CLINICAL ORAL IMPLANTS RESEARCH

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Anti-infective therapy of peri-implantitis with adjunctive local drug delivery or photodynamic therapy: six-month outcomes of a prospective randomized clinical trial

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Key words: dental implants, laser, local antibiotics, local drug delivery, peri-implantitis, photodynamic therapy, surface decontamination

Abstract

Objective: To compare the adjunctive clinical effects in the non-surgical treatment of peri-implantitis with either local drug delivery (LDD) or photodynamic therapy (PDT).

Material and methods: Forty subjects with initial peri-implantitis, i.e. pocket probing depths (PPD) 4–6 mm with concomitant bleeding on probing (BoP) and marginal bone loss ranging from 0.5 to 2 mm between delivery of the reconstruction and pre-screening appointment were randomly assigned to two treatment groups. All implants underwent mechanical debridement with titanium curettes, followed by a glycine-based powder airpolishing. Implants in the test group (n = 20) received adjunctive PDT, whereas minocycline microspheres were locally delivered into the peri-implant pockets of control implants (n = 20). At sites with residual BoP, treatment was repeated after 3 and 6 months. The primary outcome variable was the change in the number of sites with BoP. Secondary outcome variables were changes in PPD, in clinical attachment level (CAL), and in mucosal recession (REC).

Results: After 3 months, implants of both groups yielded a statistically significant reduction ($P < 0.0001$) in the number of BoP-positive sites compared with baseline (LDD: from 4.41 ± 1.47 to 2.20 ± 1.28, PDT: from 4.03 ± 1.66 to 2.26 ± 1.28). After 6 months, complete resolution of mucosal inflammation was obtained in 15% of the implants in the control group and in 30% of the implants in the test group ($P = 0.16$). After 3 months, changes in PPD, REC, and modified Plaque Index (mPlI) were statistically significantly different from baseline ($P < 0.05$). No statistically significant changes ($P > 0.05$) occurred between 3 and 6 months. CAL measurements did not yield statistically significant changes ($P > 0.05$) in both groups during the 6-month observation time. Between-group comparisons revealed no statistically significant differences ($P > 0.05$) at baseline, 3 and 6 months with the exception of the mPlI after 6 months.

Conclusions: In cases of initial peri-implantitis, non-surgical mechanical debridement with adjunctive use of PDT is equally effective in the reduction of mucosal inflammation as with the adjunctive use of minocycline microspheres up to 6 months. Adjunctive PDT may represent an alternative treatment modality in the non-surgical management of initial peri-implantitis. Complete resolution of inflammation, however, was not routinely achieved with either of the adjunctive therapies.

Date:
Accepted 10 April 2012

To cite this article:
Schär D, Ramseier CA, Eick S, Arweiler NB, Sculean A, Salvi GE. Anti-infective therapy of peri-implantitis with adjunctive local drug delivery or photodynamic therapy: six-month outcomes of a prospective randomized clinical trial. *Clin. Oral Impl. Res.* **24,** 2013, 104–110
doi: 10.1111/j.1600-0501.2012.02494.x

Peri-implantitis has been defined as an inflammatory process that affects the soft tissues surrounding an osseointegrated implant in function with concomitant loss of supporting marginal bone (Albrektsson & Isidor 1994). Peri-implant mucositis, in contrast, is a reversible inflammatory reaction of the mucosa adjacent to an implant without bone loss (Albrektsson & Isidor 1994; Salvi et al. 2012). Colonization of oral implant surfaces with bacterial biofilms occurs rapidly (van Winkelhoff et al. 2000; Quirynen et al. 2006; Fürst et al. 2007; Salvi et al. 2007). The biofilm development seems to play an important role in altering the biocompatibility of the implant surface and, thus enhancing peri-implant disease development (Mombelli & Lang 1998). The composition of bacterial

biofilms associated with peri-implant mucositis and peri-implantitis was shown to be similar with the one associated with chronic periodontitis (Mombelli et al. 1987, 1988; Becker et al. 1990; Alcoforado et al. 1991; Rams et al. 1991; Leonhardt et al. 1999; Pontoriero et al. 1994; Salvi et al. 2012). Predominantly gram-negative anaerobic bacteria are found in sites with peri-implant diseases (Pontoriero et al. 1994; Augthun & Conrads 1997; Salcetti et al. 1997; Mombelli & Lang 1998; Leonhardt et al. 1999; Quirynen et al. 2002, 2006). Therefore, implant surface decontamination represents the basic objective in the treatment of peri-implantitis. However, the reduction in the bacterial load at sites with peri-implantitis by means of mechanical debridement alone remains difficult because of the design of the suprastructure and the topography of the implant surface.

