MINERVA STOMATOLOGICA

VOLUME 66 · No. 6 · DECEMBER 2017

EDIZIONI · MINERVA · MEDICA

PUBBLICAZIONE PERIODICA BIMESTRALE - POSTE ITALIANE S.P.A. - SPED. IN A.P.D.L. 353/2003 (CONV. IN L. 27/02/2004 N° 46) ART. I, COMMA I, DCB/CN - ISSN 0026-4970 TAXE PERÇUE

Online version at http://www.minervamedica.it

Minerva Stomatologica 2017 December;66(6):255-66
DOI: 10.23736/S0026-4970.17.04054-7

ORIGINAL ARTICLE

A new multiple anti-infective non-surgical therapy in the treatment of peri-implantitis: a case series

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ABSTRACT

BACKGROUND: Peri-implantitis is a frequent disease that may lead to implant loss. The aim of this case series was to evaluate the clinical results of a new non-surgical treatment protocol.

METHODS: Fifteen patients with dental implants affected by peri-implantitis were treated with a multiple anti-infective non-surgical treatment (MAINST) which included two steps: 1) supra-gingival decontamination of the lesion and sub-gingival treatment with a controlled-release topical doxycycline; 2) after one week, a session of supra and sub gingival air polishing with Erythritol powder and ultrasonic debridement (where calculus was present) of the whole oral cavity was performed along with a second application of topical doxycycline around the infected implant. Primary outcome measures were: implant failure; complications and adverse events; recurrence of peri-implantitis; secondary outcome measure were presence of Plaque (PI), Bleeding on Probing (BOP), Probing Pocket Depth (PPD). Recession (REC), Relative Attachment level (RAL).

RESULTS: Neither implant failure nor complications nor adverse events were reported. Statistically ($P<0.01$) and clinically significant reductions between baseline and 1 year of PI (100% *vs.* 13.9%, 95% CI: 72.4% to 93.7%); BOP (98.5% *vs.* 4.5%, 95% CI: 85.4% to 98.5%) and PPD (7.89 *vs.* 3.16 mm, 95% CI: -5.67 to -3.77), were detected. At baseline, all 15 patients had a PPD>5 mm at the affected implant(s), whereas only 3.7% at 3-month follow-up a PPD>5 mm, and none at 6 and 12 months.

CONCLUSIONS: Within the limits of this study, the MAINST protocol showed improvement of clinical parameters for the treatment of peri-implantitis, which were maintained for up to 12 months.

(*Cite this article as:* Mensi M, Scotti E, Calza S, Pilloni A, Grusovin MG, Mongardini C. A new multiple anti-infective non-surgical therapy in the treatment of peri-implantitis: a case series. Minerva Stomatol 2017;66:255-66. DOI: 10.23736/S0026-4970.17.04054-7)

Key words: Oral implants - Anti-bacterial agents - Biofilms - Professional practice - Peri-implantitis.

Treatment of peri-implantitis is still a challenge. This study presents a new non-surgical approach that combines the use of a topical antibiotic and air-driven Erythritol powder for treating a contaminated implant surface. The technique proved to have good clinical results, with resolution of infection and stable outcomes, which were maintained for up to a year in a group of fifteen patients. An effective non-surgical approach would be less invasive and more cost-effective for patients.

The replacement of missing teeth with den-

tal implants is a predictable and worldwide choice of action in modern dentistry. However, a frequent biological complication associated with this treatment option is the inflammation of the tissues surrounding the implant, also known as mucositis and peri-implantitis.[1]

Mucositis has been defined as an inflammation of the peri-implant soft tissue without bone loss.[2] Signs of inflammation of the supporting tissues adjacent to an oral implant combined with bone loss has been described as peri-implantitis.[3] The diagnosis of peri-implantitis is based on increased probing pocket depth (PPD), presence of bleeding on probing (BOP) and/or suppuration (PUS) and evidence of progressive bone loss.[4]

In a recent systematic review [5] the authors concluded that the weighted mean prevalence of mucositis was 43% (95% CI: 32-54%), whereas the prevalence of peri-implantitis was estimated to be 22% (95% CI: 14-30%).

The formation of a complex biofilm on the implant surface has been recognized as the principle etiologic factor for both peri-implant diseases.[6] The composition of diseased peri-implant biofilm has been shown to be similar to the subgingival microbiota in subjects affected by chronic periodontitis.[7] A cause-effect relationship between bacterial plaque accumulation and the development of mucositis has been shown.[8] If this reversible condition is left untreated it may lead to peri-implantitis, with progressive destruction of the bone supporting the implant.[3] Therefore, preventive supportive therapy for maintaining healthy peri-implant tissues and immediate treatment of initial pathological conditions are of utmost importance.[9, 10] Lack of supportive therapy is associated with an increased risk of mucositis progressing to peri-implantitis.[11]

Unlike periodontitis, peri-implant lesions do not respond predictably to non-surgical or surgical treatment,[12] even though the inflammatory phase of peri-implant tissues clinically appears to be similar to that which occurs around natural teeth.[12, 13]

Despite the fact that both biofilm disruption and the lowering bacterial load are key factors in treating periodontal and peri-implant diseases, as of today, none of the suggested non-surgical treatments for peri-implantitis have been shown to give predictable outcomes.[12, 14] As hand or ultrasonic instrumentation have shown little clinical improvements,[15] the use of adjunctive anti-microbials has been suggested.

