

Comparison of two different techniques used for the maintenance of peri-implant soft tissue health: a pilot randomized clinical trial

Logien Al Ghazal, Jeffery O'Sullivan, Noel Claffey and Ioannis Polyzois

Department of Restorative Dentistry and Periodontology, Dublin Dental University Hospital Trinity College, Dublin, Ireland

ABSTRACT

Objectives: The aim of this pilot study was to compare the effectiveness of two different methods of debridement on maintaining and improving peri-implant soft tissue health over a period of 12 months.

Materials and methods: Twenty adult patients (25 implants) were enrolled in a randomized, single-blinded, parallel group clinical trial. All implants included showed no signs of pathologic bone loss. Patients were scheduled to be reviewed every 3 months over a 12 months period. Nine patients (15 implants) were randomly allocated to a test group and treated with a low abrasive air polishing powder (Air-Flow[®] Perio, EMS) (AFP) and another nine (10 implants) to a control group and treated with titanium curettes (TC). Peri-implant crevicular fluid samples were analyzed to quantitatively measure the concentration of six interleukins (IL-6, IL-8, IL-1 β , TNF, IL-10 and IL-12). A multilevel analysis was used to test the comparison between the two treatments. The same analysis was used to study the relationship between clinical parameters and cytokines while controlling for confounding factors.

Results: There was no significant difference in bleeding on probing (BOP) between the two treatment methods ($p = .35$). Both debridement techniques resulted in a similar reduction of BOP (40.04% and 39.93%). IL-6 was the only cytokine of the six investigated that demonstrated a correlation with a clinical parameter (BOP) ($p = .05$).

Conclusions: Both treatment methods were proven to be effective in reducing peri-implant inflammation and preventing further disease progression. Some cytokines may act as markers for peri-implant disease as the present study showed a significant relationship between IL-6 and BOP.

ARTICLE HISTORY

Received 18 January 2017

Revised 19 June 2017

Accepted 26 June 2017

KEYWORDS

Peri-implant mucositis; cytokines; maintenance; multilevel analysis

Introduction

Dental implants are now commonly used for replacing missing teeth in partially or fully edentulous patients. As it happens with teeth, inflammation and disease progression around implants may eventually lead to their failure. It is now believed that peri-implant tissues respond to plaque in a manner similar to natural teeth [1].

Peri-implant diseases represent a 'collective term for inflammatory reactions in the tissues surrounding the implants [2]. Peri-implant mucositis has been defined as the presence of inflammation of the mucosa adjacent to a dental implant diagnosed with bleeding on gentle (<0.25N) probing and no sign of loss of supporting bone' [3]. In peri-implantitis, the inflammatory process affecting the tissues surrounding a functioning implant leads to resorption of peri-implant bone and these changes are often associated with suppuration and deepened pockets [4].

We now know that the presence of gingival inflammation may lead to a shift in the microbial environment inside the gingival sulcus which in turn may lead to the progression of gingivitis to periodontitis [5]. Lang and Berglundh [6] suggested a similar path for the progression of peri-implant disease. The main aetiological factor for peri-implant disease is plaque accumulation [1,7–12]. Additionally, a number of risk

indicators have also been identified for the development of peri-implant mucositis which include residual cement, smoking and not enrolling in maintenance visits [13].

Peri-implant disease has been recognized as an important complication due to the rise in its prevalence. A meta-analysis demonstrated a prevalence of 43% (CI: 32–54%) for peri-implant mucositis and 22% (CI: 14–30%) for peri-implantitis [3]. It was suggested that monitoring peri-implant health by recording clinical parameters and taking radiographs every year following the installation of the supra-structure is essential for the early detection of signs of peri-implant disease [3,4]. As with natural teeth, bleeding on probing (BOP) around dental implants is a key clinical parameter for identifying areas with peri-implant inflammation [3].

Cytokines have been shown to act as biomarkers for peri-implant disease, as higher concentrations were detected in advanced peri-implantitis cases than in cases with mild inflammation [14]. However, controversial evidence exists regarding which cytokines would correlate to disease progression [15].

IL-6 is considered a multiple function cytokine (pleiotropic) which acts both locally in the tissues and systemically on the liver to produce acute phase proteins [16]. A recent study demonstrated that IL-1, IL-6 and IL-8 values were elevated in

patients with progressing periodontal diseases [17]. Similar to periodontal disease, the levels of inflammatory cytokines were investigated around implants and were compared with natural teeth [18]. Cytokine levels such IL-8, TNF α and IL-6 were found to be two to four times higher around implants. Further work showed that IL-1 β and TNF- α rises when bone loss occurs around natural teeth and implants, thus the rise in the value of these two cytokines can be indicative of bone loss [19–21]. Another study demonstrated that the expression of IL-6 in peri-implant mucositis cases shows a significant rise when compared to healthy implant sites [22]. In a recent study, the levels of IL-6, IL-17 and IL-33 in the per-implant crevicular fluid around peri-implantitis sites were observed to be in higher concentration when compared to healthy peri-implant sites [23].

A number of different treatment modalities for the prevention and treatment of peri-implant mucositis have been investigated including the use of hand instruments like carbon fibre or titanium curettes [24,25]. The use of ultrasonic instruments for maintenance around implants was questioned due of the possibility of implant surface damage [18]. Recently, using devices like an Air-powder abrasive system resulted in significant reduction in plaque and bleeding scores and results have been promising [26,27].