Mechanical debridement alone with carbon fiber curettes or with the Vector® system (Dürr Dental, Bietigheim-Bissigen, Germany) slightly improved the bleeding tendency, but pocket probing depths (PPD) remain unchanged or worsened (Karring et al. 2005). These outcomes were confirmed in a study comparing non-surgical mechanical debridement of peri-implantitis lesions with either titanium curettes or with an ultrasonic device (Renvert et al. 2009). In that study, plaque and bleeding scores improved, however, no significant effects on PPD reduction were observed (Renvert et al. 2009). Consequently, adjunctive therapies to mechanical debridement alone, such as local drug delivery (LDD), use of antiseptics, and laser therapy have been advocated.

Beneficial effects on the adjunctive delivery of local antibiotics were reported. Mechanical implant surface debridement in conjunction with the placement of non-resorbable tetracycline-impregnated fibers yielded clinical benefits with respect to the reduction in PPD and bleeding tendency after 12 months (Mombelli et al. 2001). The improvement of clinical and microbiological parameters in the treatment of peri-implantitis lesions was also achieved with the adjunctive delivery of local resorbable antibiotics and chlorhexidine gel (Büchter et al. 2004; Renvert et al. 2004, 2006, 2008; Persson et al. 2006; Salvi et al. 2007).

Although the results of the studies mentioned above showed an improvement in the healing of peri-implantitis lesions, a complete resolution of peri-implant mucosal inflammation remained a rare event.

Photodynamic therapy (PDT) has received increasing attention in dentistry in recent years (Konopka & Goslinski 2007). The application of photosensitive dyes into pockets and their activation with light of a specific wavelength results in the killing of periodontal pathogens. Outcomes of clinical studies in subjects with chronic periodontitis revealed beneficial effects of PDT on the reduction in gingival inflammation (Andersen et al. 2007; Braun et al. 2008; Christodoulides et al. 2008; Chondros et al. 2009).

The effects of toluidine blue O (TBO)-mediated PDT on the treatment of ligature-induced peri-implantitis were investigated in dogs. The results revealed a reduction in bacterial counts of *Prevotella intermedia/nigrescens*, *Fusobacterium* spp., and *beta-haemolytic Streptococcus* (Shibli et al. 2003). On the other hand, no differences with respect to bacterial counts reduction in *Prevotella* sp., *Fusobacterium* spp., and *beta-haemolytic Streptococcus* were found comparing the treatment of ligature-induced peri-implantitis with azulene-mediated-PDT with that of a mucoperiosteal flap and adjunctive irrigation of chlorhexidine (Hayek et al. 2005).

Studies on the non-surgical treatment of peri-implantitis with adjunctive PDT in humans, however, are lacking.

Hence, the aim of this prospective randomized clinical trial was to compare the adjunctive clinical effects of PDT with those of adjunctive LDD in the non-surgical treatment of initial peri-implantitis.

Material and methods

Subject selection

Subjects from the Department of Periodontology of the University of Bern, Switzerland and subjects referred from private practice were included in the study. The research protocol was submitted to and approved by the Ethical Committee of the Canton Bern (KEK Number 79/10). The study was carried out in accordance with the ethical principles of the World Medical Association Declaration of Helsinki.

The following inclusion criteria were applied:

(1). Age $\geq$18 years
(2). Absence of relevant medical conditions
(3). Partially edentulous subjects with healthy or treated periodontal conditions enrolled in a regular maintenance care program
(4). Initial peri-implantitis defined as:
  (a) pocket probing depth (PPD) of 4–6 mm with concomitant bleeding on probing (BoP) at $\geq$1 peri-implant site and
  (b) radiographic bone loss ranging from 0.5 to 2 mm between delivery of the prosthetic reconstruction and pre-screening appointment
(5). Implant in function for $\geq$1 year
(6). Solid-screw tissue level titanium implants with a sandblasted and acid-etched (SLA) surface (Straumann®; Dental Implant System, Institut Straumann AG, Basel, Switzerland)
(7). Full-Mouth Plaque Score (FMPS) $\leq$25
(8). Full-Mouth Bleeding Score (FMBS) $\leq$25

