CLINICAL ORAL IMPLANTS RESEARCH

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Effect of glycine powder air-polishing as an adjunct in the treatment of peri-implant mucositis: a pilot clinical trial

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Abstract

Background: Glycine powder air-polishing (GPAP) has the potential to effectively erase biofilms and may improve the treatment efficacy of peri-implant mucositis. This pilot clinical trial evaluated the effect of GPAP as an adjunct in treating peri-implant mucositis.

Materials and methods: Twenty-four subjects having at least one implant with peri-implant mucositis were randomly assigned to test (12 subjects with 17 implants) and control (12 subjects with 16 implants) groups. Following baseline assessment, all subjects received oral hygiene instruction and non-surgical debridement. In the test group, the sites with probing depth (PD) $\geq$4 mm were additionally treated by GPAP for 5 sec. Clinical parameters were measured at 1-week, 1-month, and 3-month recall visits.

Results: At the 3-month visit, the mean reductions in PD at site level were 0.93 $\pm$ 0.93 mm and 0.91 $\pm$ 0.98 mm in the test and control groups, respectively ($P < 0.05$), and no significant difference existed between two groups. Mean bleeding score was also significantly reduced in both groups after the intervention. No complications or discomfort were reported during the study.

Conclusions: This pilot clinical trial suggests that non-surgical mechanical debridement may effectively control peri-implant mucositis, and adjunctive GPAP treatment seems to have a limited beneficial effect as compared with mechanical debridement alone. However, further clinical trials with a large sample size are needed to confirm this preliminary observation.

The cause–effect relationship between plaque and gingivitis was demonstrated during the 1960s in the experimental gingivitis study (Loe et al. 1965). Thirty years later, a similar study found that 3 weeks of accumulated plaque around implants could also lead to peri-implant mucositis (Pontoriero et al. 1994). Histological studies on soft tissue have shown that inflammatory infiltrations in the mucosa around implants and the gingiva around natural teeth share many features (Berglundh et al. 1992; Ericsson et al. 1992; Trejo et al. 2006). However, if plaque is present for a longer time such as 3 months, the inflammatory infiltration in the peri-implant mucosa would be almost three times greater than in the dentogingival unit (Ericsson et al. 1992; Heitz-Mayfield & Lang 2010). Studies on animal models have also shown bone loss induced by plaque, which are accumulated by ligature (Hurzeler et al. 1995; Marinello et al. 1995; Persson et al. 1996; Isidor 1997).

Due to lack of long-term investigation, the relationship between peri-implant mucositis and peri-implantitis remains obscure. However, according to some experts, peri-mucositis, which appears to be a sign of host response to bacterial burden, might be the precursor for peri-implantitis (Heitz-Mayfield et al. 2011; Lang et al. 2011). Therefore, early diagnosis and intervention are of great clinical importance in management of peri-implant infections. Nevertheless, few clinical studies have examined the procedure for treating peri-implant mucositis (Heitz-Mayfield & Lang 2004; Renvert et al. 2008; Maximo et al. 2009; Thone-Muhling et al. 2010; Heitz-Mayfield et al. 2011). Although clinical improvement can be gained through mechanical debridement, there is still quite a high proportion of sites with deep pocket and bleeding tendencies on probing (Ciancio et al. 1995; Strooker et al. 1998; Porras et al. 2002; Lindhe & Meyle 2008; Thone-Muhling et al.

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2010; Heitz-Mayfield et al. 2011). Adjunctive methods, such as mouth rinse and local antiseptic gel, designed to enhance clinical outcomes have, however, failed to show any additional effect (Ciancio et al. 1995; Strooker et al. 1998; Porras et al. 2002; Lindhe & Meyle 2008; Thone-Muhling et al. 2010; Heitz-Mayfield et al. 2011).

