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ORIGINAL ARTICLE

Polyhexamethylene guanidine phosphate irrigation as an adjunctive to scaling and root planing in the treatment of chronic periodontitis

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ABSTRACT

Objective: To evaluate the efficacy of adjunctive polyhexamethylene guanidine (PHMG) phosphate irrigation in periodontal treatment.

Materials and Methods: The subjects comprised 59 patients with severe chronic periodontitis. Plaque index, bleeding on probing (BOP) and pocket probing depths (PPD) were recorded. The subjects were randomly allocated to one of three groups for scaling and root planning, with different adjunctive irrigants: 1% PHMG phosphate (19 subjects), 0.2% chlorhexidine (21 subjects) and distilled water (19 subjects). Patients were recalled after two weeks, one month and then after 4, 6 and 12 months.

Results: In all groups, treatment resulted in considerable improvement of the observed clinical parameters. There were no intergroup differences in plaque index and BOP at any time point, but significant differences in PPD at one, four and six months. By the end of the study no intergroup differences in PPDs persisted. While post study surgical treatment needs decreased in all three groups, no intergroup differences were observed in the number of deep periodontal pockets.

Conclusions: Irrigation with PHMG phosphate significantly reduces PPDs in the short-term, but has no significant long-term effect on the mean pocket depth.

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Introduction

Periodontitis is defined as biofilm-induced inflammation of the toothsupporting tissues. The condition leads not only to tooth loss [1], but may also have an adverse effect on general health, increasing the risk of myocardial infarction and impairing quality of life [2, 3]. Periodontitis originates from microbial plaque, but progression and severity of the disease are correlated with the immune response [4]. While host inflammatory mediators have been associated with tissue destruction, recent studies have shown that these agents may also play an important role in the control of periodontal infection [5, 6].

The aim of periodontal treatment is to arrest inflammation, prevent contamination of underlying tissue, and create favourable conditions for healing and regeneration of periodontal tissue. The association between periodontitis and microbial plaque is well-recognized, hence an essential component of periodontal treatment is to reduce the burden of periopathogens. Systemically administered antibiotics have the disadvantage of side effects, including hypersensitivity and gastrointestinal disturbances [7]. Locally delivered antimicrobials may therefore be an important element of anti-infective management of periodontal diseases [8]. Conventional methods of mechanical treatment, such as scaling and root planing (SRP), are complicated and time-consuming clinical procedures and might not always succeed in eliminating periopathogenic bacteria [8]. Moreover, in patients with chronic periodontitis at risk of developing bacteremia in association with SRP, antiseptic administration may decrease the amount of bacterial 'spill over' into the blood stream and modify the severity of the bacteremia [9]. It has been shown that subgingival instrumentation with concomitant PVP-iodine rinsing reduces the risk of development of bacteremia of oral origin [10]. Removal of subgingival dental plaque may be hampered by the rough surface of the roots and difficulty in reaching the most apical portions of pockets with curettes [11]. Thus periodontal pockets may persist after treatment. It has been shown that even after meticulous scaling, some subgingival microorganisms can persist in periodontal pockets [12]. The use of antiseptics, especially delivered subgingivally, may help reduce the titer of periopathogenic and other microbial species. The disappointing outcomes of some studies have been attributed to failure to deliver the active agent to the site in an effective concentration, or insufficient retention time at the site of action [13].

Polyhexamethylene guanidine (PHMG) derivatives are members of the polymeric guanidine family, widely used for

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many years as antiseptics in medicine and the food industry [14]. Structurally similar conjugates such as polyhexamethylene biguanide hydrochloride (PHMB-H) and PHMG phosphate (PHMG-P) were synthesized by incorporating different anions into the PHMG structure. PHMB-H has been extensively tested *in vivo* and *in vitro*. In the form of a mouthwash, PHMB-H consistently inhibits plaque regrowth and reduces oral bacterial counts [15–17]. An expert meeting in 2008 recommended PHMB as highly appropriate for use in infected wounds [18]. PHMG phosphate (PHMG-P) has been proposed for anti-infective application in dentistry. In preclinical studies, it has shown elevated antimicrobial activity against Gram-positive and Gram-negative bacteria and fungi [19]. However, there are to date no data available on the efficacy of PHMG-P in periodontal treatment.

