DOUTORADO EM ODONTOLOGIA
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BRUNO FREITAS MELLO

UTILIZAÇÃO DO LASER DE ER:YAG E TERAPIA REGENERATIVA PARA O TRATAMENTO DA PERI-IMPLANTITE: AVALIAÇÃO DE 1 ANO

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Guarulhos, 29 de fevereiro de 2020.

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RESUMO

O presente estudo avaliou os resultados clínicos do tratamento da peri-implantite utilizando o laser de Er:YAG (érbio dopado com ítrio, alumínio e granada) associado com ROG (Regeneração óssea guiada). Durante um período de 18 meses (junho de 2018 - janeiro de 2020), um total de 24 indivíduos (10 pacientes totalmente desdentados) com 31 implantes dentários cilíndricos roscados de diferentes marcas com peri-implantite foram incluídos neste estudo prospectivo. Peri-implantite foi definida como perda óssea vertical> 4mm, profundidade de sondagem (PS) > 5mm, sangramento à sondagem (SS) e / ou supuração (Sup). Anteriormente todos os implantes dentários foram submetidos a um tratamento pré-cirúrgico que consistiu na aplicação de gel complexo de hidrocarboneto-oxo-borato, profilaxia supragengival por uma semana e avaliação clínica da restauração suportada por implantes. Após acesso cirúrgico e limpeza de todos os defeitos peri-implantar, o enxerto de cerâmica bifásica embebido em sangue preencheu toda a cavidade. Uma membrana reabsorvível foi aplicada para cobrir todo o defeito enxertado para permitir uma cicatrização não submersa. Após 1 ano de acompanhamento, 3 de 31 implantes foram removidos devido à infecção persistente. 3 implantes adicionais apresentam recessão da mucosa peri-implantar, mas sem sinais de inflamação (SS, Sup e perda óssea adicional). Aos 12 meses de pós-operatório, a taxa de sobrevivência foi de 90,32%. O desfecho clínico (PS <5 mm, sem SS e / ou Sup, sem perda óssea adicional) foi alcançado em 82,75% dos implantes restantes (25 de 29 implantes dentários no final do estudo). Dentro dos limites deste estudo, pode-se concluir que o laser Er: YAG associado à regeneração óssea guiada foi capaz de melhorar o estado de saúde peri-implantar, pelo menos, após 1 ano de acompanhamento. No entanto, este protocolo não foi capaz de resolver todos os casos de peri-implantite.

Palavra-chave: Implante Dentário, Lasers de Er-YAG, Peri-implantite, Estudo Clínico, Regeneração Óssea, Cirurgia Oral.

ABSTRACT

This study evaluated the clinical outcomes of treatment of peri-implantitis using Er:YAG (Erbium dopped with yttrium, aluminum and garnet) laser associated with GBR (guided bone regeneration). Over a time period of 18 months (June 2018 – January 2020), a total of 24 subjects (10 totally edentulous patients) with 31 threaded, cylindrical dental implants of different brands with peri-implantitis were included in this prospective study. Peri-implantitis was defined as vertical bone loss ≥4mm, probing depth (PD) ≥5mm, bleeding on probing (BoP) and/or suppuration (Sup). Previously all dental implants were submitted to a presurgical treatment that consisted of application of hydro-carbon-oxo-borate complex gel, supragingival prophylaxis for one week and clinical evaluation of implant supported restoration. After surgical access and cleaning of entire peri-implant defects, biphasic ceramic graft material soaked in blood filled all the cavity. A resorbable membrane was applied to cover the entire grafted defect to allow a non-submerged healing. After 1 year follow up, 3 out 31 implants were removed due to persist infection. Additional 3 implants present peri-implant mucosa recession, but without signs of inflammation (BoP, Sup and further bone loss). At 12 months postoperative, the survival rate was 90.32%. The clinical endpoint (PD<5mm, no BoP and/or sup, not further bone loss) were achieved in 82.75% of the remaining implants (25 out 29 dental implants at the end of the study). Within the limits of this study, it could be concluded that the Er:YAG laser associated with guided bone regeneration was able to improve the peri-implant health condition, at least, after 1 year follow up. However, this protocol was not able to solve all peri-implantitis cases.

Keywords: Dental Implant, Er-YAG Lasers, Peri-implantitis, Clinical Study, Bone Regeneration, Oral Surgery.

