EFFECT OF THE TOPICAL APPLICATION OF TRICLOSAN IN PERIODONTALLY TREATED PATIENTS

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ABSTRACT

The aim of this clinical, parallel, double-blind study was to evaluate the effect of irrigating, with 0.6% triclosan, periodontal pockets ≥4 mm showing persisting signs of inflammation 90 days after subgingival scaling and root planing. 14 patients, aged 35-61 years, were randomly assigned to test group (TG) or placebo group (PG). In TG, pockets were rinsed with 10 ml of triclosan while in PG, pockets were rinsed with placebo. Irrigations were repeated fortnightly for 70 days (total 6 rinses). Clinical examinations consisted of Plaque Index (PlI), Gingival Index (GI), Bleeding on Probing (BOP), Periodontal Probing Depth (PPD) and Clinical Attachment Level (CAL). Median values of PlI, GI and BOP were analyzed over time with the Friedman test and for the multiple comparisons with Wilcoxon and Mann-Whitney tests. Means for PPD, and CAL were analyzed with repeated measurements ANOVA ($p<0.05$). There were no statistically significant differences in the PlI and GI between groups. BOP was reduced significantly in both groups in a similar fashion. Significant reductions in PPD were observed for both groups. TG showed a PPD reduction of 0.8 mm whereas PG reduced 0.4 mm. No difference was found among groups for PPD. CAL gain for the TG group was 0.7 mm and for the PG of 0.5 mm. Only the gains observed for the TG group were significant. It can be concluded that 0.6% triclosan or placebo irrigation, 3 months after non-surgical treatment, of sites with persistent signs of inflammation, produced similar results.

Key words: randomized controlled trial, periodontal pocket, triclosan.

EFEITO DA APLICAÇÃO TÓPICA DE TRICLOSAN EM PACIENTES PERIODONTAIS TRATADOS

RESUMO

O presente estudo experimental, duplo-cego, paralelo, teve por objetivo avaliar o efeito de irrigações com triclosan a 0,6% em bolsas periodontais, ≥4 mm, de dentes unirradiculares que, noventa dias após a terapêutica periodontal subgengival não-cirúrgica, ainda apresentassem sinais clínicos de inflamação. Participaram 14 pacientes entre 35 e 61 anos, os quais, por sorteio, foram divididos em grupo teste (GT) e placebo (GP). No GT foi feita aplicação tópica subgengival de 10 ml de triclosan por sítio e no GP, com placebo. Foi realizada 1 irrigação por sítio a cada 14 dias durante 70 dias (total de 6 irrigações). Foram avaliados Índice de Placa (IPL), Índice Gengival (IG), Sangramento à Sondagem (SS), Profundidade de Sondagem (PS) e os Níveis de Inserção Clínica (NIC). Os exames clínicos foram realizados no início, aos 42 dias de irrigação e 30 dias após a última irrigação ter sido realizada. Medianas e intervalos interquartis dos IPl, IG e SS foram analisados através do Teste de Friedman, ao longo do tempo, e os Testes de Wilcoxon e Mann-Whitney, para as múltiplas comparações. As médias e desvios padrão de PS e NIC foram analisadas através da ANOVA de medidas repetidas ($p<0,05$). Em relação ao IPl e IG, não foram observadas diferenças estatisticamente significantes do início para o fim do período experimental e nem entre os grupos. A redução no SS foi estatisticamente significante do início para o fim do experimento para ambos os grupos experimentais. O GT apresentou uma redução da PS de 0,8 mm e o GP uma redução de 0,4 mm. Os sítios irrigados apresentaram reduções significativas da PS do início para o final do estudo. Tanto os valores iniciais quanto os valores finais, quando comparados entre os grupos, não diferiram significativamente. Em relação aos níveis de inserção, observou-se uma redução para o GT de 0,7 mm e de 0,5 mm para o GP, o que foi estatisticamente significante para o grupo teste do início para o fim do experimento. Em sítios não tratados cirurgicamente, que após 3 meses ainda apresentavam sinais inflamatórios, a irrigação com as soluções triclosan 0,6% ou placebo mostrou-se igualmente eficaz.

Palavras-chave: ensaio controlado randomizado, bolsa periodontal, triclosan.