Overall, early detection and treatment of peri-implant mucositis can prevent its progression to peri-implantitis as it has been demonstrated that peri-implant mucositis is fully reversible. Additionally, early detection and treatment of peri-implantitis dramatically improve the prognosis of the implants affected [28–31].

This study aims to compare the effect of two different debridement methods for maintaining or improving peri-implant soft tissue health and to investigate a possible relationship between inflammatory factor changes and changes in the clinical parameters over a period of one year.

Materials and methods

Study design

The study was conducted in Trinity College Dublin and was designed as a randomized, single-blinded, parallel group, clinical trial (as recommended by the VIII European Workshop

on Periodontology) [32], comparing the use of titanium curettes to the use of glycine powder air polishing (Air-Flow® Perio, EMS, Herrliberg, Switzerland) for maintaining peri-implant health and treating peri-implant mucositis. Ethical approval was gained from the Faculty of Health Sciences, Research Ethics Committee, Trinity College Dublin.

Study population

Subjects were recruited from a population of partially dentate patients that had received one or more dental implants in the Dublin Dental University Hospital (DDUH), Trinity College, within 5 years from the commencement of this study. The hospital electronic records were searched and to those 97 patients identified as possible candidates, an information leaflet and an invitation letter were sent by a gate-keeper. Both the information leaflet and invitation letter were sent by post. Patients were given 3 months to reply. In the invitation letter, patients were asked to reply either by e-mail or by calling the Dental hospital line in order to confirm their interest to participate in the study. Twenty-five patients showed interest in participating.

These 25 patients were contacted by phone and an appointment was arranged for them. This assessment took place 2 weeks before baseline examination by the primary investigator (L. A.). During assessment, the goals and objectives of the study were explained to the patients. Additionally, they were asked about recent antibiotic intake and an oral examination was performed to ensure that they fulfilled the inclusion criteria. Four of the patients were excluded before baseline examination. Three of them due to antibiotic intake and the fourth because it was difficult for the examiner to access the periodontal pockets due to the supra-structure design. One patient made it to the baseline examination but failed to return for the follow up visits

The study started with 20 patients (13 females and seven males) with an age range of 25–70 years. Out of the 20 patients, two were ex-smokers, and five were smokers who smoked 3–10 cigarettes per day. Two patients dropped out as they could not attend all appointments for personal reasons. Eighteen participants (25 implants) completed the study (Figure 1).

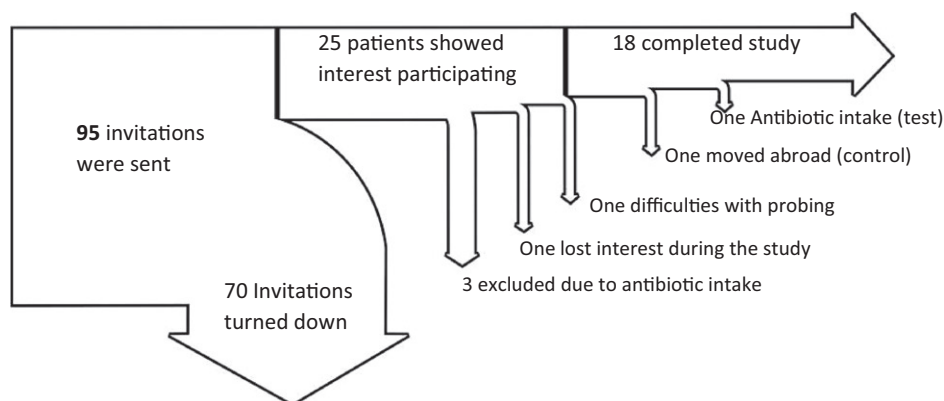


Figure 1. Flow chart.

Inclusion criteria

Each patient had to meet the following inclusion criteria:

- At least eighteen years of age.
- Patients with one or more single implant supported single crowns placed and restored in the Dublin Dental School and Hospital within the past five years. The peri-implant tissues had to be either healthy or have 1–6 bleeding sites without evidence of pathologic bone loss.
- Only implants replacing incisors canines and premolars were included.
- Bone loss of ≤ 2 mm assessed from the implant shoulder.

Exclusion criteria

- Uncontrolled diabetes.
- Patients on anti-inflammatory drugs.
- Unable to give consent to participate in the study.
- Children under 18 years of age.
- Pregnant or lactating women.

Randomization

Patients were allocated randomly to the two different treatment groups by a draw. Patients had to pick a folded paper with a number from a cardboard box. Patients who picked odd numbers were assigned to the control group, and those who picked even numbers were assigned to the test group. Both groups ended up with nine patients each. Ten implants were followed in the control group and 15 implants in the test group. A CONSORT checklist was used to report.

Baseline examination

All patients were given a detailed description of the study. At baseline, patients signed consent before starting clinical examination according to the Declaration of Helsinki. The visit included an update of their medical history, dental history, social history, oral hygiene practices as well as a detailed extra-oral and intra-oral examination, hard tissue charting and periodontal charting. The detailed periodontal charting was carried out for each patient and included full mouth probing depths, plaque and bleeding scores. Probing depth was measured by one previously calibrated examiner (IP) using a single end metal periodontal probe (UNC 15 colour-coded probe, Hu-Friedy, Chicago, IL). The examiner did not know which patient was allocated to which treatment group. Debridement for all patients was provided by a post-graduate student (L. A.).