Subjects were excluded on the basis of the following criteria:

(1). Peri-implant mucositis defined as absence of radiographic marginal bone loss between delivery of the prosthetic reconstruction and pre-screening appointment
(2). Pregnant or lactating females
(3). Tobacco smoking
(4). Uncontrolled medical conditions
(5). Untreated periodontal conditions
(6). Use of systemic antibiotics in the past 3 months
(7). Use of systemic antibiotics for endocarditis prophylaxis
(8). Subjects chronically treated (i.e. 2 weeks or more) with any medication known to affect soft tissue conditions (e.g. phenytoin, calcium antagonists, cyclosporin, coumadin, and non-steroidal anti-inflammatory drugs) within 1 month of the baseline examination
(9). Radiation therapy in the head and neck area
(10) Infectious diseases, such as HIV, TB, hepatitis
(11) Drug and alcohol abuse
(12) Failure to sign written informed consent

Null hypothesis

No statistically significant differences are observed with respect to the clinical parameters (e.g. BoP, PPD, REC, CAL) between the two treatment modalities (i.e. adjunctive PDT vs. adjunctive LDD).

Primary and secondary outcome variables

The primary outcome variable was the change in the number of peri-implant sites with BoP. Secondary outcome variables were the changes in PPD, mucosal recession (REC), and clinical attachment level (CAL).

Sample size calculation

A sample size of 20 subjects per group resulted in a power of 63% to detect a mean

difference of one BoP-positive site (of six sites per implant) with a standard deviation of 1.3 (Fisher's exact test). The calculated means and standard deviations were based on the 3-month outcomes by Schwarz et al. (2005).

Study design

The study was designed and conducted as a prospective randomized clinical trial of 12 months duration. Subjects were recruited from August 2010 to March 2011. A total of 40 subjects signed an informed consent. Periapical radiographs were taken at the prescreening appointment to confirm peri-implant bone loss. The subjects were assigned to the test or control group by a computer-generated randomization table. Each group included 20 subjects. Only one implant fulfilling the inclusion criteria was treated in each subject. If additional implants in the same subject were affected by peri-implantitis, treatment was provided according to the same protocol.

All subjects were enrolled in a regular maintenance care program and displayed high levels of self-performed plaque control.

Assessment of clinical parameters

One blinded and calibrated examiner (C.A.R.) assessed the following outcome variables at six sites per implant (e.g. disto-buccal, buccal, mesio-buccal, disto-oral, oral, mesio-oral) at baseline, 3 and 6 months:

(1). pocket probing depth (PPD)
(2). clinical attachment level (CAL)
(3). mucosal recession (REC) from the implant shoulder
(4). bleeding on probing (BoP) (Lang et al. 1986)
(5). modified Plaque Index (mPlI) (Mombelli et al. 1987).

The measurements were performed with a color-coded periodontal probe with millimeter markings (UNC15; Hu-Friedy, Chicago, IL, USA).

Minimization of bias

A computer randomization of the treatment modalities for each subject was done. To minimize potential bias, the calibrated examiner assessing the clinical parameters was masked to each subject's treatment assignment.

The treatment provider (D.S.) was a different person from the calibrated clinical examiner (C.A.R.). Following disclosure of the results, the calibrated clinical examiner and the statistician were unblinded.

Treatment of peri-implantitis

All treatment procedures were provided by the same operator (D.S.).

At baseline, all subjects were instructed in the use of superfloss (Superfloss Oral-B, Procter & Gamble, Cinncinati, Ohio and Emoform Duofloss, Natim Handels GmbH, St. Stefan, Austria) by adopting a circular cleaning technique around the neck of the implant. Before starting with mechanical debridement, the peri-implant soft tissues were anesthetized with articaine (Ubistesin™; 3M ESPE AG, Seefeld, Germany). Mechanical debridement was carried out with titanium currettes (Deppeler SA, Rolle, Switzerland) and a glycine-based powder air-polishing for subgingival biofilm removal (Air-Flow Master®, Perio Powder®, Perio-Flow® nozzle; E.M.S. Electro Medical Systems SA, Nyon, Switzerland). The movements of the handpiece with the flexible plastic tip were carried out in a circumferential mode parallel to the implant axis without contact with the implant surface.

