Comparative Evaluation of Boric Acid Gel versus Chlorhexidine Gel in the Treatment of Chronic Periodontitis: Randomized, Placebo-Controlled Clinical Study

Abstract

Background: Over the years, various antimicrobials have been tried and tested in the treatment of periodontitis. Chlorhexidine (CHX) has emerged as the gold standard. In recent years, trend has shifted toward the use of agents with antibacterial, anti-inflammatory, and osteoblastic activity. Boric acid (BA) is one such agent which possess all such properties and thus been evaluated in the treatment of periodontitis. Aim and Objective: The aim of the study is to compare and evaluate the efficacy of 0.75% BA gel versus 1% CHX gel as an adjunct to scaling and root planing in patients with chronic periodontitis both clinically and microbiologically. Materials and Methods: The present study was a randomized, placebo-controlled clinical trial where 45 systemically healthy patients with chronic periodontitis were included in the study. About 15 patients each were divided into three groups, that is, Group I received BA gel, Group II received CHX gel, and Group III received placebo gel as a local drug delivery agent. Clinical parameters such as gingival index, plaque index, modified sulcus bleeding index, probing pocket depth, and clinical attachment level were evaluated at baseline and 6-month follow-up. Microbiological analysis to check for mixed anaerobic flora was done using subgingival plaque samples at baseline and 3 months after treatment. Results: Significant reduction was seen in all clinical parameters in both BA and CHX gel groups as compared to control group (P < 0.05). However, on comparing BA gel group with CHX gel, the results were statistically insignificant (P > 0.05). Conclusion: BA gel and CHX gel both were equally effective in improving the clinical and microbiologic parameters in patients with chronic periodontitis when used as a local drug delivery agent.

Keywords: Boric acid, chlorhexidine, chronic periodontitis, local drug delivery, scaling and root planing

Introduction

Periodontitis is an inflammatory response to microbial flora characterized by periodontal attachment loss and alveolar bone resorption which ultimately leads to tooth loss.[1] The primary objective of periodontal therapy is the elimination of microbial flora leading to resolution of inflammation and halting the disease progression.[2] This objective is mainly achieved through complete removal of supragingival and subgingival deposits present on the root surface.[2] The mechanical debridement is done either with the hand instruments or power driven instruments (sonic and ultrasonic).[3] This gold standard nonsurgical therapy brings about the improvements in clinical parameters in majority of cases.[3] However, in certain conditions, mechanical nonsurgical therapy is unable to completely eradicate the causative subgingival microflora such as those invaded into periodontal tissues or in deep periodontal pockets.[4-6] As a result, recolonization of bacteria occurs resulting in delay of periodontal healing process.[4-6]

Nonsurgical periodontal therapy is aimed to minimize or eliminate microbial biofilm using both mechanical and chemotherapeutic approaches. Chemotherapeutic approaches are used to prevent further plaque accumulation and also to disinfect the affected root surfaces and adjacent periodontal tissues.[3,4] This is achieved by means of various antiseptics applied topically or drugs used as sustained-release local drug delivery agents.[3,4] Mechanical therapy may fail to eliminate plaque in deep pockets. This

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results in failure of periodontal treatment as bacterial plaque can accumulate after therapy.\(^6\) Hence, it seems beneficial to combine mechanical periodontal therapy with the use of chemotherapeutic agents.\(^7\)

Goodson et al. in 1979 introduced the concept of controlled release local drug delivery.\(^5\) This kind of treatment modality inhibits most of the problems associated with systemic therapy (such as drug toxicity and interactions and formation of resistant bacteria), limits the drug to its target site, and therefore, results in higher drug concentrations. Conventionally, various antimicrobial agents such as tetracycline, metronidazole, and chlorhexidine (CHX) have been tested as local drug delivery agents either as monotherapy or as an adjunct to scaling and root planing (SRP).

CHX is one agent, which has been extensively studied, in the periodontal research. CHX is one of the most effective topical antimicrobial agents. Friedman and Golomb\(^8\) proved that it is effective in reducing the probing pocket depth (PPD), attachment loss, and bleeding on probing. They were one of the earliest research workers who demonstrated its use as sustained-release device.

