CAMILA CAMARINHA DA SILVA CIRINO

AVALIAÇÃO CLÍNICA E MICROBIOLÓGICA DO TRATAMENTO CIRÚRGICO E NÃO-CIRÚRGICO DE PACIENTES COM PERIODONTITE AGRESSIVA GENERALIZADA: ENSAIO RANDOMIZADO COM ACOMPANHAMENTO DE 12 MESES.

CLINICAL AND MICROBIOLOGICAL EVALUATION OF SURGICAL AND NON-SURGICAL TREATMENT OF GENERALIZED AGGRESSIVE PERIODONTITIS: A 12 MONTHS FOLLOW-UP RANDOMIZED TRIAL.

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Faculdade de Odontologia de Piracicaba

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Tese apresentada à Faculdade de Odontologia de Piracicaba da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de Doutora em Clínica Odontológica, na Área de Periodontia.

Thesis presented to the Piracicaba Dental School of the University of Campinas in partial fulfillment of the requirements for the degree of Doctor in Clinical Dentistry, in Periodontic área.

Orientador: Antonio Wilson Sallum

Este exemplar corresponde à versão final da tese defendida por Camila Camarinha Da Silva Cirino e orientada por Prof. Dr. Antonio Wilson Sallum.

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Prof. Dr. RENATO CORRÊA VIANA CASARIN

RESUMO

O presente estudo teve o objetivo de avaliar clínica e microbiologicamente o efeito das terapias periodontais cirúrgica e não cirúrgica em um período de 12 meses no tratamento da periodontite agressiva generalizada (PAG). Quinze pacientes diagnosticados com PAG foram incluídos neste estudo com desenho experimental de boca dividida. Os quadrantes superiores foram submetidos ao tratamento, e foram alocados em dois grupos: Grupo TNC (terapia não-cirúrgica) – debridamento ultrassônico associado a raspagem manual; e Grupo TC (terapia cirúrgico) – acesso cirúrgico para debridamento ultrassônico associado a raspagem manual. No baseline, e aos 3, 6 e 12 meses pós terapia, foram avaliados os seguintes parâmetros clínicos: índice de placa (IP), índice de sangramento à sondagem (ISS), profundidade de sondagem (PS), nível de inserção clínica (NIC) e posição da margem gengival (PMG). Nos mesmos períodos foram determinados os níveis de concentração de *Porphyromonas gingivalis* (Pg) e *Aggregatibacter actinomycetemcomitans* (Aa) no biofilme subgengival. Os resultados indicaram que a TC foi capaz de promover maior redução de PS quando comparada à TNC, em bolsas profundas, aos 12 meses (5,9±1,2 mm e 4,8±0,6 mm, TNC e TC respectivamente, $p < 0,05$), e também em dentes posteriores aos 6 meses de acompanhamento (4,8±0,8 mm e 4,1±1,3 mm, TCN e TC, respectivamente, $p < 0,05$). Além disso, foi observada maior recessão gengival em dentes posteriores do grupo TC, aos 6 meses, comparados ao baseline (-0,2±0,2mm e -0,7±1,2 mm, TCN e TC, respectivamente, $p < 0,05$). A avaliação microbiológica não demonstrou diferença estatística nos níveis de Aa e Pg para ambos os grupos em todos os períodos de acompanhamento. Pode-se concluir que, apesar de ambas a terapias não terem sido capazes de reduzir os níveis de Aa e Pg, clinicamente a terapia cirúrgica promoveu maior redução de PS em bolsas profundas e dentes posteriores.

Palavras-chave: Periodontite agressiva. Terapia cirúrgica. Terapia não-cirúrgica.

ABSTRACT

The present study aimed to evaluate clinically and microbiologically the effects of surgical and non- surgical periodontal therapy in a 12-month period in the treatment of generalized aggressive periodontitis (GAgP). Fifteen patients with GAgP were included in this randomized controlled clinical study with experimental split-mouth design. Superior quadrants were treated, and allocated into two groups: Non-Surgical Therapy Group (NST) - ultrasonic debridement associated with manual scaling, and Surgical Therapy Group (ST) - access to surgical ultrasonic debridement associated with scaling manual. At baseline and at 3, 6 and 12 months after treatment, the following clinical parameters were assessed: plaque index (PI), bleeding on probing index (BoP), probing depth (PD), clinical attachment level (CAL) and gingival margin position (GMP). In same periods were determined the concentrations of *Porphyromonas gingivalis (*Pg*), Aggregatibacter actinomycetemcomitans (*Aa*)* in subgingival biofilm. The results showed that ST was able to promote further PS reduction compared to the NST, in deep pockets, at 12 months (5.9 ± 1.2 mm and 4.8 ± 0.6 mm, NST and ST respectively, $p < 0.05$) and also in posterior teeth at 6 months follow-up (4.8 ± 0.8 mm and 4.1 ± 1.3 mm, NST and ST, respectively, $p < 0.05$). In addition, it was observed higher gingival recession in posterior teeth of ST group at 6th month, comparing to baseline (-0.2 ± 0.2 and -0.7 ± 1.2 mm, NST and ST, respectively, $p < 0.05$). The microbiological evaluation showed no statistical difference in the levels of Aa and Pg for both groups at all follow-up periods. It can be concluded that, althought both therapy failed do reduce the levels of Aa and Pg, clinically the surgical therapy promoted more PD reduction in deep pockets and posterior teeth.

Key words: Aggressive periodontitis. Surgical therapy. Non surgical therapy.

SUMÁRIO

DEDICATÓRIA

Dedico este trabalho à minha família, meu alicerce e minha plenitude. Com vocês, aprendi a sonhar, a lutar, a voar. Em vocês, encontrei todo apoio, incentivo e amor necessários para concluir esta dura jornada. Em especial, dedico esta conquista à minha filha Beatriz, que chegou para colorir a minha vida com cores que jamais imaginei, e que me faz a cada dia mais amada, mais realizada e mais feliz. Amo vocês!

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“Que os vossos esforços desafiem as impossibilidades. Lembrai-vos de que as grandes coisas do homem foram conquistadas do que parecia impossível.”

Charles Chaplin

INTRODUÇÃO

A periodontite agressiva (PA) uma doença que acomete pessoas jovens e cuja prevalência é descrita na literatura de maneira bastante variada. Estudos conduzidos nos Estados Unidos com escolares apontaram prevalência maior em indivíduos negros (2,60% - 2,90%) quando comparada com indivíduos brancos (0,06% - 0,17%). Na Europa e Ásia, a prevalência varia de 0,1 a 1,8%, e estudos com populações africanas indicam taxa de prevalência de até 7,6%. No Brasil, pesquisas epidemiológicas apresentaram dados que variam entre 0,32 a 5,5% de indivíduos portadores de PA (Albandar, 2002, Susin e Albandar, 2005).