SUMÁRIO

1 INTRODUÇÃO E JUSTIFICATIVA

1.1 Etiologia da peri-implantite

A peri-implantite é definida como um processo inflamatório dos tecidos ao redor do implante dentário em função com perda óssea peri-implantar progressiva (Schwarz et al.2017). O sinal clínico evidente para esse diagnóstico é definido pela presença de edema, rubor, sangramento e recessão marginal da mucosa peri-implantar, presença de bolsas peri-implantares ≥ 6 mm com sangramento a sondagem e/ou supuração e perda óssea progressiva ≥ 3 mm em comparação à última avaliação radiográfica (Schwarz et al.2017; Berglundh et al. 2018).

O fator etiológico da doença está relacionado ao acúmulo de biofilme sobre os tecidos peri-implantares causados pela falta de manutenção e deficiência na higienização do implante dentário (Figuero et al. 2014; Schwartz et al. 2017; Berglundh et al. 2018). Fatores como extravasamento de cimento em sulco da mucosa peri-implantar, pacientes com fenótipo gengival fino, restaurações implantossuportadas com planejamento errôneo favorecem na dificuldade de controle de biofilme e assim tornando fatores de risco para peri-implantite (Schwartz et al. 2017). A composição do biofilme supragengival e subgengival de implantes dentários doentes é muito similar aos patógenos das doenças periodontais dando destaque às bactérias gram-negativas anaeróbias *Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola, Prevotella intermedia* e *Campylobacter rectus* (Shibli et al. 2008; Faveri et al. 2014; Pérez-Chaparro et al. 2016). Consequentemente pacientes com histórico de periodontite apresentam uma grande chance de adquirir a doença em seus implantes dentários (Shibli et al. 2008; Figuero et al. 2014; Schwarz et al.2017; Berglundh et al. 2018).

A agressão causada pelas citotoxinas produzidas pelo biofilme patogênico desencadeia a resposta inflamatória dos tecidos peri-implantares ocasionando na atividade do sistema imunológico por meio da liberação de citocinas pró-inflamatórias, anti-inflamatórias e relacionadas à osteoclastogênese e quimiocinas. A coleta do fluído crevicular peri-implantar possibilita a identificação das citocinas presentes em tecido peri-implantar doente e assim distinguir do tecido saudável. Normalmente os

tecidos com peri-implantite manifestam a presença da citocina IL-1β conforme as revisões sistemáticas (Zani et al. 2016; Mardegan et al. 2017; Schwarz et al. 2017).

A prevalência da peri-implantite varia de 1% a 47 % por conta da ausência de padronização no diagnóstico das doenças peri-implantares na literatura, muitos trabalhos diagnosticaram a peri-implantite com PS ≥ 4 a 6 mm e perda óssea ≥ 0,5 mm por ano ou perda óssea ≥ 1,5 a 2 mm em relação à remodelação óssea inicial e/ou quando houver exposição de espiras (Cosgarea et al. 2019; Tomasi et al. 2019).

1.2 Tratamento não cirúrgico

Por conta da similaridade entre a doença periodontal tanto em aspecto microbiológico quanto aos sinais clínicos muitos trabalhos relatam a raspagem associado com curetas e pontas de ultrassom com revestimento em titânio, teflon, PEEK (Poli-éter-éter-cetona), fibra de carbono, plástico e silicone para não modificar a superfície tratada do implante para uma possível reosseointegração, desorganizar e remover o biofilme patogênico contido nas bolsas subgengivais dos implantes dentários doentes (Figuero et al. 2014; Ramanauskaite et al. 2016). Entretanto, limitações como a presença das espiras e a extensão do defeito ósseo prejudicam a efetividade da raspagem deixando um biofilme remanescente (Ramanauskaite et al. 2016; Shibli et al. 2019). Consequentemente o uso adjunto de soluções e géis a base de clorexidina ou CPC ampliam a atividade antimicrobiana. Em comparação, o uso de antibióticos como minociclina aplicado localmente proporcionou melhores parâmetros clínicos, principalmente quando empregado novamente na região (Figuero et al. 2014). Por via sistêmica, a administração de amoxicilina e metronidazol não mostraram diferença significativa em relação ao placebo na redução dos parâmetros clínicos (Shibli et al. 2019). A combinação de raspagem com curetas, ultrassom, jato abrasivo de ar com glicerina e administração sistêmica de metronidazol demonstrou sucesso no tratamento da peri-implantite com ausência de sangramento, inflamação e perda óssea progressiva (Nart et al. 2020). O emprego dos lasers na descontaminação da superfície de implantes dentários doentes foi relatado na literatura como uma boa opção. A terapia fotodinâmica (PDT) consiste na ação conjunta de um laser de baixa potência com uma substância denominada azul de metileno para a destruição dos patógenos presentes no biofilme subgengival por meio de uma reação de oxidação que ocorre na membrana celular levando ao dano no seu

