Evaluation of different clinical periodontal protocols for the treatment of combined endo-periodontal lesions: a clinical and CBCT-based 6-month follow up study

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Abstract

Aim: To report a case series with three clinical protocols to treat combined endodontic-periodontal lesions (EPLs).

Materials and methods: EPLs were treated by the same endodontic protocol and allocated in three periodontal treatment groups: Scaling Root Planning (SRP, n=15), SRP associated with Amoxicillin and Metronidazole (SRP+AMX+MET, n=16), and Open Flap Debridement (OFD, n=13). Probing pocket depth (PPD), clinical attachment level (CAL), bleeding on probing (BOP-%), plaque index (PI-%), tooth mobility (TM), and volumetric analysis of EPL by cone-beam computed tomography (CBCT) were evaluated at 30 days, 3 months, and 6 months after periodontal therapies.

Results: All therapies had a significant improvement in clinical parameters showing a reduction in PPD, CAL, BOP. There was no intra- or intergroup difference in PI ($p>0.05$). The SRP+AMX+MET therapy showed the best results in terms of PPD reduction ($p<0.05$) at 6 months with a reduction in TM at 30 days, 3, and 6 months ($p<0.05$). Both the SRP+AMX+MET and OFD therapies promoted reduction in lesion volume ($p<0.05$).

Conclusion: All protocols were effective in the treatment of endo-periodontal lesions. However, the endodontic treatment protocol associated with the SRP+AMX+MET therapy seems to have the best clinical and tomographic results.

Keywords: Clinical protocols; periodontitis; anti-bacterial agents; case reports.

Introduction

Combined endodontic-periodontal lesions are defined by a pathological communication between the pulpal and periodontal tissues at a given tooth, occurring in either an acute or a chronic form (Papapanou *et al*., 2018), presenting a challenge in clinical practice. Performing an accurate diagnosis and adequate treatment combining endodontic and periodontal therapies causes some uncertainty about the best protocol to follow that results in the most ideal treatment outcomes (Solomon *et al*, 1995; Lang *et al*, 1999; Singh, 2011).

Endo-periodontal lesions can happen due to anatomical factors such as exposed dentinal tubules, accessory canals (Abbott *et al*., 2009), palato-gingival grooves, and apical foramen, which are the main connections between the periodontal and pulp tissues (Ghezzi *et al*, 2012). Other non-physiological pathways such as iatrogenic perforations, vertical root

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fractures (Narang *et al*., 2011; Aksel & Serper, 2014; Rotstein & Simon, 2006), poor-quality endodontic treatment (ET), and inadequate restorations also allow reinfection, affecting these tissues.

The etiological factors of endodontic and periodontal infection are living pathogens and bacterial biofilms, respectively, which play crucial roles in the formation and progression of pulp and periodontal disease (Rotstein, 2017). Due to the anatomical dental complexity and the possibility of several sites of contamination along with the root complex, treatment is difficult, and the prognosis is not always favorable (Lang *et al*., 1999). It is dependent on multiple factors: the initial periodontal severity, periapical infections, treatment planning and decision making, in combination with clinician skills and experience as well as patient motivation; therefore, a multidisciplinary intervention is recommended (Singh, 2011; Heasman, 2014; Simon *et al*., 2013).

It is a consensus that endodontic treatment is the first step to be followed, which may or may not be performed concomitantly with periodontal treatment (Rotstein&Simon, 2004; Al Fouzan, 2014; Schmidt *et al*., 2014; Tewari, 2018; Gupta *et al*., 2015). However, there is no consensus about the best periodontal therapy for endo-periodontal defects. A wide spectrum of different periodontal treatment options has been described, but studies fail to compare and show different treatment modalities for endodontic periodontal lesions (Hassan *et al*., 1986; Schmidt *et al*, 2014). Scaling and root planning is considered as a gold standard periodontal treatment (Cobb, 2002), but it is known that endo-periodontal lesions present deeper probing depths, and in most of the cases combined with vertical defects, non-surgical therapy may not be effective. Many studies suggest that failure to clean the roots thoroughly result in treatment failure (Knowles *et al*., 1978; Ramfjord *et al*., 1987; Rosling *et al*., 1976). An alternative would be open flap debridement, a therapy able to eliminate calculus and biofilm more effectively, leading to better root decontamination when compared to non-surgical periodontal therapy. Another alternative for non-responsive sites would be antibiotic therapy. The adjunctive use of antibiotics offers statistically significant and clinically relevant benefits over those achieved with scaling and root planning alone in the treatment of periodontitis (Borges *et al*. 2017, McGowan *et al*., 2018).

Therefore, the present study aimed to evaluate and compare three different periodontal approaches using a standardized endodontic therapy for combined endo-periodontal lesions treatment. To the best knowledge of the authors, the present is the first case series to assess different periodontal treatment protocols for the treatment of these lesions.