O desafio microbiano é um fator etiológico primário para a instalação e progressão da PA. Além de fatores imunológicos e genéticos ainda não completamente estabelecidos, algumas características microbiológicas têm sido descritas como determinantes e importantes no estabelecimento e progressão da doença. Entre elas, a presença e concentração do patógeno *A. actinomycetemcomitans* mostrou ser maior nos indivíduos com PAG, além de aumentar significativamente o risco de desenvolvimento da doença, bem como o risco de perda de inserção (Haubek et al, 2008; Slots e Ting, 1999, Casarin et al, 2010). Outros estudos ainda mostraram que, além do Aa, há a presença e alta prevalência de *Porphyromonas gingivalis*, *Tanerella forsythia, Campylobacter rectus, Prevotella intermedia, Treponema SSP*, bacilos entéricos, entre outros (Gajardo et al, 2005; Lafaurie et al, 2007, Faveri et al, 2008).

Um fator importante em relação à microbiota é que esta também afeta diretamente o processo de reparo dos tecidos, por interferir na proliferação celular e adesão dos fibroblastos do ligamento periodontal sobre o cemento dental contaminado (Aleo et al, 1974; Aleo et al, 1975). Sendo assim, a adequada biocompatibilização da superfície radicular é essencial para o restabelecimento da saúde periodontal. Nesse sentido, a terapia mecânica é o tratamento de escolha, e tem sido alvo de diversas pesquisas no intuito de alcançar melhores protocolos de

tratamento que promovam resultados previsíveis para o controle da doença periodontal.

Diversos estudos têm testado diferentes modalidades terapêuticas em busca de uma melhor resposta clínica, especialmente em casos mais avançados e severos de periodontite agressiva. A terapia periodontal não-cirúrgica se apresenta como uma opção importante no tratamento desta condição, entretanto o índice de pacientes que não responderam ao tratamento ainda é significativo (Hughes et al, 2006), o que reforça a necessidade de outras abordagens para melhorar os resultados.

A terapia cirúrgica é uma alternativa de tratamento que tem apresentado resultados mais efetivos do que a terapia não-cirúrgica em periodontite crônica, com reduções significativas de profundidade de sondagem, principalmente em bolsas profundas (Antczak-Bouckoms et al, 1993; Heitz-Mayfield et al, 2002). Entretanto, não há na literatura estudos clínicos controlados que avaliem estes benefícios na forma agressiva da doença periodontal.

Na década de 80, estudos comparativos entre a terapia cirúrgica e não-cirúrgica apresentaram resultados com maior redução de profundidade de sondagem e ganho de inserção clínica em favor do tratamento cirúrgico. (Wennstrom et al, 1986, Christersson et al, 1986). Microbiologicamente, por meio de técnicas de cultura bacteriana, Christersson e colaboradores (1986) demonstraram que a raspagem não alterou a contagem de Aa no ambiente subgengival, enquanto o acesso cirúrgico eliminou este patógeno em 88,8% das bolsas após uma semana, e em 55,5% após 16 semanas. Em outro estudo mais recente, a terapia cirúrgica, contudo, associada à terapia antimicrobiana, evidenciou ganhos significativos de inserção, com estabilização em longo prazo (Buchmann et al, 2001). Desta forma, os autores sugeriram que a terapia cirúrgica poderia, então, apresentar resultados benéficos no tratamento da periodontite agressiva, principalmente nos casos mais severos, uma vez que a terapia cirúrgica tem grande

impacto na redução da profundidade de sondagem, parâmetro este que tem grande valor preditivo para perda de inserção clínica em longo prazo (Badersten et al, 1990, Matuliene et al, 2005).

Os estudos citados anteriormente, no entanto, podem não fornecer informações suficientes para um tratamento previsível em pacientes com periodontite agressiva, em especial, na forma generalizada e severa. Deste modo, baseado na ausência de estudos clínicos randomizados controlados longitudinais que avaliem a abordagem cirúrgica em periodontite agressiva, o presente estudo tem como objetivo comparar, através dos parâmetros clínicos e microbiológicos, o efeito das terapias periodontais cirúrgica e não-cirúrgica no tratamento da periodontite agressiva generalizada, com acompanhamento clínicos de 12 meses.

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Clinical and microbiological evaluation of surgical and non-surgical treatment of generalized aggressive periodontitis: a 12 months follow-up randomized trial.

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One-sentence summary: Surgical therapy promoted additional benefits in patients with GAgP.

ABSTRACT

Background: The present study aimed to evaluate clinical and microbiological effects of surgical and non-surgical periodontal therapy in generalized aggressive periodontitis (GAgP) treatment.

Material and Methods: Fifteen GAgP patients were included in this RCT with split-mouth design. Quadrants were allocated into two groups: Non-Surgical Therapy Group (NST), and Surgical Therapy Group (ST). The following clinical parameters were assessed: plaque index (PI), bleeding on probing index (BoP), probing depth (PD), clinical attachment level (CAL) and gingival margin position (GMP). Concentrations of *Porphyromonas gingivalis (*Pg*), Aggregatibacter actinomycetemcomitans (*Aa*)* in subgingival biofilm were also determined. Clinical and microbiological parameters were assessed at baseline, 3, 6 and 12 months after treatment.

Results: ST was able to promote further PS reduction compared to NST in deep pockets at 12 months (5.9 ± 1.2 mm and 4.8 ± 0.6 mm, NST and ST respectively), and in posterior teeth at 6 months (4.8 ± 0.8 mm and 4.1 ± 1.3 mm, NST and ST, respectively; $p<0.05$). In addition, higher gingival recession were observed in posterior teeth of ST group at 6th month, comparing to baseline (-0.2 ± 0.2 and -0.7 ± 1.2 mm, NST and ST, respectively; $p<0.05$). Microbiological evaluation showed no statistical difference in levels of Aa and Pg for both groups at all follow-up periods.

Conclusion: Surgical therapy promoted additional benefits in patients with GAgP. Furthermore, both therapies failed to reduce Aa and Pg levels at different follow-up times.

Key words: Aggressive periodontitis, surgical therapy, non surgical therapy.

INTRODUCTION

Aggressive periodontitis (AgP) is a complex disease with various factors involved in its pathogenesis. Nevertheless, microbial challenge is a primary etiological factor for the onset and progression of AgP. In addition to genetic and immunologic factors, that were not yet been fully established, some microbiological characteristics have been described as determinant and important for the onset and progression of this disease. Among them, the presence and concentration of pathogen *Aggregatibacter actinomycetemcomitans* (Aa) has showed to be greater in individuals with generalized aggressive periodontitis (GAgP), besides increasing significantly the risk for the development of the disease, as well as the risk for attachent loss[1,2,3]. Other studies still showed that, beside Aa, there is the presence of high prevalence of *Porphyromonas gingivalis* (Pg)*, Tannerella forsythia (*Tf)*, Campylobacter rectus* (Cr), *Prevotella intermedia* (Pi), *Treponema ssp*, enteric rods and others[4,5,6].