Plaque scores were recorded using the O' Leary index [33]. All clinical parameters were measured at six sites (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual and disto-lingual). In the seventh European workshop of periodontology, it was suggested that BOP when probing with a force of 0.25 N is essential for the diagnosis of peri-implant mucositis [6]. BOP was assessed at six sites per implant (mesio, medio, disto/lingual and buccal). BOP %

around each implant was calculated by converting number of sites that bled out of six into a percentage. Those presented with 0% were considered healthy. The distribution of peri-implant mucositis among implants in both groups before and after treatment is shown in Table 1.

Peri-implant mucositis diagnosis was based on the presence of BOP and bone loss ≤ 2 mm assessed from the implant shoulder and taking into consideration the physiological remodelling process [6,32]. All subjects presented with the bone level around their implants at the first implant thread according to the pre-operative peri-apical radiograph at baseline. When available, radiographs taken during implant restoration were used to aid diagnosis. Peri-apical radiographs were viewed using (Planmeca Dimaxis, Helsinki, Finland). Peri-apical radiographs were taken at baseline and at 12 months and were compared for progression of bone loss. None of the implants included in the study show signs of pathologic bone loss at the end of the study period. The comparison was made through a consensus by two examiners (I. P.) and (L. A.). Table 2 presents the general scheme for both treatment groups.

Finally, the width of the keratinized mucosa (KM) was measured at the mid-buccal zone. All data were recorded and saved on the electronic data record system (Salud Dental Suite, Dublin, Ireland).

Sample collection

Peri-implant crevicular fluid was collected using perio-paperstrips (PerioPaperTM, Gingival Fluid Collection Strips, Ora-Flow, Smithtown, NY) from four sites around each implant. The area was isolated using cotton rolls and hygroformic saliva ejectors. The paperstrips were inserted into the peri-implant sulcus and left for 30s. Samples were then stored in a 1.5-ml Eppendorf tube and transferred immediately on dry ice and stored afterward in -80°C freezer. Samples were analysed on a LSR Fortessa using the commercially available (BD Cytometric Bead Array (CBA) Human Inflammatory Cytokines Kit, BD, San Jose, CA) for detection and quantitation of inflammatory cytokines. Therapeutic visits were arranged every 3 months for 12 months.

Table 1. Distribution of peri-implant mucositis before and after treatment.

	Control groups	Test groups	Total
Before treatment			
(BOP% = 0%)	3	1	4
(BOP% >0%)	7	14	21
After treatment			
(BOP% = 0%)	7	9	16
(BOP% >0%)	3	6	9
Total	10	15	25

Table 2. General scheme for both treatments.

Baseline	3 months	6 months	9 months	12 months
Radiograph	PICF sample	PICF sample	PICF sample	Radiograph
PICF sample	Clinical PM	Clinical PM	Clinical PM	PICF sample
Clinical PM	OH, advice	OH, advice	OH, advice	Clinical PM
OH, advice	Therapy	Therapy	Therapy	OH, advice
Therapy				Therapy

PICF: peri-implant crevicular fluid; PM: clinical parameters; OH: oral hygiene.

Treatment protocols for control and test groups

Patients were given oral hygiene instructions prior to treatment, instructions for the use of inter-dental aids such as dental floss, inter-dental brush and single-tufted brushes. No chemical plaque control agents were prescribed. According to the randomization of the patients, the control group received debridement using titanium curettes (TC), and the test group by the use of Air Flow[®] Perio (AFP).

Implants in the control group received debridement with the use of titanium curettes (Titan, Buffalo, NY). Debridement was done until no plaque could be detected.

In the test group, the implants were cleaned with the Air Flow[®] Perio (Air-Flow, Master Piezon[®], EMS Electro Medical Systems, Herrliberg, Switzerland). The Air Flow[®] utilizes air-powder mixture and water ejected through a disposable perio-flow nozzle tip which allows for its use sub-gingivally. The powder used for debridement was the Air-Flow[®] powder Perio, which utilizes extra-fine grains of glycine powder with low density. The Air Flow[®] unit was set according to the manufacturer instructions. The water was set to medium, and the powder chamber was filled to the indicated maximum powder level. The tip of the nozzle was inserted sub-gingivally, and each peri-implant surface was cleaned for 5 s as recommended by the instructions from the manufacturer.

The natural teeth for patients in the test and control groups were cleaned by an ultra-sonic device (EMS, Master Piezon[®], Nyon, Geneva, Switzerland). Polishing of implant supra-structure and existing teeth was provided using Nupro prophyl paste, Dentsply, Pennsylvania, PA and a slow speed prophyl handpiece with a brush tip.

Extraction of peri-implant crevicular fluid

Six out of the nine control patients and seven out of the nine test patients were randomly selected for cytokine analyses. One sample per implant was taken during each follow up visit, and from the peri-implant site with the deepest probing depth. Cytokine levels were determined for eight implants in the control group, and eleven implants in the test group. Mean and standard deviations for the concentrations of each cytokine (pg/ml) sampled from the deepest pocket were investigated.

Peri-implant crevicular fluid was extracted from the perio paper-strips by adding 180 µl of (Sigma-Aldrich[®], Dulbecco's phosphate-buffered saline) (PBS) to each Eppendorf tube. The Eppendorf containing the PBS and paper strip was

agitated by rocking for 10 min. The sample tube was then vortexed vigorously for 30 s prior to centrifugation for 10 min at 4–8 °C at 1200 rpm. Paper-strips were removed from the eppendorfs and discarded. The samples were then labelled and stored at –80 °C before further analysis.