Methodology

The present study was approved by the Ethics Committee of the Institute of Science and Technology, São Paulo State University (n01.190.850) and was conducted in accordance with the Helsinki Declaration of 1975 as revised in 2013. Patients diagnosed with combined endo-periodontal lesion between 2016 and 2018 following the inclusion and exclusion criteria were invited to participate in the present study, totalizing forty-four treated teeth.

- *Inclusion criteria*: patient aged ≥ 20 years presenting periodontitis diagnosis (Stage III or IV; localized/generalized extension or molar/incisor pattern; grade A, B or C) (Papapanou *et al*., 2018); with endo-periodontal lesions without root damage with grade 1, 2 or 3 (Herrera *et al*., 2018) probing pocket depth (PPD) ≥ 6 mm in at least one site of the tooth; negative or altered response to the pulp sensitivity test (Jafarzadeh & Abbott, 2010).

- *Exclusion criteria*: the presence of root damage (root fracture or cracking; root canal or pulp chamber perforation and external root resorption), patients without periodontitis, pregnant or lactating, smokers, patients that have taken antibiotics and/or anti-inflammatories in the last 6 months or reported a systemic disease.

All patients received information about their periodontal status and an explanation about the risks and benefits of the study. After signing the informed consent form, they were allocated according to the team judgment about what could be the best treatment (convenience sample; dental anatomy and complexity were considered to access the defects), highlighting the clinical practice reality to one of the three predetermined treatment groups: scaling and root planning (SRP, n=15), SRP associated with amoxicillin and metronidazole (SRP+AMX+MET, n=16) and open flap debridement (OFD, n=13).

The patients received oral hygiene instructions and underwent supragingival biofilm and/or calculus removal before treatment. They were instructed again about their oral hygiene in each follow-up appointment (Figure 1).

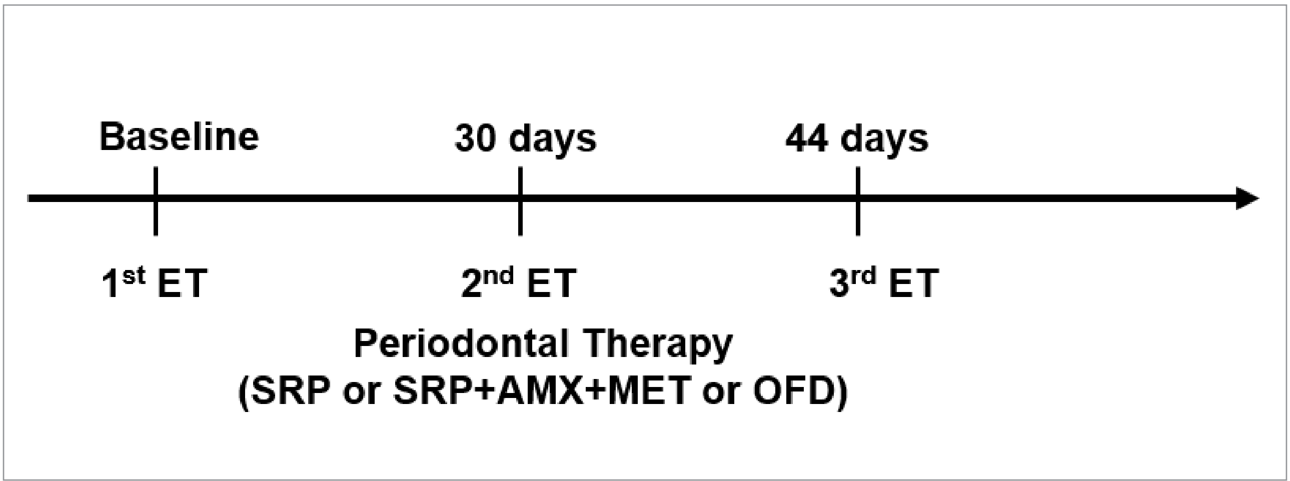

Figure 1. Treatment sequence. 1st ET: first session of endodontic treatment; 2nd ET: second session of endodontic treatment; 3rd ET: third session of endodontic treatment; SRP: scaling and root planning; SRP+AMX+MET: SRP associated with amoxicillin and metronidazole; OFD: open flap debridement.

Pulp tests

A cold pulp test was chosen since it has generally high diagnostic accuracy and is simple considering the primary pulp testing method in clinical practice (Balevi, 2019). An altered response was considered when there was a lack of time for response, minimal response, or intense response when compared with another patient tooth, giving preference to the same tooth, opposite the hemi-arcade (Jafarzadeh & Abbott, 2010).