Recently, air-polishing devices (APD) have been shown to be a feasible treatment option in periodontal care (Petersilka et al. 2003a,b, c; Moene et al. 2010; Wennstrom et al. 2011). As the initiation of peri-implant mucositis is similarly dependent on the presence of biofilms, APD may potentially be applied in peri-implant cases (Sahrmann et al. 2012). Glycine powder, which is a non-toxic and water-soluble amino acid, has been shown not to change the implant surface profile under scanning electronic microscope (SEM) (Schwarz et al. 2009). Clinical studies have revealed significant improvements in probing depth (PD), bleeding on probing (BOP), and microbiological tests when treating peri-implantitis with glycine powder air-polishing (GPAP) (Maximo et al. 2009; Renvert et al. 2011; Sahm et al. 2011). However, it is still argued that GPAP does not show superior results to other methods, such as manual curettes, ultrasonic scalers, and erbium-doped yttrium aluminum garnet (Er: YAG) laser treatment (Maximo et al. 2009; Renvert et al. 2011; Sahm et al. 2011). Nevertheless, no study has been carried out to investigate the effect of APD using glycine powder as an adjunctive method to treat peri-implant mucositis. This pilot clinical trial evaluated the effect of GPAP as an adjunct in the treatment of peri-implant mucositis.

Materials and methods

The study was a single-blind, randomized, 3-month clinical trial. All the procedures were performed in Beijing, China, from 2010 to 2011. The research protocol was approved by the Ethics Committee of Peking University Health Science Center prior to the study.

Study population

The enrolled subjects were patients who had received implant treatment at least 1 year before at Peking University School & Hospital of Stomatology. Reasons for missing teeth included caries, trauma, congenital missing, or root fracture as previously recorded. The remaining dentition was either periodontally healthy, with gingivitis, or moderate chronic periodontitis (Armitage 1999). Subjects with teeth extracted due to poor periodontal prognosis or who had aggressive or advanced periodontitis were excluded from this study.

Participants had to meet the following inclusion criteria: at least one implant site with PD $\geq$4 mm and BOP positive; molar or premolar site; no detectable loss of supporting bone as compared with periapical radiographs immediately after restoration. To avoid a range of different implant systems, only one system (ITI® Straumann®, Standard Implant, SLA surface, Waldenburg, Switzerland) was selected. For those with more than one implant, all implants that met the inclusive criteria were analyzed in the study.

Subjects who were smokers and who had systemic diseases (e.g., diabetes mellitus and osteoporosis) that might affect the study outcomes were also excluded from the study. Furthermore, those who had received any peri-implant treatment within the last 6 months and those who needed antibiotic treatment were excluded.

Clinical measurements and procedures

An initial questionnaire containing information about personal particulars, oral habits, and systemic conditions was completed by each participant. Periapical radiographs were taken to detect any loss of supporting bone. Each participant was given an explanation of the study, and a written consent form was obtained before treatment.

Then, the implant(s) and the remaining teeth were both checked, and PD, modified plaque index (mPlI), and bleeding index (BI) were recorded on a chart. All the examinations were performed by the same trained and calibrated operator (J.Y.J). The following parameters were evaluated at six sites (mesio, medio, disto/buccal, and lingual) of implants using a manual probe (122-006, PQ-W, Williams, SILVER by Hu-Friedy, Chicago, IL, USA). mPlI was graded as follows: (0) no detection of plaque, (1) plaque recognized only by running a probe across a smooth marginal surface of the implant, (2) plaque can be seen at a glance, (3) abundance of soft matter (Mombelli et al. 1987; Mayfield et al. 1998). PD was measured under 0.2–0.25 N force, to the nearest scale (Lindhe & Meyle 2008; Gerber et al. 2009). BI scores were assessed 30 sec after probing: (0) no bleeding, (1) point of bleeding, (2) line of bleeding, (3) drop of bleeding (Renvert et al. 2011).

Treatment protocol

After baseline examination, the participants were instructed and motivated in oral hygiene practice and then received non-surgical treatment including supra-gingival scaling, root debridement, and polishing according to their periodontal conditions. Before grouping, all the implants were treated by the examiner (J.Y.J.) using ultrasonic scaler with carbon fiber tips (Satelec® P5 ultrasonic scaling machine and PH2L, PH2R tips, Newtron, France). This instrumentation procedure was carried out until the operator felt it was adequate rather than for a defined time. Then, subjects were randomly assigned to the test (GPAP) or control group.

