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The efficacy of non-surgical and systemic antibiotic treatment on smoking and non-smoking periodontitis patients

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SUMMARY

In 28 adult severe periodontitis patients who did not respond to conventional periodontal therapy, full mouth clinical parameters including probing pocket depth, relative attachment level, bleeding on probing and suppuration after probing, visible plaque index and modified gingival index were recorded at the baseline and 14 months after treatment. Based on clinical and bacteriological diagnosis, a combination of systemic amoxicillin 500 mg × 3 and metronidazole 200 mg × 2 was prescribed for 7 days.

In combination with non-surgical treatment, systemic antibiotic therapy, significantly improved median values of probing pocket depth, bleeding on probing, suppuration index, visible plaque index and modified gingival index except relative attachment level. Despite the improvement of clinical parameters in general, both bleeding on probing and suppuration index had significantly lower reduction in smokers than in non-smokers.

Key words: periodontitis, non-surgical and systemic antibiotic treatment, smoking

INTRODUCTION

Periodontitis is an inflammatory disease of the supporting tissues of the teeth that results in the progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession, or both. Periodontitis is the result of complex agents and relationships, as well as specific micro-organisms and environmental, acquired and genetic risk factors [1].

Among environmental factors, smoking is increasingly accepted to be a risk factor for periodontitis, affecting various aspects of the host immune response [2-4]. Epidemiological studies indicate that smoking is a greater risk indicator for the presence of periodontitis than the presence of certain pathogens. Additionally, the severity of periodontitis has also been associated with cigarette consumption [5].

Conventional non-surgical periodontal therapy consists of mechanical supra- and subgingival tooth debridement and instruction in self-administrated oral health care measures [6]. Clinical studies have consistently shown that smokers respond less favourably to scaling and root planing, and also, tobacco users have a poorer response to surgical pocket therapy [1,7,8]. According to the literature, after non-surgical therapy smokers showed a continuing loss of horizontal attachment level, lesser probing depth reduction and bleeding on probing [7,9-11].

No statistically significant differences between treatment response in smoking and non-smoking patients after non-surgical therapy have been established by other authors [11,12]. Although understanding of the effect of smoking on periodontal healing will require more information, the non-surgical treatment outcome in smokers appears not to be as effective as in non-smokers [13].

Few studies have examined the effect of the combination of non-surgical therapy with systemic antibiotic therapy on treatment response of smoking and non-smoking patients. Systemic periodontal

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antibiotic therapy reinforces mechanical treatment and supports host defences to overcome infection by killing remaining pathogens after conventional mechanical periodontal therapy [14]. Treatment regimens directed strictly towards reducing bacterial load and altering microbial composition might be more helpful in the case of both patient groups.

The objective of this study was to compare the longitudinal effect of the combination of non-surgical periodontal therapy with systemic antibiotic treatment in smoking and non-smoking patients.

MATERIALS AND METHODS

Patient selection

This study was designed to investigate routine periodontal therapy in advanced cases as close to clinical practice as possible for better comprehension of clinical management strategy.

Patients with generalized severe chronic periodontitis that did not respond well to previous mechanical periodontal treatment were recruited consecutively from new referrals to the Policlinic of the Tartu University Dental Clinic between January 2002 and December 2004. The present patients represented periodontitis patients who came as referrals from general practitioners because of inadequate treatment response. All of the included patients received repeated full-mouth debridement under local anaesthesia 2-3 times during the last year.

The same clinician performed the initial examination, sampling, treatment and re-evaluation. Specific inclusion criteria were based on at least one pocket deeper than 6 mm in all sextants and minimum radiographic marginal alveolar bone loss >1/3 of the root length in at least two quadrants. Further a CPITN (Community Periodontal Index of Treatment Needs) score of 4 in at least three sextants was required. All of the patients had at least 22 natural teeth. The patients were healthy and had no systemic conditions known to affect periodontal tissues, nor had they had antibiotic therapy during the preceding 6 months. Cigarette consumption was determined on the basis of verbal questioning (10-20 cigarettes per day for ≥5 years).