Endodontic Treatment

A single operator, a specialist in endodontics (CHSD), performed all endodontic treatments in three visits. Initially, patients were anesthetized with 2% mepivacaine (Mepivalem®AD 2% with epinephrine 1.100.000, Dentsply Pharmaceutical, Brazil). The teeth were isolated with a rubber dam, and coronal access was made. The canals were filled with 2.5% sodium hypochlorite solution (Asfer®, Brazil), and the working length was determined using an apical locator (Root ZX II®, Morita®, Japan) and checked with a periapical radiograph. Root canals were prepared by rotary instrumentation (ProTaper® Universal, Dentsply Maillefer®-Switzerland). Five ml of 2.5% sodium hypochlorite solution (Asfer®, Brazil) was used for each instrument. The final irrigation was made with 3 ml of trisodium ethylenediaminetetraacetic acid (Trisodium EDTA Liquid. pH level 3 – Biodinamica; Brazil) and 3 ml of distilled water in each root canal. The canals were dried by aspiration and received final irrigation with 2% aqueous chlorhexidine solution (Maquira®, Brazil).

After drying by aspiration and sterile paper points, intracanal medication with calcium hydroxide (Ultracal®, Ultradent®, USA) was applied. Thus, the teeth were restored by Coltosol (Coltene®, USA) and composite resin (Surefil SDR Flow; Dentsply Maillefer®, Switzerland and FiltekTMZ350 XT; 3M ESPE; Brazil) to avoid coronal leakage and recontamination. If necessary, occlusal adjustment was performed.

After 30 days, the second endodontic visit was performed immediately after periodontal therapy. The medication was removed with 2.5% sodium hypochlorite solution irrigation and #15 Kfiles (Dentsply Maillefer®, Switzerland). Passive ultrasonic irrigation (Irrisonic tip, Helse, Brazil / DentSurg, CVDentus, Brazil) was performed by alternating 2.5% sodium hypochlorite, 3ml of trisodium EDTA and 5ml of distilled water for 60 seconds each. The canals were dried and received final irrigation with 2% aqueous chlorhexidine solution. After new drying with paper points, a new intracanal medication with calcium hydroxide was applied, and the tooth was sealed with Coltosol and composite resin.

After 14 days, the third endodontic visit was performed, the intracanal medication was removed, and the root canals were irrigated with EDTA, dried by aspiration and sterile paper points, and then filled with AHPlus cement (Dentsply Maillefer®, Switzerland) and ProTaper Gutta Percha Cones (Dentsply Maillefer®, Switzerland) using the Schilder technique. The teeth were, again, restored with composite resin.

Clinical Variables

All clinical parameters were assessed by a single examiner who was blinded, trained, and calibrated (CLF). The calibration was performed as follows: a total of ten (10) patients presenting one Endo-Periodontal defect were selected. The examiner measured the CAL and PD in all defects two times within a 24-hour interval.

The measures were then submitted to the Intra-Class test with an agreement of 0.89. The periodontal clinical parameters were taken at baseline, 30 days, 3 and 6 months after periodontal treatment as follows: probing pocket depth (PPD), clinical attachment level (CAL), gingival recession (GR), bleeding on probing (BOP-%) plaque index (PI-%) and tooth mobility (TM). A North Carolina periodontal probe (Hu Friedy; USA) was used to measure those parameters.

Periodontal Therapies

Periodontal therapy was performed 30 days after the first endodontic appointment by a single and experimental operator (NMRBA). Initially, the patients were anesthetized with 2% mepivacaine (Mepivalem®AD 2% with epinephrine 1.100.000, Dentsply Pharmaceutical, Brazil) and treated according to the therapy selected:

- SRP: ultrasonic scaler (Cavitron Dentsply, USA) with subgingival tips (UI25KSF10S; Hu-Friedy; USA) and curettes were used in a single session.

- SRP+AMX+MET: after SRP therapy, the patients received 500 mg of amoxicillin and 400 mg of metronidazole every 8 hours for 7 days.

- OFD: surgical access was done by an intrasulcular incision followed by a full-thickness flap elevation. The same patterns of periodontal debridement (ultrasonic tips and curettes) were kept with curettage of the granulation tissue around the teeth. The site was irrigated with 0.9% saline solution and sutured with 4-0 silk thread. The patients received guidelines for post-operative care (500mg dipyrone or 500mg paracetamol every 4 to 6 hours in case of pain), and the suture was removed after 7 days.

Follow-ups were performed at 30 days, 3 months, and 6 months after the periodontal therapy for all groups.

Postoperative Pain

The patients answered the Visual Analogic Scale (VAS) to evaluate pain perception. It was taken after 7 days of the first endodontic intervention (first visit) and 7 days after the periodontal treatment.

