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Adjunctive effect of the colloidal silver ions solution in the treatment of chronic periodontal disease: a preliminary clinical study

Dopunski efekat koloidnog rastvora jona srebra u lečenju hronične parodontopatije: preliminarna klinička studija

Vladan M. Kovačević*†, Dragana R. Daković*†, Dubravko R. Bokonjić*‡

***University of Defence, Faculty of Medicine, Military Medical Academy, Belgrade, Serbia; Military Medical Academy, †Clinic for Dental Diseases, ‡National Poison Control Center, Belgrade, Serbia**

Abstract

Background/Aim. Bacteria play the most important role in the development of periodontitis and chlorhexidine (CHX) is a "gold standard" in its treatment. Silver ions are also strong antiseptics, being used in dentistry for a long time. Therefore, the aim of this study was to compare the efficacy of CHX and colloidal silver ions solution (SSI) in the treatment of patients with chronic periodontitis. The additional aim was to ascertain silver ions, tolerability and efficacy comparing to CHX. **Methods.** Twenty-nine examinees of both sexes (the average age 50.6) participated in this study and were divided into two groups. The patients in the first group (n = 15) suffering from a generalized moderate chronic periodontitis, after scaling and root planning (SRP), were treated by rinsing of periodontal pockets with 0.2% solution of CHX. The patients of the second group (n = 14), in addition to the treatment of periodontal pockets, were treated with a 5 mg/mL colloidal SSI. **Results.** During the periodontal treatment, the mean values of all clinical parameters (except clinical attachment loss – CAL), in the both groups of patients were statistically significantly lower ($p < 0.001$) in relation to the initial values. The greater reduction of periodontal bleeching on probing (BOP) depth after one month was found in the SSI treated group (0.97 mm) in relation to the CHX group (0.65 mm). The local application of CHX and SSI led to statistically significant reduction of gingival parameters (gingival index – GI and BOP) in the groups after the treatment (GI for 0.65 and 0.87; BOP for 0.31 and 0.33, respectively). **Conclusion.** The results of our study showed that colloidal SSI was at least equally effective in the treatment of patients with periodontal disease as the solution of CHX. Additionally, the SSI is simple for use which speaks in favor of its more extensive use in dentistry including chronic periodontal disease.

Key words:
periodontal diseases; periodontal index; chlorhexidine; silver.

Apstrakt

Uvod/ Cilj. U nastanku parodontopatije bakterije imaju vodeću ulogu, a hlorheksidin (CHX), predstavlja „zlatni standard" među antisepticima u terapiji ove bolesti. Joni srebra, takođe jaki antiseptici, koriste se odavno u stomatologiji. Imajući to u vidu, cilj ovog rada bio je da se uporedi efikasnost CHX i koloidnog rastvora jona srebra (SSI), kao adjuvantnih antiseptika u okviru kauzalne terapije *scaling and rooth planing* (SRP) kod obolelih od hroničnog oblika parodontopatije. Dodatni cilj bio je da se utvrdi da li je SSI podnošljiviji za pacijente, a jednako efikasan rastvor kao i CHX. **Metode.** U studiji je učestvovalo 29 ispitanika oba pola (prosečne starosti 50.6 godina), podeljenih u dve grupe. Prvu grupu (n = 15) sačinjavali su ispitanici oboleli od hroničnog oblika parodontopatije, kojima su nakon SRP parodontalni džepovi ispirani 0,2% rastvorom CHX. U drugoj grupi (n = 14), nakon završene kauzalne terapije, parodontalni džepovi su ispirani rastvorom SSI koncentracije 5 mg/mL. **Rezultati**. Tokom parodontalne terapije, srednje vrednosti svih kliničkih parametara (osim gingivalnog džepa), kod obe grupe pacijenata su se statistički značajno smanjile u odnosu na početne vrednosti. Najveće smanjenje dubine parodontalnih džepova, nakon mesec dana, zabeleženo je u SSI grupi (0,97 mm) u poređenju sa CHX grupom (0,65 mm). Lokalna aplikacija rastvora CHX i SSI takođe je dovela do statistčki značajnog smanjenja gingivalnih parametara [gingivalni indeksi (GI) krvarenja na dodir (BOP)] u grupama posle lečenja (GI za 0,65 i 0,87); (BOP za 0,31 i 0,33). **Zaključak.** Rezultati su pokazali da je koloidni SSI najmanje jednako efikasan u terapiji kod osoba sa hroničnom parodontopatijom kao i CHX. Pored toga, CHX je jednostavan za upotrebu, bez neželjenih efekata, što ga preporučuje za širu upotrebu u stomatologiji, uključujući i adjuvantnu terapiju hroničnog oblika parodontopatije.