Implants in the test group received adjunctive PDT. This was performed with a set-up for PDT (HELBO®; Photodynamic Systems GmbH, Wels, Austria), including a hand-held diode laser (HELBO® TheraLite Laser, HELBO® 3D Pocket Probe; Photodynamic Systems GmbH) with a wavelength of 660 nm and a power density of 100 mW. The dye phenothiazine chloride (HELBO® Blue Photosensitizer; Photodynamic Systems GmbH) was applied submucosally from the bottom to the top of the peri-implant pockets and was left *in situ* for 3 min. Subsequently, the pockets were irrigated with 3% hydrogen peroxide according to the manufacturer's instructions. Each pocket was exposed to the laser light for 10 s. Adjunctive PDT was repeated 1 week later according to the manufacturers' instructions. Subjects were instructed to continue flossing the day after treatment.

Implants in the control group received adjunctive delivery of one unit-dosage of minocycline hydrochloride microspheres (Arestin®; HANSAmed Ltd, Ontario, Canada). Each unit-dosage cartridge delivers minocycline hydrochloride microspheres equivalent to 1 mg of minocycline. As with the implants in the test group, prior to Arestin® application the pocket was irrigated with 3% hydrogen peroxide. Subjects in the control group were instructed to discontinue submucosal flossing for 10 days to avoid mechanical removal of the minocycline microspheres.

Check-ups and reinforcement of oral hygiene instructions followed at week 1, 2, 4, and 8. Clinical follow-up assessments were performed after 3 and 6 months from baseline. If BoP at one or more peri-implant sites after 3 and 6 months was recorded, an additional treatment procedure equivalent to initial therapy was provided.

Data analysis

Only one implant per subject was included in the study. Therefore, each variable was analyzed on a subject level.

Descriptive statistics present an overview of the study sample. Mean values and standard deviations (SD) were calculated for every variable and for every assessment timepoint. Mean values ± SD of the parameters assessed around implants in the test group (PDT) and in the control group (LDD) were compared with the unpaired student's *t*-test. Levels of significance within each group between baseline and the 3 and 6 months assessments were calculated with the paired student's *t*-test and the Wilcoxon's signed rank test.

The difference in proportion of subjects with a history of treated periodontitis was tested using the chi-square test. The Mann–Whitney *U*-test was used to assess the differences in the mean number of implants and in the mean number of implants with peri-implantitis between subjects in the test and control group.

The level of significance was set at $\alpha = 0.05$.

Results

A total of 40 subjects with at least one implant diagnosed with initial peri-implantitis were recruited for the study. All subjects completed the observation period of 6 months. Each group consisted of 20 subjects. Baseline demographics including mean age and age range of the subjects and time after implant placement are summarized in Table 1.

A statistically, significantly higher ($P = 0.002$) proportion of subjects who received adjunctive PDT (18/20) had a history of treated periodontitis compared with that in the control group (8/20). Moreover, subjects in the PDT group had a statistically, significantly higher mean number of implants (3.5 vs. 1.9, $P = 0.003$) and a statistically, significantly higher mean number of implants with peri-implantitis (2.1 vs. 1.2, $P = 0.009$) compared with those in the LDD group.

Bleeding on probing

Table 2 presents the mean values ± SD of BoP-positive sites at baseline and after 3 and 6 months. At baseline, the mean number of

Table 1. **Demographics of the study sample at baseline**

	All	Local drug delivery (LDD) group (control)	Photo dynamic therapy (PDT) group (test)
Number of subjects	40	20	20
Gender (male/female)	20/20	10/10	10/10
Mean age (years) (range)	58 (27–78)	57 (29–75)	59 (27–78)
Mean time (years) after implant placement (range)	7.4 (2.6–15)	7.2 (2.6–15)	7.3 (4–14.8)
Subjects with a history of treated periodontitis	26	8	18
Number of implants placed	107	37	70
Mean number of implants per subject	2.7	1.9	3.5
Number of implants with peri-implantitis	67	24	43
Mean number of implants per subject with peri-implantitis	1.8	1.2	2.1

Table 2. **Mean number of BoP-positive sites ± SD at each implant at baseline, 3 and 6 months**

	Baseline	3 months	6 months
LDD group (n = 20)	4.41 ± 1.47	2.20 ± 1.28*	2.10 ± 1.55¶
PDT group (n = 20)	4.03 ± 1.66	2.26 ± 1.28*	1.51 ± 1.41¶

*statistically significant change from baseline to 3 months.
¶statistically significant change from baseline to 6 months.
LDD, local drug delivery; PDT, photo dynamic therapy; SD, standard deviation.