Volumetric analysis

The CBCT images were acquired before the first endodontic treatment (baseline) and after six months of follow-up. An experienced and calibrated radiologist (SLPCL; ICC > 0.90) evaluated the images. The endo-periodontal lesion volumes at baseline and after 6 months of treatment (final volume) for all groups were compared. Images were acquired from an ICAT Next Generation CT scanner (Imaging Sciences International, Hatfield, PA, USA) with the same parameters (voxel 0.25 mm, the field of view [FOV] 8.0x8.0cm, 37.07mA, 120kV in 26.9s). DICOM (Digital Imaging and Communications in Medicine) format files were exported to the ITK-Snap 3.4.1 software (Kitware, New York, USA) to obtain lesion volumes. The semi-automatic method was chosen following the methodology proposed by Kauke *et al.* (2018). In the multiplanar reconstruction (MPR) window, through the axial, coronal, and sagittal sections, the region to be studied - corresponding to the lesion - was delimited using the region of interest (ROI) with the "Segment 3D" tool. Bone threshold adjustment was performed, and "bubbles" were sequentially inserted in all regions of the lesion, which were progressively expanded and collapsed to encompass the full extent of the endo-periodontal lesion. The entire process was followed through with MPR images, thus avoiding the possibility of the volume not corresponding to the lesion. After this process, the volumetric value in mm3 corresponding to the lesion was obtained by the "volume and statistics" tool. (Figure 2).

Statistical Analysis

All data were expressed as mean ± standard deviation (SD), and normality was tested by the Shapiro–Wilk. Clinical and CBCT parameters, where treatment and time were counted as factors, were evaluated using the Two-way Repeated Measures ANOVA followed by the Tukey´s test for intra- and intergroup comparisons. The changes in clinical parameters were evaluated by one-way ANOVA. The proportions were analyzed by the chi-square test. All tests were performed using the SigmaPlot 14.0 package at a significance level of 5% and 95% of CI.

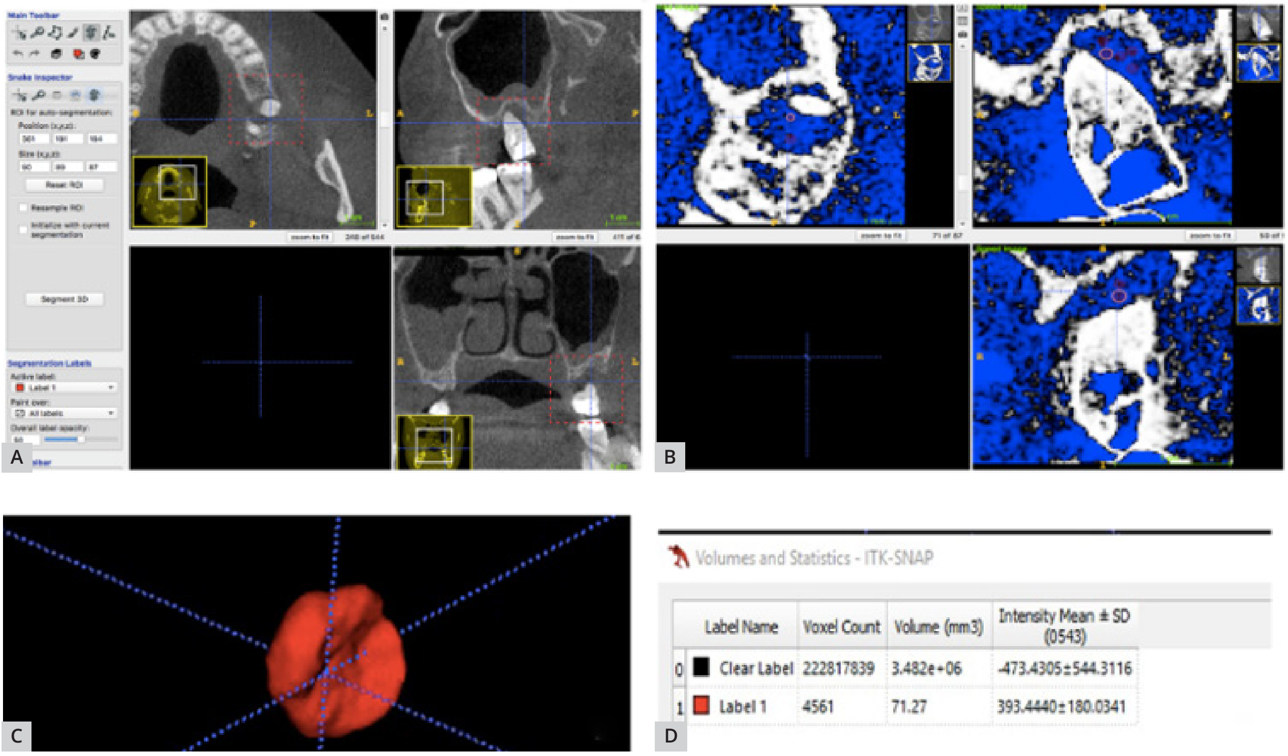

***Figure 2.** Lesion volume capture (mm³). ITK-Snap 3.1.4 software displaying the lesion segmentation process: (A) MPR window and region of interest (ROI) delimitation; (B) Threshold adjustments and bubbles insertion into the lesion; (C) three-dimensional image of segmentation; (D) Statistical results of lesion volume.*

