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Adjunctive use of a nanocolloidal silver-based local antiseptic solution in the nonsurgical treatment of periodontitis: A split-mouth clinical study

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ABSTRACT

Objectives. The aim of the present study was to evaluate the potential additional clinical benefit of a commercial nanocolloidal silver-based local antiseptic used as irrigation solution after subgingival mechanical instrumentation.

Material and methods. Periodontitis patients were treated following the current guidelines. Two randomly assigned hemiarches of each patient received subgingival mechanical instrumentation plus irrigations with the commercial product (experimental group); the other two hemiarches received mechanical instrumentation plus saline irrigations (control group). A clinical periodontal examination at baseline moment and after 3 months was performed. The parameters considered for analysis were oral hygiene index (IHI), bleeding on probing score (BoP), periodontal pocket probing depth (PD), gingival recession (GR) and clinical attachment level (CAL). 72 sites were included in the analysis, the site with the highest PD/quadrant for each patient. Data were analyzed using GraphPad Prism version 8.0.1 (GraphPad Software Inc., La Jolla, CA, USA). $p<0.05$ was set as statistical significance level. Outcomes. Eighteen periodontitis patients were treated. All clinical parameters improved at re-evaluation, compared to baseline, both in experimental and control group. The differences were statistically significant in terms of IHI, BoP and PD reduction. At re-evaluation, there were no statistically significant differences between periodontal parameters registered in the experimental and control sites.

Conclusions. The present study failed to prove an adjunctive clinical benefit of the antiseptic product in the nonsurgical treatment of periodontitis. These results support the gold standard role of subgingival mechanical instrumentation in the periodontitis' therapeutic protocol.

Keywords: nonsurgical periodontal treatment, subgingival mechanical instrumentation, antiseptic, silver nanoparticles, periodontitis

INTRODUCTION

The mechanical removal of soft and hard supra- and subgingival deposits from the dental surface is performed in the first and second stages of treatment of periodontitis in order to obtain periodontal stability. The goal of nonsurgical periodontal therapy is to disrupt and remove the bacterial biofilm and reduce the number of periodontal pathogens

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[1], thereby stimulating the resolution of local inflammation and the healing processes. Subgingival mechanical instrumentation together with supragingival plaque control are effective in improving clinical periodontal parameters, namely reducing gingival bleeding, periodontal pockets' probing depths (PD) and improving the clinical attachment levels (CAL) [1].

Subgingival mechanical instrumentation alone results in a mean reduction of bleeding on probing (BoP) of 63%, mean PD reduction between 1.7-2.6 mm, 74% pocket closure [2] and an average CAL gain of 0.5 mm [3]. The literature reported that up to 30% of instrumented subgingival surfaces may present residual calculus deposits, especially in areas that are more difficult to access (furcation lesions, deep periodontal pockets, infrabony defects, root concavities) [4]. Thus, the adjunctive use of antimicrobial agents to eliminate or inactivate pathogenic microflora in these retentive sites seems a logical gesture to implement in practice [5].

In cases of incipient and moderate periodontitis, with shallow periodontal pockets and without complexity factors, subgingival mechanical instrumentation appears to be sufficient for stabilizing the disease and healing of the periodontal tissues [2,6]. Yet, some adjunctive methods mostly based on antimicrobial products have been investigated for their additional benefit to subgingival mechanical instrumentation, especially in severe cases of periodontitis, associated with local complexity factors, in patients with systemic risk factors such as smoking, diabetes or genetic susceptibility [5,7].

The subgingival bacterial biofilm is a highly organized structure that, in its intact form, can be impenetrable to chemical agents. Bacteria behave fundamentally differently in the organized biofilm compared to their planktonic state [8]. Thus, the biofilm must be disrupted by the mechanical action of the scaling tools, which further allows the antimicrobial substance to act on the vulnerable residual bacterial deposits [5].

The effectiveness of adjunctive periodontal therapy consists in the selection of the appropriate antimicrobial agent [9]. Systemic antibiotic therapy requires administration in high doses for bactericidal concentrations to be obtained at the subgingival level. Due to systemic adverse effects and the issue of bacterial resistance to antibiotics, oral administration should be limited to well-selected cases of periodontitis [2,10]. Locally administered antibiotics, especially sustained-release products, could be taken into consideration [2] as they avoid the beforementioned general adverse effects, but have inconveniences such as insufficient antimicrobial spectrum, risk of inducing antibiotic resistance in the local environment and high costs [11]. Antiseptics are chemical agents capable of eliminating microorganisms from living tissues. They have several advantages: wider antimicrobial spectrum and reduced risk of resistance induction due to multiple intracellular targets [11].