Although conventional antimicrobial agents have shown comparable results, the search is constantly on for an alternative medicine in the treatment of chronic periodontitis. Till now, various agents with antibacterial, antioxidant, and anti-inflammatory property have been used for local drug delivery in the treatment of periodontitis.\(^9,10\) One such agent is boric acid (BA) which has been recently evaluated to be used locally in the treatment of chronic periodontitis.

BA and borates are naturally present as boron with numerous metallic and nonmetallic properties.\(^11,12\) They are also found in other sources such as vegetables, nuts, legumes, and fruits.\(^11,12\) It has been demonstrated that boron which a bioactive trace element is known to possess antibacterial activity. Apart from its antibacterial activity, it also possesses regulatory effect on inflammatory and immune responses.\(^12,13\) Balci Yuce et al., in 2014,\(^14\) conducted an animal study where they found that BA application caused reduction in inflammation of periodontal tissue and alveolar bone loss in a ligature-induced experimental periodontitis in diabetic rat model.\(^14\) Antibacterial and anti-inflammatory property of the BA is due to boron-containing compound called as AN0128.\(^12,15\) This compound reduces tumor necrosis factor-\(\alpha\) release from human monocytes which are induced from lipopolysaccharides. This further imparts antibacterial and anti-inflammatory activity to BA.\(^14\) BA increases osteogenic effects by stimulating osteogenic differentiation-related marker gene synthesis during the proliferation and differentiation cycle in human bone marrow stromal cells.\(^12,14,16\)

Based on this body of evidence that BA can potentially act as antibacterial, anti-inflammatory, and osteoblastic agent, the present study was conducted with a hypothesis that its local application within the periodontal pocket can lead to reduction in microbial counts and also modulate the healing by downregulating the inflammatory process. Thus, the aim of the current clinical trial was to compare, clinically and microbiologically, the efficacy of 0.75% BA gel versus 1% CHX gel as a local drug delivery agent in patients with chronic periodontitis.

**Materials and Methods**

**Source of data**

This was a single-center, three-group, parallel-designed, randomized, placebo-controlled clinical trial conducted for a period of 1 year from May 2017 to June 2018. The participants enrolled in this study were selected from the outpatient department of periodontology. Institutional ethical committee board gave the approval for the study and the guidelines of the Declaration of Helsinki were strictly followed. After obtaining the ethical approval, written informed consent was signed from all the patients for participation in the study.

**Intraexaminer calibration**

An experienced periodontist performed all the initial periodontal parameter evaluation and collection of any samples. The examination was performed at six sites per tooth and accepted if \(>90\%\) of measurements were reproduced with 1 mm of difference with respect to per tooth 48 h apart. The examiner who performed measurements were blinded to the type of treatment given to the participants and other examiner performed all treatment procedures.

**Sample size calculation**

The sample size was calculated for \(\alpha\)-error fixed at <5% with a power of 80%. Based on this calculation, the minimum sample size required in each group was 15 participants which provided a true difference of 1 mm between the groups. Participants were enrolled and randomly divided into three groups using computer-generated random sequence table. At initial visit, full-mouth supragingival and subgingival SRP was performed by one examiner in all the patients diagnosed with chronic periodontitis. Local anesthesia was used if required. Patients having periodontal pockets with a probing depth of \(\geq5\) mm were selected for the study. A total of 45 participants having mild-to-moderate periodontitis from both the sexes with age ranging from 18 to 55 years (mean ± standard deviation of 35.8 ± 3.11), willing to participate in the study, were included in this study\(^17,18\) [Table 1].

**Selection criteria**

Inclusion criteria for the study were (i) patients diagnosed with chronic periodontitis and having periodontal pocket depth of \(>5\) mm postinitial therapy and (ii) systemically healthy patients.
Exclusion criteria for the study were (i) patients with a known or suspected allergy to the drugs used in the study (BA or CHX), (ii) patients who were undergoing any systemic BA therapy, (iii) tobacco users in any form, and (iv) lactating or pregnant females.

Enrollment process was done after the examiners were calibrated. One examiner performed all enrollment process. Using the randomly generated computerized table, patients were divided into three groups, that is, the BA gel group (n = 15), the CHX gel group (n = 15), and the placebo gel group which acted as a control (n = 15). The examiner who performed the enrollment process was blinded to the randomization procedure. After randomization, SRP + local delivery of 0.75% BA gel, SRP + 1% CHX gel, or SRP + placebo gel was done by the same operator who performed the initial periodontal therapy.