DNA, sendo uma alternativa aos antibióticos e antissépticos. Os lasers de alta potência como Er;YAG e Er:CrYSSG demonstraram um excelente desempenho na remoção do tecido de granulação inflamatório das bolsas peri-implantares, previne a danificação da superfície do implante sendo uma excelente alternativa aos instrumentos raspadores e ultrassônicos sem contar que após a irradiação a superfície do implante se torna resistente à adesão bacteriana e assim oferecendo resultados clínicos satisfatórios (Shibli et al. 2006; Figuero et al. 2014; Ramanauskaite et al. 2016; Shibli 2018). Por outro lado, a terapia não cirúrgica apresenta ineficiência no tratamento da peri-implante ilustrada em poucas mudanças nos parâmetros clínicos e alterações do nível ósseo marginal (Figuero et al. 2014; Ramanauskaite et al. 2016).

1.3 Terapia cirúrgica

Limitações da terapia não cirúrgica como a presença de espiras nos implantes dentários, ineficiência na descontaminação da superfície do implante e defeito ósseo extenso requerem a necessidade de acessar a lesão peri-implantar por meio da técnica de retalho mucoperiostal para efetuar o debridamento otimizado valendo-se, novamente, dos instrumentos de raspagem, dispositivos ultrassônicos, jato abrasivo de ar e/ou irradiação com lasers de baixa e alta potência. A indicação dessa técnica ocorre em casos de bolsas peri-implantares rasas (Figuero et al.2014; Ramanauskaite et al. 2016; Berglundh et al. 2018; Heitz-Mayfield et al. 2018; Stewart et al. 2018). A técnica de ressecção consiste na remoção da porção cervical da mucosa peri-implantar doente seguido de uma osteoplastia (caso seja necessário), descontaminação da superfície e reposiconamento do retalho com exposição do implante que posteriormente será feito o desgaste das espiras expostas (implantoplastia). Essa técnica tem indicação para regiões que não comprometa a estética, defeitos supreósseos e defeitos intraósseos de uma parede (Figuero et al. 2014; de Waal et al. 2015; Ramanauskaite et al. 2016; Carcuac et al. 2017). A técnica regenerativa apresenta indicação em casos de devolução da arquitetua óssea para prevenção de recessão da mucosa peri-implantar e estimular a reosseointegração com manobras de reconstrução óssea, após a acesso por retalho mucoperiostal e o debridamento do implante e do defeito aplica-se enxerto ósseo e/ou membrana para manutenção do arcabouço (Figuero et al.2014; Roos-Jansåker et al. 2014; Bassi et al.

2015; Ramanauskaite et al. 2016; Roccuzzo et al. 2017; Monaca et al. 2018; Isehed et al. 2018; Tomasi et al. 2019).

2. PROPOSIÇÃO

O objetivo deste estudo foi avaliar o efeito do laser de Er:YAG associado a terapia regenerativa no tratamento cirúrgico da peri-implantite.

3. ARTIGO CIENTÍFICO:

ER:YAG LASER AND GUIDED BONE REGENERATION IN THE SURGICAL TREATMENT OF PERI-IMPLANTITIS: 1 YEAR CLINICAL AND RADIOGRAPHIC EVALUATION

Artigo preparado nas normas do *Clinical Oral Implants Research*

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Running title: Er:YAG in the surgical treatment of peri-implantitis

Key-Words: Dental Implants; Peri-implantitis; Surgical Treatment; Guide Bone Regeneration, Submerged Healing; Clinical Study.

Introduction

The use of dental implants to replace missing teeth in daily clinical practice has been shown to be a reliable treatment. However, peri-implant infections have been reported in the current literature[1]. Peri-implantitis is characterized by the presence of inflammatory reactions that affect the soft and hard peri-implant tissues under loading leading to peri-implant bone loss. The clinical signs vary from inflammatory process of the peri-implant mucosa, bleeding on probing, suppuration, clinical attachment loss and peri-implant bone loss[2]

Although the prevalence of peri-implantitis has been reported between 8% and 29%[1], the treatment of peri-implant diseases has aroused much interest[3,4]. Nowadays, there are several sources of evidence for a bacterial etiology of peri-implantitis[5-7]. The increase of probing depth and clinical attachment loss often have been associated with a dysbiosis and an immunoinflammatory mediators produced by the host response. These factors are crucial for the onset of peri-implant diseases.