Locally administrated antiseptic substances are delivered either as irrigation solutions for subgingival application after the mechanical instrumentation, or as sustained-release preparations which gradually discharge the active substance in the subgingival environment (gels, fibers, microspheres, chips, varnishes) [12]. The literature has failed to demonstrate a significant clinical benefit of the adjunctive use of antiseptic subgingival irrigations in the treatment of periodontitis [5].

Recent therapeutic guidelines suggest the adjunctive use of sustained-release local antiseptic preparations based on chlorhexidine (*PerioChip*), with a statistically significant additional effect in terms of PD reduction on short term [2].

Given the current circumstances in which there is no ideal antiseptic product recommended by the literature [2], silver nanoparticles emerged as interesting molecules for periodontitis treatment due to their antibacterial *in vitro* effect against multiple oral bacterial species, including some periodontal pathogens (*Agreggatibacter actinomycetemcomitans, Fusobacterium nucleatum*) [13–15]. Silver nanoparticles, through their antimicrobial activity, have improved the biological properties of various dental materials such as nanocomposites, acrylic resins, dentinal adhesives, surface treatments of implants or guided tissue regeneration membranes in periodontology [16,17]. However, the effect on the biofilm has not been investigated.

The aim of the present study was to evaluate the adjunctive benefit of a commercial local silver nanoparticle-based product compared to a control, locally applied saline solution, both utilized after subgingival mechanical instrumentation. The null hypothesis assumed that there are no differences in terms of PD reduction or CAL gain between periodontal pockets treated with both abovementioned approaches. To our knowledge, this split-mouth randomized clinical study is the first to evaluate the potential additional benefit of this commercial product in the nonsurgical treatment of periodontitis.

MATERIALS AND METHODS

Study design and experimental product composition

After obtaining the approval from the Ethics Committee of "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca (472/19.12 .2018), respectively of the Cluj-Napoca Emergency County Clinical Hospital (24211/B 25.10.2018), the study was carried out in accordance with the Declaration of Helsinki (1975) revised in 2013.

Perioflush® (Dental Life Sciences, Niemce, Poland) is a nanocolloidal silver-based subgingival irrigation solution commercially available in ready-to-use 3 mL syringes containing distilled water, nanocolloidal silver (100 ppm), sodium nitrate, orthophosphoric acid, lactic acid, and flavors. The solution is injected as such at the subgingival level, from the base of the periodontal pocket.

The study was designed as a randomized (coin method), prospective, split-mouth clinical study. Each patient with periodontitis included in the study received the experimental treatment (subgingival mechanical instrumentation plus subgingival irrigation with *Perioflush*®) applied in two hemiarches and the control treatment (subgingival mechanical instrumentation plus subgingival irrigation with saline) applied in the other two hemiarches. The experimental group was formed by the sites receiving the experimental treatment, and the control group was formed by the sites receiving the control treatment.

At study initiation, the team received instructions on the study protocol provided by two senior periodontologists (AR, AS). The principal investigator (SI) participated in two examination sessions supervised by two investigators (AC, ICM) calibrated previously for other studies [18].

The study group included subjects with periodontitis, diagnosed according to the Papapanou et al. case definition [19], referred for specialized treatment at the Periodontology Department of the Cluj-Napoca Emergency County Clinical Hospital and at a private office.

The following inclusion criteria were set:

- adult patient
- the absence of systemic diseases associated with severe immune dysfunctions or interfering with the evolution of periodontitis/response to treatment
- presence of stage II-IV periodontitis
- at least 10 teeth.

The exclusion criteria from the study were:

- patient with systemic diseases associated with severe immune dysfunctions
- patient with systemic diseases that contraindicate periodontal therapy or influence the evolution of the disease/response to treatment
- pregnant or breastfeeding woman
- periodontal treatment or systemic antibiotic therapy in the last 6 months.