Results

There was no statistically significant difference in age, gender, or mono- and multi-rooted teeth among the groups (Table 1). All treatments showed a significant improvement in PPD, CAL, and BOP at 3 and 6 months (Table 2). The most notorious PPD reduction was seen in the SRP+AMX+MET at 3 and 6 months compared to the other groups. TM improved for the SRP group at 3 and 6 months. However, the SRP+AMX+MET showed improvement in 30 days. SRP+AMX+MET and OFD therapies had the most significant lesion volume reduction and there was no significant difference between them (Table 3) (Figure 3).

Considering postoperative pain, the patients from the SRP+AMX+MET and OFD therapies reported low pain after the endodontic treatment, and patients from the OFD reported the same after the periodontal therapy (Table 4).

Table 1. Baseline group demographics.

	SRP (n=15)	SRP+AMX+MET (n=16)	OFD (n=13)	P-value
Age (mean ± SD)	48.00 ± 11.29	40.94 ± 6.71	46.38 ± 11.46	0.2[a]
Gender (M/W)	05/10	05/11	04/09	NS[b]
Teeth types (monorradicular/ multirradicular)	07/08	08/08	03/10	NS[b]

SD: standard deviation; M: men; W: women; [a] P- value – One-way ANOVA on Ranks; [b] Qui-Square Test; NS: not significant difference.

Table 2. Clinical Parameters over time.

Clinical Parameters	Period	SRP (n=15) (mean ± SD)	SRP+AMX+MET (n=16) (mean ± SD)	OFD (n=13) (mean ± SD)
PPD (mm)	Baseline	8.84 ± 2.50Aa	7.57 ± 2.52Aa	8.55 ± 2.91Aa
	30 days	9.24 ± 2.51Aa	7.76 ± 2.74Ab	8.34 ± 3.16Aab
	3 months	6.67 ± 2.38Ba	4.71 ± 1.91Bb	6.09 ± 3.10Ba
	6 months	6.16 ± 2.48Ba	4.41 ± 1.85Bb	6.13 ± 3.42Ba
	ΔPPD	2.69 ± 2.76a	3.16 ± 2.38b*	2.30 ± 3.41a
CAL (mm)	Baseline	9.96 ± 3.05Aa	8.22 ± 2.71Ab	9.77 ± 2.82Aa
	30 days	10.58 ± 3.0Aa	8.65 ± 2.91Ab	9.83 ± 3.47Aab
	3 months	8.44 ± 2.70Ba	6.92 ± 2.96Bb	8.74 ± 3.52Ba
	6 months	8.31 ± 2.65Bab	6.90 ± 2.90Ba	9.00 ± 3.68Ab
	ΔCAL	1.64 ± 2.85a*	1.33 ± 2.34a	0.74 ± 3.28a
GR (mm)	Baseline	1.11 ± 1.72Aa	0.65 ± 1.30Aa	1.15 ± 1.84Aa
	30 days	1.33 ± 1.68Aa	0.90 ± 1.42Aa	1.49 ± 2.26Aa
	3 months	1.78 ± 1.61Ba	2.20 ± 2.25Ba	2.66 ± 2.89Ba
	6 months	2.16 ± 1.65Ba	2.49 ± 2.56Ba	2.87 ± 2.90Ba
	ΔGR	-1.04 ± 1.24a	-1.84 ± 1.98b	-1.72 ± 2.43b
BOP (%)	Baseline	77.78 ± 42.04Aa	83.67 ± 37.34Aa	80.85 ± 39.77Aa
	30 days	82.22 ± 38.66Aa	67.35 ± 47.38Aa	82.98 ± 37.99Aa
	3 months	64.44 ± 48.41Ba	55.10 ± 50.25Ba	53.19 ± 50.44Ba
	6 months	66.67 ± 47.67Ba	53.06 ± 50.42Ba	51.06 ± 50.53Ba
PI (%)	Baseline	60.00 ± 50.71Aa	56.25 ± 51.23Aa	15.38 ± 37.55Ab
	30 days	60.00 ± 50.71Aa	43.75 ± 51.23Aa	30.77 ± 48.04Aa
	3 months	53.33 ± 51.64Aa	50.00 ± 51.64Aa	38.46 ± 50.64Aa
	6 months	53.33 ± 51.64Aa	75.00 ± 44.72Aa	46.15 ± 51.89Ab
TM (1 / 2 / 3 degree)	Baseline	5 / 3 / 6A	3 / 5 / 6A	6 / 2 / 2A
	30 days	5 / 4 / 5A	7 / 4 / 4B	9 / 2 / 2A
	3 months	8 / 2 / 3B	9 / 6 / 0B	6 / 6 / 0A
	6 months	8 / 0 / 3B	8 / 4 / 0B	4 / 5 / 0A
Number of tooth loss		2	0	0