In spite of differences in pathogenesis, biocompatibilization of root surface is essential for reestablishment of periodontal health. In this context, mechanic therapy is the treatment of choice, and has been target of several studies aiming to reach better treatment protocols that could promove predictable results for AgP control. However, although non-surgical periodontal therapy appears as an option for the treatment of this condition, it is associated to a reduction in clinical response[7] and a high percentage of non-responder sites[8], which reinforces the need for other approaches to reach better results.

Surgical therapy is an alternative that has showed more effective results than non-surgical therapies regarding chronic periodontitis (CrP), with significant reduction on pocket probing, mainly in deep pockets[9,10]. In 13 AgP subjects followed-up for 5 years after a surgical therapy plus systemic antimicrobial intake, a significant gains in CAL and a long-term stabilization of results could be seen[11]. However, there

are no controlled clinical trials comparing surgical to non-surgical approach in AgP therapy.

Thus, based on the absence of longitudinal randomized clinical trials that evaluate surgical approaches in aggressive periodontitis, this study aims to compare, through clinical and microbiological parameters the effect of surgical and non-surgical periodontal therapies in the treatment of generalized aggressive periodontitis, with a 12-month follow-up.

MATERIAL E METHODS

Study Design

This study was designed as a randomized controlled clinical trial with split-mouth experimental design, in order to determinate microbiological and clinical outcomes of surgical and non-surgical therapy in the treatment of generalized aggressive periodontitis. This study was approved by Ethics Committee Piracicaba Dental School of the University of Campinas, under protocol 024/2006. Written informed consent was obtained from included participants.

Population Screening

Twenty-one individuals were selected from postgraduate clinic of Piracicaba Dental School, University of Campinas, southeastern region of Brazil, from March of 2011 to September of 2012. All selected patients received complete periodontal examination, complete periapical radiographic examination and complete medical and dental anamnesis.

Inclusion criteria were: (i) diagnosis of generalized aggressive periodontitis, according to American Academy of Periodontology: generalized loss

of periodontal attachment affecting at least three teeth other than first molars and incisors (Lang et al, 1999); (ii) presence of at least 20 teeth; (iii) at least 8 teeth presenting PD ≥ 5 mm with bleeding on probing and at least 2 with PD ≥ 7 mm); (iv) good general health; and (v) < 35 years of age . Exclusion criteria were (i) periodontal treatment conducted within the last 6 months; (ii) utilization of drugs such as antibiotics, continuous use of anti-inflammatories; (iii) presence of systemic diseases or active infectious disease (diabetes, cardiovascular, hepatitis, etc.); (iv) presence of the habit of smoking; (v) pregnancy or lactation.

Calibration, Randomization, and Sample Size Calculation

For calibration, two non-study patients presenting with GAgP examined by designated examiner (CCSC) measuring CAL and PD in all patients twice within 24 hours with an interval of 1 hour between examinations. The intraclass correlation was calculated for each parameter, resulting in 90% for PD and 87% for CAL. Quadrants to be treated were allocated to groups according to a computer-generated list (under responsibility of HFV). This code was not broken until the follow-up was concluded. Sample size calculation was done before the study with a statistical software program[¶]. This analysis indicated that with 15 patients, the study would have 80% power to detect a 1 mm difference in the PD reduction, considering a mean standard deviation of 1.3mm[12].

Treatment

1. Study groups

Upper jaw in contralateral quadrants were randomly assigned to the following treatment protocols:

[¶] Bioestat release 5.3, Fundação Mamirauá, Belém, Pará.

- Non-surgical therapy (NST) Group: ultrassonic instrumentation[#] with specific subgingival acess tips[**], associated with scaling and root planing using Gracey and Mini-five curetes[††].
- Surgical Therapy (ST) Group: intrasulcular incision and elevation of a mucoperiosteal flap to access root surfaces; and then ultrassonic instrumentation with specific subgingival acess tips, associated with scaling and root planing using Gracey and Mini-five curetes.

2. Patients Preparation

After anamnesis and clinical examination to confirm adequacy to study criteria, patients were clarified about AgP characteristics. Subsequently, they underwent initial periodontal therapy, which included oral hygiene instructions, supragingival scaling, prophylaxis and removal of biofilm retentive factors.

3. Treatment

After initial therapy, treatments were conducted by a single operator (HFV) in one session. Lower jaw also received scaling and root planing, however data were not included in this study.

Patients were anesthetized for the completion of treatment. After procedures, patients received on quadrants of ST group vertical internal mattress sutures with mononylon 5-0. Postoperative instructions and drug prescription were given, which included 500 mg sodium dipyrone every 6 hours if they felt pain or discomfort, and mouthwash with chlorhexidine gluconate 0.12% twice daily for 14 days. After 7 days, sutures were removed.

[#] Cavitron, DENTSPLY, NY, USA.
[**] 25K FSI®-SLI®-10S, DENTSPLY, NY, USA.
[††] Hu-Friedy, IL, USA

Clinical Evaluation

Clinical parameters were assessed in 6 points around each tooth with a North Carolina periodontal probe with 1mm markers‡‡ as follow:

1) full-mouth plaque index (FMPI), according to Ainamo and Bay[13] and full-mouth bleeding score (FMBS), according to Mühlemann and Son[14]; 2) Probing Depth (PD), distance from the bottom of pocket to gingival margin; 3) gingival margin position (GMP), distance from the gingival margin to enamel cement junction (CEJ); and 4) Clinical Attachment Level (CAL), distance from the bottom of the pocket to the CEJ.

In each evaluation, reinforcement in oral hygiene and professional plaque control were performed. Parameters were assessed for initially moderate (5 and 6 mm) and deep pockets (≥ 7 mm).

Biofilm Collection

Subgingival biofilm samples were obtained from 02 moderates and 02 deep sites randomly selected. Collection were performed in baseline, and after 03, 06 and 12 months after treatment.

After careful removal of supragingival biofilm, relative isolation with cotton rolls and drying, collection was performed sterile paper point (#35) was inserted into the bottom of the periodontal pocket for 30 seconds. The paper points were placed into sterile tubes containing 300 µL 0.5-mM Tris-EDTA.

Microbiologic analysis

The presence and concentration of Pg and Aa were evaluated by

‡‡ PCPUNC 15® Hu Friedy, IL, USA

quantitative polymerase chain reaction (qPCR) as previously described in Casarin et al, 2012. Briefly, DNA was extracted from the subgingival biofilm, using commercial kits[§§]. A qPCR was performed using the hot start reaction mix for PCR[¶¶]. The concentration of the DNA used in each run was 10 mg/mL. The amplification profiles were as follows: 95°/10', 55°/5', 72°/4' – 40 cycles for Pg; 95°/10', 55°/5', 72°/3' - 40 cycles for Aa Absolute quantification of target bacteria in clinical samples was performed using Pg (ATCC 33277) and Aa (JP2) as controls. The determination of DNA genome copies in controls was based on the genome size of each bacteria[15]. The microbiologic analyses were performed separately for moderate and deep pockets.

