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Case Report

Antimicrobial Photodynamic Therapy Combined with Photobiomodulation Therapy in Teeth with Asymptomatic Apical Periodontitis: A Case Series

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Abstract: Introduction: Apical periodontitis (AP) is an inflammatory disease of the periapical tissues that is often asymptomatic and diagnosed through radiographic examination. A challenge in traditional endodontics is disinfection of the root canal system (RCS), which anatomically presents numerous variations, often leading to persistent infections. Antimicrobial photodynamic therapy (aPDT) and photobiomodulation therapy (PBMT) offer promising adjuncts, due to their antimicrobial and tissue-healing properties. Objective: The aim of this article was to report five cases of teeth with pulp necrosis and asymptomatic apical periodontitis (AAP) treated with aPDT and PBMT protocols. Materials and Methods: Five cases of pulp necrosis and AAP were treated with conventional endodontic therapy supplemented with aPDT and PBMT. The treatment protocol included chemomechanical preparation (CMP), aPDT using a 660 nm diode laser (DL) with methylene blue (MB) as a photosensitizer (5 min pre-irradiation time), and PBMT using a 940 nm DL. Treatment results were evaluated through cone-beam computed tomography (CBCT)-based evaluation over 1 year of clinical follow-up. Results: All cases showed significant bone regeneration and tissue healing, demonstrating the efficacy of the combination of aPDT and PBMT. Post-operative pain did not occur in any of the patients, suggesting a possible analgesic effect of PBMT. Conclusions: The combination of aPDT and PBMT in endodontic therapy promoted tissue recovery and improved the prognosis of AAP. Further research and randomized control trials are needed to optimize treatment protocols and evaluate the long-term effects.

Keywords: photobiomodulation therapy; antimicrobial photodynamic therapy; laser; bone regeneration; apical periodontitis; root canal system

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1. Introduction

Apical periodontitis (AP) is an inflammatory disease of the periapical tissues, which develops as a host immune response to microbial infection inside the root canal system

(RCS) [1]. AP is typically asymptomatic and diagnosed through radiographic examinations. Its etiology is associated with the commensal oral microbiota, which invades and multiplies in the RCS following pulp necrosis due to factors such as caries, tooth trauma, defective restorations, or unsuccessful endodontic procedures [2]. Necrotized root canals are quickly inhabited by diverse bacterial communities, which extend to the surrounding connective tissues via the apical foramen, leading to the development of a periapical lesion [3].

Endodontic therapy seeks to reduce the bacterial load to levels that permit the modeling and healing of the affected bone tissue. However, to date, it has not been possible to find a therapeutic combination that is effective in every case. Existing endodontic treatment methods have been inadequate in lowering endodontic pathogens below detectable levels. In fact, AP remains notably prevalent [4]. This shortfall is likely due, in part, to the complex anatomy of the RCS, which hinders the elimination of bacteria in areas that are difficult for antimicrobial agents to reach, such as apical deltas, accessory canals, isthmuses, and dentinal tubules [5]. Additionally, the effectiveness of sodium hypochlorite (NaOCl) (the irrigant of choice in conventional endodontic therapy) can be limited by factors such as its concentration, exposure time, and volume within the root canals [6]. Consequently, it is evident that more advanced disinfection techniques are necessary for the thorough eradication of endodontic microbial biofilms.

In this context, antimicrobial photodynamic therapy (aPDT) has been suggested to complement conventional endodontic therapy, in order to combat a wide range of endodontic infectious diseases [7]. The inactivation of micro-organisms by aPDT is based on the use of a chromophore or photosensitizer (PS)—a harmless natural or synthetic chemical solution—which is activated by low doses of visible light in the presence of oxygen to cause targeted cellular damage. The photodynamic process begins when an electron in the PS is excited to a higher energy level, leading to the formation of an excited state. This state is transient, as the energy can be dissipated as fluorescence or transferred to nearby molecular oxygen through an inter-system crossing mechanism [8] (Figure 1A).