Ključne reči:
periodontalne bolesti; periodonatlni indeks; hlorheksidin; srebro.

Correspondence to: Vladan Kovačević, Military Medical Academy, Clinic for Dental Disease, Crnotravska 17, 11 000 Belgrade, Serbia.
E-mail: vladankovacevic@yahoo.com

Introduction

The problems caused by periodontitis have been identified as serious health issues in many populations for a long time [1]. Chronic periodontitis has a slow to moderate rate of disease progression, which may be associated with local predisposing factors, such as dental plaque, subgingival calculus deposits, some iatrogenic factors and systemic diseases, such as diabetes mellitus [2]. The severity and extent of periodontal tissues damage vary from person to person and depend largely on the individual immune responses to microorganisms [3, 4]. Through their products, such as acids, endotoxins, antigens, the microorganisms cause changes in the periodontium, ranging from gingivitis, inflammation of the alveolar bone, and formation of periodontal pockets, to the terminal destruction of alveolar bone and loss teeth [5].

Nowadays, a very efficient and widely accepted periodontal therapy is a mechanical removal of bacterial biofilm and bacterial toxins from the teeth surfaces [6]. This kind of therapy including scaling and polishing the teeth surfaces and periodontal pocket curettage is also known as a causal therapy (Scaling and Root Planing – SRP). SRP is applied in the first phase of the treatment for all patients with periodontitis, regardless of the type and severity of the disease as well as the future therapy direction and course.

Routine dental checks show significantly better results of the treatment when local antiseptics combined with a causal therapy were used, compared to the cases when causal therapy was implemented without the additional therapy [7]. Chlorhexidine (CHX) is certainly one of the most widely studied antiseptic with the outstanding plaque inhibitory properties and as a such, is considered the „gold standard“ for the adjuvant treatment of patients with periodontal disease [8]. It provides a constant bactericidal and fungicidal effect for more than six hours [9]. Depending on concentration and sensitivity, CHX can act both as bacteriostatic and bactericidal agent [10] and can be used in a form of a solution spray or perio-chips [11]. Some studies suggest the adverse effects of CHX, such as discoloration of teeth (dark brown pigmentation), numbness of the tongue dorsal surface and some taste disturbances. More serious side effects include an extensive erosion of the oral mucosa and swelling of parotid glands [12].

On the other hand, silver is a non-toxic, very powerful disinfectant, which can significantly reduce bacterial infection [13]. The use of silver as a strong antiseptic is very frequent today, but it has not been tested sufficiently in the field of periodontics. The effects of silver ions are mostly based on three mechanisms: firstly, interaction with the DNA of bacteria, secondly, the destruction of the cell membrane, and thirdly, the blocking of essential enzymes that regulate transport of electrons [14]. Silver has a long lasting bacteriostatic effect because it is bind to proteins tissue and chlorides. The resulting compounds gradually release silver ions. Higher concentrations have a caustic effect by depositing proteins [15].

Some recent studies have provided data on the use of silver nitrate solution in aphthous stomatitis treatment during the past years [16]. Additionally, a strong antimicrobial effect of silver nitrate solution (0.5 μg/mL) on microorganisms that cause periodontal disease is described in some *in vitro* studies [17]. Some authors investigated the effect of long-term release of silver ions from resorptive periochips soaked in 12% silver nitrate, set in periodontal pockets [18]. Recently, tests have been conducted on the impact of silver zeolite enriched with extracts of polyphenols from an alga *A. nodosum* investigating the potential role of this solution in the prevention of periodontal disease [19].

According to our electronic data base search, there was no information in the existing literature on the effects of aqueous silver ions solution on subgingival dental plaque microorganisms and periodontal tissue during the causal therapy phase for chronic generalized periodontitis. Therefore, the aim of this study was to compare the efficacy of CHX as a “golden standard” in the treatment of patients with periodontitis with silver ions, which have not been used so far in this respect. The assumption was that silver ions, in addition to better tolerability, would be at least equally effective as CHX.