The patients were asked to fill in and sign an informed consent form. An individualized treatment plan was developed, according to the recommendations in effect [20,21]. Briefly, the treatment plan included personal oral hygiene instruction and the individualization of techniques and means according to the periodontal situation, and the management of risk factors. Then the supra- and subgingival professional cleaning was performed. At 3 months post-treatment, the patients returned for evaluation of the results, undergoing a complete periodontal examination. Results were quantified in clinical terms of BoP, PD and CAL, and then subjected to statistical analysis. No subject was lost from the study. After that, the patients were subsequently referred for other stages of the complex treatment plan (surgical therapy for the reduction of residual periodontal pockets, orthodontic treatment, prosthetic rehabilitation, periodontal maintenance].

Baseline clinical examination and personal oral hygiene instructions

All periodontitis patients were reexamined after being included in the study. The IHI oral hygiene index of O'Leary et al. [22] was evaluated in four areas of the tooth, by staining the dental plaque on teeth's surfaces with Rondells Blue (Directa Dental, Upplands Väsby, Sweden). Gingival bleeding, as the clinical expression of local inflammation, was quantified using the bleeding on probing score [23], by probing to the bottom of the sulcus/pocket in six sites/tooth. Both scores were expressed as a percentage according to the calculation: (number of positive areas/total number of examined areas) x 100.

The periodontal parameters evaluated in six sites/tooth (mesio-buccal, centro-buccal, disto-buccal, mesio-palatal, centro-palatal, disto-palatal) were PD, gingival recession (GR) and CAL following current protocols. They were measured using an UNC-15 periodontal probe (Hu-Friedy, Chicago, IL) to the nearest mm.

Subgingival mechanical instrumentation

After the management of local risk factors, according to the therapeutic protocols in effect, the treatment plan continued with the professional control of the dental plaque: supra- and subgingival scaling and root planing, using hand (Mini-Five Gracey curettes, Hu-Friedy, Chicago, IL, Inited States) and ultrasonic (Acteon Satelec P5 Booster, Acteon Group, Mount Laurel, NJ, United States) instruments. The procedure was performed under local anesthesia (Septanest with adrenaline 1/100000 40mg/0,01mg/mL, Septodont), in one or two separate sessions, 24 h apart, following the randomization plan provided for the split-mouth design. Thus, for each patient, two hemiarches were treated by subgingival mechanical instrumentation plus subgingival irrigation with *Perioflush*®, and the other two hemiarches by subgingival mechanical instrumentation plus saline irrigation.

For the experimental sites, the blunt tip of the *Perioflush*®' syringe (3 mL) was inserted subgingi-

val, parallel to the long axis of the root, up to 1 mm coronally to the base of the periodontal pocket. The liquid was expressed continuously, by gentle pressure of the syringe piston, slowly moving the needle inside the periodontal pocket in a vertical direction, under continuous suction. Irrigation with saline was performed using a similar technique. In total, equal amounts (approximately 9 mL) of *Perioflush*® and saline were used for each half of the oral cavity. At the end of the irrigation, the patient was asked to rinse with water for 10 sec.

Re-evaluation

Three months after subgingival mechanical instrumentation, patients were re-evaluated. The full-mouth clinical examination was performed for the same parameters followed at the baseline examination.

Statistical analysis

From the collected data, in the statistical analysis were included four sites per patient, 1 proximal site/quadrant represented by the one with the highest PD (mm); in addition to PD value, GR and CAL values (mm) were also considered, as well as the presence (+) or absence (-) of the dental plaque and bleeding on probing, at the two examination moments. The primary variable of interest was PD.

The data were collected in a Microsoft Excel database. It included demographic-behavioral information, the values of the periodontal parameters, the number of missing teeth (the teeth that were to be extracted, according to the treatment plan, were also considered absent).

Statistical analysis was performed using GraphPad Prism version 8.0.1 (GraphPad Software Inc., La Jolla, CA, USA). The values of IHI index and BoP score, and the periodontal parameters were expressed as mean (± standard deviation).

The homogeneity of the groups (experimental vs. control) was tested using the t-test (Student). Also, the evolution of the IHI and BoP was evaluated using the t-test, comparing the values at baseline with the values recorded at re-evaluation. The results of the t-test were expressed as (t; p; df), where "t" represents the calculated value of the test, "p" is the statistical significance value, and "df" represents the number of degrees of freedom.