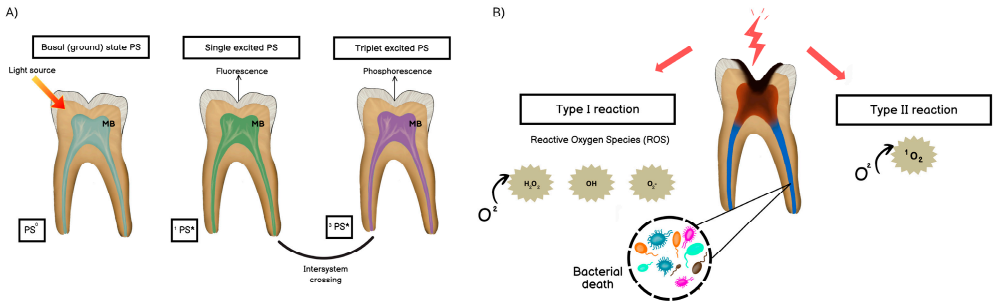

Figure 1. Schematic representation of mechanisms of antimicrobial photodynamic therapy: (**A**) When light is absorbed, the PS is activated, shifting from its ground state to an excited singlet state. This excited state may undergo inter-system crossing, where the spin quantum number changes, resulting in a lower-energy, longer-lasting triplet state. The triplet state can then react through one or both of the oxygen-dependent mechanisms, known as Type I and Type II photoprocesses; (**B**) in the type I pathway, electron transfer reactions occur from the triplet PS state, involving a substrate to form radical ions (free radicals), which can then interact with oxygen to generate cytotoxic species such as superoxide, hydroxyl radicals, and lipid radicals. In contrast, in the Type II pathway, energy transfer from the triplet PS state to ground-state molecular oxygen occurs, producing singlet oxygen which can oxidize biological molecules such as proteins, nucleic acids, and lipids, leading to cytotoxic outcomes.

When a PS is excited by an affine wavelength, it generates a cascade of photochemical reactions, causing the generation of reactive oxygen species (ROS), such as hydroxyl radicals, hydrogen peroxide, and superoxide (type 1 reaction) and singlet oxygen ($^1O_2$) molecule (type 2 reaction) (Figure 1B), which have toxic effects on bacteria and fungi [9]. The cytotoxic effects of aPDT are primarily due to the oxidative stress induced by light

(photo-oxidative stress), which leads to severe damage to bacteria cell membranes and nucleic acids [10].

Various light sources have been mentioned for aPDT, including light-emitting diodes (LEDs), halogen lamps, and lasers [11]. Among these, diode lasers (DLs) are particularly favored due to their portability, ease of use, and lower cost. Additionally, the wavelength range emitted by DLs aligns well with the electronic absorption spectrum of the majority of available PS [12]. The wavelength for irradiating a PS is determined by its absorption coefficient. It has been specified that appropriate wavelengths are 620–700 nm for toluidine blue O (TBO) and methylene blue (MB), 600–805 nm for cyanine, 620–650 nm for hematoporphyrins, 300–500 nm (ultraviolet/blue light) for curcumin and its derivatives, and 660–700 nm for phthalocyanines [13].

Several aPDT protocols have been published for the disinfection of root canals in patients with endodontic infections; however, there is noticeably high variability in the parameters used among them. Despite this wide variation in parameters, aPDT has been shown to be effective in reducing the bacterial load within the root canal [14,15].

On the other hand, photobiomodulation therapy (PBMT) involves using non-thermal light at wavelengths ranging from 650 to 1350 nm to induce a biological response through photonic energy transfer. This non-ablative energy modulates the biological processes of the target tissue, directing its action mainly to tissue repair and pain reduction [16]. PBMT, also called low-level laser therapy (LLLT), operates through a photochemical effect, where the absorbed light triggers a chemical reaction known as photobiostimulation. This process influences the release of various growth factors, which are essential for the development of epithelial cells, fibroblasts, collagen, and vascular proliferation [17]. The effects generated can be described as anti-inflammatory, analgesic, and accelerated wound healing, while also stimulating the synthesis of enzymes that play roles in lysosomes and mitochondria [18]. Visible and infrared laser radiation produces photophysical effects that alter intracellular activities, impacting the respiratory chain by boosting ATP within the mitochondrial membrane (Figure 2A). Promising results have been reported for PBMT on human gingival fibroblast proliferation [19,20] or in bone tissue regeneration processes [21,22] (Figure 2B). It is believed that LLLT reduces post-operative pain primarily by stimulating the production of endorphins, which, in turn, mitigates discomfort [23].

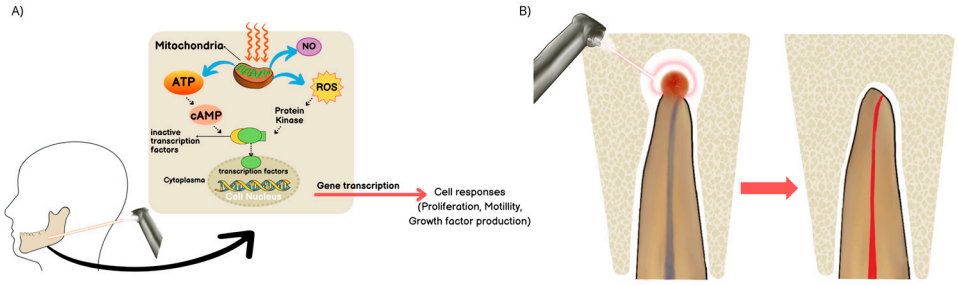

Figure 2. Schematic of the mechanisms of action and clinical effects of photobiomodulation: (**A**) Cytochrome C oxidase (CCO), the primary chromophore located in complex IV of the mitochondrial respiratory chain, plays a critical role in PBMT. When CCO absorbs light (particularly in the red and near-infrared wavelengths), it leads to the photodissociation of nitric oxide (NO). This process reduces oxidative stress and subsequently boosts the production of reactive oxygen species (ROS), ATP, and calcium ions (Ca^{2+}). As a result of increased ATP and protein synthesis, the growth factor response within cells and tissue occurs. These changes promote the desired biological responses, including anti-inflammatory, analgesic, and healing effects, while also enhancing cellular processes such as differentiation, proliferation, and migration. For these effects to occur, light must be absorbed by chromophores, which are interrelated molecules (e.g., enzymes, cell membranes, and extracellular substances) that have the capacity to absorb light. (**B**) Extraoral application of laser (red/infrared) directed toward the apical area of the affected tooth. By irradiating this area as a supplement to the endodontic treatment, accelerated bone tissue regeneration can be achieved.