Data Management and Statistical Analyses

The statistical analysis considered the intent-to-treat. Initially, the values were analyzed for normality by Shappiro-Wilk test. The null hypothesis tested was that ST added no clinical or microbiologic benefits to the treatment of GAgP patients compared with NST. To test this hypothesis, a statistical software program was used and the primary variable was the reduction in PD, followed by CAL gain, alteration in GMP and reduction in periodontal pathogens. The homogeneity of groups at baseline was tested using the Student's t test. For clinical parameters, a repeated-measures ANOVA was used to detect intragroup differences in clinical parameters (GMP, PD, CAL), considering the patient as a statistical unit. The results of GMP, PD, and CAL refer strictly to the qualifying sites. When a statistical difference was found, an analysis of the difference was determined using the Tukey method. The Student's t test was used to determine the differences between groups regarding changes in clinical parameters and the percentage of residual pockets. The Friedman test was used to detect intragroup differences, and the Kruskal-Wallis test was used for intergroup analysis of full-mouth plaque and bleeding indices in all periods. The experimental level of significance was determined to be 5%.

RESULTS

Figure 2 illustrate the flowchart of the study. During patients' recruitment, 21 individuals were selected as possible participants of the study. After initial exam, 5 of them were excluded (two diagnosed with localized AgP, two refused to participate and one smoker). Then, 16 patients filled inclusion criteria and were included in the study. One patient were excluded for not accomplish 03 months follow-up. At 12 months follow-up, 07 patients were also excluded – two due to antibiotics intake, one due to pregnancy and four moved to other city.

Table 1 shows patient's characteristics at baseline. There was no difference between groups regarding oral hygiene status (PI and BoP), and there was no difference in clinical parameters ($p>0.05$).

Data about plaque and bleeding scores are presented in Table 2. There were no statistically significant changes in Plaque Index (PI) considering different times and different groups. Considering Bleeding on Probing (BoP), there were a great reduction for all pockets from baseline to 03 months, with no differences between groups. For moderate pockets, at 06 months the percentage of positive sites did no presented differences also for 03 months and baseline, whereas at 12 months both groups showed significant reduction compared to baseline. For deep pockets, there was also a significant reduction from 03 months to baseline and no differences of them for 6 months, and in 12 months evaluation no statistical significant changes from other examinations.

Data from clinical parameters are described in Table 3. Considering all pockets, both treatments promoted significant reduction in PD and CAL gain ($p<0.05$), with no differences between groups ($p>0.05$). However, although both treatments promoted significant increase in GMP ($p<0.05$), ST group presented, at 6^{th} month, higher gingival recession than NST group ($p<0.05$). At 12^{th} month, no difference were observed anymore ($p>0.05$).

Concerning moderate pockets, changes in CAL and GMP were similar between groups ($p>0.05$). PD also did not presented difference comparing surgical and non-surgical approach ($p>0.05$). However, in deep pockets, ST group presented at 12th month of follow-up a statistically difference in PD (5.9±1.2mm and 4.8±0.6mm in NST and ST respectively, $p=0.03$). Moreover, ST promoted a higher PD reduction (2.9±0.7 mm) than NST (1.5±1.1mm), although a borderline p-value has been achieved ($p=0.0572$). CAL and GMP for deep pockets did not presented significant differences between groups.

Considering only anterior teeth, all clinical parameters similarly changed during 12th follow-up ($p<0.05$), in NST and ST group, with no statistical difference between them ($p>0.05$). Differently, in regards to posterior teeth, ST group presented a significantly lower PD mean at 6th month (4.1±1.3 mm) when compared to NST group (4.8±0.8mm), with $p=0.03$. Moreover, ST group also presented a higher gingival recession in posterior teeth than NST at 6th month (NST: -0.2±0.2mm, ST: -0.7±1.2mm; $p=0.05$).

DISCUSSION

The present study clinical and microbiologically evaluated surgical and non-surgical periodontal therapy in the treatment of GAgP patients. There remains a challenge for clinicians the treatment of aggressive periodontitis, due to its rapid progression and the paradigm of worse response. Several studies have been conducted in order to achieve better results, but there are few studies in the literature that support surgical therapy as an effective alternative in treatment of this condition.

The findings of the present study demonstrated that surgical approach promoted additional probing depth reduction in deep pockets (1.1 mm at 12 months follow-up) and posterior teeth (0.7mm at 6 months follow-up), although also

promoted additional gingival recession in all pockets (0.3 mm) and only in posterior teeth (0.5 mm).

Systematic reviews and meta-analysis have showed that reduction in probing depth are greater in surgically treated site, particularly in deep pockets, in patients with chronic periodontitis[9,10]. Nevertheless, few studies have addressed surgical therapy in aggressive periodontitis, but these often reports promising results. In a small sample size trial, Christersson et al[16], treating deep sites of localized AgP patients, showed no significant changes in PD for scaled and root planed group. On the other hand, for surgically treated group, PD measures decreased approximately 2.6 mm after 16 weeks.

Surgical therapy has also demonstrated to be an effective approach with regard to long term periodontal stability. Wennstrom et al[17], in long term follow-up, also demonstrated a great reduction of probing depth between baseline and 6 months in sites treated with open flap scaling and root planing, with minor variation between 2 and 5 years follow-up, in patients with localized AgP. Considering GAgP patients, a prospective case series[11] treated sites with PD greater of equal to 6 mm with surgical access associated with systemic amoxicillin/metronidazole intake. At 3 months evaluation, gain of CAL was of 2.23 mm, reaching 2.57 mm at 5 years of follow up. Compared to results achieved in present study, in which CAL gain was about 2.5 mm at 1 year follow-up, it appears that surgical therapy, alone, could also reach promising results on GAgP treatment. Though, it is undoubted that antimicrobials play an important role in clinical parameters improvements.

A recent review indicated that adjunctive use of antimicrobials to non-surgical therapy promotes statistically significant improvements in CAL gain and PD reduction[18,19]. Several studies have evidenced additional benefits of antimicrobial therapies in aggressive periodontitis[11,12,20,21,22,23,24,25,26], even though it has not yet been established which the most appropriate antimicrobial protocol. Some clinical trials[12,21,25] evaluated the association of amoxicillin and metronidazole with non-

surgical approach, and found a reduction in PD ranging between 3.1 and 4.27 mm, and CAL gain ranging between 2.3 a 3.43 mm in deep pockets. Those data, when compared to the ones achieved in present study (2.9 mm of PD reduction and 2.5 mm of CAL gain in deep pockets), evidenced an additional benefit of systemic antibiotics when associated to non-surgical therapy. Nonetheless, there are no controlled clinical trial that presents clear answers about benefits achieved, particularly in association with surgical therapy[27].