The overall effect of the treatment (intragroup differences for periodontal parameters baseline vs. re-evaluation, respectively intergroup differences at re-evaluation) was determined using ANOVA (Analysis of Variance), followed by Tukey's post hoc test with multiple comparisons. ANOVA results were expressed as (F; p), where "F" represents the calculated value of the test and "p" is the statistical significance value.

The statistical significance level was set at $p<0.05$.

RESULTS

Following the application of the inclusion and exclusion criteria, 18 patients were included in the study, with an average age of 48 years (30-65 years). Of the participants, 8 were men and 10 were women.

An average of 22 teeth per patient were examined and treated, with a total of 397 teeth. In the statistical analysis, 72 teeth were included, one per quadrant, namely the proximal site with the highest PD value.

At the full-mouth examination, the values determined at baseline for IHI were between 36% and 100% (with an average of 74.94%±22.8), and at re-evaluation they were between 11% and 40% (with an average of 18.5%±6.96). Testing the evolution of IHI (baseline vs. re-evaluation) using the t-test indicated an extreme, statistically significant reduction in the oral hygiene index ($t=10.97$; $p<0.0001$; $df=17$). At re-evaluation, IHI was greater than 20% in 5 of the 18 patients. When evaluating changes in IHI score depending on the treatment, the average IHI score of the hemiarches treated with *Perioflush*® (experimental IHI) registered a statistically significant reduction at re-evaluation (17.56%±6.42), compared to baseline value (73.70%±22.85) ($p<0.0001$). The same dynamic was recorded by the average IHI score of the hemiarches treated with saline (control IHI) ($p<0.0001$), reducing from 76.06% (±23.28) at baseline, to 19.42% (±7.94) at re-evaluation (Fig.1A). Comparatively, there were no statistically significant differences between experimental IHI and control IHI at re-evaluation ($p>0.05$).

In the case of the global BoP score, the values determined at baseline were between 10% and 100% (with a mean of 35.33%±22.88), and at re-evaluation they were between 2% and 31% (with an average of 9.33%±6.18). Testing the evolution of BoP score (baseline vs. re-evaluation) using the t-test indicated an extreme, statistically significant reduction ($t=5.01$; $p=0.0001$; $df=17$). At re-evaluation, 4 of the 18 patients had BoP greater than 10%. These 4 patients also presented an IHI score greater than 20%. When evaluating changes in BoP score depending on the treatment, the average BoP score of the hemiarches treated with *Perioflush*® (experimental BoP) registered a statistically significant reduction at re-evaluation (8.18%±4.79), compared to baseline value (35.65%±21.73) ($p<0.0001$). The same dynamic was recorded by the average BoP score of the hemiarches treated with saline (control BoP) ($p=0.0004$), reducing from 35.34% (±24.32) at baseline, to 10.86% (±9.61) at re-evaluation (Fig.1B). Comparatively, there were no statistically significant differences between experimental BoP and control BoP at re-evaluation ($p>0.05$).