**Preparation of 0.75% boric acid gel**

BA gel was prepared by adding the required amount of different gelling agents in water for a specific time period. Gelling agents used were Carbopol (Lubrizol Advanced Materials India Private, Mumbai, India), sodium carboxymethylcellulose, and methylcellulose (3% w/v). A weighed amount of BA and zinc oxide were dissolved separately in ethanol, and this solution was then slowly added to the polymer dispersion. Following this, glycerin (0.5 ml) and preservative propylparaben (0.02 mg) were added to the dispersion and stirred continuously until a homogeneous product was formed. In this way, 0.75% of BA in situ gel was prepared. Placebo gel was prepared by the same procedure apart from the addition of the BA. After preparation of the gels, they were stored at room temperature in an autoclaved wide-mouthed glass bottles.

The CHX gel used was commercially available under the name Hexigel®.

**Local drug delivery**

Local delivery of the agents was performed according to the procedure mentioned by Oosterwaal et al. where a drug is placed into the periodontal pocket with the help of syringe having blunt needle. In this process, the blunt needle is placed at the bottom of the pocket and gel is delivered until it becomes visible at the entrance of the pocket three times within 10 min. The drug was delivered according to the above-mentioned procedure in all the three groups (0.75% BA gel, 1% CHX gel, and the placebo gel group) for standardization. For the sustained release of the drug and to avoid washout of drugs into the oral cavity or ingress of oral fluids into periodontal pocket, periodontal dressing was placed. Patients were given the posttreatment instruction which included refraining from brushing over the sites where dressing was placed, avoiding any use of mouth rinses and any form of interdental aids. Patients were asked to report immediately if any swelling, pain, burning sensation, or any other problem occurred over the selected teeth. Patients were recalled after 7 days for removal of periodontal pack.

**Clinical analysis**

Clinical parameters such as Gingival Index (GI), Plaque Index (PI), Modified Sulcus Bleeding Index (mSBI), PPD, and clinical attachment level (CAL) were evaluated at baseline and 6 months. PPD served as a primary outcome variable, whereas GI, PI, mSBI, and CAL served as secondary outcome variables. PPD was recorded using a University of North Carolina No. 15 periodontal probe (Hu Friedy®) and a custom-made acrylic stent was used to standardize the measurement of site-specific PPD. CAL was calculated as the distance between the cementoenamel junction and base of the periodontal pocket.

**Microbial analysis**

Blood agar plates were used to conduct the microbial analysis. Blood agar was chosen because it is a general purpose, nonselective, and enriched medium that promotes the growth of microorganisms. Subgingival plaque samples were collected from the patients using a curette. This was then transferred to a saline containing test tube. After thorough mixing of the sample in the saline, 0.1 ml of this saline was plated on a blood agar plate using a spreader. The plates were then incubated anaerobically for 24 h at 37°C. This procedure was carried out for all the patients at baseline and 3 months.

**Statistical analysis**

Statistical analysis of the results was performed for colony-forming units (CFUs), PI, GI, mSBI, PPD, and CAL using Statistical package for social science (SPSS 20, IBM, Chicago, IL, USA). The ANOVA test was used for continuous variables after confirming normality of the data distribution. The method of Bartlett was used to confirm that the data had a Gaussian distribution. Statistical significance was defined as P < 0.05.

**Results**

A total of 45 patients completed the study [Figure 1]. Clinical parameters were evaluated in all these patients at baseline and 6 months, whereas microbial parameters were evaluated at baseline and 3 months. No adverse reactions were reported, and the gel was well tolerated by patients. Demographic characteristics of the test and the control groups are shown in Table 1.

**Table 1: Demographic characteristics of the participants at baseline**

| Group | n=45 | Male | Female | Mean age±SD |
|-------|------|------|--------|-------------|
| Group I | 15 | 7 | 8 | 35.4±7.9 |
| Group II | 15 | 8 | 7 | 39.1±5.29 |
| Group III | 15 | 8 | 7 | 32.9±9.86 |

n: Sample size; SD: Standard deviation

**Figure 1**
At baseline, there was no difference with regard to all the clinical parameters (PI, GI, mSBI, PPD, and CAL). Table 2 shows an intragroup comparison of all the clinical parameters at baseline and 6-month follow-ups. On intragroup comparison of PI, it was found that there significant difference in all the three groups at 6-month follow-up as compared to baseline \( (P < 0.05) \). However, with regard to GI, mSBI, PPD, and CAL, there were significant differences found only in BA gel and CHX gel groups \( (P < 0.05) \), whereas in placebo gel group, the difference was nonsignificant \( (P > 0.05) \) at 6-month follow-up.