Moreover, one of the main goals of periodontal therapy is to arrest the progression of the disease. It was observed that patients subjected to non-surgical therapy showed exhibited signs of disease progression in long term[28]. Furthermore, Badersten et al[29] demonstrated that sites with increase in PD > 1 mm showed increase of about 78% of predictive value for attachment loss. The outcome of the present study demonstrated a stability of CAL during all monitoring period, however sites treated with non-surgical instrumentation showed a tendency to recurrence in deep pockets and posterior teeth, with additional CAL gain and increase in PD over the time. This result could be attributed to a greater difficulty in instrumentation, especially in those critical areas such as deep sites and furcation.

Surgical approach seems to be more effective to access to root surfaces, promoting a more thorough debridement and additional benefits especially in areas with difficult access, such as deep sites and furcation areas[30]. This could result in a better calculus and biofim removal on scaled area and a, consequently, an optimized microbiota reduction. However, the microbiological findings of this study failed in reach significant differences between groups.

Both surgical and non-surgical approaches failed to promote reduction in amounts of Pg and Aa. The presence of these pathogens in subgingival environment increases significantly risk to disease development, as well as the risk of attachment loss[1,2]. A substantial suppression of Aa could not be achieved by scaling and root planing alone in some studies, however a surgical approach was able to suppress

Aa in 55.5% of pockets after 16 months[16] when antimicrobial therapy was prescribed adjunctively. Another study achieved significant lower counts of Aa in scaling and root planing (SRP)+antimicrobials compared to SRP alone or SRP+placebo[12,20,23]. This highlight the impact of antimicrobials on pathogens, in special, Aa reduction.

Periodontal tissue breakdown in GAgP seems to be influenced by Aa ability of overpass junctional epithelium and invade connective tissue[31]. Accordingly, systemic antimicrobials could have an impact over these pathogens, promoting further reduction in its amount that was not observed in the present study. Anyway, the subgingival biofilm present more than 400 species and actually, more than Aa and Pg has been associated to AgP, in which could be included *Streptococcus, Eubacterium, Peptostreptococcus, Selenomonas,* and other phylotypes that have not yet been cultivated[6,32]. So, further analysis with a high-throughput approach could give us a more definitive idea of how surgical and non-surgical approaches alter subgingival environment and, possibly, indicate the most predictable form to treat GAP subjects.

Indeed, since this is the first randomized clinical trial treating GAgP patients with surgical approach, further controlled clinical trials with larger sample size, with long-term follow-up, and/or in association with other adjunct approaches, are required to confirm those benefits and possibly reach better clinical and microbiological outcomes and promote a more predictable treatment of this population.

CONCLUSION

Based on obtained outcomes, it can be concluded that surgical therapy promoted additional benefits in patients with GAgP, with greater PD reduction in deep pockets and posterior teeth. Moreover, both surgical and non-surgical

approaches were not able to reduce levels of Aa and Pg in both groups over follow-up periods.

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FIGURES

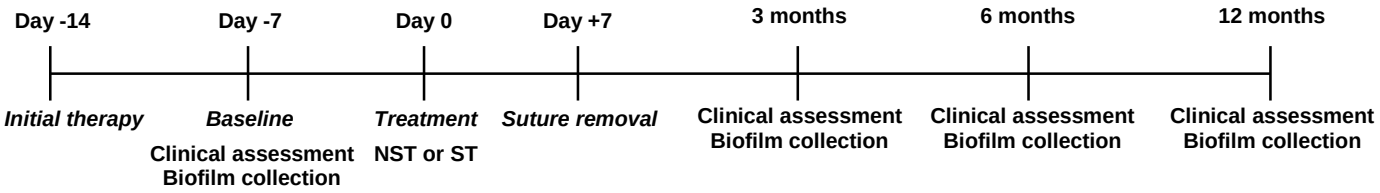

Figure 1. Timeline of patient's follow-up.