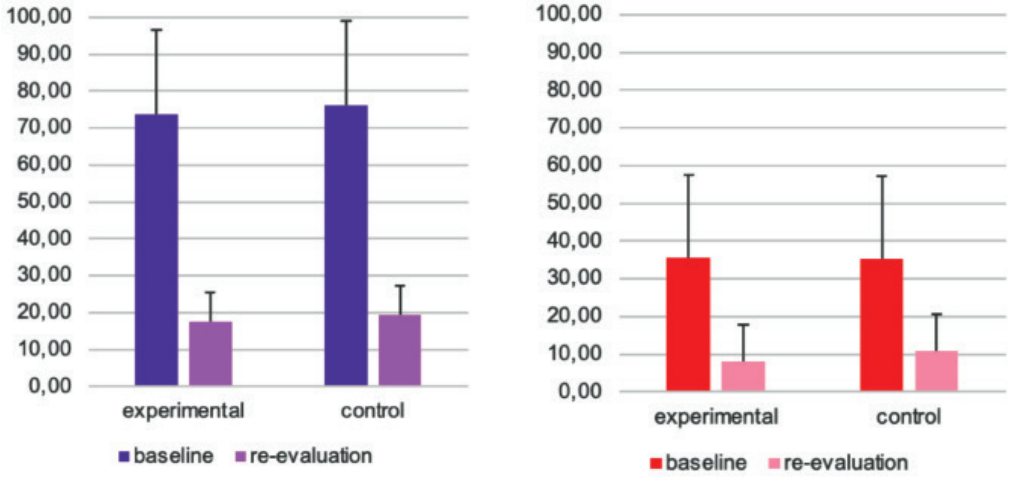

FIGURE 1. The evolution of the values (%) of **A.** Oral Hygiene Index (IHI) and **B.** Bleeding on Probing score (BoP). The height of the columns represents the mean value (%) and the "whiskers" represent the standard deviation

To test the homogeneity of the groups at baseline in terms of PD, GR and CAL, the paired samples t-test was applied. The baseline PD values in the experimental group were between 4 and 8 mm (with an average of 5.8 mm±1.16), and in the control group they were also between 4 and 8 mm (with an average of 5.55 mm±1.2), without statistically significant differences between the two groups (t=1.22; p=0.22; df=35). In the case of GR, the baseline values in the experimental group were between -2 and 3 mm (with an average of 0.47 mm±1.08), and in the control group they were between -3 and 4 mm (with an average of 0 .38 mm±1.6), without statistically significant differences between the two groups (t=0.34; p=0.73; df=35). The baseline CAL values in the experimental group were between 3 and 9 mm (with a mean of 6.27 mm±1.42), and in the control group they were between 1 and 9 mm (with a mean of 5.94 mm±1 .98), without statistically significant differences between the two groups (t=1.18; p=0.24; df=35). At baseline, all 72 sites included in the study presented bleeding on probing, and apart from two sites in the control group, all the others were positive for dental plaque.

When investigating the evolution of PD, the ANOVA test, used to determine the effect of the treatment in the experimental and control group at baseline and at re-evaluation, showed statistically significant differences (F=34.28; p<0.0001). Then, Tukey's post hoc test was applied to observe which groups had statistically significant differences. In the experimental group, mean PD decreased by 2.02 mm, from 5.8 mm (±1.16) at baseline to 3.77 mm (±0.89) at re-evaluation, a statistically significant difference (p <0.0001) (Fig.2A). Statistically significant differences were observed in the control group, achieving a mean PD reduction of 1.75 mm, from 5.55 mm (±1.20) at baseline to 3.8 mm (±1.91) at re-evaluation (p<0.0001) (Fig.2B). By comparing the mean PD reduction at re-evaluation, between the two groups,

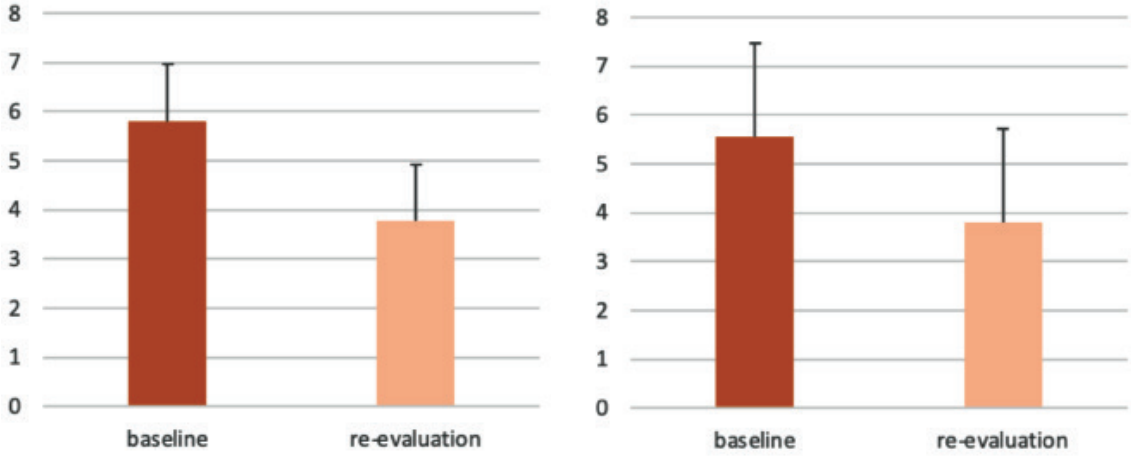

FIGURE 2. The evolution of the periodontal pockets' probing depths (PD) in the **A.** experimental group and **B.** control group. The height of the columns represents the mean value (mm) and the "whiskers" represent the standard deviation