Randomization was performed by the toss of a coin (Needleman et al. 2005; Chondros et al. 2009). The allocation was based on subject level, which meant that if there were more than one implant in one individual, all the implants would receive the same treatment modality. The allocation and additional air-polishing procedure were accomplished in an isolated dental room by an operator (C.J.), which was concealed from the examiner (J.Y.J.). Only implants in the test group were further treated by the GPAP (AIR-FLOW master® and AIR-FLOW Perio®, EMS, Nyon, Switzerland). The water and powder were set to medium as a default when the machine was switched on. The outlet of the appliance handpiece was connected to a disposable subgingival nozzle. The nozzle was inserted deep into the pockets with PD $\geq$4 mm until resistance was felt, and then the pedal was pressed for 5 sec on each site (Fig. 1). All air-polishing procedures were performed by the same operator (C.J.) who was not involved in clinical examination and data collection, and the study subjects were asked not to discuss their treatment with the examiner until the end of the study. All the treatments, both on implants and natural teeth, were accomplished within the first visit in both groups.

During the follow-up visits, oral hygiene instruction (OHI) was reinforced when necessary. PD were re-examined at the 1- and 3-month post-treatment visits. mPlI and BI were

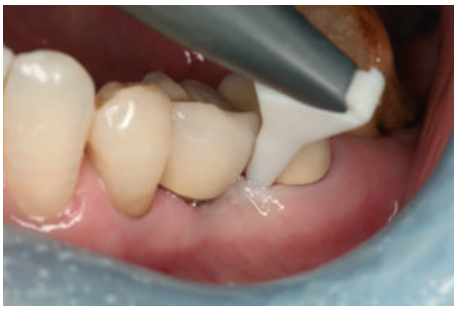

Fig. 1. Clinical photograph of GPAP usage with a disposable nozzle.

recorded at the 1-week, 1-month, and 3-month visits. Adverse events and complaints of discomfort were recorded if any.

Intra-examiner reproducibility

Five subjects were randomly selected for the assessment of intra-examiner (J.Y.J.) reproducibility. After baseline PD examination, treatment on remaining dentition was carried out, which usually lasted 1 h. Then, before any treatment on the implants, they were probed again for calibration. The weighted kappa analysis was applied, and the reproducibility was 69%.

Statistical analysis

The statistical analysis was performed with commercially available software (SPSS, version 14.0, SPSS Inc., Chicago, IL, USA). Mean values and standard deviations (mean ± SD) for the clinical parameters were calculated. Data for both subject level and treated site level were obtained. Fisher's exact test was applied in baseline comparison. At subject level, mean data were calculated using an average of all sites around the implant(s) for each participant. At treated site level, however, only data on deep pockets with PD $\geq$4 mm were used and analyzed. Independent and pairwise *t*-tests were applied. Mixed-effect and longitudinal analysis was also carried out by R (version 2.15.2) and nparLD (version 2.1). The difference with a *P*-value <0.05 was considered statistically significant.

Results

Twelve subjects (17 implants) in the GPAP group and 12 subjects (16 implants) in the control group were enrolled in this study. No subject with more than two implants was included. Data from the 1-week and 1-month follow-ups were missing in one and two subjects, respectively. No complaint of discomfort was reported after any treatment.

Baseline demographic characteristics were collected at the first visit and are presented in Table 1. The two groups were evenly distributed in terms of age, sex, periodontal condition, prosthesis pattern, and oral hygiene habits, except for mPlI, which was higher in the GPAP group than in the control.

Table 1. **Baseline demographics and clinical examination results for subjects in two groups**

Background	GPAP group (*N* = 12)	Control group (*N* = 12)	*P*-value
Mean age (years)	46.2	41.3	0.311
Female	50%	67%	0.414
Periodontal condition			
Healthy	0	1 (8%)	0.843
Gingivitis	8 (66.7%)	7 (58.3%)	
Periodontitis	4 (33.3%)	4 (33.3%)	
Connected crown	1	3	0.514
Oral hygiene habit			
Brushing frequency (per day)	2	2.3	0.114
ID brushing (user)	4 (33%)	6 (50%)	0.514
Flossing (user)	6 (50%)	7 (58%)	0.755
Mouth rinse (user)	5 (42%)	3 (25%)	0.514
Number of subjects with			
One implant	7	8	
Two implants	5	4	
Probing depth (± SD)	3.6 (±0.47)	3.5 (±0.50)	0.538
Bleeding index (mean± SD)	1.4(±0.57)	1.5(±0.65)	0.912
Modified plaque index (mean ± SD)	1.2(±0.85)	0.6(±0.40)	**0.030**

N, number of subjects; connected crown includes connected crown and crown with a pontic; SD, standard deviation; $P < 0.05$ was bold.