INTRODUCTION

The success of periodontal therapy is based on supra and subgingival plaque control[1-5]. Longitudinal evaluations have demonstrated that adequate control of the subgingival biofilm leads to stability of the periodontal destruction and, to a limited extent, gain in attachment[4].

The use of chemical adjuncts for periodontal therapeutic approaches has been the subject of study. In the supragingival environment, antiseptics have

been widely used with predictable results. For example, chlorhexidine and triclosan have received great attention[6-9].

In the subgingival area, the use of antiseptics and antibiotics has been studied in different settings[11-13]. However, the results obtained with these approaches are contradictory[14-19].

Triclosan is a liposoluble, non-ionic agent that has been extensively tested in order to determine its interaction in the oral environment and its effect on biofilms, gingivitis, periodontitis and its role in the inflammatory process[10,20,21]. It has been used as a personal hygiene product for more than 30 years. In the dental field, dentifrices and rinsing solutions are the most common forms of utilization.

In oral hygiene products, it is normally combined with a copolymer, with antimicrobial properties, reducing the supra and subgingival microbiota[22]. Additionally to the antimicrobial property, it has been demonstrated that triclosan has antiinflammatory properties[12,21,23-26]. The antiiniflammatory property could be of interest both for the prevention and treatment of gingivitis as well as a complementary effect in the subgingival wound healing.

It is noteworthy that the majority of studies that have utilized adjuncts to periodontal therapy do not try to separate the mechanical from the chemical effect. It would be of interest to determine the role of the mechanical instrumentation and the chemical effect individually. Subgingival irrigation seems to have a beneficial effect. However, to determine the real effect of different substances is interesting, especially in non-responsive sites.

The aim of the present study was to evaluate the effect of subgingival irrigation with triclosan in periodontal sites of single-rooted teeth which, ninety days after non-surgical periodontal therapy, presented persisting signs of inflammation.

MATERIALS AND METHODS

Study design

The present study is a double-blind, parallel, randomized, placebo-controlled clinical trial. The protocol was reviewed by the Institutional Review Board of the Lutheran University of Brazil, and is in accordance with the Declaration of Helsinki**.** All participants were aware of the study aims and methods and signed an informed consent form.

Study sample

Fourteen males, aged 35 to 61 years, non-smokers at the time of the study (former smokers had to have quit smoking at least 6 months prior to the study) were included in the present trial. Individuals with diabetes, blood disorders, hepatic or renal problems were not included. Also, individuals under anti-coagulant therapy or that had undergone antibiotic or oral prophylaxis in the 3 months prior to the study were not considered eligible.

Periodontal sites

The present trial was performed on periodontal sites from upper and lower single-rooted teeth without restorations close to the gingival margin and without endodontic lesions or pulp necrosis. Included sites comprised those which, 90 days after non-surgical periodontal treatment, presented PD≥4 mm without marginal bleeding, but that bled upon probing of the bottom of the pocket.

Randomization

By means of a draw, the 14 individuals were randomly assigned to test (TG) or placebo (PG) groups. TG comprised 7 individuals totalizing 29 sites and PG comprised 7 individuals with 24 sites. The number of sites per individual ranged from 2 to 5.

Experimental solutions

Test and placebo solutions were based on a gel described by Furuichi et al.[13] The only difference between the two solutions was the presence of 0.6% triclosan. Both solutions contained 1.976% Gantrez®; 0.6% sodium lauril sulphate (SLS); 0.25% tauranol; 0.3% phenolic oil; 0.65% iota Carrageenan Viscarin TP 389; 2% sodium CMC 12M31P; 20% glicerine S-97 (99,5%); 0.5% propilene glycol; 2.5% sylox 15; 15% sorbitol; 0.107% sodium sacharine; 0.243% sodium fluoride; 0.1% color; 41.95% deionized water.