BoP-positive sites per implant amounted to 4.03 ± 1.66 in the test group and to 4.41 ± 1.47 in the control group. No statistically significant difference ($P > 0.05$) was observed at baseline between test and control groups. Therapy resulted in a statistically significant reduction ($P < 0.0001$) in BoP-positive sites in both groups after 3 months. The achieved reduction was 50% in the LDD and 44% in the PDT group, respectively. Again, no statistically significant difference ($P > 0.05$) between groups was observed. Almost no changes were observed in both groups from 3 to 6 months. The reduction in BoP-positive sites after 6 months was 52% in the control and 63% in the test group, respectively. The between-group difference after 6 months did not reach statistical significance ($P > 0.05$).

A complete resolution of mucosal inflammation after 3 months was found in two (10%) subjects in the control group and in two (10%) subjects in the test group ($P = 0.39$). After 6 months, the corresponding values were three (15%) in the control group and six (30%) in the test group, respectively ($P = 0.16$).

Pocket probing depth

Mean values ± SD of PPD at baseline and after 3 and 6 months are summarized in Table 3. Mean baseline PPD was 4.39 ± 0.77 mm at implants in the control and 4.19 ± 0.55 mm at implants in the test group, respectively. A statistically significant reduction ($P < 0.02$) in PPD was found between baseline and 3-month follow-up (LDD group: 0.46 mm, PDT group: 0.27 mm) as well as between baseline and 6-month follow-up ($P < 0.005$) (LDD group: 0.49 mm, PDT group: 0.36 mm). The between-group comparison revealed no statistically significant difference ($P > 0.05$) at baseline, 3 and 6 months.

Clinical attachment level

Table 4 presents the mean CAL ± SD values at baseline, 3 and 6 months. Baseline CAL amounted to 2.72 ± 0.72 mm at implants in the control group and to 2.66 ± 0.73 mm at implants in the test group. No statistically significant difference was observed neither between baseline and the follow-up assessments ($P > 0.05$) nor between implants in the test and the control groups at any time point ($P > 0.05$).

Mucosal recession

Mean values ± SD of the mucosal recessions at baseline, 3 and 6 months are presented in Table 5. Baseline values were 1.68 ± 1.04 mm in the control group and 1.53 ± 0.91 mm in the test group, indicating that most of the crown margins were slightly submucosally and could be located with a periodontal probe. Changes in mucosal recession were statistically, significantly different in both groups between baseline and the 3-month ($P < 0.02$) as well as between baseline and the 6-month ($P < 0.05$) assessments, respectively. No statistically significant difference ($P > 0.05$) was found between groups at baseline, 3 and 6 months.

Modified Plaque Index

Mean values ± SD of the mPlI are presented in Table 6. Oral hygiene instructions resulted in a statistically significant reduction ($P < 0.03$) between baseline and the 3- and 6-month evaluations at implants in both groups. Again, no statistically significant difference ($P > 0.05$) was found between implants in the test and control groups at baseline and after 3 months. After 6 months, implants in the test group harbored no detectible amounts of bacterial plaque ($P < 0.0001$) compared with those in the control group.

Discussion

The aim of this prospective randomized trial was to compare the clinical outcomes of PDT with LDD, both as an adjunct to non-surgical mechanical debridement in subjects with initial peri-implantitis. Treatment was performed at baseline and was repeated at BoP-positive sites after 3 and 6 months. The outcomes demonstrated that both treatment modalities were comparable with respect to the reduction in mucosal inflammation, PPD, and gain of clinical attachment up to 6 months. Hence, the null hypothesis could not be refused.

Based on the fact that therapy of peri-implantitis with mechanical debridement alone was shown to have minimal impact on the reduction in mucosal inflammation, PPD, and microbiological parameters, adjunctive local delivery of minocycline microspheres was selected as control therapy.

The effect of locally delivered minocycline microspheres as an adjunct to non-surgical mechanical debridement with carbon fiber currettes was investigated in a case series of peri-implantitis lesions (Salvi et al. 2007). Although the results of that study showed a significant reduction in the percentage of mucosal inflammation and reduction in PPD over 12 months, the need for additional surgical intervention could not be excluded in some cases (Salvi et al. 2007).