TABLE 1. Comparisons of mean differences of the investigated periodontal parameters (mm); p = value of statistical significance

Groups	Probing Depth (PD)		Gingival Recession (GR)		Clinical Attachment Level (CAL)	
	Mean difference	p	Mean difference	p	Mean difference	p
Experimental baseline vs re-evaluation	2,02	<0,0001	-1,11	0,0055	0,94	0,0916
Control baseline vs re-evaluation	1,75	<0,0001	-0,91	0,0319	0,83	0,1666
experimental vs control re-evaluation	0,02	0,9996	-0,27	0,8355	-0,22	0,9455

the differences were not statistically significant (p>0.05) (Table 1).

When investigating the GR changes, the ANOVA test, used to determine the effect of the treatment in the experimental and control group at baseline and at re-evaluation, showed statistically significant differences (F=6.51; p=0.0004). Then, Tukey's post hoc test was applied to observe which groups had statistically significant differences. In the experimental group, mean GR increased by 1.11 mm, from 0.47 mm (±1.08) at baseline to 1.58 mm (±1.15) at re-evaluation, a statistically significant difference (p<0.05). Statistically significant differences were observed in the control group, achieving an increase in mean GR of 0.91 mm, from 0.39 mm (±1.60) at baseline to 1.3 mm (±1.67) at re-evaluation (p<0.05). By comparing the mean GR increase at re-evaluation, between the two groups, the differences were not statistically significant (p>0.05) (Table 1).

To evaluate CAL changes, the ANOVA test was applied, followed by a post hoc Tukey test. In the experimental group, mean CAL gain was 0.94 mm, from 6.27 mm (±1.42) baseline CAL loss to 5.33 mm (±1.41) CAL loss at re-evaluation, differences that were not statistically significant (p>0.05). In the control group the differences were not statistically significant, yielding a mean CAL gain of 0.83 mm, from 5.94 mm (±1.98) baseline CAL loss to 5.11 mm (±1.90) CAL loss at re-evaluation (p>0.05). By comparing the mean CAL gain at re-evaluation, between the two groups, the differences were not statistically significant (p>0.05) (Table 1).

Dental plaque was present at re-evaluation in one of the 36 experimental sites and 2 of the 36 control sites. Bleeding on probing at re-evaluation was positive in 15 of the 36 experimental sites and 17 of the 36 control sites. Bleeding on probing remained positive after treatment in association with PD of at least 4 mm.

DISCUSSION

In the present research, periodontitis patients were treated with a split-mouth approach: two hemiarches (experimental group) were treated with a commercial local antiseptic irrigation solution based on silver nanoparticles in association with subgingival mechanical instrumentation (experimental treatment) and the other two hemiarches (control group) with subgingival mechanical instrumentation plus saline irrigation (control treatment). The eventual additional clinical benefit of the experimental treatment over control treatment was appreciated. After 3 months, both groups resulted in statistically significant improvements in the periodontal status in terms of inflammation as revealed by the reduction of BoP and PD, which is in high agreement with the data that have accumulated over the last decades [2,5,9]. However, comparatively, there were no statistically significant differences of these parameters between the experimental and control group at the follow up moment, which sustains the null hypothesis. These results do not necessarily show the inefficacy of the antimicrobial product, but mostly highlight the gold standard position of the subgingival mechanical instrumentation in periodontitis therapy [2,7]. Moreover, the lack of additional benefit brought by subgingival adjuvant irrigation in subgingival mechanical instrumentation may be caused by the rapid clearance of the solution from the periodontal pockets due to the flow of crevicular fluid and the short time of action of the active substance (irrigation for approximately 3 minutes) [12,24].