The aim of the study was to evaluate clinical effects of intrasulcular irrigation with PHMG-P and chlorhexidine as an adjunctive to periodontal debridement in patients with severe chronic periodontitis.

The following research hypothesis was formulated: That there will be a significant difference in clinical efficacy between groups using antiseptics and the group using water as adjunctives to periodontal debridement.

Materials and Methods

The participants were recruited into the study between autumn 2011 and spring 2014, from patients referred to the Periodontal Clinic of the School of Dentistry of Belarusian State Medical University. The inclusion criteria stipulated that the subjects should be aged between 18 and 75 years, in normal health, with diagnosed generalized or local severe chronic periodontitis, having at least 3 teeth with periodontal pockets with minimum probing depths of 6 mm, and radiographic evidence of extensive bone loss (≥one third of root length). Further reasons for exclusion were: periodontal treatment less than six months prior to the study, pregnancy, nursing mother, health conditions which could affect progression of periodontal disease or which require antibiotics, allergy to CHX, PHMG-P, or a course of antibiotics in the previous 6 months.

To avoid selection bias, a simple randomization technique was used, based on the roll of a dice. All patients were allocated into one of 3 groups according to the score on the dice, cast by the nurse: scores of 1 or 4 went to the first group, 2 or 5 to the second group and 3 or 6 – to the third group. In the first group (19 subjects) Aquin (Inkraslav©, Minsk, Belarus), containing PHMG-P 1% (w/v) as the active substance, was used as an adjunctive irrigant for SRP; in the second group (21 subjects) the irrigant used was 0.2% (w/v) chlorhexidine (Public Pharmaceutical Service, Minsk, Belarus), and the third group (19 subjects) served as a control, with distilled water used as the irrigant. The first appointment took approximately one hour and comprised oral examination and completion of a periodontal status chart, informed consent, allocation to one of the groups and sample collection. The second appointment, for full mouth debridement with adjunctive irrigation, took up to two hours. Over the study period, subsequent appointments for debridement took less time, as the need for scaling decreased. Local anesthetics were used if necessary Ubistesin® (3M ESPE, Seefeld, Germany). As stipulated in the study protocol, all the irrigant solutions were prepared by a nurse, who randomly chose the code and distributed the solutions in identical opaque bottles with corresponding numbers. The legend was sealed until statistical analysis. The study ended when the last enrolled patient had undergone final follow-up examination.

At baseline the patients underwent a comprehensive periodontal examination. Panoramic radiographs were used to verify the diagnosis of chronic severe periodontitis. The presence of dental plaque at the gingival margin along the mesial, buccal, distal and lingual aspects was determined, and the plaque index (PI, %) was calculated. Gingival inflammation was registered as bleeding on probing (BOP) and expressed as the proportion of bleeding sites relative to the total number of sites. Pocket probing depth (PPD) was designated as the primary outcome and measured to the nearest mm using a calibrated Williams' periodontal probe (Falcon®, Sialkot, Pakistan). PPD was registered as the distance between the gingival margin and the most apical point of probe penetration into the periodontal pocket and was measured at six sites on each tooth. Periodontal pockets with PPD >4 mm were considered to be pathological and were selected for the analysis [20]. A PPD value of 6 mm was chosen as the threshold for surgical treatment need. After the baseline examination, all subjects received initial periodontal therapy, which included motivation, oral hygiene instruction and full-mouth debridement, using a combination of ultrasonic and manual instrumentation, with one of the test solutions as an irrigant. The irrigants were delivered to the periodontal pockets by means of a syringe with a blunt needle, at a dose of 2 ml per periodontal pocket. At each follow-up appointment, all treatment procedures were repeated. After baseline, five follow-up appointments were scheduled: after 2 weeks, 1 month, and then after 4, 6 and 12 months. All examinations and treatment were undertaken by the same experienced periodontist (A.V.).