The commercially available kit used for this study quantitatively measures six cytokines interleukin-8 (IL-8), interleukin-6 (IL-6), interleukin-1β (IL-1β), interleukin 10 (IL-10), interleukin 12p70 (IL-12p70) and tumour necrosis factor (TNF).

Statistical analysis

All statistical analysis was performed using statistical software R (version 3.3.3, Vienna, Austria) and software packages lme4 (Linear Mixed-Effects Models using 'Eigen' and S4) and arm (Data Analysis Using Regression and Multilevel/Hierarchical Models). The analyses were performed both at a patient and an implant level. The mean for clinical parameters for both groups were calculated. A multilevel analysis was used to investigate the effect that these two treatments had on specific clinical parameters as well as on the concentration of a selected number of cytokines while adjusting for other confounding factors such as age and smoking. A gradual multi-level analysis test was performed to eliminate nuisance parameters (non-significant variables).

Results

Eleven out of the 18 patients had a history of chronic periodontitis. From these 11 patients, six were in the control group and five in the test group and they all had their teeth extracted due to periodontitis. One participant lost his teeth due to trauma and the remaining six patients due to dental decay. For both groups, no pathologic radiographic bone loss had been observed during the 12-month period.

Clinical parameters around implants

Mean values of BOP % and PD around the implants for both groups at the four time points are presented in Table 3. Control and test groups demonstrated a similar reduction in the mean values of BOP%. Whereas, treatment resulted in a mean reduction of PD of the value of 0.8 mm for the control group and 0.9 mm for the test group over the

Table 3. BOP%, plaque score and PD for both groups during the 12-month period.

Visits	Group	% Sites BOP Mean (±SD)	Change	% Plaque Mean (±SD)	Change	PD mm Mean (±SD)	Change
Baseline	TC	50.03 (±38.51)		16.67 (±20.79)		5.0 (±0.81)	
	AFP	57.71 (±30.75)		35.56 (±28.80)		4.3 (±1.49)	
3 months	TC	28.33 (±32.44)	–21.70	6.66 (±11.65)	–10.01	4.8 (±1.31)	–0.2
	AFP	33.33 (±33.33)	–24.38	16.67 (±24.40)	–18.89	4.1 (±1.35)	–0.2
6 months	TC	13.33 (±15.31)	–36.70	26.67 (±11.65)	+ 10.00	4.6 (±1.17)	–0.4
	AFP	34.44 (±41.53)	–23.27	44.44 (±29.99)	+ 08.88	3.7 (±1.38)	–0.6
12 months	TC	9.99 (±16.10)	–40.04	8.33 (±11.79)	–08.34	4.2 (±0.78)	–0.8
	AFP	17.78 (±26.33)	–39.93	26.67 (±28.03)	–08.89	3.4 (±0.83)	–0.9

TC: titanium curettes; AFP: AIR Flow Perio.

12-month period. The mean values for the plaque scores per implant can be seen in also in [Table 3](#).

Full mouth clinical parameters

Full mouth BOP and plaque score were also recorded for all patients. It was noticed that both groups started with a similar average number of sites with BOP at baseline. A more gradual reduction was observed for the control group when compared to the AFP group. Whereas for full mouth plaque scores, a fair reduction was observed for both groups throughout the 12 months ([Table 4](#))

Patient level analysis

A significant relationship was recorded between percentage of BOP around the investigated implants in each patient and visit 4 ($p = .000283$) with percentages of BOP around the implants decreasing over time. A significant relationship was also observed between full mouth plaque scores and BOP ($p = .05$) with percentages of BOP around the implants decreasing as overall plaque scores decreased. At a patient level, none of the cytokines included showed any significant relationship with BOP ([Table 5](#)). No significant relationship was observed between any of the investigated variables and PDs at a patient level.

Implant level analysis

Percentage of BOP around the investigated implants

Primary results ([Table 6](#)) show that a significant relationship was recorded between percentage of BOP around the investigated implants and visit 4 ($p = .0000412$) with percentages of BOP around the implants decreasing over time. A significant relationship was also observed between full mouth plaque scores and BOP ($p = .001$) with percentages of BOP around the implants decreasing as overall plaque scores decreased. It is worth noting that the relationship between percentage of BOP per implant and IL-6 levels in the deepest pocket around these implants reached statistical significance

Table 4. Mean values for BOP and full mouth plaque score.

Visits	Group	% Full mouth BOP	% full mouth plaque score
Baseline	TC	24.98 (± 26.01)	44.27 (± 24.86)
	AFP	24.13 (± 17.53)	55.80 (± 16.45)
3 months	TC	18.30 (± 13.69)	36.60 (± 17.82)
	AFP	18.87 (± 13.58)	32.27 (± 7.66)
6 months	TC	7.30 (± 9.00)	34.20 (± 16.23)
	AFP	18.40 (± 22.80)	49.67 (± 15.66)
12 months	TC	2.60 (± 2.45)	34.80 (± 9.80)
	AFP	4.73 (± 4.13)	31.67 (± 10.65)

TC: titanium curettes; AFP: AIR Flow Perio.

Table 5. Results of model fit for the multilevel analysis BOP at a patient level.