As far as we are aware, there is limited information available regarding treatments that incorporate both aPDT and PBMT as adjunct therapies in in vivo studies. The case reports presented here contribute to the documentation of the effectiveness of laser-based therapies, showing results obtained in real clinical situations. Moreover, most of the previously reported in vivo methodologies lack three-dimensional cone-beam computed tomography (CBCT) imaging controls, which introduces bias in the analysis of the therapy's outcome [24–27].

Therefore, the aim of this paper was to present a series of five cases involving pulp necrosis and asymptomatic apical periodontitis (AAP), which were managed with conventional endodontic therapy, supplemented by aPDT and PBMT, and evaluated through CBCT imaging.

2. Case Report

The study was carried out in accordance with the Helsinki Declaration, and all patients signed the informed consent. The study was also conducted in accordance with the CARE guidelines (https://www.care-statement.org/) (accessed on 3 July 2023). The approval for the study protocol was granted by the Scientific Ethics Committee of Universidad de La Frontera (062/21). Table 1 summarizes the clinical and medical history of each of the five treated patients.

Table 1. Summary of relevant clinical information of the five cases presented.

	Tooth	Endodontic Diagnosis	Painful Symptomatology	Age	Gender	Relevant Medical History	Ethnicity	Weight	Height	Cigarette Smoking	Alcohol Consumption
Case 1	1.2	Pulp necrosis/AAP	No	27	Male	No	Amerindian	90 kg	180 cm	No	Yes
Case 2	1.1/2.1	Pulp necrosis/AAP	No	33	Female	No	Amerindian	61 kg	160 cm	No	Yes
Case 3	1.2	Pulp necrosis/AAP	No	43	Male	No	Amerindian	76 kg	162 cm	No	No
Case 4	3.3	Pulp necrosis/AAP	No	41	Female	No	Amerindian	55 kg	157 cm	No	Yes
Case 5	2.7	Pulp necrosis/AAP	No	33	Female	No	Amerindian	61 kg	160 cm	No	Yes

2.1. First Case

The first case is a male patient, 27 years old, with no relevant medical history. Panoramic and periapical radiography showed a radiolucent lesion associated with tooth 1.2. CBCT examination showed an osteolytic lesion of dimensions 14 × 11 × 9 mm, causing expansion and fenestration of the vestibular table (Figure 3A–C).

Clinical examination revealed normal soft tissues, and both percussion and sensitivity tests (gutta-percha and ethyl chloride) were negative. The diagnosis was pulp necrosis and AAP. Endodontic treatment of tooth 1.2 was performed in two sessions. The root canal was prepared in the first session using the mechanized instrumentation Reciproc #40/0.06 (VDW, Munich, Germany). Between each instrumentation, an irrigation volume of 10 mL of 2.5% NaOCl was delivered through a 30-gauge side-vented needle (Becton Dickinson, Madrid, Spain) at a 1 mm working length (WL). The canals were irrigated with ethylene-diaminetetraacetic acid (EDTA) 17% (Ultradent, South Jordan, UT, USA) for 1 min, followed by 1 mL of saline and 1 mL of 2.5% NaOCl successively. The final disinfection protocol consisted of Passive Ultrasonic Activation (PUI) (Ultra X, Eighteeth, Changzhou, China) of 2.5% NaOCl, 3 cycles of 20 s, with the ultrasound tip positioned 2 mm from the WL. Subsequently, ultrasonic activation (Ultra X, Eighteeth, Changzhou, China) of 0.005% MB (Chimiolux, DMC, Sao Paulo, Brazil) was performed for 30 s and the pre-irradiation time was 5 min (Figure 4A). The PS supernatant was aspirated before performing photoactivation. Afterward, intracanal disinfection was carried out using

aPDT with a DL (Therapy EC, DMC, Sao Paulo, Brazil) set to the following parameters: a wavelength of 660 ± 10 nm, a power output of 100 mW, and a total energy of 9 J (Figure 4B).