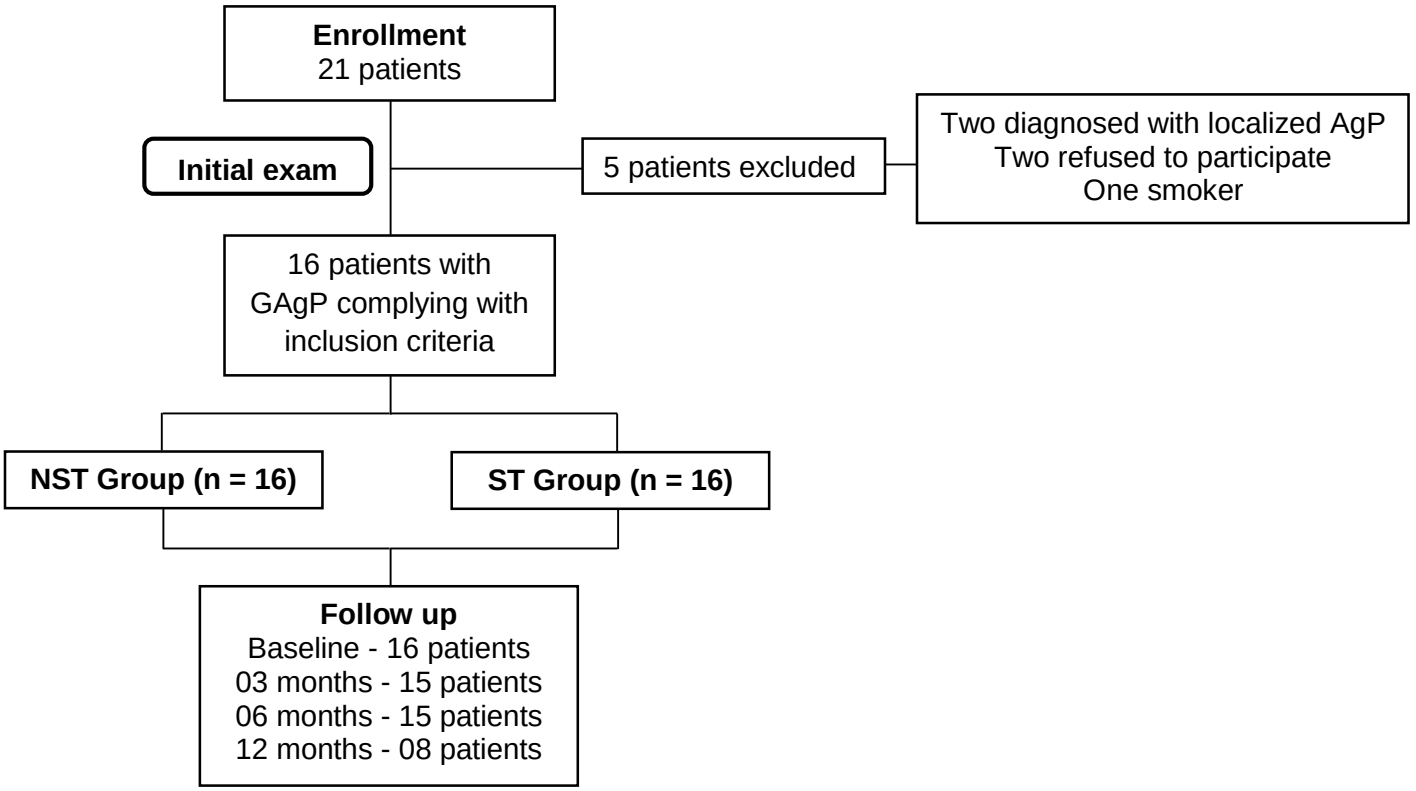

Figure 2. Flowchart of study

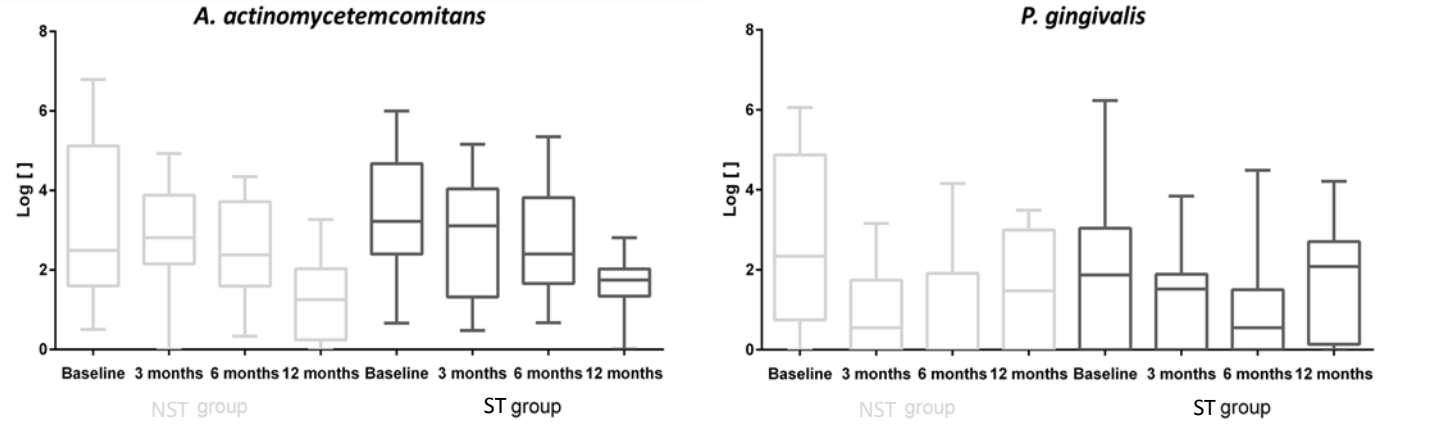

Figure 4. *A. actinomycetemcomitans* (left) and *P. gingivalis* (right) amounts (log[ ]) in each group in all pockets during 12-months of follow-up. *No difference between groups (Friedman and Wilcoxon's tests, p>0.05).*

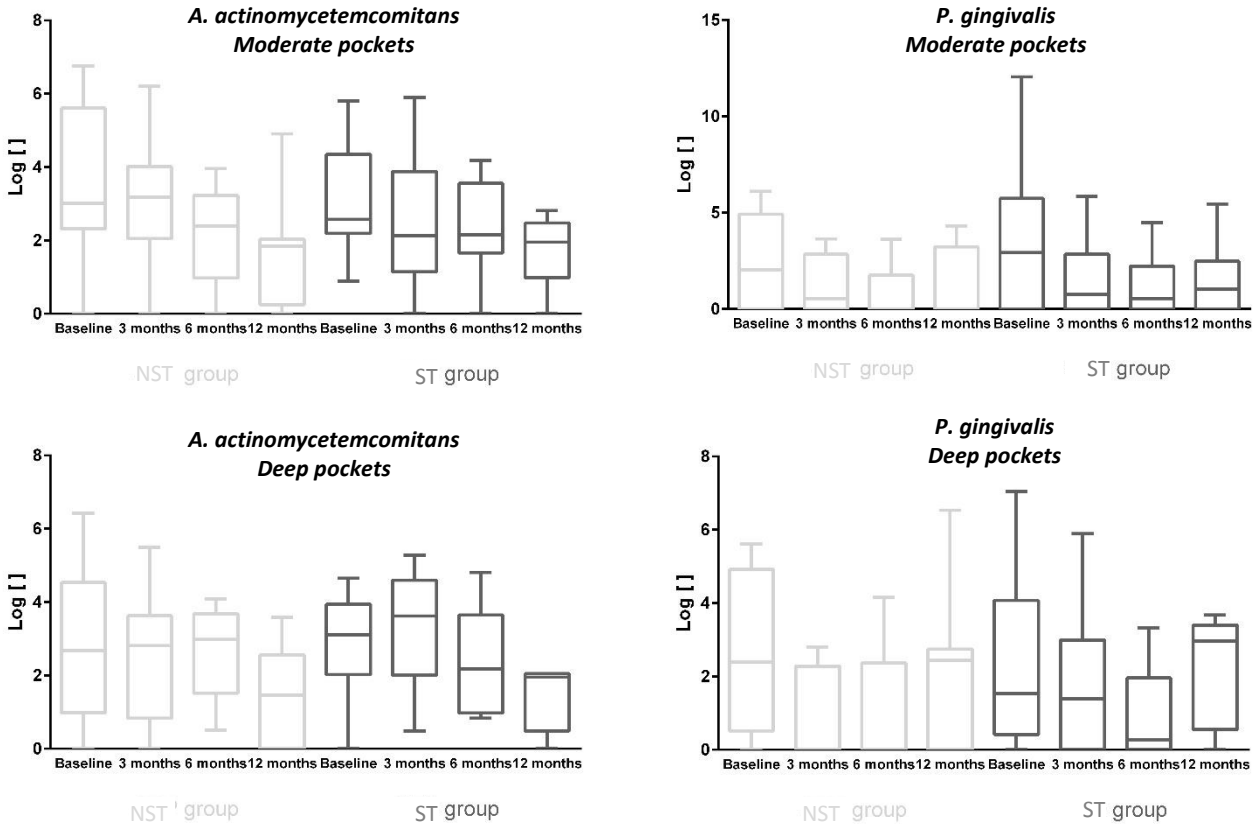

Figure 5. *A. actinomycetemcomitans* (left) and *P. gingivalis* (right) amounts (log[ ]) in each group in moderate and deep pockets during 12-months of follow-up. *No difference between groups (Friedman and Wilcoxon's tests, p>0.05)*