The study was conducted according to the principles outlined in the Helsinki Declaration and approved by the Ethical Board of Belarusian State Medical University (Resolution 5 of 18.04.2011). Prior to study start the participants were briefed about the research objectives, the medications to be applied and the methods of treatment. Each participant gave written informed consent. As part of the treatment routine, all patients were informed of the examination results and diagnoses.

Statistical analysis

Patients were analyzed as they were randomized. If the patient withdrew from the study the data were kept and analysed for the actual participation time. Description statistics were computed and expressed as the mean ± standard deviation (SD). The Friedman Test was applied to assess differences within treatment groups and the Kruskal-Wallis Test was applied for intergroup comparisons. To determine the

Table 1. Demographic data.

Variables		PHMG-P	CHX	Water	Total
Enrolled volunteers number		19	21	19	59
Number of patients who completed the study		16	19	18	53
Average age (SD)		46.9 ± 11.4	49.4 ± 12.3	45.4 ± 9.8	47.3 ± 11.2
Male		10	9	11	30
Female		9	12	8	29
Smoking habits		1	2	6	9
Number of periodontal pockets measured initially	≥4 mm	359	444	422	1225
	≥6 mm	245	250	243	738
Number of periodontal pockets around front teeth		118 (32.9%)	209 (47.1%)	187 (44.3%)	514

significance of differences between two groups, the Mann-Whitney Test was applied to independent groups and the Wilcoxon Signed Rank Test to dependent groups. A p value $\leq .05$ was defined as statistically significant. To achieve 80% power to detect an average intergroup difference in PPD of 1 mm (assumed SD 1.5 mm), sample size was estimated as 14 patients for each group. Oversampling was done to allow for the possibility of drop-outs and data corruption. The software package SPSS Statistics 25 (IBM©, SPSS© Statistics, NY) was used for data analysis.

Results

Fifty-nine patients (30 males and 29 females) with severe chronic periodontitis, aged 29–70 years, mean age 47.2 (SD 11.2) years were enrolled in the study. The demographic data are presented in Table 1. Fifty-three patients completed the study: six withdrew for various reasons, resulting in an overall retention rate of 89.8%. The details are summarized in a flow diagram [Figure 1].

At baseline, there were no intergroup differences with respect to PI and BOP ($p > .05$), hence the groups were comparable [Table 2]. During the course of the study, significant differences in PI and BOP were observed within all three groups ($p < .05$). Pairwise intragroup comparison at the one-month follow-up revealed considerable improvement in PI and BOP within all three groups ($p < .05$). Moreover, BOP tended to decrease significantly within the groups after six months and this was also observed at the 12-month examination ($p < .05$). However, no intergroup differences in PI and BOP were observed at any follow-up examination.

Periodontal pockets deeper than 4 mm were considered to be pathological and selected for the PPD analysis. The results are presented in Table 3. At baseline, there were no intergroup differences in PPD. Over the course of the study, PPD decreased significantly in all three groups ($p < .05$). Intergroup comparison revealed marked differences at one, four and six months' follow up ($p < .05$). Pairwise comparison disclosed significant differences between PHMG-P and CHX applications, and between PHMG-P and water, but no difference was observed between CHX and water ($p > .05$). The largest reduction in PPD was recorded one month after study start, with significant intergroup differences ($p < .05$) after one, six and 12 months. The reduction in PPD was substantial in all three groups ($p < .05$), while no significant intergroup differences were found in the overall PPD reduction (Baseline – 12 months) ($p > .05$).

At baseline, the mean PPD value of deep periodontal pockets (≥ 6 mm) did not differ between the groups ($p > .05$). Significant intergroup differences in PPD, in favour of PHMG-P, were detected at one, four and six month follow-ups. However, by the end of the study, no differences were detected [Table 4].

Neither the total nor the average number of deep periodontal pockets (≥ 6 mm) per patient differed between treatment groups at baseline [Table 5]. During the study, the number of pockets decreased significantly within the groups. No differences were observed between the groups at any follow-up examination. However, in the PHMG-P group, there was a tendency towards more rapid reduction in deep periodontal pockets ($p > .05$). By the end of the study, only patients in the antiseptic groups no longer needed surgical treatment. All the deep periodontal pockets of two patients in the PHMG-P group and one patient in CHX group decreased below the threshold for surgical treatment need.