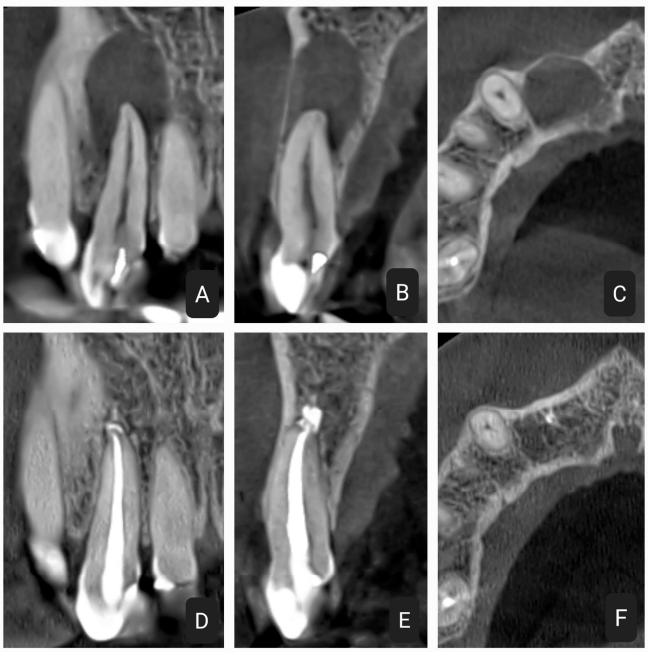

Figure 3. Three-dimensional CBCT images of tooth 1.2. (**A**–**C**) Coronal, sagittal, and axial pre-treatment sections. The CBCT examination showed an osteolytic lesion of dimensions 14 × 11 × 9 mm, causing expansion and fenestration of the vestibular table. (**D**–**F**) Coronal, sagittal, and axial post-laser treatment images show evident bone tissue gain, including recovery of the vestibular bone table.

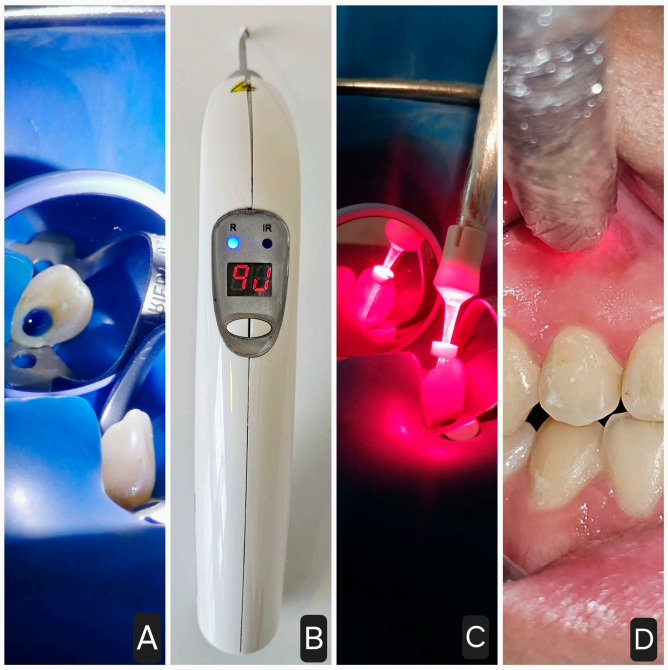

Figure 4. Intracanal disinfection with aPDT was conducted utilizing a DL with the following specifications: wavelength 660 ± 10 nm, power 100 mW. (**A**) MB inside the root canal and pulp chamber; (**B**) the laser used for all cases was therapy EC; (**C**) activation of MB using laser light inside the root canal; (**D**) the PBMT treatment entailed employing a wavelength of 940 ± 10 nm, one spot measuring 0.2 cm^2, and a power of 0.1 W.

The laser tip was positioned at WL and activated by performing helical movements to ensure an equal light distribution for 90 s (Figure 4C). Finally, 5 mL of 2.5% NaOCl was activated using PUI to remove the PS. Once dry, the canal was treated with calcium hydroxide ($Ca(OH)_2$) (Ultracal XS, Ultradent, USA) and provisionally restored with ionomer glass (Ketac Molar). Then, PBMT using a DL at 940 ± 10 nm (Biolase, EpicX) was applied. The treatment involved using one spot with a size of 0.2 cm^2 and a power of 0.1 W. Each point was treated for 40 s in continuous mode [22]. The treatment was distributed to 1 extraoral buccal point per lesion, resulting in a total energy of 4 J. The energy density used was 20 J/cm^2 (Table 2). A tipless surgical handpiece was used for PBMT extraoral therapy (Figure 4D).

Table 2. Laser parameters used for PBMT.

Wavelength (nm)	Power (W)	Energy Per Point (J)	Time (s)	Energy Density (J/cm^2)	Number of Points	Spot Size (cm^2)
940	0.1	4	40	20	1	0.2

After 7 days, a second disinfection and aPDT session were carried out, following the same protocol as in the first session. After completion, the canal was irrigated with 10 mL of 2.5% NaOCl (activated using PUI for 60 s), dried, and obturated using the synchronized hydraulic technique with Bioroot bioceramic sealer (Septodont, Saint-Maur-des-Fossés, France). The PBMT protocol described above was then applied. After the second session, a weekly session of PBMT was applied for the following 4 weeks, resulting in a total of 6 applications. Three-dimensional images were obtained using a Promax 3D CBCT (Planmeca, Helsinki, Finland), with parameters of 90 kV, 12 mA, FOV 8 × 8 cm, and voxel size 0.15 mm, and analyzed using the Romexis 4.5.1.R software (Planmeca, Helsinki, Finland). The defect and bone volume were measured initially and at 1-year follow-up (Figure 3D–F).