Table 3 shows the intergroup comparison of all the clinical parameters at baseline and 6-month follow-ups. Comparison of GI, mSBI, PPD, and CAL showed a significant difference between the three groups after 6-month follow-up \( (P < 0.05) \). However, with regard to PI, there was nonsignificant difference between in all the groups at 6-month follow-up \( (P > 0.05) \).

Table 4 shows an intergroup pairwise comparison of all the clinical parameters at baseline and 6-month follow-ups. On comparing Group I versus Group II, it was found that there was nonsignificant difference with regard to all clinical parameters after 6-month follow-up \( (P > 0.05) \). Similar results were seen while comparing Group II versus Group III \( (P > 0.05) \). However, on comparing the Group I versus Group III, it was found that there was a significant difference between all the clinical parameters at 6-month follow-up \( (P < 0.05) \). These pairwise results signify slight beneficial effects of BA gel on the clinical parameters over both CHX and placebo gels.

Significant reduction in the CFUs was seen on the blood agar plates from baseline to 3 months in both BA and CHX groups [Figures 2 and 3].

**Discussion**

The present study was a randomized, placebo-controlled clinical trial where the effect of 0.75% BA gel was evaluated as an alternative to 1% CHX on the clinical and microbiological parameters in patients with chronic periodontitis. The above agents were compared against placebo gel and were used as a local drug delivery agent. The results of this study demonstrated significant improvement in clinical and microbial parameters in the test groups, as compared to the control group (placebo gel).

In the present study, 0.75% concentration of BA was used as this concentration is found to be nontoxic to periodontal connective tissue cells. This is based on the previous study conducted by Sağlam et al.\(^{[25]}\) where they evaluated the cytotoxic effect of different concentrations of BA solution.
Mamajiwala, et al.: Boric acid gel in chronic periodontitis

using water-soluble tetrazolium salt assay. They concluded that 0.75% concentration of BA solution was nontoxic to gingival and periodontal ligament fibroblast cells. However, in the present study, the drug was delivered in gel form as compared to the previous study where 0.75% BA irrigation was done. BA was delivered locally into periodontal pocket in gel form as it delivers higher concentration of drug at the site of application. It also has added the advantage of bypassing the systemic metabolism and potential side effects from its systemic administration. This form of delivery provides sustained release of the drug into the subgingival area after its placement and thus maintaining longer period of substantivity.

A total of 45 patients completed the study at the end of the 6-month follow-up period. No adverse reactions to the drug were found, and the drug was well tolerated by patients, with no complications. This fact suggests that 0.75% concentration of BA is well tolerated by the participant without any subsequent side effects such as irritation or burning sensation at the local site of treatment, and any alteration in taste.

In the present study, 0.75% BA gel was compared with 1% CHX gel in the treatment of chronic periodontitis. To the best of our knowledge, only one study has been conducted where the comparison between the two is made. However, the present study is not comparable to the previous one as the concentration of the drug (CHX 0.2%), and vehicle for delivery used was different. In the present study, gel

Table 2: Intrigroup comparison of mean values of clinical parameters expressed as mean ± standard deviation

| Parameter | Baseline | 6 months | Baseline | 6 months | Baseline | 6 months | P |
|-----------|----------|----------|----------|----------|----------|----------|---|
| PI (mm)   | 1.56±0.20 | 1.11±0.86 | 1.42±0.21 | 1.02±0.13 | 1.63±0.35 | 1.31±0.24 | <0.05* |
| GI (mm)   | 1.21±0.22 | 0.74±0.35 | 1.34±0.22 | 0.69±0.38 | 1.28±0.36 | 0.98±0.21 | <0.05* |
| mSBI (mm)| 1.52±0.43 | 0.76±0.52 | 1.49±0.25 | 0.71±0.85 | 1.50±0.36 | 1.05±0.14 | >0.05* |
| PD (mm)  | 6.78±1.48 | 4.35±0.62 | 7.21±1.12 | 4.60±0.89 | 6.98±0.97 | 5.54±1.01 | <0.05* |
| CAL (mm) | 2.15±1.01 | 1.21±0.89 | 2.32±0.98 | 1.32±1.10 | 2.21±0.98 | 1.98±1.11 | >0.05* |