Methods

A randomized prospective clinical study was conducted at the Periodontology Department and Implantology Department of the Clinic for Dental Diseases, the Military Medical Academy in Belgrade. Twenty-nine examinees of both sexes (26 men and 3 women, the average age 50.6) participated in the study and they were divided into two groups. The patients from the first group (n = 15) were treated by rinsing with 0.2% solution of CHX after SRP of periodontal pockets. The second group (n = 14), in addition to the treatment of periodontal pockets, was treated with a 5 mg/mL colloidal silver ions solution (SSI).

The parameters for inclusion of patients into the study were as follows: clinical diagnosis of generalized chronic periodontitis with radiographic confirmation of the presence of alveolar bone resorption (≥ 30%), patients who had a sufficient number of teeth in the upper and lower jaw (≥ 20) and those who had ≥ 5 sides of the teeth with periodontal pockets whose depth was ≥ 5mm. The study excluded the patients whose treatment of periodontitis was conducted more than 12 months ago, the presence of systemic diseases that may affect the treatment of periodontal disease, the use of antibiotics and anti-inflammatory drugs in the last 6 months, pregnancy, lactation and the use of contraception drugs as well as systemic infections of the oral cavity.

After taking a medical history and making diagnosis and indications for the treatment of the periodontal disease, the examinees were offered a form of voluntary consent for participation in the study for which we received the approval of the Ethics Committee of the Military Medical Academy in Belgrade.

All teeth were measured (third molars were not included) with a graduated probe (the community periodontal index of treatment needs – CPITN: US, Williams, Pro-Dentec, Batesville, Ark). For the assessment of oral hygiene the following indices were used: Plaque index (PI), measured on four sides (mesio-vestibular, vestibular, disto-vestibular,

oral), whose score was marked with values 0–3 [20]; Gingival index (GI), measured on the same four sides, whose score is also marked with 0–3 [21]. The GI score of 2 and 3 indicated bleeding on probing (BOP). In order to assess the periodontal status, the clinical attachment level (CAL) – the distance from the cement-enamel junction to the bottom of the periodontal pocket, was measured in mm, and the periodontal pocket depth (PPD) in mm – the distance from the free gingiva margin to the bottom of the periodontal pocket.

After the measurements were completed, the causal therapy was performed using a method of periodontal pockets curettage per a quadrant (in the following four days one quadrant was processed). After the curettage was conducted around each of the designated teeth, the application of a particular adjuvant antiseptic (SSI or CHX) was carried out by injecting 10 mL into the periodontal pockets. The patient was asked to mouthwash a given amount of antiseptic for 60 seconds and not to take food in a following hour after the treatment.

Each patient, depending on the allocated group, was given the same solution for home use for the following 10 days, with precise usage instructions. A month after scaling and root planning, including a particular adjuvant antiseptic, the control measurement of all parameters was performed in order to compare the values to the baselines.

Complete statistical analysis of data was done with the statistical software package, SPSS Statistics 18. Variables were presented as mean value ± standard deviation (SD). The Kolmogorov-Smirnov test was used for the evaluation of distribution of clinical data. A statistical significance within and between groups was tested by *t*-test for the paired and independent samples. All the analyses were estimated at $p < 0.05$ level of statistical significance.

Results

The results of the study are shown in Table 1 and Figure 1.

Table 1 shows the mean values of clinical parameters before and one month after the treatment in both groups of patients. During the SRP treatment, the mean values of all clinical parameters (except CAL), in both groups of patients, were statistically significantly lower ($p < 0.001$) comparing to the initial values. The greater reduction of periodontal probing depth after one month was found in the SSI treated group (0.97 mm) comparing to the CHX group (0.65 mm), however, without a statistical significance ($p = 0.420$).

The values of CAL inside the studied groups after the treatment were little lower in relation to their initial values, without statistically significant difference.

A local application of CHX or SSI led to the statistically significant reduction of gingival parameters (GI and BOP) in the groups after the treatment. There were no differences found between those two groups of patients after the treatment ($p = 0.492$ and $p = 0.918$, respectively). The index of oral hygiene (PI) was statistically significantly lower in both groups of patients after the treatment ($p = 0.001$), but it was also lower in the SSI group in relation to the CHX group ($p < 0.05$).