2.2. Second Case

The second case is a female patient, 33 years old, with no relevant medical history. Panoramic and periapical radiography showed an apical lesion associated with teeth 1.1 and 2.1. The CBCT showed an osteolytic lesion of dimensions 11 × 10 × 8 mm, causing expansion and fenestration of the vestibular table (Figure 5A–C).

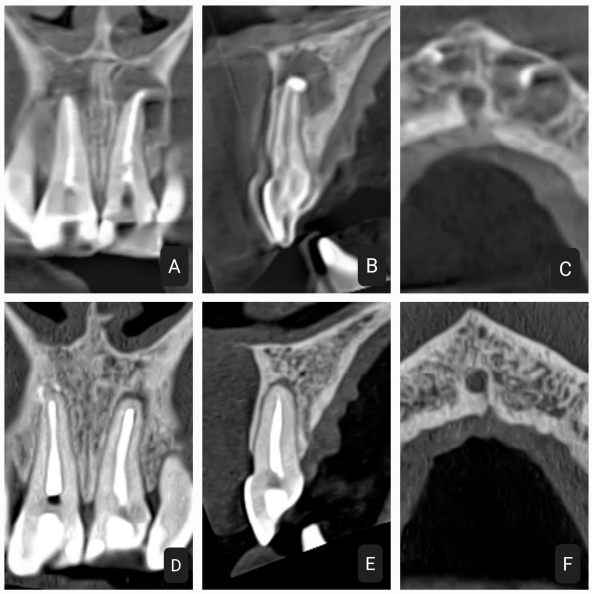

Figure 5. CBCT images of teeth 1.1 and 2.1: (**A**–**C**) Coronal, sagittal, and axial pre-treatment images show an osteolytic lesion measuring 11 × 10 × 8 mm, resulting in expansion and fenestration of the vestibular table and (**D**–**F**) coronal, sagittal, and axial post-treatment images, which evidence significant bone regeneration in the affected area.

Clinical examination revealed normal soft tissues, and both percussion and sensitivity tests (gutta-percha and ethyl chloride) were negative. The diagnosis was pulp necrosis and AAP. Endodontic treatment was performed in two sessions, and the root canal preparation was carried out with an instrument of size #40/0.06 (Reciproc, VDW, Germany). The protocols used for chemomechanical preparation (CMP), disinfection by aPDT, and PBMT were the same as in case 1. The defect and bone volume were measured initially and after 1-year of follow-up (Figure 5D–F).

2.3. Third Case

The third case is a male patient, 43 years old, with no relevant medical history. Panoramic and periapical radiography showed an apical lesion associated with tooth 1.2. The CBCT revealed an osteolytic lesion of dimensions 10 × 10 × 8 mm in tooth 1.2, causing expansion and fenestration of the vestibular table (Figure 6A–C). Both the percussion and sensitivity tests (gutta-percha and ethyl chloride) were negative. The diagnosis was pulp necrosis and AAP. The protocols used for the CMP, disinfection by aPDT, and modulation by PBMT were the same as in case 1. The root canal preparation was conducted with an instrument of size #40/0.06 (Reciproc, VDW, Germany). The defect and bone volume were measured initially and after 1-year follow-up (Figure 6D–F).

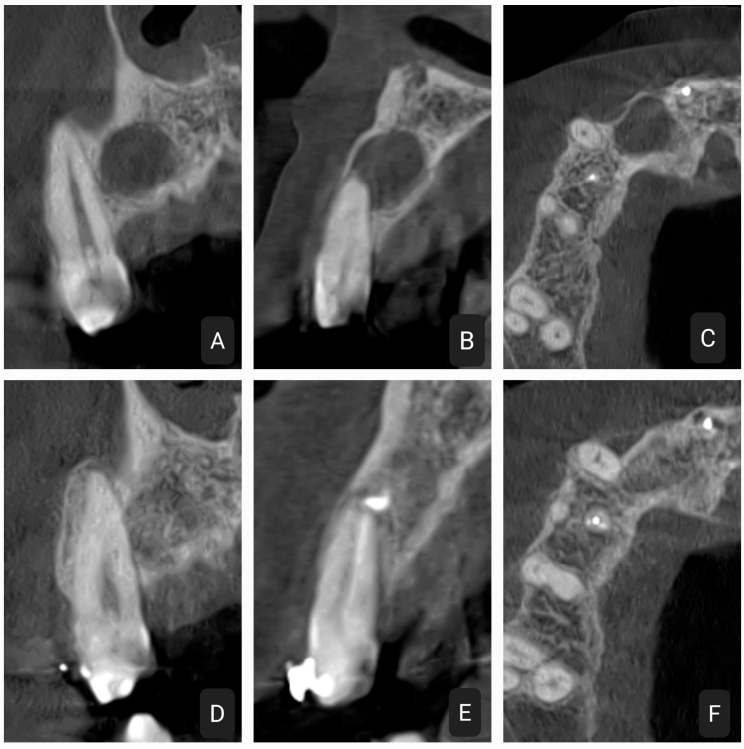

Figure 6. CBCT images of tooth 1.2: (**A**–**C**) Coronal, Sagittal, and axial pre-treatment images revealed an osteolytic lesion measuring 10 × 10 × 8 mm, resulting in expansion and fenestration of the vestibular table and (**D**–**F**) coronal, sagittal, and axial post-treatment images. Notice the gain of bone tissue throughout the affected area.