*P>0.05 derived from ANOVA considered nonsignificant, †P<0.05 derived from Student’s t-test considered significant. BA: Boric acid; CHX: Chlorhexidine; GI: Gingival Index; PI: Plaque Index; mSBI: Modified Sulcus Bleeding Index; PPD: Probing pocket depth; CAL: Clinical attachment level

Table 3: Intergroup comparison of mean values of clinical parameters expressed as mean ± standard deviation

| Clinical parameters | BA group | CHX group | Placebo group | P |
|---------------------|----------|-----------|---------------|---|
| PI                  | 1.56±0.20 | 1.42±0.21 | 1.63±0.35     | >0.05* |
| 6 months            | 1.11±0.86 | 1.02±0.13 | 1.31±0.24     | >0.05* |
| GI                  | 1.21±0.22 | 0.74±0.35 | 1.34±0.22     | >0.05* |
| 6 months            | 0.76±0.52 | 0.69±0.38 | 0.98±0.21     | <0.05* |
| mSBI                | 1.52±0.43 | 1.49±0.25 | 1.28±0.36     | >0.05* |
| 6 months            | 0.76±0.52 | 0.71±0.85 | 1.05±0.14     | <0.05* |
| PPD                 | 6.78±1.48 | 7.21±1.12 | 6.98±0.97     | >0.05* |
| 6 months            | 4.35±0.62 | 4.60±0.89 | 5.54±1.01     | <0.05* |
| CAL                 | 2.15±1.01 | 1.21±0.89 | 2.32±0.98     | >0.05* |
| 6 months            | 2.32±0.98 | 1.32±1.10 | 2.21±0.98     | <0.05* |

*P>0.05 derived from ANOVA considered nonsignificant, †P<0.05 derived from ANOVA considered significant. BA: Boric acid; CHX: Chlorhexidine; GI: Gingival Index; PI: Plaque Index; mSBI: Modified Sulcus Bleeding Index; PPD: Probing pocket depth; CAL: Clinical attachment level

Figure 2: Changes in colony-forming units
the glutathione levels, which is a known potent antioxidant and thus prevents the oxidative damage. BA apart from increasing glutathione levels also neutralizes other agents of reactive oxygen species which halts the further oxidative damage. In the study concluded that there is a direct correlation between gingival crevicular fluid lipid peroxidation levels, total oxidant status, PPD, and the clinical attachment loss in patients with periodontitis. This fact validates the beneficial effect of local delivery of an agent with antioxidant property in the treatment of chronic periodontitis. The fact is confirmed with results of the present study where significant improvement was seen with regard to PPD and CAL in BA gel group as compared to placebo gel group. However, when compared to CHX group, there was insignificant difference with regards to PPD and clinical attachment loss. These results are contradictory to the previous study conducted by where they found that there was significant reduction in PPD and CAL in BA gel group as compared to CHX group. It was thought that it might have occurred due to cytotoxic activity of CHX fibroblasts which might not have been the case in the current study. In the current study, it can only be hypothesized that BA can act as a potential antioxidant as no biochemical investigations were done in the present study. Thus, no conclusive remarks could be made regarding the mechanism by which reduction in probing depth and gain CAL occurred in patients treated with BA.

Another reason why there was significant improvement in CAL and PPD may be due to the ability of the boron atom to inhibit the serine proteases. The serine proteases such as elastase, chymase, and cathepsin G are major proteolytic enzymes. These proteolytic enzymes degrade the integrity of the periodontal fibers such as elastin, collagen, ground substance, and basement membrane. As BA is known to inhibit those enzymes which cause degradation of periodontal tissue may be another reason that the BA gel group showed more improvements in CAL compared with the CHX and placebo groups.