Of the patients aged between 25 and 65, 14 smokers (S) and 14 non-smokers (NS) were consecutively selected.

The Ethics Review Committee on Human Research of the University of Tartu approved the study protocol.

Clinical measurements and sampling

Clinical parameters were recorded at the baseline, 2-3 weeks after the first mechanical treatment and 14 months after combined treatment during a regular check-up visit. Our study was designed as single blind research.

The clinical examination included recordings of visible plaque index (VPI), modified gingival index (MGI), bleeding on probing (BOP) and suppuration after probing (SUP), probing pocket depths (PPD) and relative attachment levels (RAL). Probing pocket depths were measured to the nearest mm

Table 1. Changes in response to combined treatment

Clinical parameters	Before-treatment median (ranges)	14 mos. follow-up median (ranges)
Visible plaque index (%)	56.8 (24.1-84.6)*	33.3 (5.0-69.4)*
Bleeding on probing (%)	46.9 (16.9-81.0)*	27.7 (9.2-46.2)*
Suppuration index (%)	2 (0-12)*	0 (0-5)*
Probing pocket depth (mm)	4.0 (3.1-6.3)*	3.6 (2.4-4.7)*
Relative attachment level (mm)	4.2 (3.2-6.3)	4.1 (3.0-6.1)
Modified gingival index (1-3)	2 (1-3)	2 (1-3)

*P<0.05

Table 2. Changes in response to combined treatment in smoking patients

Clinical parameters	Before-treatment median (ranges)	14 mos. follow-up median (ranges)
Visible plaque index (%)	51.9 (24.1-82.3)*	33. 6 (13.4-69.4)*
Bleeding on probing (%)	44.8 (21.9-81.0)*	32.2 (15.8-46.2)*
Suppuration index (%)	2.5 (0-8)	2 (0-5)
Probing pocket depth (mm)	4.2 (3.1-6.3)*	3.8 (3.1-4.2)*
Relative attachment level (mm)	4.2 (3.3-6.3)	4.4 (3.5-5.1)
Modified gingival index (1-3)	2 (1-3)	2 (1-2)

*P<0.05

using a WHO periodontal probe. The recordings were performed at 6 sites around all teeth (except for the third molars): buccomesially, mid-buccally, buccodistally, distolingually, mid-lingually and mesiolingually. Each site was measured twice in order to assess the variability of the probing measurements. An attachment level change exceeding 2 mm between two examinations was regarded as a probing attachment gain or loss. The presence or absence of gingival bleeding (BOP) and suppuration (SUP) were registered after probing.

These particular patients needed a complex treatment modality and we started from non-surgical therapy. Following initial examination, each patient subsequently underwent quadrant scaling and root planing under local anaesthesia over a 4-week period at up to 6 appointments. Two to three weeks after the last non-surgical treatment visit, patients were reviewed, and initial healing was evaluated.

As the patients did not respond to the conventional periodontal therapy, showing an inadequate resolution of inflammation (visible signs of inflammation, bleeding on probing and suppuration) microbiological analyses were taken and a combination of systemic amoxicillin 500 mg × 3 and metronidazole 25 0mg × 2 for 7 days was prescribed [15,16].

Pooled subgingival samples from the six deepest periodontal pockets were taken with a sterile Gracey 11/12M and 13/14M curette after non-surgical therapy. Samples were transferred to the vials that contained 2ml of the VMGA III medium and serially diluted in the Brucella broth (Oxoid, Basingstoke, Hampshire, UK), and 100 µl aliquots from the dilutions were inoculated onto the Brucella agar (Oxoid), enriched with 5% horse blood and 1% menadione, and TSBV (Oxoid) agar. The Brucella Agar plates were incubated in an anaerobic chamber (Shelon Manufacturing Inc.) and on TSVB plates under microaerobic (Oxoid, CampyPak) conditions. The isolates were identified according to colonial and cellular morphology, the potency disk pattern (Vancomyin, Kanamycin, Colistin, Brilliant Green, and Oxgall), catalase, oxidase and spot indole reactions, long-wave UV light fluorescence, and MGU assay. The total level of microbial load of specimen collected from gingival pockets was calculated as the logarithm value of colony forming unit per millilitre ($\log_{10}$CFU/ml).