Clinical parameters

Individuals were clinically evaluated for the presence of plaque, gingivitis, periodontal probing depth, bleeding on probing and clinical attachment level. Plaque index was evaluated according to the Silness & Löe Plaque Index (PlI)[27]; Gingival inflammation was evaluated by Gingival Index (GI)[27]. Periodontal probing depth (PPD) was assessed by a manual periodontal probe and was deter-

mined as the distance from the most apically probable portion of the pocket and the gingival margin. Bleeding on probing was assessed after the removal of the probe during the PPD measurement. Clinical attachment level (CAL) was determined as the distance from the most apically probable portion of the pocket and the cemento-enamel junction. All clinical parameters were assessed at 6 sites per tooth by a trained and calibrated examiner. Calibration was checked before the initiation of the study and was calculated after duplicate measurements with 1 hour interval for PPD and CAL. For PPD, the weighted kappa (±1 mm) was 0.61 and for CAL this value was 0.65.

Experimental procedures

Ninety days after the end of non-surgical periodontal therapy, individuals were invited to participate in the trial. Clinical examinations were performed on single-rooted teeth. Topical applications were performed according to group allocations with the aid of a 15 ml syringe. The solution was applied 1mm from the bottom of the pocket. 10ml of the test or placebo solution was applied during 20 seconds. The individuals were instructed to continue with regular supragingival homecare. Toothbrushes and dental floss were provided at every consultation. The topical applications were repeated fortnightly up to 6 irrigations. Clinical parameters were recorded at baseline, 42 days after initiation of subgingival application and 30 days after the last application (day 100). Fig. 1 demonstrates the flowchart of the study.

Analysis of the results

The individual was the unit of analysis in the present study. PlI, GI and BOP were analyzed by median and interquartile ranges. Alterations over time were analyzed by Friedman test, and Wilcoxon and Mann-Whitney tests were utilized for multiple comparisons. PPD and CAL are summarized as mean and standard deviation. Data were analyzed by repeated measurements ANOVA, followed by Tukey test. In order to control for type I error, multiple comparisons were adjusted by the Bonferroni method.

RESULTS

All participants in the present study completed the protocol, with 100% compliance for all visits.

Median values and interquartile range of PlI during the study are shown in Table 1. At baseline (day 0), PlI median values were 1 for TG and 0 for PG. No statistically significant difference was observed among groups. At days 42 and 100, median values for PlI were of 0 for both groups, without statistically significant differences. Median values for GI were 0 throughout the experiment for both groups, without statistically significant differences (Table 2).

Table 3 shows data concerning PPD. It can be observed that in TG the baseline mean value was 4.5 mm, which declined to 3.8 and 3.7 mm on days 42 and 100, respectively. In the PG, the mean value for PPD was 4.3 mm, declining to 3.7 and 3.9 mm on days 42 and 100, respectively. No statistically significant difference was observed between groups at any experimental evaluation. However, both groups showed a statistically significant improvement from day 0 to day 42, which was maintained until the end of the trial.

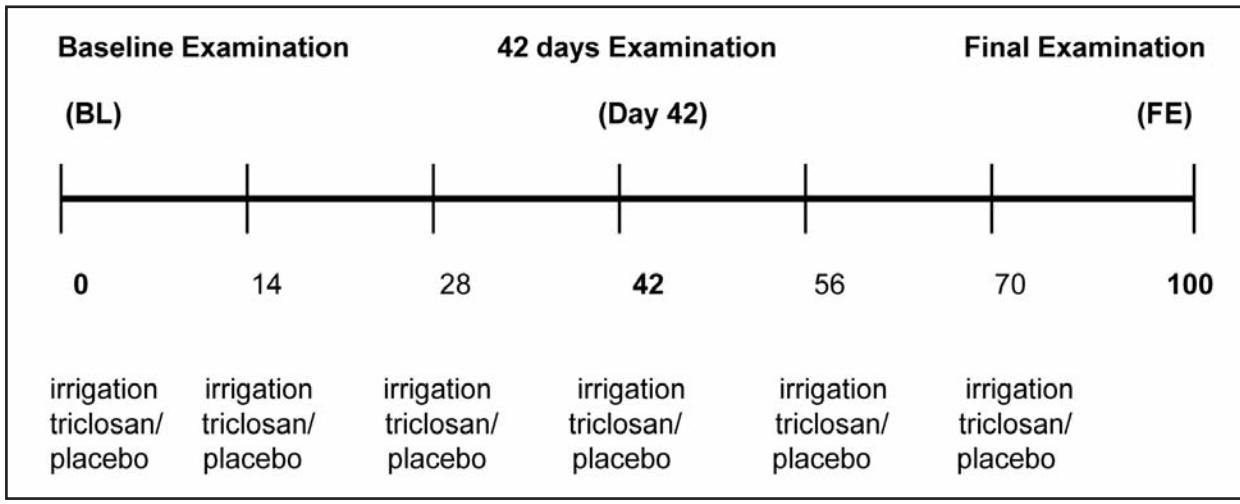

Fig. 1: Schematic presentation of the study outline.