The participants' oral hygiene standards were not affected by age: PI did not differ between age subgroups, when split at the age of 50. The correlation between age and oral plaque index was low and not significant. Oral hygiene standards were higher in women at baseline and at all follow-up examinations ($p < .05$). During the study no adverse effects of antiseptics were observed.

Discussion

Despite extensive evaluation of the clinical efficacy of mechanical instrumentation in combination with various locally applied antimicrobials, comparison of different studies is complicated by the lack of standard protocols, diverse methods of application, varying concentrations of antimicrobials etc. [21–23]. Thus current data on the use of antiseptics in periodontal treatment are inconsistent. Some reports claim that CHX does not provide additional benefit as an adjunctive to SRP [23, 24]. The lack of efficacy has been attributed to the low concentration (0.02%) of the antimicrobial agents used for irrigation.

The current double-blind clinical trial was undertaken to assess the efficiency of repeated sessions of mechanical debridement, supplemented by adjunctive administration of antiseptics in the form of irrigants. To estimate the short-term effects, clinical parameters were scored one month after startup and then at four, six and 12 months, to evaluate medium-term efficiency. The fact that oral examination and treatment were undertaken by the same clinician is a possible source of bias. However, the risk was minimized by

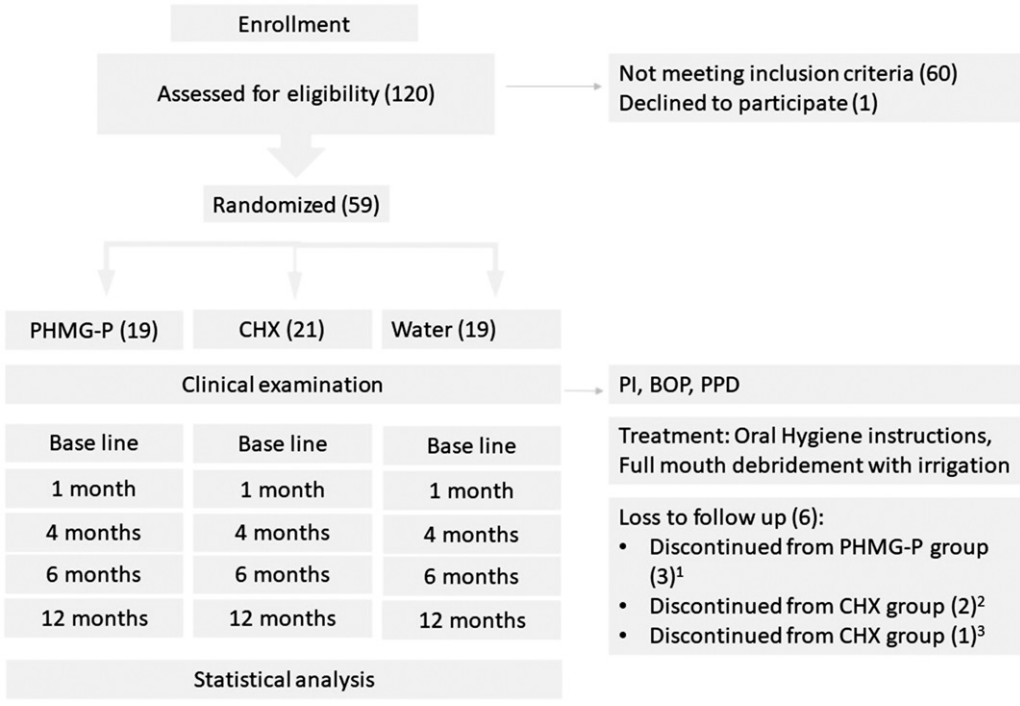

Figure 1. Flow Diagram.1. One retired man withdrew from the study after 4 months because he had moved to the country and could no longer attend the clinic. One woman withdrew from the study after 4 months in order to undergo prosthetic rehabilitation. One man withdrew from the study after 6 months because he missed an appointment while away on business. 2. Two subjects withdrew from CHX intervention group after 4 months, giving no reason. 3. One person withdrew from the water intervention group after 4 months, giving no reason.