Statistical analysis of data

The baseline clinical data between smokers and non-smokers was compared using the Mann-Whitney test. The Signed Rank test was used to compare the changes in clinical parameters after systemic antibiotic therapy. Differences in the total level of microbial load were determined using the Spearman test (Jandel SigmaStat 2.0).

RESULTS

The effect of systemic antibiotic therapy in combination with non-surgical treatment

Systemic antibiotic therapy in combination with non-surgical treatment was effective in all cases.

Table 3. Changes in response to combined treatment in non-smoking patients

Clinical parameters	Before-treatment median (ranges)	14 mos. follow-up median (ranges)
Visible plaque index (%)	62.5 (34.8-84.6)*	33.3 (5.0-65.7)*
Bleeding on probing (%)	51.5 (16.9-76.3)*	22.1(9.2-38.2)*
Suppuration index (%)	2 (0-12)*	0 (0-2)*
Probing pocket depth (mm)	3.9 (3.3-5.5)*	3.4 (2.4-4.7)*
Relative attachment level (mm)	4.1 (3.4-6.1)	4.0(3.0-6.0)
Modified gingival index (1-3)	3 (2-3)*	2 (0-3)*

*P<0.05

Table 4. Comparison of clinical parameters of smokers and non-smokers after systemic antibiotic therapy in combination with non-surgical treatment, 14 months observation period

Clinical parameters	Non-smokers' median (ranges)	Smokers' median (ranges)
Visible plaque index (%)	33.3 (5.0-65.7)	33. 6 (13.4-69.4)
Bleeding on probing (%)	22.1(9.2-38.2)*	32.2 (15.8-46.2)*
Suppuration index (%)	0 (0-2)*	2 (0-5)*
Probing pocket depth (mm)	3.4 (2.4-4.7)	3.8 (3.1-4.2)
Relative attachment level (mm)	4.0(3.0-6.0)	4.4 (3.5-5.1)
Modified gingival index (1-3)	2 (0-3)	2 (1-2)

*P<0.05

There were significant improvements in most clinical parameters (Table 1). The level of post-treatment oral hygiene also improved significantly.

Comparison of clinical parameters between smokers and non-smokers

Table 2 demonstrates smoking patients and Table 3 demonstrates non-smoking patients' clinical parameters before and after the combined treatment. Despite the general improvement of clinical parameters, there were no significant post-treatment changes in SUP, RAL and MGI in smokers. The smokers' group showed continuing attachment loss and less reduction in BOP values compared to non-smokers. Post-treatment clinical parameters (except suppuration index) in non-smokers improved significantly ($p<0.05$). The poorer response to therapy may not be due to oral hygiene levels, because there were no significant differences between VPI values between smokers and non-smokers.

Although at baseline the clinical parameters of smokers and non-smokers were similar ($p>0.05$), the differences in treatment responses were estimated (Table 4). The reduction in bleeding on probing and suppuration at 14 months was significantly lower in the smokers than in the non-smokers.

Microbiological results

After instrumentation, no periodontal pathogens were isolated in 11 patients (39%), while 17 patients (61%) were infected with one to three different pathogens. Among the pathogens, *Prevotella intermedia/nigrescens* (10 patients) and *Actinobacillus actinomycetemcomitans* (8 patients) were predominant. The total level of microbial load ($\log_{10}$ CFU/ml) and the spectrum of pathogens in S and NS patients remained similar.

DISCUSSION

This study was designed to investigate routine periodontal therapy in advanced cases as close to clinical practice as possible for better comprehension of a clinical management strategy.