In a comparative study, the clinical adjunctive effects of repeated local delivery of minocycline microspheres was compared with that of chlorhexidine gel application in subjects with peri-implantitis (Renvert et al. 2008). Adjunctive minocycline microspheres delivery resulted in a statistically superior reduction in PPD and bleeding sites compared with that of chlorhexidine gel application (Renvert et al. 2008).

Table 3. **Mean pocket probing depth (mm) ± SD at each implant at baseline, 3 and 6 months**

	Baseline	3 months	6 months
LDD group (n = 20)	4.39 ± 0.77	3.93 ± 0.59*	3.90 ± 0.78¶
PDT group (n = 20)	4.19 ± 0.55	3.92 ± 0.61*	3.83 ± 0.58¶

*statistically significant change from baseline to 3 months.
¶statistically significant change from baseline to 6 months.
LDD, local drug delivery; PDT, photo dynamic therapy; SD, standard deviation.

Table 4. **Mean clinical attachment level (mm) ± SD at each implant at baseline, 3 and 6 months**

	Baseline	3 months	6 months
LDD group (n = 20)	2.72 ± 0.72	2.62 ± 0.68	2.53 ± 0.65
PDT group (n = 20)	2.66 ± 0.73	2.66 ± 0.83	2.50 ± 0.77

LDD, local drug delivery; PDT, photo dynamic therapy; SD, standard deviation.

Table 5. **Mean mucosal recession (mm) ± SD at each implant at baseline, 3 and 6 months**

	Baseline	3 months	6 months
LDD group (n = 20)	1.68 ± 1.04	1.30 ± 0.10*	1.38 ± 1.02¶
PDT group (n = 20)	1.53 ± 0.91	1.26 ± 0.88*	1.33 ± 0.90¶

*statistically significant change from baseline to 3 months.
¶statistically significant change from baseline to 6 months.
LDD, local drug delivery; PDT, photo dynamic therapy; SD, standard deviation.

Table 6. **Mean mPII ± SD at each implant at baseline, 3 and 6 months**

	Baseline	3 months	6 months
LDD group (n = 20)	0.21 ± 0.27	0.01 ± 0.04*	0.03 ± 0.15¶
PDT group (n = 20)	0.13 ± 0.21	0.01 ± 0.04*	0.00 ± 0.00¶§

*statistically significant change from baseline to 3 months.
¶statistically significant change from baseline to 6 months.
§statistically significant difference between groups.
LDD, local drug delivery; PDT, photo dynamic therapy; SD, standard deviation; mPII, modified plaque index.

Controversial results exist with respect to the use of adjunctive PDT in the treatment of periodontitis lesions. In particular, the most frequently reported clinical benefit of PDT was the reduction in gingival inflammation (Andersen et al. 2007; Braun et al. 2008; Christodoulides et al. 2008; Chondros et al. 2009; Ge et al. 2011). The outcomes of two reviews, on the other hand, concluded that there is insufficient evidence to confirm a benefit of PDT for the treatment of periodontitis (Azarpazhooh et al. 2011; Herrera 2011). Differences in the study samples and in the treatment protocols, however, precluded to draw robust conclusions.

Scarce evidence is available concerning the treatment of peri-implantitis lesions with PDT. *In vitro* studies (Dobson & Wilson 1992; Haas et al. 1997) and results from one experimental study (Shibli et al. 2003) documented the antibacterial effect of PDT on periodontal pathogens detected in peri-implant pockets. Moreover, treatment of experimentally induced peri-implantitis with azulene-mediated-PDT resulted in a comparable clinical success as access flap surgery with adjunctive irrigation of chlorhexidine (Hayek et al. 2005).

Although a significantly higher proportion of subjects who received adjunctive PDT had a history of treated periodontitis when compared with those in the control group, the clinical outcomes after 6 months were comparable. Outcomes from comparative studies revealed that implants in subjects treated for periodontitis may experience more biological complications compared with those in non-periodontitis subjects (Hardt et al. 2002; Karoussis et al. 2003). Furthermore, subjects with treated periodontitis not compliant with a regular maintenance care program displayed a higher incidence of peri-implant bone loss and implant loss over a follow-up period of 10 years (Roccuzzo et al. 2010, 2012). All subjects in the present study were enrolled in a regular supportive periodontal therapy (SPT) program. This highlights the importance of SPT in enhancing the long-term outcomes of implant therapy in subjects susceptible to periodontitis.