Coefficient	Estimate	Std. error	t Value	p Value
Treatment	-0.06	0.08	-0.76	.46
Visit 2	-0.16	0.09	-1.74	.09
Visit 3	-0.23	0.09	-2.40	.021
Visit 4	-0.41	0.10	-3.99	.00028
Plaque score overall	0.07	0.03	2.01	.05
IL-10	0.08	0.04	1.78	.08

($p = .05$). The rest of the cytokines included, did not show a significant relationship with BOP.

Regarding the treatment effect on BOP, there was a difference between both treatments but having controlled for a number of variables this difference did not reach statistical significance ($p = .35$).

Probing depth around the investigated implants

As for the PD ([Table 7](#)), when after running the model, it showed that the effect of treatment was not significant ($p = .097$). A gradual decline in the mean value of PD was observed between the four visits. This effect was produced while controlling for other confounding variables ($p = .05$) and was shown to be significant. An effect was detected between bleeding scores and probing depths in the deepest sites around the treated peri-implant tissues. Bleeding scores increased with increasing probing depths ($p = .04$).

After adjusting for the confounding factors, there was a negative effect between the KM and the deepest PD. Meaning more width of KM, the shallower were the probing depths. The value although did not reach statistical significance ($p = .09$).

Discussion

The study herein included 18 patients (25 implants) which were randomly allocated to two groups. One control (debridement with Titan, Langer, 5/6 and 1/2, Buffalo, NY) and one-test debridement using Air Flow[®] Perio (Air-Flow, Master Piezon[®], EMS Electro Medical Systems, Herrliberg, Switzerland). The use of such material and method of debridement was shown to be safe on natural teeth as well as implants and also effective in biofilm removal [34–37]. In an earlier study, more patient comfort was reported with the use of Air-flow[®] when compared with manual debridement [38]. However, the level of comfort was not taken into consideration in the present study.

The clinical parameters considered were BOP and PD since their increasing values could be a sign of disease progression [6]. The results from the study herein demonstrated that

Table 6. Results of model fit for the multilevel analysis BOP at an implant level.

Coefficient	Estimate	Std. error	t Value	p Value
Treatment	-0.08	0.08	-0.95	.35
Visit 2	-0.12	0.08	-1.55	.12
Visit 3	-0.18	0.07	-2.47	.016
Visit 4	-0.36	0.08	-4.39	.00004
Plaque score overall	0.68	0.19	3.43	.001
IL-6	0.01	0.009	1.97	.05

Table 7. Results of model fit for the multilevel analysis PD at an implant level.

Coefficient	Estimate	Std. error	t Value	p Value
Treatment	0.72	0.41	1.76	.097
Visit 2	-0.03	0.26	-0.12	.90
Visit 3	-0.31	0.26	-1.16	.24
Visit 4	-0.54	0.28	-1.91	.05
Bleeding score	0.73	0.35	2.05	.04
Keratinized mucosa	0.10	0.06	-1.68	.09

both groups achieved a similar mean reduction in BOP and the difference between both treatments having controlled for other variables did not reach statistical significance. It was also observed that treatment resulted in a similar reduction in PD for both the control and the test groups. Similar results have been observed in earlier studies regarding BOP and PD reduction following the use of curettes, ultrasonics or glycine powder air-polishing devices to debride peri-implant sites [27,39]. The use of mechanical debridement over a number of visits as a treatment for peri-implant mucositis, has been shown to be effective [27,34,39–41]. Similar improvements were observed in the study herein as BOP and PD significantly improved over a 12-month period.

In a human clinical trial conducted on 29 patients diagnosed with peri-implant mucositis, the patients were randomly assigned to two treatment groups [25]. The control group received mechanical debridement alone, whereas the test group received the additional use of antiseptic therapy using 0.5% chlorhexidine gel. This trial showed no significant difference between the two groups in overall probing depth reduction after 3 months. From the data above, it can be concluded that mechanical debridement alone is sufficient to reduce PD values in sites diagnosed with peri-implant mucositis.

The effect of Air Flow[®] Perio on PD values was tested by Renvert et al. [42] in a clinical trial which included 21 patients diagnosed with peri-implantitis and were randomly allocated to two treatment groups. The first group received debridement of the implant surface using the Air Flow[®] Perio, and the second group received treatment with a laser monotherapy. The mean PD reduction was 0.9mm for the Air Flow[®] Perio and 0.8mm for the laser group. The mean reduction of PD in the Air Flow[®] Perio group was equal to the mean probing depth reduction in the study herein which was 0.9mm.

The present study showed a significant relationship between BOP and PD as the deeper the PD the higher was the bleeding score. Additionally, it seems that the wider the keratinized tissue buccal to the investigated implants the shallower were the PDs. Such observation could be of interest because it has been previously reported that higher BOP and plaque scores were noticed around implants with a thin KM [43–45]. We could speculate that the presence of adequate width of KM around implants may help in the prevention of peri-implant mucositis and peri-implantitis. Similar observations were reported in another study where PDs were deeper around implants with insufficient width of KM [46]. However, the findings of a later study [47] are in contrast with the findings of the study herein as they reported no significant relationship between PD and the width of keratinized mucosa. Finally, a recent study [48] demonstrated that more cases with peri-implant mucositis were present when KM was present. Overall, the significance of KM around dental implants to maintain peri-implant health remains controversial [49,50].