We found that smoking habits affected the results of combined treatment. Few data are available about the validation of the effect of the combination of non-surgical therapy with systemic antibiotics on treatment response in smokers and non-smokers. According to Palmer et al., smokers had a poorer treatment response to scaling and root planing, regardless of the application of adjunctive metronidazole [17]. In our study, differences in bleeding on probing and the suppuration index were assessed between smoking and non-smoking patients, while in the use of metronidazole, only the reduction in probing depth was less in the smoking group [17].

In our study, the combination of non-surgical and systemic antibiotic treatment with two antimicrobial compounds was effective in the treatment of generalized severe chronic periodontitis. There was a significant improvement in some clinical parameters after the treatment: a reduction in the visible plaque index, bleeding on probing and probing pocket depths. Additionally, from the literature it seems possible that some patients with deep generalised periodontitis may benefit from systemic antimicrobial therapy in stage of initial active treatment [18]. We chose a time for administration of systemic antibiotics 2-3 weeks after the completion of non-surgical treatment because this gave us the opportunity to ensure that these patients needed additional anti-inflammatory treatment by evaluation of primary heeling reaction. Also, from the literature it is well known, that antimicrobial treatment is much more effective after the biofilm disruption [19]. Besides, this appropriate time supports the host defence mechanisms in overcoming the infection by killing subgingival pathogens that remain after conventional mechanical treatment.

The selection of potent antibiotics presupposes adequate microbiological analysis and susceptibility testing where indicated [15,16]. In the present study, the predominant pathogens before the administration of systemic antibiotics were *P. intermedia/nigrescens*, *A. actinomycetemcomitans*, Enterobacter spp. and *T. forsythensis*. Therefore the decision was to use a combination of metronidazole and amoxicillin as an adjunct to mechanical periodontal debridement [15,16,20]. The improvement of clinical parameters indicates the effectiveness of the chosen treatment method.

Nevertheless, the precise investigation of both patient groups showed a better improvement of clinical parameters among non-smoking patients, which in turn had an effect on combined treatment modality. Therefore, the essential risk factors should be considered in estimating treatment effect.

The deposition of plaque is associated with environmental, behavioural, and health care variables. According to Skaleric et al., poorer health conditions were associated with male gender, lower levels of education and lower frequency of tooth brushing [21]. All of our patients received an oral hygiene tra ining program consisting of oral hygiene instruction, regular plaque control and a motivation session during every scheduled treatment visit. Thus the poorer response to therapy may not be due to oral hygiene

levels, because there were no significant differences between visible plaque index values between smokers and non-smokers at the baseline. The current report is in agreement with similar findings from the literature [22,23]. There are also reports in which alveolar bone destruction has been found in patients with an excellent level of oral hygiene [24].

We found that smoking mostly influenced parameters associated with disease activity, such as suppuration and bleeding. The poorer response of smokers is probably a result of the general effect of smoking, which compromises the response to periodontal treatment. In smokers, the host's immune response is adversely affected by impaired production of immunoglobulins, which makes smokers more susceptible to infections and re-infections [25,26]. *In vitro* exposure to nicotine suppresses the ability of macrophages to kill oral pathogens 27], and leads to lowered elastase and neutrophil levels in the oral cavity [28]. Cigarette smoking also compromises periodontal ligament cell adhesion to root planed surfaces, which might affect periodontal regeneration following therapy [8].

These findings may explain the disadvantages of smoking, especially in the case of clinical markers closely related with inflammation. Although smoking affects treatment results, the qualitative and quantitative extent of the effect remains unclear. However, a homogenous study population and examination of the whole dentition were anticipated to allow more powerful conclusions of the treatment response in patients with well-defined periodontitis rather than it would be achieved by examining selected teeth or few dental sites in patients exhibiting various periodontal diseases.

CONCLUSIONS

The combination of non-surgical and systemic antibiotic treatment was effective in the treatment of generalized severe chronic periodontitis. However, smoking habits adversely affected the results of combined treatment, especially bleeding, on the index of probing and suppuration.

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