Table 2. Oral hygiene and bleeding on probing before and after treatment.

Treatment group	PI, % (Mean ± SD)					BOP, % (Mean ± SD)				
	Baseline	1 month	4 months	6 months	12 months	Baseline	1 month	4 months	6 months	12 months
PHMG-P	35 ± 24	20 ± 18	26 ± 17	22 ± 18	16 ± 13	33 ± 22	15 ± 16	16 ± 15	12 ± 09	7 ± 7
CHX	33 ± 26	16 ± 13	15 ± 12	15 ± 15	11 ± 11	31 ± 25	15 ± 13	13 ± 09	12 ± 13	7 ± 8
Water	39 ± 24	20 ± 15	23 ± 18	19 ± 14	17 ± 14	33 ± 19	14 ± 11	13 ± 10	12 ± 11	6 ± 4

Table 3. PPD and PPD reduction of periodontal pockets over 4 mm prior to and after treatment.

Treatment Group	PPD, mm (Mean ± SD)					PPD reduction, mm (Mean ± SD)				
	Baseline	1 month	4 months	6 months	12 months	1 month	4 months	6 months	12 months	Total (12 months-baseline)
PHMG-P	6.5 ± 1.5	5.5 ± 1.6	5.2 ± 1.5	5.0 ± 1.5	5.0 ± 1.6	−1.1 ± 1.3	−0.3 ± 1	−0.1 ± 1	0.02 ± 0.9	−1.5 ± 1.4
CHX	6.4 ± 1.7	5.8 ± 1.7	5.6 ± 1.8	5.4 ± 1.9	5.1 ± 1.9	−0.7 ± 1.2	−0.2 ± 1.4	−0.3 ± 1.1	−0.2 ± 1.2	−1.4 ± 1.7
Water	6.4 ± 1.7	5.8 ± 1.7	5.5 ± 1.8	5.3 ± 1.7	5.1 ± 1.9	−0.6 ± 1.2	−0.3 ± 1.4	−0.2 ± 1.3	−0.2 ± 1.2	−1.3 ± 1.5

Table 4. Average PPD and PPD reduction of periodontal pockets over 6 mm prior to and after treatment.

Treatment Group	PPD, mm (Mean ± SD)					PPD reduction, mm (Mean ± SD)				
	Baseline	1 month	4 months	6 months	12 months	1 month	4 months	6 months	12 months	Total
PHMG-P	7.2 ± 1.2	6.0 ± 1.5	5.8 ± 1.4	5.5 ± 1.5	5.5 ± 1.6	−1.2 ± 1.3	−0.2 ± 1.1	−0.2 ± 1.1	0.02 ± 0.9	−1.8 ± 1.5
CHX	7.6 ± 1.4	6.6 ± 1.6	6.3 ± 1.9	6.0 ± 2.0	5.8 ± 2.1	−1.0 ± 1.2	−0.3 ± 1.2	−0.3 ± 1.1	−0.2 ± 1.3	−1.7 ± 1.9
Water	7.5 ± 1.3	6.6 ± 1.7	6.1 ± 1.9	6.0 ± 1.7	5.8 ± 1.9	−0.9 ± 1.2	−0.5 ± 1.5	−0.2 ± 1.3	−0.2 ± 1.3	−1.7 ± 1.7

Table 5. Absolute and average number per patient of deep periodontal pockets (>6 mm) prior to and after treatment.

Treatment Group	Absolute number of deep periodontal pockets					Average number of deep periodontal pockets				
	Baseline	1 month	4 months	6 months	12 months	Baseline	1 month	4 months	6 months	12 months
PHMG-P	245	157	128	102	89	12.9 ± 6.7	8.3 ± 3.4	6.7 ± 3.4	6.0 ± 3.5	5.6 ± 4.1
CHX	250	201	174	146	133	11.9 ± 8.4	9.6 ± 7.3	8.3 ± 8.1	7.7 ± 7.4	7.0 ± 8.7
Water	243	206	179	169	152	12.8 ± 11.0	10.8 ± 9.4	9.4 ± 8.0	9.4 ± 8.2	8.4 ± 8.2