Table 2. **Probing depth ± SD at baseline, 1 month, and 3 months in both groups**

PD (±SD) (mm)	Baseline	1-month	*N*/*n*	Δ	*P*-value[1]	3-month	*N*/*n*	Δ′	*P*-value[2]
GPAP Group									
S	3.6 (±0.47)	3.2 (±0.52)	10	0.28	**0.039**	3.2 (±0.48)	12	0.43	**0.017**
TS	4.6 (±0.50)	3.8 (±1.0)	36	0.78	**<0.001**	3.7 (±0.95)	46	0.93	**<0.001**
Control Group									
S	3.5 (±0.50)	3.3 (±0.26)	12	0.17	0.172	3.1 (±0.38)	12	0.40	**0.012**
TS	4.5 (±0.55)	3.8 (±1.0)	46	0.70	**<0.001**	3.6 (±1.0)	46	0.91	**<0.001**
P-value[3]									
S	0.538	0.405				0.587			
TS	0.551	0.735				0.831			

PD, probing depth; SD, standard deviation; S, subject level; TS, treated site level; *N*, number of subjects; *n*, number of treated sites; Δ, difference between 1 month and baseline; Δ′, difference between 3 months and baseline; *P*-value[1] and *P*-value[2] are the results analyzed from 1 month to baseline and 3 months to baseline within one group, respectively; *P*-value[3] is the result analyzed between two groups at subject level and site level, respectively; $P < 0.05$ was bold.

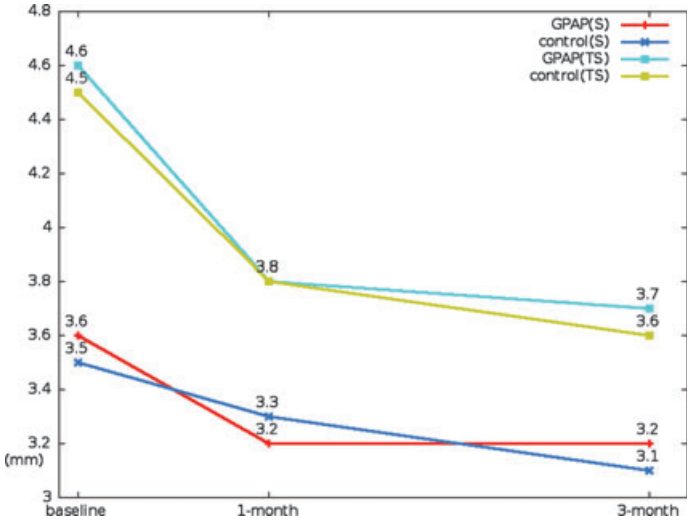

Fig. 2. Probing depth changes in the GPAP group and control group. GPAP – Glycine powder air-polishing; S – subject level; TS – treated site level.

Probing depth changes

Mean values of PD at subject and site levels are shown in Table 2. At subject level, 1-month and 3-month data in the GPAP group and 3-month data in the control group showed significant PD reductions. The 3-month reductions were 0.43 ± 0.53 mm and 0.40 ± 0.47 mm in the GPAP and control group, respectively. No significant difference was found within any visit between the two groups. At treated site level, significant PD reductions were shown at the 1- and 3-month points as compared with the baseline (P-value < 0.001). At the 3-month point, the reductions were 0.93 ± 0.93 mm in the GPAP group and 0.91 ± 0.98 mm in the