Table 1. Median and interquartile range of the Plaque Index for test and placebo groups during the experimental period.

	Test		Placebo	
Day	*n*	*median (25% - 75%)*	*n*	*median (25% - 75%)*
0	7	1 (0 – 1) Aa	7	0 (0 – 0) Aa
42	7	0 (0 – 1) Aa	7	0 (0 – 0) Aa
100	7	0 (0 – 2) Aa	7	0 (0 – 2) Aa

Medians followed by the same capital letter do not differ statistically (5% level) in the intra-group comparison during the experimental period.
Medians followed by the same lowercase letter do not differ statistically (5% level) in the inter-group comparison in the same clinical examination.

Table 2. Median and interquartile range of the Gingival Index for test and placebo groups during the experimental period.

	Test		Placebo	
Day	*n*	*median (25% - 75%)*	*n*	*median (25% - 75%)*
0	7	0 (0 – 0) Aa	7	0 (0 – 0) Aa
42	7	0 (0 – 1) Aa	7	0 (0 – 0) Aa
100	7	0 (0 – 0) Aa	7	0 (0 – 0) Aa

Medians followed by the same capital letter do not differ statistically (5% level) in the intra-group comparison during the experimental period.
Medians followed by the same lowercase letter do not differ statistically (5% level) in the inter-group comparison in the same clinical examination.

Table 3. Mean values and standard deviation, in millimeters for Periodontal Probing Depth for test and placebo groups during the experimental period.

	Test		Placebo	
Day	*n*	*mean ± standard deviation*	*n*	*mean ± standard deviation*
0	7	4.5 ± 0.46 Aa	7	4.3 ± 0.31 Aa
42	7	3.8 ± 0.70 Ba	7	3.7 ± 0.65 Ba
100	7	3.7 ± 0.64 Ba	7	3.9 ± 0.70 Ba

Mean values followed by the same capital letter do not differ statistically (5% level) in the intra-group comparison during the experimental period.
Mean values followed by the same lowercase letter do not differ statistically (5% level) in the inter-group comparison in the same clinical examination.

Table 4. Median and interquartile range of the % of sites with Bleeding on Probing for test and placebo groups during the experimental period.

	Test		Placebo	
Day	*n*	*median (25% - 75%)*	*n*	*median (25% - 75%)*
0	7	100 (100 – 100) Aa	7	100 (100 – 100) Aa
42	7	25 (0 – 60) Ba	7	33 (0 – 50) Ba
100	7	33 (0 – 40) Ba	7	33 (0 – 40) Ba

Medians followed by the same capital letter do not differ statistically (5% level) in the intra-group comparison during the experimental period.
Medians followed by the same lowercase letter do not differ statistically (5% level) in the inter-group comparison in the same clinical examination.

Table 5. Mean values and standard deviation, in millimeters for Clinical Attachment Level for test and placebo groups during the experimental period.

	Test		Placebo	
Day	*n*	*mean ± standard deviation*	*n*	*mean ± standard deviation*
0	7	7.1 ± 1.7 Aa	7	6.1 ± 1.3 Aa
42	7	6.3 ± 1.9 Ba	7	5.6 ± 1.6 Aa
100	7	6.4 ± 2.3 Ba	7	5.6 ± 1.5 Aa

Mean values followed by the same capital letter do not differ statistically (5% level) in the intra-group comparison during the experimental period.
Mean values followed by the same lowercase letter do not differ statistically (5% level) in the inter-group comparison in the same clinical examination.

Table 4 shows median values for BOP. In TG, a statistically significant reduction was found from day 0 to the subsequent evaluations. The same pattern was observed for the PG. However, no statistically significant difference was observed among groups.