There is limited evidence on the efficacy of systemic antibiotics in the treatment of peri-implantitis [12] and systemic administration can have clinical and microbiological implications in terms of bacterial resistance and alteration of a patient's resident flora.[16, 17] Peri-implantitis lesions represent well-hidden defects, therefore controlled and sustained local drug delivery devices, originally developed for the treatment of localized periodontal lesions, have been used in the treatment of peri-implant infections.[13]

Significant reduction in BOP was found when mechanical therapy was combined with the use of a controlled-release tetracycline-containing fiber.[18] Furthermore, in a series of randomized controlled clinical trials, better outcomes have been seen when minocycline-containing microspheres were locally added,[19, 20] and sustained release of doxycycline, in addition to repeated mechanical debridement, has demonstrated a statistically significant increased reduction of PPD and probing attachment levels.[21]

Recently, an air-powered abrasive system using a low abrasive amino acid (glycine), has shown to be effective in the removal of biofilm without causing damage to the hard or soft tissues surrounding natural dentition.[22] Sahm *et al.*[23] in 2011 compared the effectiveness of a glycine-based powder air-polishing system against debridement with carbon curettes combined with chlorhexidine application in the non-surgical treatment of peri-implantitis. Air-polishing treatment resulted in significantly higher reductions in BOP. Similar reductions in BOP and PUS have been observed when the therapeutic effect of an Er:YAG laser was compared to an air polishing device in the treatment of peri-implantitis.[24]

Erythritol, a new low abrasive powder, with comparable physical properties to glycine

powder has been introduced for sub-gingival air polishing. Erythritol is a non-toxic, chemically neutral, and completely water-soluble polyol, widely used as an artificial sweetener and food additive. Due to its particle size, comparable to that of glycine, and promising chemical characteristics, allowing it to bond to antiseptic substances, it has been recently proposed for sub-gingival biofilm removal.[25] Furthermore, data published recently has suggested that Erythritol also has an inhibitory effect on some perio-pathogenic bacteria such as *Porphyromonas gingivalis*.[26]

To date, there are no studies which analyze the use of an air abrasive system based on Erythritol, combined with local antibiotics in the treatment of peri-implantitis. Therefore, the aim of the present study was to report the one-year results of a new non-surgical therapeutic protocol (Multiple Anti-Infective Non-Surgical Therapy [MAINST]) in the non-surgical treatment of acute peri-implantitis lesions.

Materials and methods

This was a case series, private clinic-based study, approved by the Ethical committee of Brescia's hospital (Spedali Civili of Brescia, Ethical Committee of District of Brescia) on May 7th, 2016 (Chairperson: Carmen Terraroli, protocol No. 0). All patients referred to the clinic for peri-implantitis between January and July 2014 were considered eligible for the study. The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were followed. Each patient signed a written informed consent.

The Strobe (Strengthening the Reporting of Observational Studies in Epidemiology) statement [27] was followed in this report.

Patients were included when they met the following inclusion criteria:

— at least 1 dental implant which had served successfully as a fixed prosthetic reconstruction abutment for more than one year, with absence of mobility;

— the implant showed radio-graphical and clinical signs of peri-implantitis, defined as presence of suppuration (PUS), bleeding upon gentle probing of the peri-implant pocket (BOP) and a probing pocket depth (PPD) of ≥6 mm in at least one site around the implant and radiographical evidence of crestal bone resorption (BR) from moment of implant placement of 2 mm or more. If the radiography at implant placement was not available, the implant shoulder was used as reference;

— the subjects were systemically healthy (no systemic diseases requiring medication).

Exclusion criteria were:

— patients who could not be treated with the MAINST protocol due to allergy to tetracyclines;

— patients who were treated with systemic antibiotics or any local antimicrobial 3 months prior to beginning the clinical treatment;

— patients who could not comply with the planned recall visit;

— patients who needed antibiotic prophylaxis for routine dental therapy;

— pregnant or women who were breast-feeding.

Data and clinical parameters

Age, gender, smoking, and medical history were recorded for each patient.

Primary outcomes measures were:

— implant failure: recorded as implant mobility or implant removed due to infection;

— complications and adverse events: every complication and/or adverse event was recorded;

— number of recurrence of peri-implantitis: recorded as number of exacerbations of peri-implantitis (swelling, pus, deepening of the PPD) that would require another course of treatment.