PPD: probing pocket depth; CAL: clinical attachment level; GR: gingival recession; BOP: bleeding on probing; PI: plaque index; TM: tooth mobility (Tooth without mobility was not included) ; Δ: variation; SD: standard deviation; Different capital letters: statistically significant difference in the intragroup comparison ($p < 0.05$) - Two-Way Repeated Measures ANOVA; Different lowercase letters: statistically significant difference in the intergroup comparison ($p < 0.05$) – Two-Way Repeated Measures ANOVA; *ANOVA on Ranks

Table 3. Tomographic lesion volume at baseline and 6 months.

	Period	SRP (n=15) (mean ± SD)	SRP+AMX+MET (n=16) (mean ± SD)	OFD (n=13) (mean ± SD)
Lesion	Baseline	311.65 ± 277.00Aa	284.06 ± 193.30Aa	401.02 ± 215.50Aa
Volume (mm³)	6 months	220.74 ± 286.42Aa	132.77 ± 90.15Ba	230.28 ± 194.64Ba
	ΔV	-90.91a*	-150.30b	-170.74ab

SD: standard deviation; ΔV: volume change; Different capital letters: statistically significant difference in the intragroup comparison ($p < 0.05$) – Two-Way Repeated Measures ANOVA; Different lowercase letters – statistically significant difference in the intergroup comparison ($p < 0.05$) – Two-Way Repeated Measures ANOVA; *: One-Way ANOVA.