The relationship between a number of inflammatory cytokines and the clinical parameters was investigated as there have been suggestions that changes in the levels of certain inflammatory factors can be helpful for early diagnosis of

disease initiation/progression [18,19]. In a structured review by Preshaw and Taylor [51], it was demonstrated that increasing levels of inflammatory cytokines and their interaction around teeth are an important contribution to the pathogenesis of periodontitis. It was suggested that the over production of inflammatory cytokines by the host in response to bacteria may affect bone metabolism and cause bone resorption around natural teeth [52]. Since periodontitis and peri-implantitis are inflammatory lesions around teeth and implants, respectively, resulting in the loss of supporting bone, it has been suggested that the rise in cytokine levels such as IL-6, IL-8 and IL-12 in the peri-implant crevicular fluid may act as a markers of peri-implant bone loss [15,53]. In this study, one cytokine (IL-6) demonstrated a positive relationship with BOP.

The present study demonstrated low concentrations of IL-10, IL-12 and TNF for both groups which did not follow a certain trend of increase or decrease over the 12-month period. This could be attributed to the fact that both IL-12 and IL-10 are associated with the activation and inhibition of T-cell response, respectively, and are more related to the cellular mediated immunity which takes place during the later stages of inflammation and tissue destruction [54]. A number of studies reported that IL-10 and IL-12 were found in high concentrations only around implants with advanced peri-implantitis [15,21,55]. Regarding the TNF concentrations, earlier studies reported that this cytokine is elevated in sites around teeth and implants with signs of bone loss [19,20]. It was also detected in very high concentrations in cases with severe peri-implantitis [23,54]. In the present study, all implants included were either healthy or diagnosed with peri-implant mucositis and none of the fixtures showed signs of pathologic peri-implant bone loss. This could explain the low concentration of cytokines like IL-10, IL-12 and TNF.

A fluctuation in the mean concentrations of IL-1 β was observed in both groups. Some studies reported that the rise in the level of IL-1 β was present in cases of bone loss, while another study demonstrated that IL-1 β rises in areas with gingival inflammation [14,19,20,56]. It could be speculated that the fluctuation in the concentration levels of IL-1 β could reflect the different states of peri-implant mucosal inflammation at different time points rather than disease progression.

In previous studies, the concentrations of certain cytokines showed an increase in the presence of peri-implant disease [15,23]. The present study showed a positive relationship between the IL-6 concentrations and BOP. Statistical results showed no relationship between IL-6 and changes in PD. This observation is in agreement with results reported by Liskmann et al. [57]. In their study, the IL-6 in saliva was rising when there was an increase in bleeding, PD and gingival index.

Finally, It is well accepted that plaque is the main etiological factor for peri-implant disease [1,11], and it is no surprise that our data demonstrated a significant relationship between high full mouth plaque scores and BOP. This study clearly demonstrates the importance of plaque levels on the long-term supportive maintenance of dental implants as following treatment and resolution of inflammation, peri-implant health was maintained for 12 months.

To minimize selection bias, the participants in the study herein were randomly assigned to the study or the control group. The method of selection of the participants though might have introduced such bias as all the patients had been treated in the DDUH before, and as a result, might not have been a representative cohort of the wider population.

One of the main limitations of this study should be the limited number of observations. Additionally, inclusion of smokers and patients with history of periodontal disease might have significantly affected clinical measurements. A number of the individual characteristics of each patient and the effect that they might have had on the peri-implant tissue response thought were taken into account when running the multilevel model.

Another limitation of the study is that connection types and implant surface characteristics were not recorded. These implant characteristics might have affected plaque retention and BOP levels.

Conclusion

Providing maintenance treatment for implants over regular visits helps to maintain peri-implant health and reduce inflammation in the peri-implant pockets. As presented by the study herein, IL-6 has a positive relationship with the increase in BOP, suggesting that cytokine levels could reflect the state of inflammation. Cytokine levels can act as markers for peri-implant disease; however, clinical parameters remain the main criteria for diagnosis. Reliance on cytokines for defining disease state could be misleading. Similar studies in future should focus on larger sample sizes, clinical parameters and the effect of IL-6 on treatment success or failure.

The present study indicates that maintaining or improving peri-implant hygiene over a 12-month period helps to reduce the level of peri-implant inflammation. However, it could be recommended that to compare the effects of the two-debridement methods for the prevention of peri-implantitis a longer period of follow up would be required.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