Although peri-implant bone defects may also be affected by occlusal overload[9] the elimination of pathogenic dental biofilm from dental implant surface and surrounding peri-implant defect plays an important factor to attempt re-osseointegration[10,11].

Treatments applied to recover peri-implant tissue are mainly the those applied in Periodontics[10,12,13]: mechanical treatment, chemical treatment, physical treatment, surgical treatment associated with guided bone regeneration and biomaterials, but in most of the cases there is a combination of these techniques. These therapeutic strategies have two distinct objectives in common: to decontaminate the implant surface and the affected peri-implant area, and also to restore peri-implant health and the architectural conditions of the soft and hard peri-implant tissues.

Previous systematic reviews[14,15] evaluated the efficacy of the Guided Bone Regeneration (GBR) in the treatment of peri-implant defects. The main factor associated with lack of success in this therapeutic technique were the early exposure of the barriers/membrane and or infection/contamination, causing a low percentage of bone filling and frequently, lack of re-osseointegration. In addition, it has also been reported that the main factor contributing to the percentage of bone filling is decontamination of the entire peri-implant area. This factor could be potentialized using adjunctive systemic use of medications, such as metronidazole and amoxicillin help the bacterial treatment of peri-implantitis[16].

In this sense decontamination and sterilization of the implant surface topograhy as well as the peri-implant area by means of high and low-intensity laser therapy using CO_2, Nd:YAG, Er:YAG, Er,Cr:YSGG and GaAlA has been evaluated.[17-19] High power lasers remove not only the inflammatory soft tissue around the peri-implant defect, but also decontaminates the implant surface without damage the implant surface. Therefore, the aim of this study was to evaluate the clinical outcomes of treatment of peri-implantitis using Er:YAG laser associated with GBR.

Material and Methods

Subjects population

Over a time period of 18 months (June 2018 – January 2020), a total of 24 subjects (10 totally edentulous patients) with 31 threaded, cylindrical dental implants of different brands with peri-implantitis were included in this prospective study. Peri-implantitis was defined as vertical bone loss $\geq$4mm, probing depth $\geq$5mm, bleeding on probing and/or suppuration. The study protocol was explained to each subject and

signed informed consent was obtained. The study protocol was approved by Ethics Committee of Human Research of University of Guarulhos, Brazil.

Inclusion and exclusion criteria

Subjects were included in the study if they had at least one screw-type dental implant in function with probing depth ≥5mm and alveolar bone loss ≥4mm observed in periapical radiography. Subjects were excluded if they had peri-implant bone defect >75% of the length of the implant, had clinically detectable mobility of the implant (lack of osseointegration), coated surfaces with HA, TPS and anodized (these implants were removed), had a chronic medical disease or condition that could influence the surgical therapy.

Clinical and radiographic examination

Clinical parameters as presence (1) or absence (0) of plaque, gingival bleeding, bleeding on probing, suppuration, probing depth (mm) and clinical attachment level (mm) were measured previously to surgery at 6 sites per implant (mesiobuccal, buccal, distobuccal, distolingual, lingual and mesiolingual) by trained and calibrated examiner (R.S.S). The PD and CAL measurements were recorded to the nearest millimeter using a North Carolina periodontal probe (Hu-Friedy, Chicago, IL, USA).

Standardized intra-oral periapical radiographs were obtained, using a dental x-ray machine equipped with a 35-cm-long cone. Exposure parameters were 70 kilovolt (peak), 15 mA, and ¼ second at a focus-to-sensor distance of 30cm. The radiographs were captured with a digital camera and transferred to a personal computer. Image processing software was used to store the digitized images. Subsequently, the images were displayed on a monitor, and linear measurements were taken with software (Image Pro-Plus 4.5 Media Cybernetics Inc., Silver Spring, MD, USA). The linear distance in millimeters between the implant shoulder and the first clear bone-to-implant

contact, mesially and distally, were registred. Mesial and distal surface values were averaged.

Pre-treatment phase

Presurgical treatment consisted of application of hydro-carbon-oxo-borate complex gel **(**BlueM Oral Gel, Curitiba, Brazil), supragingival prophylaxis for one week and clinical evaluation of implant supported restoration. In addition, if the implant-supported prostheses presented mobile abutments and/or screws, as well as fractured prosthetic crown of ceramic or resin, these restorations were substituted by fabricated interim prosthesis made of autopolymerizing acrylic resin to avoid any occlusal interference in healing process.