The results for CAL are shown in Table 5. A statistically significant improvement was observed only for TG. In this group, the baseline mean value was 7.1mm, declining to 6.3 and 6.4 mm at days 42 and 100, respectively. In the PG, no statistically significant reduction was observed for CAL. The mean reduction from baseline to the subsequent evaluations was 0.5 mm. However, when groups are compared at each time point, no statistically significant difference was detected.

DISCUSSION

The present study showed significant alterations in the periodontal parameters after consecutive subgingival irrigation with triclosan or placebo. The rationale for the protocol is based on the fact that the literature suggests that irrigation might be beneficial for periodontal wound healing[18,28]. On the other hand, in order to establish the real effect of triclosan, the use of a placebo solution is warranted, in order to rule out the sole mechanical effect of irrigation. The use of a randomized controlled trial design aimed to provide the best possible design, limiting bias and achieving higher validity. A very important aspect of the experimental design of the present study relates to the moment that irrigation started. Several studies that have utilized adjuncts to scaling and root planing, do it immediately after the mechanical debridement[14,18]. It should be noted that despite the presence of controls in such studies, split-mouth designs are frequently used and the possibility of spillover effect should not be ruled out. This effect could be related to the systemic absorption of the chemical, as happens with triclosan[29]. The choice of a parallel design in the present study relates to this situation. Parallel design studies frequently require greater sample sizes. However, since strict eligibility criteria were used, the numbers in the present study do not differ from other published studies in the literature[12,30,31].

Another important question in discriminating the effect of the mechanical and the chemical approaches is the moment of application of triclosan. The resolution capacity of subgingival scaling and root planing cannot be underestimated[4]. In the present study, 90 days were given to allow for healing after non-surgical periodontal therapy. Therefore, the individuals and sites included were those considered non-responsive, with remaining bleeding on probing. It could be argued that the irrigation performed in the present study, without the concomitant instrumentation would not affect the subgingival biofilm[32]. There is no doubt that this could be true, however, it is important to emphasize the anti-inflammatory effect of triclosan[20,21]. In fact, it has been suggested that triclosan is more effective in its anti-inflammatory than in its antimicrobial effects[10]. The results of the present study could only point to this in the higher gain in clinical attachment in the TG. One of the important biases in studies involving periodontal therapy is supragingival plaque control, which could affect the results. The results demonstrated for PlI and GI suggest that the included group had good standards of plaque control, which is absolutely necessary for periodontal would healing, having impact on the subgingival area[33].

The reductions in PPD observed in the present study are similar for TG and PG. It should be noted that the greater reductions were observed from baseline to Day 42. After that, results were found to be stable. This suggests that the eventual effects of such an approach can already be observed after 42 days. As other different studies have demonstrated, these reductions are probably more related to the act of irrigation than to the substance used. This can also be observed with BOP, with the possibility of similar interpretation[18].

Furuichi et al.[13] have demonstrated that 14 days after subgingival irrigations with triclosan reductions in GI and BOP are already present. However, this was not associated with higher improvements in PPD. Clearly the protocols are different; however, the results tend to be in the same direction, with limited effect on the subgingival área. In the present study, a significant improvement in CAL was observed for TG but not for PG. It has been shown that triclosan is capable of reducing progression of attachment loss[12,24,26]. It would be tempting to attribute the results of the present study to the effect of triclosan. However, some considerations are warranted. The CAL of the test group was 1mm greater than the control group at baseline. When percent alterations are considered, the reduction in mean CAL was 9.9% for the TG and 8.2% for PG. Therefore, the differences observed could be attributed to the initial characteristics. In either case, the clinical significance of the difference observed might be questioned.

The results of the present study do not question the anti-inflammatory properties of triclosan. The absence of significant differences between TG and PG indicate that the tested procedure (irrigation) was not efficacious in demonstrating the anti-inflammatory properties of triclosan for subgingival wound healing. Similar studies that have utilized triclosan in a more intensive way point out to the possibility of a beneficial effect subgingivally[13,22]. Additional studies with different dosages are therefore warranted

In conclusion, topical applications of triclosan were not different from topical application of placebo in reducing subgingival inflammation as demonstrated by PPD and BOP. However, during the study, irrigation was associated with improvement of periodontal parameters. When CAL is considered, significant gains were observed with the use of triclosan, which were not demonstrated with the use of placebo.

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