Our results align with those of a recent review on adjuvant antiseptics used in nonsurgical periodontal therapy: subgingival irrigation solutions applied after subgingival mechanical instrumentation do not significantly change clinical parameters, compared to subgingival mechanical instrumentation alone [5]. Statistically significant improvements in PD, bleeding indices and CAL were achieved only after the use of sustained-release local adjuvant antiseptics [5]. 10% povidone-iodine solution used as an irrigation solution after subgingival mechanical instrumentation resulted in similar reductions of PD to the control group (0.9% saline) at 3- and 6-months post-treatment [25]. At 3- and 6-months post-treatment, the adjunctive use, for 5 min/tooth, of 0.5% povidone-iodine solution as an irrigation solution after subgingival mechanical instrumentation led to similar results in terms of PD reduction and CAL gain, compared to subgingival mechanical instrumentation alone or subgingival mechanical instrumentation associated with saline irrigation [26]. Similar results were highlighted by comparing 0.9% saline solution (control group) with 0.12% chlorhexidine digluconate and 7.5% povidone-iodine, as ad-

juvant subgingival irrigation solutions after subgingival mechanical instrumentation. At 3- and 12-months post-treatment, no statistically significant differences in PD or CAL were identified between the treated groups [27]. Different concentrations of chlorhexidine digluconate solutions (0.02%-0.2%) were evaluated as adjunctive therapy after subgingival mechanical instrumentation, but without statistically significant better results compared to subgingival mechanical instrumentation alone [12].

The 3-month re-evaluation moment was chosen as an early-healing time point in which future therapy approaches are considered depending on the improvements of the periodontal parameters [2]. The experimental product could have had a positive microbiological impact in terms of improving subgingival dysbiosis, which was not appreciated and could be considered as a limitation of the present research. Current data reported the positive effect of silver nanoparticles in reducing periodontal pathogens [13–15]. There is scientific proof that the contact time between the nanosized silver particles and the bacterial biofilm plays an important role in the effectiveness of the solution. Wu et al. [24] evaluated the antimicrobial effect of some silver nanoparticles-based preparations as irrigation or intracanal medication in endodontic treatment. An irrigation solution was used for two minutes, while a gel was applied endodontically for 7 days. The irrigation solution did not significantly change the structure of the bacterial biofilm, but the use of the gel resulted in structural changes in the biofilm and very few viable bacteria detected at the end of the treatment [24]. Similarly, other studies have demonstrated the antibacterial efficiency proportional to the contact time of solutions based on nanometer-sized silver particles [28,29].

Regarding the *full-mouth* results, in terms of oral hygiene and bleeding on probing, in the present study there were obvious, statistically significant differences between baseline examination and the re-evaluation. The significant reduction of the oral hygiene index is primarily a condition for the rest of the treatments to be carried out, and at the same time, the logical consequence of training and motivating patients vis-á-vis to their personal oral hygiene. Five of the 18 participants still presented an IHI higher than 20% at the re-evaluation, the rest of the values being considered relevant for the patients' compliance in terms of personal oral hygiene [30]. The reduction of the bleeding on probing score is the clinical translation of the remission of local inflammation as response to treatment, at the same time being an indicator of periodontitis stabilization [23]. All 4 subjects with BoP greater than 10% at re-evaluation also had poor oral hygiene compliance (IHI at re-evaluation greater than 20%). Investigated separately, according to the applied irrigation substances, both IHI and BoP scores registered statistically significant reductions from baseline to re-evaluation, in the experimental and control group. However, at re-evaluation, the differences between the experimental group and control group were not statistically significant.

To our knowledge, the present research is the first clinical study to investigate the effectiveness of subgingival irrigation with *Perioflush*® as adjunctive therapy to subgingival mechanical instrumentation in the treatment of periodontitis. More data is necessary to explore its effect at short- and long-term intervals.

This clinical study had certain limitations: a small number of participants, the relatively short follow-up period, the failure to consider general risk factors such as smoking or diabetes and the inclusion of subjects in all stages of periodontitis, without differentiating the results based on the severity of the initial lesions. Other studies are planned with a design that includes the aspects mentioned above.

CONCLUSIONS

The present randomized clinical study, with a split-mouth design, failed to prove an additional clinical benefit of the silver nanoparticles-based product as an adjuvant to subgingival mechanical instrumentation compared to subgingival mechanical instrumentation plus saline irrigations. The absence of adjunctive clinical benefit induced by *Perioflush*® supports the gold standard role of subgingival mechanical instrumentation in periodontitis therapy.

There was a statistically significant reduction in plaque and bleeding on probing scores between baseline and re-evaluation moments, in both experimental and control group.

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