2.4. Fourth Case

The fourth case is a female patient, 41 years old, with no relevant medical history. The CBCT revealed an osteolytic lesion measuring 10 × 9 × 8 mm in the anteroinferior region of the mandible, associated with tooth 3.3. The lesion´s expansion caused significant bone loss, directly affecting the buccal cortical and resulting in fenestration (Figure 7A–C). Sensitivity and percussion tests yielded negative results. Ethyl chloride and gutta-percha were used for the sensitivity tests. The diagnosis was pulp necrosis and AAP. It was decided to proceed with conventional endodontic treatment, instrumenting up to size #40/0.06

(Reciproc, VDW, Germany), using the same CMP and obturation protocol as explained in case 1. To supplement the endodontic treatment, aPDT was used for disinfection and PBMT for modulation. The laser parameters were the same as in case 1. To ensure standardized monitoring, the patient was asked to undergo a CBCT to evaluate the defect and bone volume initially and after 1 year of follow-up (Figure 7D–F). It is important to highlight that, in this case, significant bone gain was observed at the 6-month follow-up.

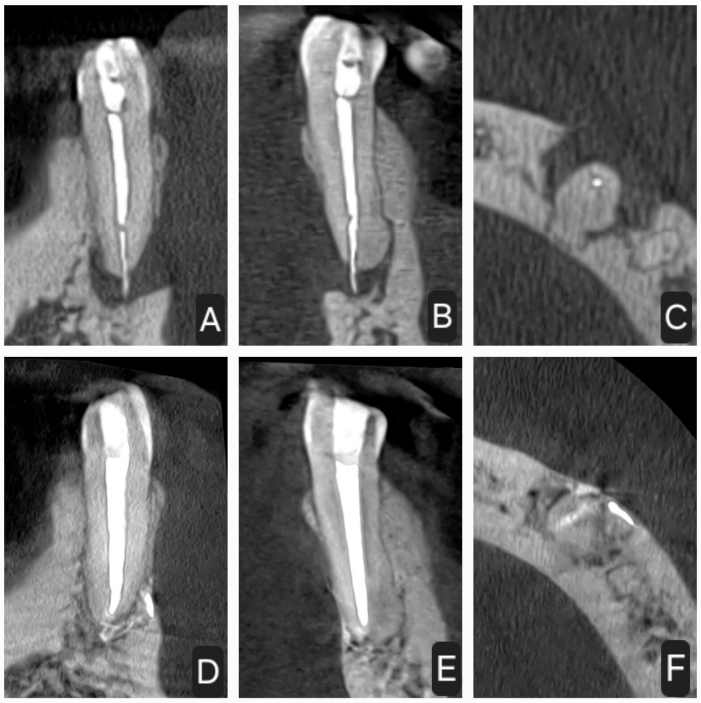

Figure 7. CBCT images of tooth 3.3. Coronal, axial, and transverse CBCT views at pre-treatment (**A**–**C**) and post-treatment (**D**–**F**). The apical lesion initially measured 10 × 9 × 8 mm. A clear recovery of trabecular and buccal cortical bone can be observed, when comparing images C and F, after using conventional endodontic therapy combined with laser therapy in both its aPDT and PBMT modalities.

2.5. Fifth Case

The fifth case is a female patient, 33 years old, with no relevant medical history, and clinically asymptomatic. Radiographic examination revealed a lesion associated with the mesiobuccal and distobuccal roots of tooth 2.7. The CBCT study provided a more detailed view of the lesion´s volume in three dimensions (Figure 8A–C), measuring 9 × 9 × 6 mm. The treatment of choice was conventional non-surgical endodontics, combined with aPDT disinfection and PBMT. In this case, the buccal roots were instrumented up to a size of #35.06 (Zenflex, Kerr, EE.UU), and the palatal root up to #40/0.06 (Reciproc, VDW, Germany). The protocols used for both the endodontic treatment and laser therapy were the same as those described in case 1. After 1 year of follow-up, there was clear evidence of bone tissue gain in the affected area (Figure 8D–F). The patient remained asymptomatic. It is important to highlight that, in this case, significant bone gain was observed at the 3-month post-treatment follow-up.