- [1] Salvi GE, Aglietta M, Eick S, et al. Reversibility of experimental peri-implant mucositis compared with experimental gingivitis in humans. *Clin Oral Implants Res.* 2012;23:182–190.
- [2] Zitzmann NU, Berglundh T. Definition and prevalence of peri-implant diseases. *J Clin Periodontol.* 2008;35:286–291.
- [3] Jepsen S, Berglundh T, Genco R, et al. Primary prevention of peri-implantitis: managing peri-implant mucositis. *J Clin Periodontol.* 2015;42:S152–S157.
- [4] Lindhe J, Meyle J. Peri-implant diseases: Consensus Report of the Sixth European Workshop on Periodontology. *J Clin Periodontol.* 2008;35:282–285.
- [5] Bartold PM, Van Dyke TE. Periodontitis a host mediated disruption of microbial homeostasis unlearning learned concepts. *Periodontol 2000.* 2013;62:203–217.
- [6] Lang NP, Berglundh T. On Behalf of Working Group 4 of the Seventh European Workshop on Periodontology: periimplant diseases: where are we now? – Consensus of the Seventh European Workshop on Periodontology. *J Clin Periodontol.* 2011;38:178–181.
- [7] Sanz M, Alander J, Lazaro P, et al. Histo-pathologic characteristics of peri-implant soft tissues in Branemark implants with 2 distinct clinical and radiological patterns. *Clin Oral Implants Res.* 1991;2:128–134.
- [8] Berglundh T, Lindhe J, Marinello C, et al. Soft tissue reaction to de novo plaque formation on implants and teeth. An experimental study in the dog. *Clin Oral Implants Res.* 1992;3:1–8.
- [9] Ericsson I, Berglundh T, Marinello C, et al. Long-standing plaque and gingivitis at implants and teeth in the dog. *Clin Oral Implants Res.* 1992;3:99–103.
- [10] Pontoriero R, Tonelli MP, Carnevale G, et al. Experimentally induced peri-implant mucositis. A clinical study in humans. *Clin Oral Implants Res.* 1994;5:254–259.
- [11] Zitzmann NU, Abrahamsson I, Berglundh T, et al. Soft tissue reactions to plaque formation at implant abutments with different surface topography. An experimental study in dogs. *J Clin Periodontol.* 2002;5:456–461.
- [12] Abrahamsson I, Zitzmann NU, Berglundh T, et al. The mucosal attachment to titanium implants with different surface characteristics: an experimental study in dogs. *J Clin Periodontol.* 2002;29:448–455.
- [13] Renvert S, Polyzois I. Risk indicators for peri-implant mucositis: a systematic literature review. *J Clin Periodontol.* 2015;2:S172–S186.
- [14] Ataoglu H, Alptekin NO, Haliloglu S, et al. Interleukin-1beta, tumor necrosis factor-alpha levels and neutrophil elastase activity in peri-implant crevicular fluid. *Clin Oral Implants Res.* 2002;13:470–476.
- [15] Candel-Martí ME, Flichy-Fernández AJ, Alegre-Domingo T, et al. Interleukins IL-6, IL-8, IL-10, IL-12 and periimplant disease. An update. *Med Oral Patol Oral Cir Bucal.* 2011;16:518–521.
- [16] Akira S, Hirano T, Taga T, et al. Biology of multifunctional cytokines: IL 6 and related molecules (IL 1 and TNF). *FASEB J.* 1990;4:2860–2867.
- [17] Giannopoulou C, Kamma JJ, Mombelli A. Effect of inflammation, smoking and stress on gingival crevicular fluid cytokine level. *J Clin Periodontol.* 2003;30:145–153.
- [18] Nowzari H, Phamduong S, Botero EJ, et al. The profile of inflammatory cytokines in gingival crevicular fluid around healthy osseointegrated implants. *Clin Implants Dent Relat Res.* 2012;14:546–552.
- [19] Machtei EE, Oved-Peleg E, Peled M. Comparison of clinical, radiographic and immunological parameters of teeth and different dental implant platforms. *Clin Oral Implants Res.* 2006;17:658–665.
- [20] Cosgarea R, Dannewitz B, Sculean A, et al. Bacterial and inflammatory behaviour of implants in the early healing phase of chronic periodontitis. *Quintessence Int.* 2012;43:491–501.
- [21] Faot F, Nascimento GG, Bielemann AM, et al. Can peri-implant crevicular fluid assist in the diagnosis of peri-implantitis? A systematic review and meta-analysis. *J Periodontol.* 2015;86:631–645.
- [22] Ata-Ali J, Ata-Ali F, Galindo-Moreno P. Treatment of periimplant mucositis: a systematic review of randomized controlled trials. *Implant Dent.* 2015;24:13–11.
- [23] Severino VO, Beghini M, Araujo M, et al. Expression of IL-6, IL-10, IL-17 and IL-33 in the peri-implant crevicular fluid of patients with peri-implant mucositis and peri-implantitis. *Arch Oral Biol.* 2016;72:194–199.
- [24] Strooker H, Rohn S, Winkelhoff AJ. Clinical and microbiologic effects of chemical versus mechanical cleansing in professional supportive implant therapy. *Int J Oral Maxillofac Implants.* 1998;13:845–850.
- [25] Heitz-Mayfield LJA, Salvi GE, Botticelli D, On Behalf of the Implant Complication Research Group (ICRG), et al. Anti-infective treatment of periimplant mucositis: a randomised controlled clinical trial. *Clin Oral Implants Res.* 2011;22:237–241.