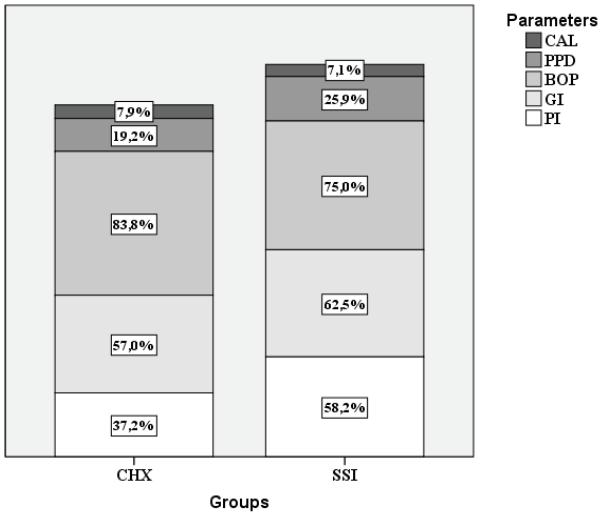

Fig. 1 – The percentage values of clinical parameters shown in Table 1 (see abtreviations) one month before and after the SRP treatment in the groups in which the solution of CHX and SSI were applied.

Table 1

Mean values of clinical parameters one month before and after the treatment in both groups of patients

Groups (before/ after treatment)	PI mean ± SD	GI mean ± SD	BOP mean ± SD	PPD mean ± SD	CAL mean ± SD
CHX (n = 15)					
baseline	0.86 ± 0.08	1.14 ± 0.46	0.37 ± 0.24	3.39 ± 0.67	3.64 ± 1.43
month 1	0.54 ± 0.27	0.49 ± 0.30	0.06 ± 0.07	2.74 ± 1.01	3.35±1.37
p_1	< 0.001	< 0.001	< 0.001	< 0.001	< 0.109
SSI (n = 14)					
baseline	1.22 ± 0.34	1.39 ± 0.34	0.44 ± 0.26	3.74 ± 0.74	3.65 ± 1.02
month 1	0.51 ± 0.37	0.52 ± 0.36	0.11 ± 0.16	2.77 ± 1.02	3.39 ± 1.14
p_1	< 0.001	< 0.001	< 0.001	< 0.001	0.069
p_2	< 0.05	0.492	0.918	0.420	0.913

p_1 – significance within the groups before and after the treatment; p_2 – significance between the groups after the treatment; PI – plaque index; GI – gingival index; BOP – bleeding on probing; PPD – periodontal probing depth; CAL – clinical attachment level; CHX – chlorhexidine; SSI – solution silver ions.

Figure 1 shows that the highest reduction of percentage values among clinical parameters was found concerning the BOP. In the CHX group, it was 83.8% lower, while in the SSI group it was somewhat even more lower (75%). The reduction of the percentage values in the GI values was also favorable in both groups as well as the PI values after the application of SSI (62.5% and 58.2%, respectively). It was distinct in relation to the CHX group amounted to 57% and 37.2%, respectively. The periodontal parameters also had lower values after the SRP treatment in both groups in which the corresponding solutions were applied. The higher percentage reduction was found in PPD, amounting in the CHX group of patients to 19.2%, and in the SSI group even more significant reduction (25.9%). The value of CAL was approximately equally lowered in both groups of patients (CHX = 7.9%; SSI = 7.1%).

Discussion

Our results showed that the CHX and SSI as adjuvant antiseptic within the SRP have an equal, statistically significant effect on all studied clinical parameters PI, GI, BOP, PPD, CAL in the patients with a chronic form of periodontal disease. The most significant result was a reduction in the PPD – it was reduced in the SSI group to 0.97 mm compared to the CHX group where the reduction was 0.65 mm. Very good results in reducing the PPD were also obtained by other authors who used CHX as a control with the SRP. The PPD values for CHX ranged from 6.28 mm to 4.90 mm one month after the therapy [22]. A significant improvement in the PPD reduction was shown by Krück et al. [21], whereas for the same parameters Cobb [22] obtained the value of 1.29 mm. These results were explained primarily by the antiseptic influence on the growth of aerobic bacteria and the reduction of the total number of anaerobic bacteria which may consequently affect the anti-inflammatory processes and the impaired maturation of plaque after conducting the causal therapy with antiseptics irrigation.