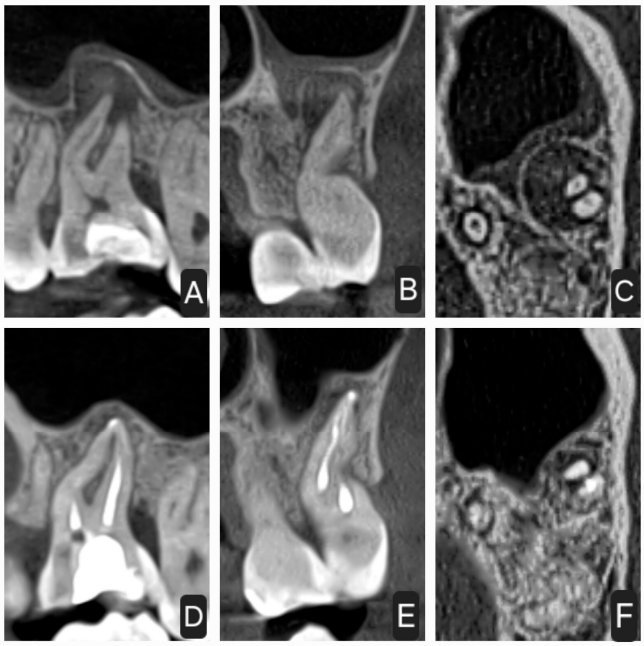

Figure 8. CBCT images of tooth 2.7. Coronal, sagittal, and axial CBCT images before (**A**–**C**) and after treatment (**D**–**F**). The three-dimensional CBCT study reveals an osteolytic lesion measuring 9 × 9 × 6 mm at the apical level, affecting the mesiobuccal and distobuccal roots. Comparing images C and F, it can be observed that, after 1 year of laser therapy, the lesion had satisfactorily resolved.

2.6. Control Periapical X-rays

X-rays play a key role in diagnosis, treatment planning, execution, and follow-up. As part of the endodontic protocol applied in the five cases presented here, conventional periapical X-rays were taken to complement the information provided by CBCT (Figure 9).

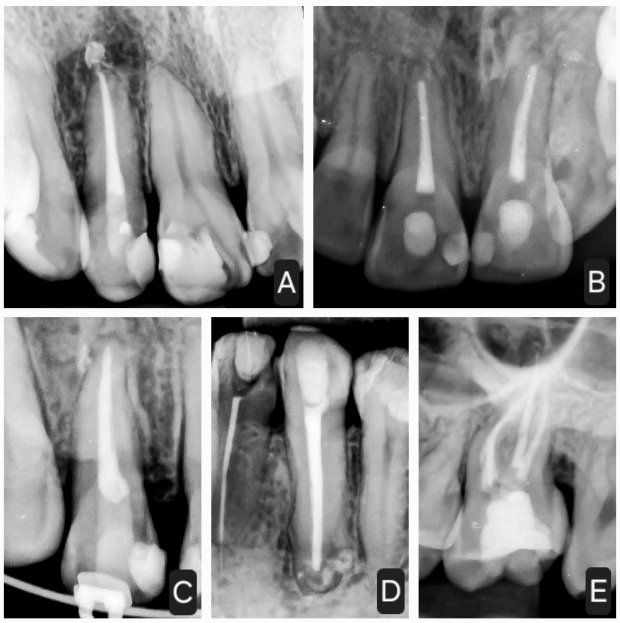

Figure 9. Control periapical X-rays of the five cases treated with conventional non-surgical endodontics supplemented with aPDT and PBMT: (**A**) Case 1, Tooth 1.2. An apical puff can be observed. (**B**) Case 2, Teeth 1.1 and 2.1. The root canals appear fully obturated. (**C**) Case 3, Tooth 1.2. A straight root canal is completely sealed. (**D**) Case 4, Tooth 3.3. The tooth is obturated in the cervical, middle, and apical thirds. (**E**) Case 5, Tooth 2.7. Endodontic obturation of the mesiobuccal, distobuccal, and palatal canals is visible. In all cases, bone tissue regeneration can be observed at the apical level.

3. Discussion

The prevalence of AP continues to increase, despite technical and technological advances in endodontic procedures. It has recently been reported that more than half of the world's adult population presents at least one tooth with AP, making its resolution a critical issue from a public health point of view [28].

aPDT has been presented as a valuable, non-invasive, and promising alternative for the eradication of bacterial infectious diseases [29]. Some articles have used planktonic models to evaluate the antimicrobial activity of aPDT [30]. However, biofilms have been proven to be much more resistant to antimicrobial agents than planktonic bacteria (even up to 1000 times more resistant). Including patients as cases makes it possible to truly evaluate the efficacy of aPDT against complex and mature bacterial organizations. aPDT has been reported to be highly effective against endodontic biofilms. Chrepta et al. [31] have reported, in their systemic review, that aPDT can reduce the bacterial load by 91.3% to 100%. Another study has demonstrated that aPDT effectively removes *E. faecalis* biofilm from the RCS before or after reciprocating instrumentation [32]. A recent randomized controlled study has assessed the ability of PUI and $Ca(OH)_2$ dressings to reduce bacterial counts in 45 single canal anterior teeth with medium-sized periapical lesions, comparing them to aPDT. While aPDT yielded higher and more promising results than $Ca(OH)_2$ dressings, it did not show a statistically significant advantage over PUI [33]. Furthermore, in vitro studies have not revealed comparative advantages in using aPDT [34,35]. This could be due to the short pre-irradiation time used and the low production of ROS species.