Nevertheless, based on the outcomes of the present study, adjunctive PDT may represent an alternative treatment modality to local delivery of minocycline microspheres in the non-surgical management of initial peri-implantitis.

In this study, optimal conditions in terms of full-mouth plaque and bleeding scores (i.e. FMPS and FMBS $\leq$25%) were instituted, before active therapy was delivered. Thus, in this study minimal bacterial reservoirs were present, before anti-infective therapy of peri-implantitis was initiated. It was reported that in partially edentulous subjects microbial transmission from residual periodontal pockets to implant surfaces represents a common phenomenon (Mombelli et al. 1995; Quirynen et al. 1996, 2006; Sumida et al. 2002; De Boever & De Boever 2006; Fürst et al. 2007; Salvi et al. 2008). Moreover, during the first 6 months of the study, excellent levels of self-performed plaque control contributed significantly to the reduction in mucosal inflammation.

Mechanical debridement with titanium currettes and a glycine-based powder airpolishing, followed by irrigation with 3% hydrogen peroxide was the first step for all implants in this study. A significant reduction in bleeding scores was reported when the rough implant surface was debrided with a glycine-based air-abrasive device compared with mechanical debridement with carbon fiber curettes and local delivery of chlorhexidine (Sahm et al. 2011).

Furthermore, all peri-implant sites were irrigated with 3% hydrogen peroxide. Hydrogen peroxide was reported to be effective against bacterial lipopolysaccharides attached to the implant surface (Zablotsky et al. 1992).

In this study, mucosal inflammation was completely resolved in 10% of implants in each group after 3 months. Complete resolution of mucosal inflammation, however, was achieved in 30% of implants receiving adjunctive PDT and in 15% of implants with adjunctive LDD after 6 months. This means that 85% of implants in the control group and 70% of implants in the test group were retreated after 6 months. So far, non-surgical anti-infective treatment protocols failed to yield complete resolution of mucosal inflammation after observation periods from 6 to 12 months (Mombelli & Lang 1992; Karring et al. 2005; Salvi et al. 2007; Renvert et al. 2008, 2009; Sahm et al. 2011).

In agreement with the outcomes from studies adopting different anti-infective protocols in subjects with peri-implantitis, this study supports the fact that peri-implant soft tissue healing was mostly pronounced in the first 3 months (Renvert et al. 2008, 2009). In the present study, significant reductions in PPD were observed around implants in both treatment groups in the first 3 months after therapy ranging from 0.27 to 0.46 mm. No additional significant reductions occurred between 3 and 6 months. Greater reductions in PPD (e.g. 0.8 mm) were reported after 3 months in the non-surgical treatment of peri-implantitis lesions with comparable baseline PPD to those in this study by using an air-abrasive device or mechanical debridement and local chlorhexidine application (Sahm et al. 2011). In the non-surgical treatment of peri-implantitis with local delivery of minocycline microspheres, a mean PPD reduction of 1 mm was reported after 3 months around implants with mean baseline PPD (e.g. 4.5 mm) comparable to those in this study (Salvi et al. 2007). On the other hand, at sites with mean baseline PPD of 3.85 and 3.87 mm, reductions in PPD of 0.17 mm and 0.19 mm were achieved 3 months after treatment of peri-implantitis with local delivery of minocycline microspheres or application of chlorhexidine gel, respectively (Renvert et al. 2008). In that study, however, no mechanical debridement preceded the application of the antiseptic drugs (Renvert et al. 2008).

Such differences among study outcomes may be explained, at least in part, by different frequency distributions of baseline PPD and/or the invasiveness of the treatment protocols.

In this study, although mucosal recessions increased significantly in both groups after 3 months, no significant changes were observed with respect to CAL gain after 3 and 6 months. This indicated that PPD reduction was accompanied by shrinkage of the marginal mucosa rather than gain of clinical attachment.

In conclusion, the outcomes of this randomized clinical study demonstrated that both treatment modalities yielded comparable reductions in peri-implant mucosal inflammation and PPD up to 6 months. Complete resolution of inflammation, however, was not routinely achieved with either of the adjunctive therapies.

Acknowledgement: The study was funded by Bredent Medical GmbH & Co. KG, Geschäftsbereich HELBO, Walldorf, Germany. The authors gratefully acknowledge the statistical expertise of Mr. Walter B. Bürgin, Biomed. Ing.

Conflict of interest: The authors do not report any conflict of interest related to this study.

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