment of persistent periapical lesions after conventional endodontic therapy. However, studies indicate that the recurrence or persistence rate of these lesions varies between 10% and 15%, highlighting the need for improvements in the techniques used (Lieblich, 2012). Although the number of cases is very low, we didn't have yet recurrence in these cases when utilizing this combination. The combination of PRF and ozone therapy appears to offer a synergistic effect that maximizes the regenerative potential of each treatment. PRF provides the necessary biological factors to stimulate cell proliferation, osteogenesis, and tissue repair, while ozone therapy works to minimize infection, reduce inflammation, and promote soft tissue healing. This dual approach not only accelerates the healing process but also enhances the predictability and success rates of endodontic and periodontal procedures, as shown in the case reports. The long-term follow-up, with a four-year post-operative evaluation, demonstrates the lasting efficacy of this combined treatment modality, highlighting its potential for use in clinical practice as a less invasive yet highly effective treatment for periapical defects (El-Bialy *et al*, 2014; Pires *et al*, 2019). The success of this treatment protocol underscores the potential of PRF and ozone therapy in regenerating bone defects without the need for grafting materials. This is a significant advantage, particularly in patients who may not be ideal candidates for more invasive procedures involving bone grafts. The long-term follow-up of the cases further supports the sustainability of the regenerative effects achieved with this approach. However, while these results are promising, it is important to note that the treatment was performed on a small number of patients, and further studies with larger sample sizes and more diverse patient populations are needed to fully validate these findings. Additionally, the long-term clinical outcomes in terms of functional success (e.g., tooth longevity, chewing function) should be further evaluated to ensure that these regenerative techniques result in not just radiographic healing but also long-term clinical success (Toma *et al*, 2015).

CONCLUSIONS

The combination of PRF and ozone therapy presents an innovative and effective approach for the regeneration of periapical defects, providing patients with a treatment option that is both less invasive and highly effective in promoting bone healing as demonstrated by the cases presented in this article, this synergistic therapy offers an alternative to traditional grafting materials, with significant potential for improving patient outcomes. Future research with larger patient populations and long-term functional evaluations will be crucial to confirm the applicability of this treatment in clinical practice.

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