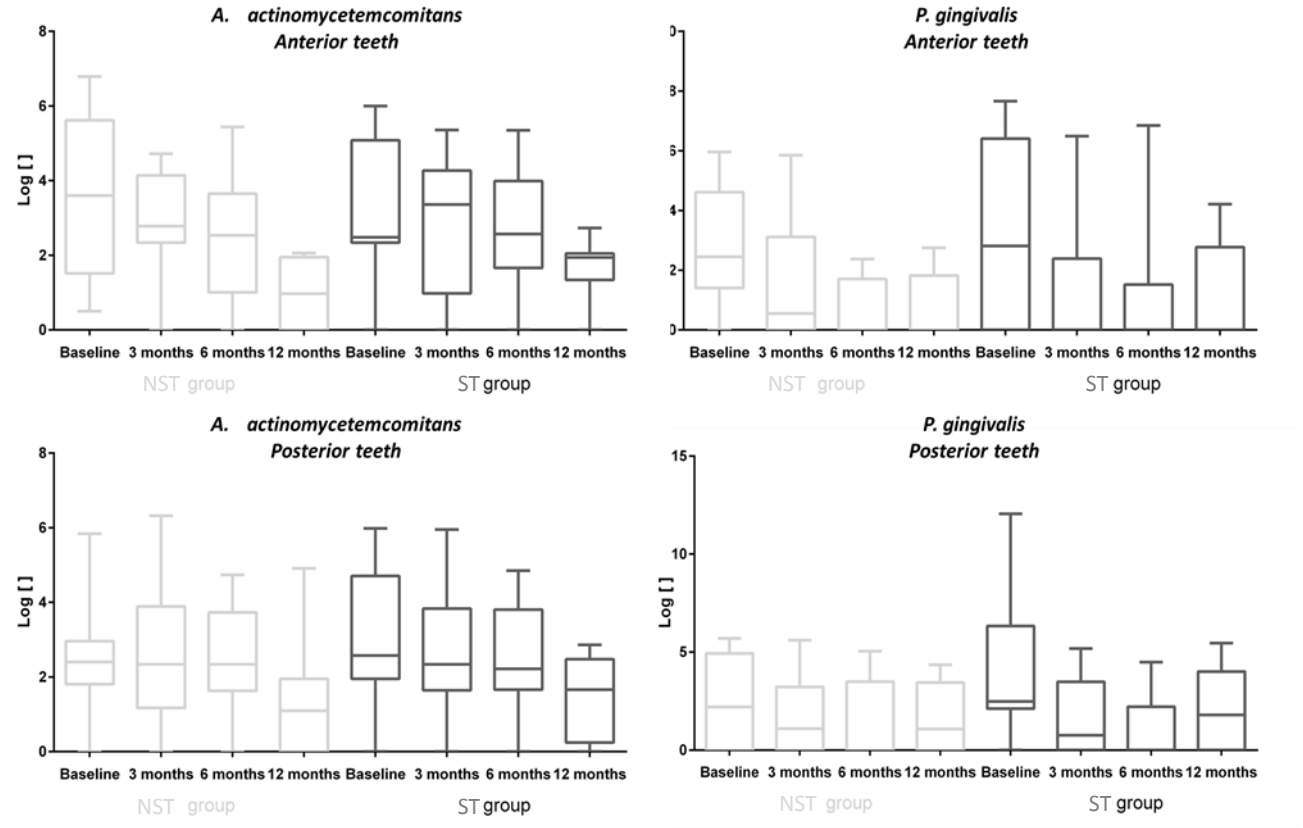

Figure 6. *A. actinomycetemcomitans* (left) and *P. gingivalis* (right) amounts (log[ ]) in each group in anterior and posterior teeth during 12-months of follow-up. *No difference between groups (Friedman and Wilcoxon's tests, p>0.05)*

TABLES

Table 1. Patient's characteristics at baseline.

Characteristics	NST	ST
Age (years) (mean±SD)	27.2±5	
Females (%)	93.75	
PI (mean±SD)	46.2	38.5
BoP (mean±SD)	92.3	92.3
PD (mean±SD)	6.2±0.7	6.2±1.3
CAL (mean±SD)	6.4±0.8	6.4±1.3
GMP (mean±SD)	0.2±0.4	0.5±0.8

At baseline, no significant differences were observed in any characteristic analyzed (ANOVA/Tukey).

Table 2. Plaque and Bleeding on Probing indexes (% of positive sites) at baseline, 3, 6, and 12 months at both groups.

		All pockets		Moderate Pockets		Deep Pockets	
		NST	ST	NST	ST	NST	ST
BoP	*Baseline*	92.3 Aa	92.3 Aa	92.3 Aa	84.6 Aa	92.3 Aa	92.3 Aa
	3 months	53.8 Ab	46.2 Ab	23.1 Ab	15.4 Ab	30.8 Ab	38.5 Ab
	6 months	61.5 Ab	61.5 Ab	53.8 Aab	30.8 Aab	53.8 Aab	53.8 Aab
	12 months	66.7 Ab	66.7 Aab	50.0 Ab	16.7 Ab	66.7 Aab	66.7 Aab
PI	*Baseline*	46.2 Aa	38.5 Aa	53.8 Aa	30.8 Aa	46.2 Aa	38.5 Aa
	3 months	46.2 Aa	46.2 Aa	46.2 Aa	46.2 Aa	46.2 Aa	46.2 Aa
	6 months	53.8 Aa	46.2 Aa	38.5 Aa	38.5 Aa	46.2 Aa	53.8 Aa
	12 months	50.0 Aa	37.5 Aa	37.5 Aa	37.5 Aa	25.0 Aa	37.5 Aa

Distinct letters (lower case within time and capital between groups) indicate statistical significant difference by Chi-Square test ($p<0.05$).

Table 3. Clinical parameters (mm±sd) of NST and ST groups, regarding all, moderate and deep pockets, as well as in anterior and posterior teeth, at baseline, 3, 6 and 12 months of follow-up.