randomization and blinding. Because the observation period was limited to only 12 months, the final outcome of 'tooth loss' in relation to use of antiseptics as adjunctives to periodontal treatment could not be assessed in this trial [25]. As patients were gradually enrolled, on referral, the simple randomization method was used despite a major limitation,

namely inability to ensure totally equal groups. Consequently, the intergroup distribution of smokers is unequal and this must be regarded as a limitation of the study. Noninclusion into the study medically compromised patients might hamper extrapolation of the results to the general population. This restriction to a generally healthy population with severe chronic periodontitis might also be considered as a limitation of the study. Water was used as a negative control because it was used to dissolve CHX in the pharmacy and it was not possible to achieve the solvent composition of Aquin (Inkraslav©, Minsk, Belarus).

The baseline PI and BOP scores were considerably higher than at the end of treatment. There were no intergroup differences in PI and BOP at any of the subsequent observations. Thus, this study confirms the results of previous studies that application of antiseptics in the form of irrigants during SRP does not offer any additional benefits [21, 22]. The absence of significant differences in PI and BOP among the treatment groups at any time point suggests similar good standards of oral hygiene and levels of motivation in the subjects. The lack of antiseptic effect could be attributed to the fact that exposure to the antiseptics during debridement was brief and sporadic and possibly inadequate for achievment of clinically detectable change: the optimal retention time of minimal inhibitory concentrations of antimicrobials towards periopathogens has yet to be determined. Moreover, antiseptics in liquid form are rapidly removed from the application site by gingival crevicular fluid [26]. A further contributing factor might be that the pathophysiological mechanisms underlying the parameters PI and BOP are not particularly responsive to the action of antiseptic solutions.

In general, the mean PPD value was reduced by 1.3–1.5 mm. The average PPD decreased from 6.5 to 5.0 mm, which is in accordance with the results of other studies [27–29]. In some cases a decrease in PPD from over 6 mm to 5 mm or less after conservative periodontal therapy might reduce the need for surgical treatment. In the PHMG-P group, PPD declined more rapidly, reaching its minimum after six months. Six months later, mean PPD in the CHX and water groups had caught up with PHMG-P values. Thus by the end of the study, there were no significant intergroup differences. One reason that PHMG-P reduced PPD more rapidly could be the higher concentration of the active ingredient: 1% PHMG-P, compared with 0.2% CHX. The lack of intergroup differences at 12 months may be attributable to the infrequent chairside administration of the antiseptics and the fact that in periodontal treatment, adequate plaque control is a greater determinant of success than antimicrobial supplements. Another factor to be considered is the clinical importance of the greater average PPD reduction of 0.3–0.4 mm associated with PHMG-P, compared with CHX. On the one hand such a minor difference may not seem critical. On the other hand, it is important to consider not only the mean reduction of PPD, but also the range. Changes in PPD ranged in both directions, up to 1.2 mm, whereas a total difference of 2 mm could signify an important clinical effect. High variability of PPD with a wide SD means that this parameter fluctuated in both directions, i.e. not all sites responded equally to treatment and while some pockets were reduced, others deepened.

Reduction of deep periodontal pockets decreases surgical treatment need. However, a patient with only one residual deep pocket still requires surgical treatment, although not as extensive. In this study, all the deep periodontal pockets in three patients in the antiseptic groups healed to below the threshold for surgical treatment. However, the numbers were insufficient to analyse and draw conclusions.

Age did not influence the ability of the participants to maintain adequate oral hygiene. However, as the study included relatively few participants of each age, no clear conclusions about the influence of age should be drawn. At the same time, gender affected oral hygiene. That males neglect their oral hygiene has been reported previously [30, 31]. However, the reason is unclear.

Conclusions

According to the protocol used in this study, irrigation with PHMG-P in the nonsurgical phase of periodontal treatment significantly reduced PPD in the short-term. However, at the end of the one-year trial, antiseptic irrigation had no long-term benefit on mean pocket depth.

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Disclosure Statement

The authors declare that they have no conflict of interests.

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