Table 3. **Modified plaque index levels at baseline, 1-week, 1- and 3-month in both groups**

mPII (±SD)		Baseline	1-week	*N/n*	*P*-value*	1-month	*N/n*	*P*-value†	3-months	*N/n*	*P* value‡
GPAP Group	S	1.2 (±0.85)	0.7 (±0.62)	12	0.064	0.4 (±0.57)	10	**<0.001**	0.4 (±0.32)	12	**0.003**
	TS	1.4 (±1.06)	0.7 (±0.81)	46	**0.001**	0.4 (±0.60)	36	**<0.001**	0.4 (±0.61)	46	**<0.001**
Control Group	S	0.6 (±0.40)	0.5 (±0.35)	11	0.283	0.5 (±0.46)	12	0.416	0.4 (±0.38)	12	0.186
	TS	0.6 (±0.68)	0.5 (±0.60)	43	0.278	0.4 (±0.65)	46	0.086	0.4 (±0.53)	46	**0.018**
p-value§	S	**0.030**	0.344			0.787			0.924		
	TS	**<0.001**	0.224			0.862			0.716		

mPII, modified plaque index; SD, standard deviation; S, subject level; TS, treated site level; *N*, number of subjects; *n*, number of treated sites.
*,†,‡*P*-value are the results analyzed from 1-week to baseline, 1-month to baseline and 3-month to baseline, respectively, within one group.
§*P*-value is the result analyzed between two groups at subject level and site level respectively; $P < 0.05$ was bold.

control group. No significant difference was detected within the two groups at any visit. Fig. 2 describes the PD changes according to different time points.

Plaque index changes

Mean values of mPlI were calculated from subject data and are presented in Table 3. The GPAP group had higher mPlI score than the control group at baseline, which was statistically significant ($P = 0.030$). Significant mPlI improvement was shown at the 1-month visit in the GPAP group as compared with baseline. However, in the control group, mPlI was comparable with baseline in all the visits. Plaque index was also analyzed at treated sites. Levels of mPlI in the GPAP group were significantly higher than in the control group at baseline. mPlI levels in the GPAP group were shown to have reduced significantly at all the follow-up visits. In the control group, however, only data from the 3-month visit showed significant reduction as compared with baseline. Fig. 3 shows the changes in mPlI levels according to different visits.

Bleeding index changes

Mean values of BI were calculated at both subject and site levels, and the outcomes are listed in Table 4. Independent and pairwise comparisons showed that BI levels were significantly reduced only at the 1-week point in both groups. At treated site level, there was a significant reduction in BI at all the visits. Additionally, at the 1-week point, the control group demonstrated a significantly greater BI reduction than the GPAP group ($P = 0.013$). The changes in BI levels over time course are shown in Fig. 4. 42.1% and 29.3% of sites turned BOP negative at 3-month point, for the control and GPAP groups, respectively ($P = 0.010$).

Mixed-effect and longitudinal analysis

Brunner and Langer models were followed to analyze the repeated measurements over time. There were no significant difference in PD, BI, and mPlI between two groups among all visits, and the *P*-values were 0.74, 0.26, and 0.08, respectively. However, PD, BI and mPlI in both groups had significant improvement over time course (*P*-values < 0.001).

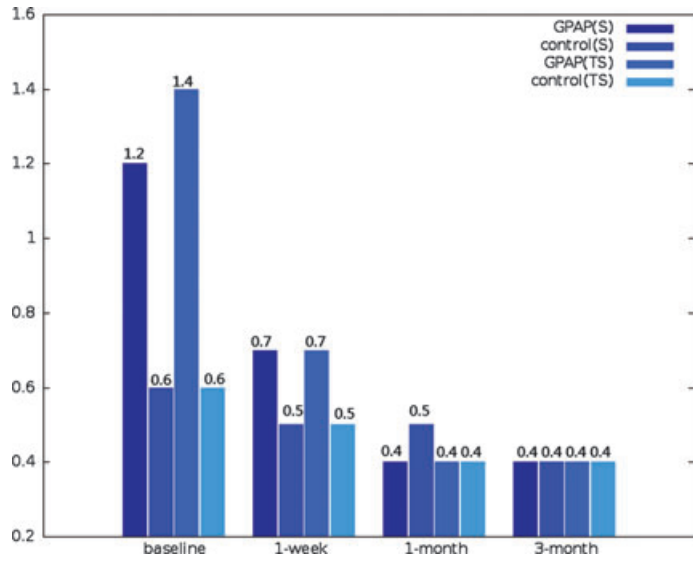

Fig. 3. Modified plaque index level changes in the GPAP group and control group. GPAP – Glycine powder air-polishing; S – subject level; TS – treated site level.