			Baseline	3 months	6 months	*Δ 0-6 months*	12 months	*Δ 0-12 months*
All pockets	**PD**	**NST**	6.2±0.7	4.4±0.7	4.4±0.8	*1.8±1.0*	4.5±0.6	*1.7±1.1*
		ST	6.2±1.3	4.1±0.7	4.2±0.9	*2.0±1.1*	4.2±0.7	*2.0±1.1*
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.28	*0.42*	*0.26*	*0.39*	*0.93*
	CAL	**NST**	6.4±0.8	4.9±0.8	5.0±1.0	1.4±0.9	5.2±0.8	1.2±1.0
		ST	6.7±1.3	5.2±1.3	5.4±1.6	1.3±1.0	5.1±1.6	1.1±1.2
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.61	*0.59*	*0.42*	*0.97*	*0.91*
	GMP	**NST**	0.2±0.4	0.5±1.1	0.6±0.6	**-0.4±0.5**	0.7±0.5	-0.5±0.4
		ST	0.5±0.8	1.1±1.2	1.2±1.3	**-0.7±0.7**	1.0±1.2	-0.5±0.5
				p value (ANCOVA)	*p value (ANCOVA)*	***p value (paired Student's t test)***	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.3	*0.2*	***0.03****	*0.57*	*0.6*
Moderate pockets	**PD**	**NST**	5.3±0.4	3.9±0.7	3.9±0.9	*1.4±0.9*	4.1±1.3	*1.3±1.4*
		ST	5.2±0.4	3.8±0.6	3.8±0.9	*1.5±0.9*	4.2±0.9	*1.0±1.0*
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.71	*0.68*	*0.79*	*0.98*	*0.33*
	CAL	**NST**	5.5±0.6	4.5±0.8	4.5±0.9	1.0±0.8	4.8±1.1	0.7±1.3
		ST	5.5±0.5	4.5±0.7	4.6±1.2	0.9±1.0	4.6±0.9	0.9±1.0
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.95	*0.69*	*0.62*	*0.73*	*0.71*
	GMP	**NST**	0.3±0.5	0.5±0.7	0.6±0.8	-0.3±0.6	0.7±0.7	-0.4±0.4
		ST	0.3±0.6	0.7±0.5	0.9±0.8	-0.6±0.5	0.4±0.5	-0.1±0.3
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.62	*0.31*	*0.14*	*0.81*	*0.77*
Deep pockets	**PD**	**NST**	7.6±0.5	5.2±0.9	5.2±1.1	*2.4±1.5*	5.9±1.2	*1.5±1.1*
		ST	7.7±0.8	5.2±1.1	4.7±1.3	*3.0±1.4*	4.8±0.6	*2.9±0.7*
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.96	*0.31*	*0.26*	*0.047**	*0.06*

	CAL	NST	7.8±0.6	5.8±0.8	6.0±1.2	1.8±1.5	6.5±5.4	1.3±1.1
		ST	7.9±1.2	6.1±1.8	5.6±2.1	2.3±1.7	5.4±1.2	2.5±1.2
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.71	*0.49*	*0.29*	*0.31*	*0.15*
	GMP	NST	0.2±0.5	0.6±0.7	0.8±0.7	-0.5±0.7	0.7±0.7	-0.5±0.5
		ST	0.3±0.8	0.9±1.4	0.9±1.3	-0.6±1.0	0.7±0.9	-0.4±1.0
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.65	*0.78*	*0.63*	*0.82*	*0.53*
Anterior teeth	PD	NST	6.5±1.2	4.3±0.8	4.3±1.0	*2.2±1.3*	4.0±1.0	*2.5±1.1*
		ST	6.3±1.1	4.2±0.7	4.2±0.7	*2.1±1.0*	4.4±1.3	*1.9±1.8*
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.83	*0.58*	*0.74*	*0.87*	*0.24*
	CAL	NST	6.8±1.3	5.1±1.1	5.3±1.5	1.5±1.4	5.1±1.7	1.7±0.9
		ST	6.8±1.1	5.1±0.9	5.3±1.2	1.5±0.9	4.8±1.5	2.0±1.9
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.94	*0.91*	*0.78*	*0.97*	*0.76*
	GMP	NST	0.3±0.8	0.8±1.1	1.0±1.3	-0.7±0.9	1.1±1.4	-0.8±0.5
		ST	0.5±0.9	0.9±0.9	1.1±1.1	-0.6±0.8	0.4±0.8	0.1±0.5
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.97	*0.9*	*0.79*	*0.11*	*0.07*
Posterior teeth	PD	NST	6.3±0.9	4.8±0.9	4.8±0.8	*1.5±0.8*	5.5±1.3	*0.8±1.4*
		ST	6.5±1.2	4.3±0.9	4.1±1.3	*2.4±1.9*	4.6±1.0	*1.9±1.9*
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.18	*0.03**	*0.08*	*0.20*	*0.10*
	CAL	NST	6.5±0.9	5.2±1.1	5.2±0.9	1.3±0.8	5.9±1.2	0.6±1.4
		ST	6.5±1.2	4.9±1.0	4.9±2.1	1.6±2.5	5.2±1.3	1.3±1.3
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.87	*0.6*	*0.64*	*0.89*	*0.68*
	GMP	NST	0.2±0.4	0.3±0.5	0.4±0.5	-0.2±0.2	0.4±0.5	-0.2±0.3
		ST	0.0±0.0	0.6±0.8	0.7±1.2	-0.7±1.2	0.5±0.7	-0.5±0.7
				p value (ANCOVA)	*p value (ANCOVA)*	*p value (paired Student's t test)*	*p value (ANCOVA)*	*p value (paired Student's t test)*
				0.09	*0.12*	*0.05**	*0.2*	*0.06*

**indicate significant difference between groups. SD – Standard deviation; PD – Probing Depth; CAL – Clinical Attachment Level; GMP – Gingival Margin Position.*

CONCLUSÃO

Com base nos resultados obtidos, pode-se concluir que, apesar de ambas as terapias cirúrgica e não-cirúrgica não terem sido capazes de reduzir os níveis de Aa e Pg em ambos os grupos nos diferentes tempos de acompanhamento, clinicamente a terapia cirúrgica promoveu maior redução de profundidade de sondagem em bolsas profundas e dentes posteriores.

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* De acordo com a norma da UNICAMP/FOP, baseado na norma do International Committee of Medical Journal Editors – Grupo de Vancourver. Abreviatura dos periódicos em conformidade com o Medline.

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COMITÊ DE ÉTICA EM PESQUISA
FACULDADE DE ODONTOLOGIA DE PIRACICABA
UNIVERSIDADE ESTADUAL DE CAMPINAS

CERTIFICADO

O Comitê de Ética em Pesquisa da FOP-UNICAMP certifica que o projeto de pesquisa **"Avaliação da utilização de metronidazol e amoxicilina associados ao debridamento periodontal no tratamento da periodontite agressiva"**, protocolo nº 024/2006, dos pesquisadores Renato Corrêa Viana Casarin e Márcio Zaffallon Casati, satisfaz as exigências do Conselho Nacional de Saúde - Ministério da Saúde para as pesquisas em seres humanos e foi aprovado por este comitê em 06/10/2008.

The Ethics Committee in Research of the School of Dentistry of Piracicaba - State University of Campinas, certify that the project **"Evaluation of the metronidazole and amoxicillin association and periodontal debridment on the aggressive periodontitis treatment"**, register number 024/2006, of Renato Corrêa Viana Casarin and Márcio Zaffallon Casati, comply with the recommendations of the National Health Council - Ministry of Health of Brazil for research in human subjects and therefore was approved by this committee at 10/06/2008.

Prof. Dr. Pablo Agustin Vargas
Secretário
CEP/FOP/UNICAMP

Prof. Dr. Jacks Jorge Junior
Coordenador
CEP/FOP/UNICAMP

Nota: O título do protocolo aparece como fornecido pelos pesquisadores, sem qualquer edição.
Notice: The title of the project appears as provided by the authors, without editing.