Surgical Treatment and Laser parameters

At baseline, the implant supported restorations and when necessary, the the prosthetic abutments, were removed and after local anesthesia, a crestal incision was made through the mucosa, and buccal and lingual full thickness flaps surgery was performed to remove the granulation tissue present in bone craters around the dental implants.

An Er:YAG laser (Lite Touch, Light Instruments, Israel) was used to remove the soft tissue and to clean the contamined implant surface. The removal of soft tissue used an irradiation energy of 150mJ, frequency of 20Hz, output power of 2W, and energy density of 120J/cm^2. The detoxification/cleaning process used an irradiation energy of 20 mJ, frequency of 20 Hz, output power of 0.4 W, and an energy density of 2.76 J/cm^2. Both procedures were performed with a sapphire tip with a length of 8 mm was employed in the respective handpiece and not in contact with the surface of the titanium, with concomitant water spray irrigation, under air 6 and water spray 7, the

irradiation angle was 90 degrees, at a focal distance of 2 mm, the spot size diameter was 1.3 mm.

After cleaning the entire peri-implant defects, biphasic ceramic graft material (70% hydroxyapatite and 30% BTCP - Plenum Oss, Jundiai, SP, Brazil) soaked in blood filled all the cavity. A membrane of poly-dioxanone (Plenum Guide, Jundiai, SP, Brazil) was applied to cover the entire grafted defect. The membrane was adjusted to extend circumferentially 3 to 5mm over the adjacent alveolar bone, avoiding ingrowths of the soft connective tissue. To allow flap apposition and closure after placement, incisions were made buccally and lingually after membrane placement. Primary wound closure was achieved with horizontal mattress sutures alternated with interrupted sutures to ensure a non-submerged healing procedure in diseased implants. The implant-supported restoration was then installed with minimum contact to the peri-implant soft tissue margin.

Postoperative care

Postoperative care consisted of an application of hydro-carbon-oxo-borate complex gel twice a day for 21 days without mechanical cleaning at the surgical areas. Anti-inflammatory medication (4mg betamethasone) was administered twice a day and appropriate analgesia (paracetamol) for 3 days following surgery in order to reduce postoperative swelling and pain. A postoperative antibiotic regimen with Metronidazole (400mg x 3 daily) and amoxicillin (500mg x 3 daily) was prescribe for 14 days (Shibli et al. 2019). Nylon sutures were removed 14 days after surgery. This healing phase was supplemented by occlusal adjustments when necessary and professional supragingival plaque control every month, for 12 months.

Data evaluation

The data were assessed per subject and per site. The clinical and radiographic data between baseline and 12 months after surgery were assessed by Wilcoxon test ($p<0.05$).

Results

A total of 24 patients completed the 12 months follow up evaluation with no dropouts. There were 16 females and 8 males ranging from 43 to 69 years of age. The majority of the dental implants were located in molar and premolar region. All the clinical parameters and treatment outcomes are presented in **Table 1.**

After 1 year follow up, 3 out 31 implants were removed due to persist infection. Additional 3 implants present peri-implant mucosa recession, but without signs of inflammation (BoP, Sup and further bone loss). After 12 months periods, the survival rate was 90.32%. The clinical endpoint (PD<5mm, no BoP and/or sup, not further bone loss) were achieved in 82.75% of the remaining implants (25 out 29 dental implants at the end of the study).

The treatment protocol improved statistically all clinical parameters ($p < 0.05$ between baseline and 1 year), including the percentage of implants achieving treatment success at 1 year (PD < 5 mm, no BoP, and no bone loss). Between baseline and 1 year, PD reduction was 2.8 ± 0.2 mm, while CA gain was 1.9 ± 0.8 mm. The BoP was reduced to 22.12 ± 9.34%, showing also the remission of inflammation signs. The

peri-implant bone remodelation ranged from 0.5 to 4mm, with a mean of 2.67 ± 1.02mm.