Discussion

As implant insertion to replace missing teeth is increasing from the past decade, attention has been naturally focused on peri-implant supportive care. Reports show that the prevalence of peri-implant mucositis occurs in up to 80% of patients and 50% of implant sites. Peri-implantitis was identified in 28% and ≥56% of subjects and in 12% and 43% of implant sites in two different studies, respectively (Renvert et al. 2008). Therefore, there is clearly a need to identify an effective method of controlling peri-implant infections.

Implants in the anterior region were excluded from this study to avoid esthetic considerations that might affect the results. Unlike previous studies, in which only subjects with good oral hygiene were recruited, in our study no limit in plaque index at baseline was set (Heitz-Mayfield et al. 2011, 2012). Participants improved their levels of oral hygiene during the course of the study. This was thought to be more realistic to clinical practice.

In terms of the statistical analysis, data were first analyzed at subject level. Participants' background and clinical parameters were compared between the two groups at baseline. Each subject was treated as a unit. However, only deep sites with PD ≥4 mm were treated by GPAP in the test group, and this minor effect might be diluted by shallow pockets. Therefore, site-level analysis was applied as well. Finally, mixed-effect and longitudinal analysis was used to evaluate the effects of GPAP over time.

Mechanical debridement with or without GPAP demonstrated significant reduction in PD and BI; therefore, both were effective in reducing peri-implant mucositis. When comparing these two, however, only at the 1-week point, did the control group demonstrate greater BI reduction. Similar results were reported by another study on natural teeth, which showed a higher percentage of BOP positive sites on Day 7 after the GPAP treat-

Table 4. **Bleeding index at baseline, 1-week, 1 month, and 3 months in both groups**

BI (±SD)	Baseline	1 week	*N/n*	*P*-value[1]	1 month	*N/n*	*P*-value[2]	3 months	*N/n*	*P*-value[3]
GPAP Group										
S	1.4 (±0.57)	0.8 (±0.53)	12	**0.006**	1.0 (±0.91)	10	0.257	1.1 (±0.58)	12	0.150
TS	1.7 (±0.93)	1.0 (±1.0)	46	**<0.001**	1.1 (±1.2)	36	**0.027**	1.1 (±0.98)	46	**0.002**
Control Group										
S	1.5 (±0.65)	0.5 (±0.25)	11	**0.001**	1.1 (±0.50)	12	0.057	1.0 (±0.85)	12	0.058
TS	1.7 (±1.0)	0.5 (±0.67)	43	**<0.001**	1.0 (±0.95)	46	**<0.001**	0.9 (±1.1)	46	**<0.001**
P-value[4]										
S	0.912	0.067			0.878			0.764		
TS	0.751	**0.013**			0.718			0.361		

BI, bleeding index; GPAP, Glycine powder air-polishing; SD, standard deviation; S, subject level; TS, treated site level; *N*, number of subjects; *n*, number of treated sites; *P*-value[1], *P*-value[2] and *P*-value[3] are the results analyzed from 1 week to baseline, 1 month to baseline, and 3 months to baseline, respectively, within one group; *P*-value[4] is the result analyzed between two groups at subject level and site level, respectively; $P < 0.05$ was bold.

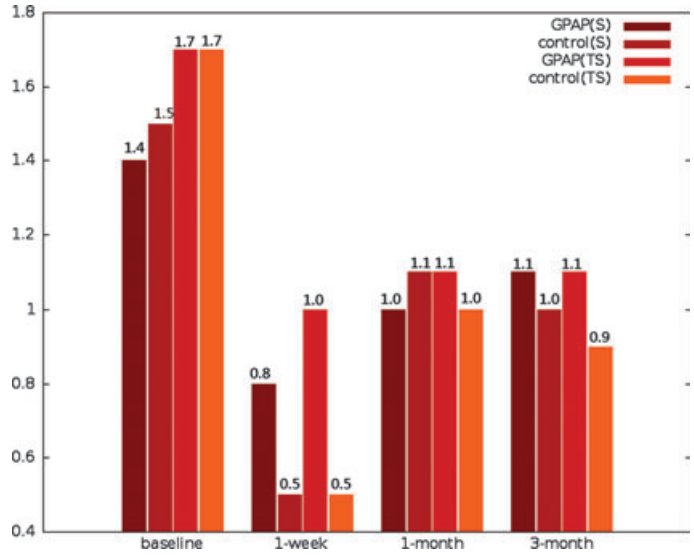

Fig. 4. Bleeding index changes in the GPAP group and control group. GPAP – Glycine powder air-polishing; S – subject level; TS – treated site level.