Considering PI scores, there was no additional benefit found from BA gel or CHX gel as an adjunctive treatment for patients with chronic periodontitis. There was a

| Clinical parameter | Groups | Significance |
|-------------------|--------|--------------|
| PI                | Group I versus Group II | >0.05* |
|                   | Group I versus Group III | <0.05* |
|                   | Group II versus Group III | >0.05* |
| GI                | Group I versus Group II | >0.05* |
|                   | Group I versus Group III | <0.05* |
|                   | Group II versus Group III | >0.05* |
| Msbi              | Group I versus Group II | >0.05* |
|                   | Group I versus Group III | <0.05* |
|                   | Group II versus Group III | >0.05* |
| PPD               | Group I versus Group II | >0.05* |
|                   | Group I versus Group III | <0.05* |
|                   | Group II versus Group III | >0.05* |
| CAL               | Group I versus Group II | >0.05* |
|                   | Group I versus Group III | <0.05* |
|                   | Group II versus Group III | >0.05* |

*P>0.05 considered nonsignificant, †P<0.05 considered significant.

GI: Gingival Index; PI: Plaque Index; mSBI: Modified Sulcus Bleeding Index; PPD: Probing pocket depth; CAL: Clinical attachment level
significant improvement in PI scores in all the groups after the 6-month period. However, changes in PI scores are dependent on patients’ compliance, and the fact that the PI scores were improved significantly in all groups in the present study suggests that patients had properly maintained the oral hygiene. It can also be suggested that enhanced oral hygiene maintenance might have occurred due to the Hawthorne effect.\textsuperscript{[34]}

In the present study, significant reduction in bacterial CFU’s counts was seen in BA gel group as compared to placebo group. The results of the current study are in accordance with a previous study conducted by Luan et al.\textsuperscript{[35]} where they found that boron-containing compound AN0128 had shown antibacterial activity against \textit{Prevotella intermedia}, \textit{Porphyromonas gingivalis}, \textit{Enterococci}, and \textit{Treponema denticola}. These results are contradictory to a previous study conducted by Sağlam et al.\textsuperscript{[25]} where they concluded that BA irrigation did not have additional advantage over the reduction of microbes. They proposed that 0.75% concentration of BA used might not be able to produce any cytopathic effect on periodontopathogens and thus was ineffective. However, this might have occurred due to different vehicle for drug delivery used as compared to the current study. As with the subgingival irrigation, the chances of washout of drug from the targeted site is more might be the reason why there was insignificant effect of BA on periodontopathogens in the previous study.\textsuperscript{[25]}

Positive results reported in the current study with regard to antibacterial activity of BA might have been due to the sustained release of drug to the target site imparting its effect over the microorganism for a longer period. This can also be partly explained by the result seen in CHX group where mean CFU counts were more after 3 months as compared to BA group in spite of improvements in clinical parameters. This is because CHX gel is thought to be rapidly diluted in a periodontal pocket due to rapid turnover of crevicular fluid rendering it ineffective.\textsuperscript{[25]}

Another mechanism as reported by Grenier et al.\textsuperscript{[36]} is also that certain organisms such as \textit{Porphyromonas gingivalis} releases vesicles that bind to CHX and makes them ineffective.

The results of this study are in accordance with a previous study by Kanoriya et al.\textsuperscript{[28]} who showed that BA gel application produces a significant improvement in clinical parameters compared with placebo.\textsuperscript{[28]} Singhal et al.\textsuperscript{[12]} have also reported that BA gel showed significant improvement in clinical parameters, along with the percentage of bone depth reduction when used as an adjunct to SRP in degree II furcation defects in chronic periodontitis patients.

However, the results of the present study cannot be directly compared to the previous studies conducted because of certain reasons, such as lack of knowledge regarding the exact mechanism by which improvement in clinical parameters occurred, also difference in methodology and vehicle for delivery used. Thus, further randomized, controlled clinical trials supported by biochemical and histological analysis and longitudinal studies with larger sample size needs to be conducted to give a conclusive evidence regarding the beneficial effect of BA in the treatment of chronic periodontitis.

The present study had certain limitations such as no biochemical investigation was done to support antioxidant activity of BA, no histological analysis was done to evaluate the healing mechanism, and effect of BA on bone defects was not evaluated.

**Conclusion**

Within the limitations of this study, it can be concluded that the use of BA gel or CHX gel in periodontal pockets as a local drug delivery agent produces a significant improvement in clinical and microbial parameters compared with placebo gel. Additional use of BA gel in nonsurgical periodontal treatment seems to be safe and effective in the treatment of patients with chronic periodontitis.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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