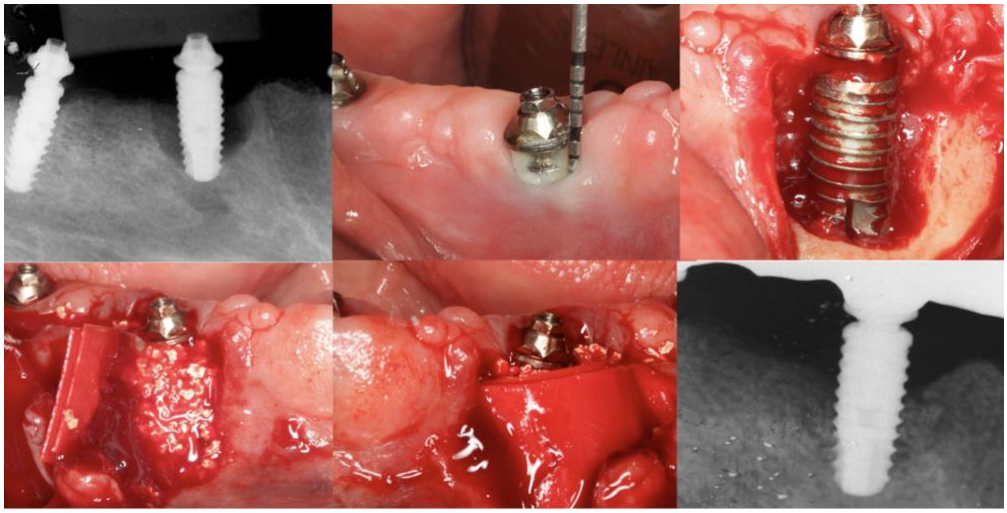

Figure 1: Clinical view of the sequence of treatment: radiographic view, clinical assessment, debridement using laser, guided bone regeneration with biphasic material and polymeric membrane, and final radiographic view after 12 months.

Discussion

This study evaluated the effect of combine local (Er:YAG laser) and systemic (antibiotics) detoxification of peri-implant defects plus guided bone regeneration provided a significative improvement in both clinical and radiographic parameters. The amount of bone regeneration was significantly influenced by size and shape of the peri-implant bone defect. In this present investigation, the clinical evaluation pre- and post-treatment revealed a variable degree of appreciable hard-tissue fill of the peri-implant defects even around deeper peri-implant defects.

The use of Er:YAG laser not only facilitates the surgical debridement but also were effective to clean up the implant surfaces even around sharp edges of the present threads and different implant surface topographies. Laser light interacts with the implant surface without touch the metal. In addition, the power output used in this

surgical procedure helps to remove organic particles and bacterial deposits. Finally, the secondary additional effect of the laser will allow a photobiomodulation to modulate the inflammatory process. In the contrary, mechanical debridement using metallic curettes could also be effective, but often results in titanium particle release and scratching into the surfaces being able to act as reservoirs to future bacterial accumulation and calculus.

Complementary, the systemic use of metronidazole (MTZ) associated with amoxicillin (AMX) treatment to resolve peri-implantitis despite its demonstrated efficacy in the treatment of severe periodontitis may be due to the difficulty inherent in decontaminating dental implant treads. The Er:YAG laser as adjunctive to the surgical peri-implant therapy has been reported to be more predictable in cases associated with moderate pockets. In this regard, it should be highlighted that the implants included in this study presented very deep pockets, many times exceeding 7 mm. Our positive findings support the notion that severe peri-implantitis may be best treated with open-flap debridement and regenerative and/or ressective therapy. It is not known whether adjunct MTZ+AMX would improve outcomes in patients treated by open-flap debridement alone, without guided bone regeneration. Thus far, randomized clinical trials testing open-flap debridement with other antibiotic protocols, such as adjunctive AMX or azithromycin, have failed to show clinically important advantages of systemic antibiotic use. Heitz-Mayfield et al. demonstrated that an anti-infective protocol including surgical access and antibiotics were able to restore, at least partially, the health conditions around implant supported restorations.

The main limitation of this study was its small sample size. It is possible that more statistically significant results would have been obtained with a study with greater power. Nonetheless, taken together, the clinical findings suggested that the use of

Er:YAG laser associated with systemic antibiotics improved all clinical parameters, at least, after a short-term period of 1 year.

Within the limits of this study, it could be concluded that the Er:YAG laser associated with guided bone regeneration was able to improve the peri-implant health condition, at least, after 1 year follow up. However, this protocol was not able to solve all peri-implantitis cases.

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CONFLICT OF INTERESTING

Prof. Shibli and Dr. Blay are founder and shareholder of Plenum, Jundia, Brazil. All the other authors have no conflict of interested with any material related with the study.

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4. CONCLUSÃO

O laser de Er:YAG associado à ROG pode melhorar as condições de saúde peri-implantar, pelo menos, em 1 ano de acompanhamento. Entretanto nem todos os casos de peri-implantite pode-se valer desse protocolo de tratamento.

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