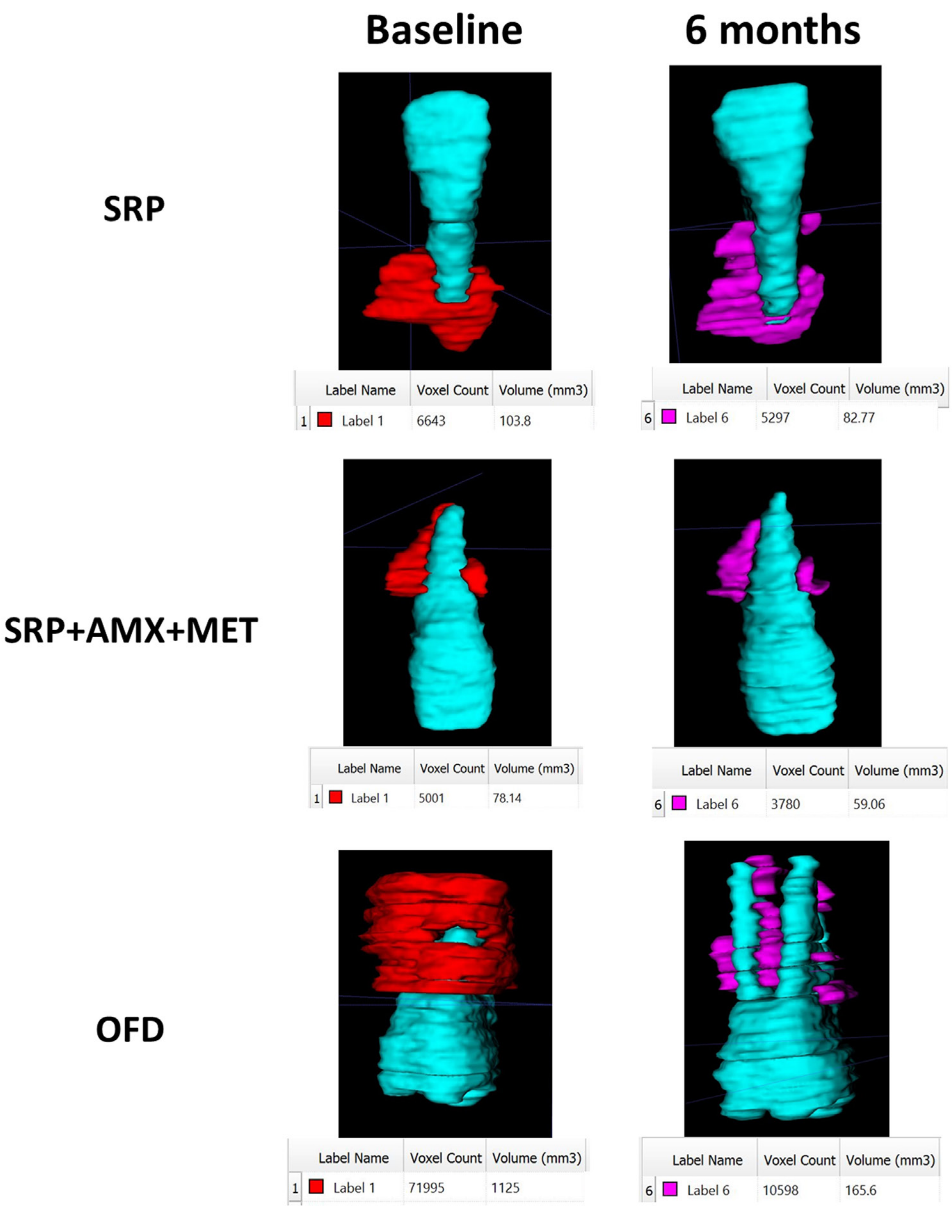

Figure 3. Examples of volumetry results. Examples obtained by the ITK Snap software, through CBCT images, in 03 groups in baseline and 6-month follow up. * The images of the teeth were generated only for to estimate the volumes of the respective lesions.

Table 4. Post-operative pain.

	Period	SRP (n=15) (mean ± SD)	SRP+AMX+MET (n=16) (mean ± SD)	OFD (n=13) (mean ± SD)
	7 days Endo	0.13 ± 0.52a	1.56 ± 2.87b	0.85 ± 2.51b
VAS	7 days Perio	0.13 ± 0.52a	0.00 ± 0.00b	1.38 ± 3.40c

VAS: visual analogic scale; SD: standard deviation; Different lowercase letters: statistically significant difference in the intergroup comparison (p <0.05) – One-Way ANOVA.

Discussion

In selected cases of combined endo-periodontal lesions, we evaluated clinical, tomographic, and pain perception data after the therapies. We found, as main results, that all therapies improved at 3 and 6 months, that the association with antibiotic therapy had significant clinical and tomographic improvement and that the perception of pain was a mild discomfort in the first days after therapy.

The endodontic-periodontal lesion condition has been described as lesions with a variety of inflammatory products and different severities in both the periodontium and pulpal tissues (Singh, 2011). These lesions are known to require management of both an endodontic and periodontal approach, and the prognosis of endodontic-periodontal injuries depends on the severity of the periodontitis, as well as its response to periodontal treatment. If the ET is appropriate, part of the endodontic repair process will be solved, (Rotstein & Simon, 2004) but the other portion of the outcome depends on the periodontal response.

Since all the patients had combined endo-periodontal lesions, a concomitantly endodontic and periodontal approach was defined as essential in achieving a good outcome. All cases had the same endodontic treatment with a twice intracanal medication change using a calcium hydroxide dressing, which has positive effects on the prognosis of periodontal treatments as it reduces lipopolysaccharides, cytokines, and matrix metalloproteinase in the periodontal pockets. (Duque *et al.*, 2019) It is also the most effective intracanal medication in endodontics (Carrote, 2004; Sathorn *et al.*, 2007; Delgado et al., 2013) due to its ability to change the pH and act in an external environment by permeabilization via the dentinal tubules and bactericidal action, which are factors that help treatment response. Due to the possibility that the periodontal pocket could be the source of the root canal reinfections and favor the cross seeding through the apical or lateral foramina after periodontal therapy (Raheja *et al.*, 2014), it was decided to change the intracanal medication after the periodontal treatment to establish a favorable environment for repair.

Although the periodontal response also presents some complexity in the clinical outcome of endo-periodontal lesions due to the characteristics of each defect, i.e., deep and narrow defects, the three (3) periodontal therapies employed showed satisfactory improvement at 6 months of evaluation.

SRP, as a non-surgical periodontal treatment, is considered the gold standard for the treatment of periodontitis (Coob, 2002). The primary objective of SRP treatment is to stop the inflammatory process and the progression of periodontitis through the effective disorganization of the biofilm, reduction of pathogenicity, and repair of the region. Since true (combined) EPL presents a complex microflora associated with deep pockets this might explain the SRP outcomes compared to other groups, suggesting that a new intervention may be necessary to reduce the residual pocket. Deep pockets may increase the risk of tooth loss in the long term (Matuliene *et al.*, 2008). However, SRP leads to significant improvement in PPD, CAL, and BOP at 3 and 6 months (Cobb, 2002; Suvan, 2005).