- [26] Maximo MB, De MAC, Santos VR, et al. Short-term clinical and microbiological evaluation of peri-implant diseases before and after mechanical anti-infective therapies. *Clin Oral Implants Res.* 2009;20:99–108.
- [27] Riben-Grundstrom C, Norderyd O, Andre U, et al. Treatment of peri-implant mucositis using a glycine powder air-polishing or ultrasonic device: a randomized clinical trial. *J Clin Periodontol.* 2015;42:462–469.
- [28] Lang NP, Wilson TG, Corbet EF. Biological complications with dental implants their prevention, diagnosis and treatment. *Clin Oral Implants Res.* 2011;11:146–155.
- [29] Lang NP, Berglundh T, Heitz-Mayfield L, et al. Group 4 Consensus statements and recommended clinical procedures regarding implant survival and complications. *Int J Oral Maxillofac Implants.* 2004;19:150–155.
- [30] Jepsen S, Berglundh T, Genco R, et al. Primary prevention of peri-implantitis: managing peri-implant mucositis. *J Clin Periodontol.* 2015;42:152–157.
- [31] Salvi GE, Zitzmann NU. The effects of anti-infective preventive measures on the occurrence of biologic implant complications and implant loss: a systematic review. *Int J Oral Maxillofac Implants.* 2014;29:292–307.
- [32] Sanz M, Chapple IL. Clinical research on peri-implant diseases: consensus report of Working Group 4. *J Clin Periodontol.* 2012;39:202–206.
- [33] O, Leary TJ, Drake BR, Naylor EJ. The plaque control record. *J Periodontol.* 1972;43:38.
- [34] Petersilka GJ, Steinmann D, Haberlein I, et al. Subgingival plaque removal in buccal and lingual sites using a novel low abrasive air-polishing powder. *J Clin Periodontol.* 2003;30:328–333.
- [35] Flemmig TF, Hetzel M, Topoll H, et al. Subgingival debridement efficacy of glycine powder air polishing. *J Periodontol.* 2007;78:1002–1010.
- [36] Flemmig TF, Arushanov D, Daubert D, et al. Randomized controlled trial assessing efficacy and safety of glycine powder air polishing in moderate-to-deep periodontal pockets. *J Periodontol.* 2012;83:444–452.
- [37] Schwarz F, Ferrari D, Popovski K, et al. Influence of different air-abrasive powders on cell viability at biologically contaminated titanium dental implants surfaces. *J Biomed Mater Res Part B Appl Biomater.* 2009;88:83–91.
- [38] Wennstrom JL, Dahlen G, Ramberg P. Subgingival debridement of periodontal pockets by air-polishing in comparison with ultrasonic instrumentation during maintenance therapy. *J Clin Periodontol.* 2011;38:820–827.
- [39] Moëne R, Decaillet F, Andersen E, et al. Subgingival plaque removal using a new air-polishing device. *J Periodontol.* 2010;81:79–88.
- [40] Trejo PM, Bonaventura G, Weng D, et al. Effect of mechanical and antiseptic therapy on peri-implant mucositis: an experimental study in monkeys. *Clin Oral Implants Res.* 2006;17:294–304.
- [41] Corbella S, Fabbro DM, Taschieri Siena DF, et al. Clinical evaluation of an implant maintenance-protocol for the prevention of peri-implant diseases in patients treated with immediately loaded full-arch rehabilitations. *Int J Dent Hyg.* 2011;9:216–222.
- [42] Renvert S, Lindahl C, Roos JAM, et al. Treatment of periimplantitis using an Er:YAG laser or an air-abrasive device: a randomized clinical trial. *J Clin Periodontol.* 2011;38:65–73.
- [43] Kim BS, Kim YK, Yun PY, et al. Evaluation of peri-implant tissue response according to the presence of keratinized mucosa. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;107:24–28.
- [44] Boynuegri D, Nemli SK, Kasko YA. Significance of keratinized mucosa around dental implants: a prospective comparative study. *Clin Oral Implants Res.* 2013;24:928–933.
- [45] Rocuzzo M, Grasso G, Dalmasso P. Keratinized mucosa around implants in partially edentulous posterior mandible: 10-year results of a prospective comparative study. *Clin Oral Implants Res.* 2016;27:491–496.
- [46] Zigdon H, Machtei EE. The dimensions of keratinized mucosa around implants affect clinical and immunological parameters. *Clin Oral Implants Res.* 2008;19:387–392.
- [47] Esper LA, Ferreira Junior SB, Kaizer RF, et al. The role of keratinized mucosa in peri-implant health. *Cleft Palate Craniofac J.* 2012;49:167–170.
- [48] Roos-Jansaker AM, Renvert H, Lindahl C, et al. Nine- to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. *J Clin Periodontol.* 2006;33:296–301.
- [49] Wennstrom JL, Derks J. Is there a need for keratinized mucosa around implants to maintain health and tissue stability? *Clin Oral Implants Res.* 2012;23:136–146.
- [50] Brito C, Tenenbaum HC, Wong BK, et al. Is keratinized mucosa indispensable to maintain peri-implant health? A systematic review of the literature. *J Biomed Mater Res.* 2014;102:643–650.
- [51] Preshaw PM, Taylor JJ. How has research into cytokine interactions and their role in driving immune responses impacted our understanding of periodontitis? *J Clin Periodontol.* 2011;38:60–84.
- [52] Cochran DL. Inflammation and bone loss in periodontal disease. *J Periodontol.* 2008;79:1569–1576.
- [53] Berglundh T, Zitzmann NU. Are peri-implantitis lesions different from periodontitis lesions? *J Clin Periodontol.* 2011;38:188–202.
- [54] Passoja A, Puijola I, Knuutila M, et al. Serum levels of interleukin-10 and tumour necrosis factor- α in chronic periodontitis. *J Clin Periodontol.* 2010;37:881–887.
- [55] Duarte PM, De MAC, Maximo MBB, et al. Differential cytokine expressions affect severity of peri-implant disease. *Clin Oral Implants Res.* 2009;20:514–520.
- [56] Heasman PA, Collins JG, Offenbacher S, et al. Changes in crevicular fluid levels of interleukin-1 beta, leukotriene B4, prostaglandin E2, thromboxane B2 and tumor necrosis factor alpha in experimental gingivitis in human. *J Periodontol.* 1993;28:241–247.
- [57] Liskmann S, Vihalemm T, Salum O, et al. Correlations between clinical parameters and interleukin-6 and interleukin-10 levels in saliva from totally edentulous patients with peri-implant disease. *Int J Oral Maxillofac Implants.* 2006;21:543–550.