In the cases presented here, the PS used was MB, due to its proven ability to inactivate Gram-negative and -positive bacteria [11], including *E. faecalis* [36]. The literature has reported that, in addition to eliminating bacteria, aPDT can accelerate bone formation processes in the periradicular zone and modulate bone healing [24]. Similarly, one of the main outcomes of PBMT is collaborating with bone remodeling [21]. The results reported here demonstrate that, through jointly employing aPDT and PBMT using wavelengths of 660 and 940 nm, an evident and sustained bone regeneration process was achieved after 3, 6, and 12 months of follow-up. These observations complement the results reported by Firmino et al. (2016) [24], who observed bone regeneration and periodontal ligament restructuring at 6 months after applying PBMT and aPDT using 660 nm DLs. On the other hand, Rubio et al. (2022) [22] have also reported bone repair at 6 months using dry disinfection with a 940 nm DL and PBMT. The resolution of the lesion was associated with the local application of aPDT, which has shown great potential in significantly reducing the presence of bacteria and effectively disrupting biofilms. However, longer follow-up periods are recommended to obtain more accurate conclusions [37].

While the parameters for pre-irradiation and irradiation times have been extensively discussed in the literature, a consensus has not yet been reached. Typical pre-irradiation times vary between 5 and 15 min [22,24,38–40], while the irradiation time ranges between 30 and 60 s [22,27,32,41,42]. These observations are consistent with the protocol used in the present study. However, it is important to note some limitations of the use of PS in aPDT.

The first limitation is the potential discoloration that the PS can cause in the treated tooth, particularly in anterior teeth [43]. Several reports have indicated that 5 min of pre-irradiation with MB or TBO is enough to generate a color change at day 30 [43] and day 60 [44], compared to the baseline measurement. Some authors have reported that the combination of Endo-PTC cream with 2.5% NaOCl is effective in removing MB or TBO from the RCS [45,46]. It should be noted that, in the present study, 2.5% NaOCl was used as the final irrigation, which was activated with an ultrasonic system. No discoloration was observed in any of the teeth in follow-ups beyond 60 days. The second limitation is the volume of residual PS at the time of light activation. For optimal performance, it is necessary to aspirate the excess PS, as was performed in our protocol. This prevents the excess solution from absorbing the applied light, thereby making the disinfection process more effective.

Post-operative pain is a fundamental variable to analyze when evaluating new antimicrobial therapies. LLLT combined with PBMT is recognized as one of the most potent non-pharmacologic methods for alleviating pain [47]. Several articles have reported that applying aPDT in endodontic treatments does not ensure a decrease in post-operative pain [48–50]. In contrast, Lopes et al. (2019) [25] concluded, through a randomized controlled clinical trial, that PBMT after endodontic treatment had a significant effect on post-operative pain. Yildiz et al. (2018) [51] observed a decrease in pain within the LLLT group on both the first and third days. Similarly, Nabi et al. (2018) [52] and Asnaashari et al. (2011) [53] found that pain following endodontic treatment was notably reduced in the LLLT group at intervals of 4, 8, 12, 24, and 48 h post-treatment. Additional studies have confirmed significant pain relief from 4 to 48 h in LLLT groups [25,54,55].

Similarly, none of the patients in this study reported signs of pain after completing the therapeutic regimen. This may be due to the analgesic action that PBMT can exert. However, characteristics such as wavelength, energy and power density, beam spot area, and the time and number of irradiations should be taken into consideration, as they may affect the outcomes.

Research has suggested that the analgesic effects are attributed to the anti-inflammatory and neurological actions of LLLT, such as enhancing lymphocyte and nerve cell respiration, stabilizing membrane potentials, and releasing neurotransmitters into inflamed tissues [53]. Moreover, LLLT significantly increases fibroblast activity, accelerates the healing of connective tissues, and exerts anti-inflammatory properties [56].

4. Future Perspectives and Conclusions

Interestingly, phenothiazines—which are synthetic non-porphyrin compounds (like MB and TBO)—are among the most extensively researched PS in the endodontics field. However, traditional PSs face significant drawbacks, including limited water solubility, an unpredictable drug release profile, inadequate target specificity, and a low extinction coefficient, all of which impede their clinical effectiveness. As a result, encapsulating these PSs in nanostructured materials has emerged as a promising strategy to enhance their performance within the RCS [57].

In summary, our results demonstrated that aPDT combined with PBMT using 660 nm and 940 nm DL has a dual effect of promoting tissue recovery in cases of AAP and improving the overall prognosis, even after 1 year of follow-up. However, further research and randomized control trials are needed to fully understand the optimal protocol parameters, as well as the long-term effects of these therapies.

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