In our study, we demonstrated that the SSI led to a significant reduction in PPD because of its successful antibacterial efficiency. This efficacy against periodontal pathogenic species was also shown in some other studies. The compounds containing silver are attractive because of their strong antimicrobial activity, high stability and wide-spread antibacterial spectrum [23]. The results of Reise et al. [24] indicate that silver compounds 3 and 4 represent the new possible antibacterial agents to be used in different therapeutic procedures of periodontitis, caries and endodontic diseases.

The values of the CAL within our tested groups were slightly lowered after the treatment, and thus there was not statistically significant difference whithin group as well as between the CHX and SSI group. In the study [25] that compared the CHX effects with other antiseptic, there were also no statistically significant differences in terms of this parameter. Their studies showed that 15, 30 and 60 days after the treatment, no statistically significant effect on the CAL level was noted ($p = 0.21$).

For the assessment of oral hygiene, the PI was used, which was statistically significantly reduced after the treatment in both of the tested groups ($p = 0.001$); however, it was significantly lower in the SSI group compared to the CHX group ($p < 0.05$). We can explain these results by the fact that silver ions prevent adhesion of bacteria and thus influence the prevention of biofilm formation which precedes creation of dental plaque [26]. It is also important to emphasize that testing of silver activity against periodontal pathogens from the biofilm has been increased recently. The study of Lu et al. [25] also focused on the antibacterial effect of silver nano-particles of various sizes on anaerobic bacteria – the smallest tested nano-particles (5 nm) showed greater antimicrobial effects compared to larger particles (15–55 nm).

Yilmaz and Bayindir [26] got almost identical results at the level of testing the CHX effects on the PI a month after the therapy, with a significant reduction in the PI value. They explained this as the CHX ability to penetrate into the areas that are inaccessible for mechanical instruments. The CHX ability to inhibit the plaque growth and its formation, in the first hours after mouthwashing, is reflected in its high affinity for the oral cavity tissues and a tooth surface [27, 28]. Otherwise, according to the CHX chemical definition, it is a positively charged cationic bisbiguanide, which has a very high ability to attract negatively charged areas, including mucous membrane, salivary dental pellicle as well as various biofilm components on a tooth surface such as bacteria, extracellular polysaccharides and glycoproteins [29, 30]. Thus, CHX represents an excellent antimicrobial agent of a broad spectrum which significantly reduces growth and development of both facultative and obligate anaerobic bacteria inside the dental plaque [31]. This was reflected in our results as the positive clinical effect on GI and BOP which were statistically significantly lower one month after the treatment ($p < 0.001$); however, similar result was noticed for the SSI, too.

Considering the CHX effect in the case of these parameters, similar results were obtained in the study of Sağlam et al. [30], where a month after the treatment, BOP was decreased to approximately 79% and GI to 0.66 mm. However, CHX has a high cytotoxic effect on a human periodontal ligament content by inhibiting the double-stranded nucleic acid molecules, protein synthesis and mitochondria activity [32]. Pucher and Daniel [33] also demonstrated that CHX is cytotoxic for human fibroblasts through inhibition of protein synthesis.

Following the positive antibacterial effects of different sizes of silver nanoparticles on anaerobic bacteria, the assumption is that this effect stems from silver adstrigent potential associated with the direct or even indirect antibacterial effects of silver ions [34]. Passing through the bacteria cell wall, silver ions prevent replication of the DNA molecule. In this way, the interactive inactivation of bacterial proteins occurs and as a result of the catalytic activity of silver**,** oxygen radicals are released, which cause structural damages inside the bacteria. This phenomenon leads to damage or even the death of bacteria.

Conclusion

The use of adjuvant antiseptics within the SRP for patients with chronic forms of periodontal disease has been justified. In our study, the tests showed that the CHX and SSI as adjuvant antiseptics as a part of the SRP, have practically the same statistically significant effect on all the studied clinical parameters. In the SSI group, a month after the therapy, a significant reduction of GI and PI was obtained compared to the CHX group. This is of great importance, because the SSI was not used as the adjuvant antiseptic in this category of patients and, as the CHX was accepted as a "gold standard" of this type, it seems that silver ions should be re-evaluated for adjuvant treatment within the causal therapy of patients with chronic periodontal disease.

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