ment as compared with a scaling and root planing (SRP) group (Moene et al. 2010). This might be caused by the damage to the mucosa from high-pressure glycine slurry. One histological study has investigated the trauma from the glycine powder hitting the gingiva when GPAP was used. Biopsies from the gingiva showed that the superficial parakeratinized layer was only slightly detached (Petersilka et al. 2008). However, in the present study, the distance between the slurry and pocket surface was so close that they almost touched, so the damage was more intensive although the nozzle usage would have meant a large decrease in slurry pressure. Interestingly, at 3-month visit, 42.1% and 29.3% of sites turned BOP negative for the control and GPAP groups, respectively, where the peri-mucositis has been completely resolved ($P = 0.010$). Further study is required to elaborate this point.

In a study of anti-infective treatment of peri-implant mucositis, mechanical debridement alone was shown to lead to a 0.63-mm PD reduction after 3 months (Heitz-Mayfield et al. 2011). Porras and his colleagues reported a 0.93-mm PD reduction 3 months after mechanical cleansing and OHI, which was comparable with our study (Porras et al. 2002). In another trial aiming to compare two full-mouth approaches to treating peri-implant mucositis, PD reduction reached 0.23 mm in a full-mouth scaling without chlorhexidine (Thone-Muhling et al. 2010). As these are the first data so far using GPAP as an adjunctive treatment in peri-implant mucositis, it is hard to compare them with other studies. Mixed-effect and regression analysis showed deeper PD at baseline led to greater PD reductions. Interestingly, the result also showed that lower BI levels tended to have greater PD reductions after therapy. It should be noted that the effects reported in this study may be mainly due to ultrasonic debridement plus oral hygiene improvement.

Although there were significant improvements in PD and BI through treatment, not all the deep pockets and bleeding sites were eliminated. The same outcomes have been reported in other studies (Porras et al. 2002; Thone-Muhling et al. 2010; Heitz-Mayfield et al. 2011). Explanations may be as follows. Firstly, the submucosal margin has a negative effect on PD reduction. A multiple regression analysis carried out in one study found the submucosal margin of restoration at baseline had a negative effect on pocket reduction (Heitz-Mayfield et al. 2011). Unfortunately, information on sub- or supra-mucosal margins was not recorded in this study. However, based on the authors' observation, most of the implants had submucosal margins. Secondly, excellent plaque control was not acquired even after three sessions of OHI reinforcements, which was evident in the large amount of visible plaque in several subjects. Thirdly, there may be host response heterogeneity to plaque and treatment provided.

Considering the insignificant adjunctive effect of GPAP, it may be possible that mechanical debridement is fairly effective at removing the plaque biofilms in peri-implant mucositis. Hence, in situations with deep pockets, narrow defects, or implant threads exposure where conventional mechanical debridement is hard to eliminate pathogenic biofilms, GPAP may show some additional effects (Sahrmann et al. 2012; Schar et al. 2013). Another possibility is that the power setting in our study was too mild to remove biofilms and hence not enough to show clinically significant improvement. The 5-sec duration for each site was adopted in this study based on previous studies and the recommendation of the manufacturer (Petersilka et al. 2003a,b,c; Sahm et al. 2011).

The complication of emphysema was not reported in this trial. It was shown that treating each site with GPAP for 5 sec is safe in peri-implant mucositis. Another concern is

possible GPAP damage to the implant surface. An *in vitro* study has shown that GPAP would not cause visible changes to either smooth or sand-blasted, large grit, and acid-attacked (SLA) surfaces under SEM (Schwarz et al. 2009).

In conclusion, within the limitations of the study, this pilot clinical trial suggests that non-surgical mechanical debridement may effectively control peri-implant mucositis and adjunctive GPAP treatment seems to have a limited beneficial effect as compared with mechanical debridement alone. However, further clinical trials with a large sample size are needed to confirm this preliminary observation.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1. A CONSORT flowchart of the enrollment, allocation, follow-up and analysis.