Regarding the group that associated antibiotics with SRP, much evidence (Segura-Egea *et al.*, 2017; Feres *et al.*, 2015; Goodson *et al.*, 2012; Harks *et al.*, 2015) suggests that the combination of amoxicillin and metronidazole with SRP is the most effective protocol for stages III and IV, generalized periodontitis resulting in clinical benefits compared to an SRP-only treatment approach. Amoxicillin is a moderate spectrum bacteriolytic antibiotic that is effective for orofacial infections, able to withstand stomach acid damage, has a much broader spectrum against the gram-negative cell wall than penicillin, and can maintain adequate blood levels for a relatively long time (Slots, 2002). Metronidazole is used as both an antiprotozoal agent and an antibiotic and has been suggested as an adjuvant to amoxicillin because of its excellent anaerobic activity (Baumgartner *et al.*, 2003). The literature reports that a 7-day regimen of 500/400 mg of amoxicillin and metronidazole would be most appropriate to reduce the risk of antibiotic resistance. (McGowan *et al.*, 2018)

The combination of these antibiotics increased the susceptibility of aerobic and facultative bacteria by 93% and 99%, respectively (Kaldahl *et al.*, 1996). These findings may explain the improvements observed in the results of the SRP+AMX+MET group, such as the significant reduction in PPD, which at 6 months presented residual pockets of approximately 4 mm, whereas the other groups presented a mean PPD of 6 mm and an effective reduction of lesion volume. While antibiotic use is a clinical reality in periodontal treatment, antibiotics in endodontics are usually used when there is evidence of systemic involvement and a rapid and diffuse spread of the infection or may be indicated in risk patients with immune suppression since most endodontic infections can be successfully managed by disinfection of the root canal system. (Segura-Egea *et al,* 2017; Aminoshariae & Kulild, 2016; Mohammadi Z., 2009)

Regarding the OFD periodontal therapy, the focus was to facilitate access to the dental root and consequently provide a gingival contour that helps the patient's plaque control, indicated for sites/teeth that present persistent clinical signs of inflammation (Serino *et al.* 2001). In addition, endo-periodontal lesions usually have deep pockets (Kaldahl *et al.*, 1996; Serino *et al.*, 2001), and surgical periodontal therapy typically has the most effective results in this condition within 12 months (Heitz-Mayfield *et al.*, 2002; Heitz-Mayfield&Lang, 2013). The OFD showed significant improvements in the treatment itself, but when compared to the others, the result fluctuated; it became similar to the SRP+AMX+MET and now the SRP. There was a higher number of molars in the OFD group compared with the other groups. This could have greatly influenced the differences between the results of OFD and antibiotics, which was considered a limitation of this study. The antibiotics had better results suggesting that it was a better therapy, but it should be taken into account that OFD was performed most multirooted teeth, which are usually in unfavorable cases. Tewari *et al.*, 2018 evaluated the appropriate time to perform OFD on an endo-periodontal lesion and found that OFD performed 21 days after ET achieved the same periodontal repair compared to groups waiting 3 months. This was also seen in SRP treatment in endo-periodontal lesions without communication (Gupta *et al.*, 2015), suggesting that both therapies can be performed simultaneously, contributing to a shorter treatment time.

The real amplitude of the endo-periodontal lesion, before and after treatment, was evaluated by a CBCT, which indicated a significant reduction in the endo-periodontal lesion after SRP+AMX+MET and OFD treatments. Clinically, a decrease in PPD, improvement of CAL, and reduction of TM seem to affect the volumetric outcomes.

Patient-centered data has its clinical importance. Using an analogical visual scale, we collected the patient's pain perception in relation to the endodontic and periodontal treatment. It was assessed 7 days into the first session of endodontic treatment and periodontal therapies. Patients in the SRP+AMX+MET group reported mild discomfort after endodontic therapy, whereas, among periodontal therapies, OFD had a higher level of discomfort. Other patient-centered data may be collected from future studies since they presented clinical importance.

The treatment groups designed were based on the best scientific evidence available on this topic. Although endo-periodontal lesions are difficult to treat, having a doubtful prognosis (Lang *et al.*, 1999; Rotstein, 2017), we present three treatment protocols with effective improvement in EPLin terms of reduced PPD and lesion volume. It is worth mentioning the importance of a multidisciplinary approach for the success and survival of the dental element. In general, there is limited evidence to define the treatment of teeth affected by EPL, and most are case reports or small-sample clinical studies.

Some limitations of the present investigation should be pointed out. First, the study did not include microbiologic and immunological evaluations. Thus, it was not possible to assess the impact of each therapy on bacterial load and inflammatory mediators. Moreover, the design of the present study was a case series; no randomization of the teeth was performed. It is known that molars respond less favorably to treatment and there are differences in the number of molar teeth for each group. Finally, the follow-up was 6 months, a short-term interval to show the stability of the results. Therefore, long-term randomized clinical trials are required to confirm our findings. As far as we know, it is the first clinical study that carried out forty-four teeth presenting true endo-periodontal lesions addressed to one of the three approaches with a 6-month follow-up. Another strength is that it investigated an approach with SRP along with antibiotic therapy (AMX+MET) for the treatment of EPL.

Conclusions

All tested treatment protocols for combined endo-periodontal lesions were effective. However, SRP associated with antibiotic therapy obtained the best clinical and tomographic results at the end of the 6-month follow-up.

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