Secondary outcome measures were:

— presence of Plaque (PI): measured by recording the presence or absence of plaque;[28]

— presence of BOP (BOP): measured by recording the presence or absence of bleeding for up to 30 seconds after gentle probing;

— probing pocket depth (PPD): measured to the nearest millimeter as the distance from the mucosal margin to the base of the peri-implant pocket. The deepest value on the four

surfaces (mesial, buccal, distal, lingual) of the implant was recorded;

— recession of the mucosal margin (REC), measured to the nearest millimeter as the distance from a fixed reference point to the mucosal margin;

— relative attachment level (RAL), measured to the nearest millimeter as the distance from a fixed reference point to the base of the clinical pocket, was recorded.

It was recorded if patient took antibiotics for other reasons during the one-year follow-up or if a new treatment of peri-implantitis was required.

Clinical parameters were assessed with a PCP-UNC 15 periodontal probe (Hu-Friedy, Chicago, IL, USA) in four sites around the implant affected by peri-implantitis (mesial, buccal, distal, and lingual) with a gentle probing force by a single experienced periodontist (MM) at baseline (T0) and, thereafter, at 1 week (T1), at 3 (T2), 6 (T3) and 12 months (T4). Reproducibility within 1mm was greater than 98%. Intra-examiner reproducibility was evaluated as the difference between duplicate measurements of the same site taken one day apart. Ten teeth on five patients were chosen and a total of 300 duplicate measurements were taken with a reproducibility within 1 mm greater than 98%. Follow-up visits were scheduled at 3, 6, 9 and 12 months following the active treatment.

Treatment of peri-implantitis

Affected implants were treated with the following two step protocol (Table I).

At baseline (step 1), acute peri-implant lesions were drained manually then an air-abrasive system (Air-flow® Master Piezon®, EMS Electro Medical Systems S.A., Nyon, Switzerland) with an Erythritol and Chlorhexidine (0.3%) based powder (Air-Flow® Powder Plus, EMS Electro Medical Systems S.A.) was used supra-gingivally. The peri-implant pockets were then flushed with a chlorhexidine 0.20% solution (Corsodyl®, GlaxoSmithKline, Brentford, UK) and thereafter filled with a 14% doxycycline controlled-release topical antibiotic (Ligosan®, Heraeus Kulzer GmbH, Hanau, Germany) following the manufacturer instructions. Patients received oral hygiene instructions and were asked to refrain from interdental cleaning of the affected sites for the whole period in which the local antibiotic was *in situ*.[29]

After 7 days (step 2), an experienced periodontist (MM) with 4× magnification loops, performed a single session of Full Mouth Erythritol Powder Air Polishing (FM-EPAP) to treat the entire oral cavity based on the protocol described by Flemmig *et al.* (Full Mouth Glicine Powder Air Polishing [FM-GPAP]).[30] Plaque was rendered visible by a disclosing plaque agent and Erythritol Powder (PLUS EMS) was used. The affected implants were treated without limitation of time. Supra-structures were removed only if screwed on the implant and mechanical treatment was stopped when all visible surfaces where inspected under a 4× magnification loop and judged as clean by the operator (MM). The Erythritol-Chlorhexidine (0.3%) based powder (Air-Flow® Powder Plus, EMS Electro Medical Systems S.A.) was used.

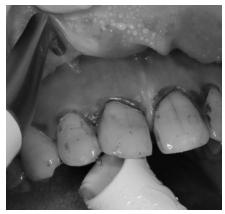
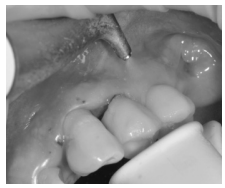
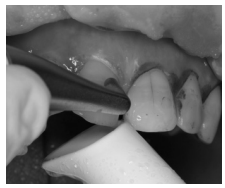
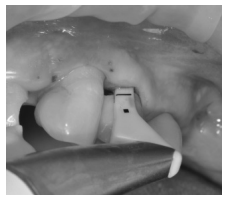
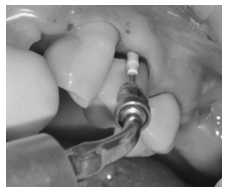
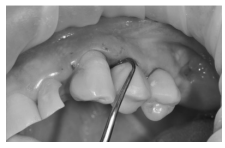
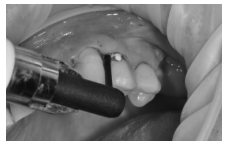
The procedure followed these steps (Table I).

Under local anesthesia the peri-implant mucosa was treated with an air-abrasive system (Air-flow® Master Piezon®, EMS Electro Medical Systems S.A.). The supra-gingival hand-piece was used with a power of 50% and maximum irrigation. The biofilm on the exposed implant surface and on the prosthetic reconstruction was removed using the same tool and same setting, directing the hand-piece at a 45° angle coronally Each site (buccal, mesial, distal and lingual) was treated for 5 seconds.

The peri-implant pockets <5 mm were then treated by directing the hand-piece towards the mucosal margin at a 45° angle, for 5 seconds again at each site.

The sub-gingival hand-piece with a flexible nozzle attached (Perio-flow® Air Flow Master Piezon®, EMS Electro Medical Systems S.A.), in Perio modality setting at 50% power and maximum irrigation was used for peri-implant pockets which were deeper than 5 mm. The nozzle was inserted in the depth of the pocket

TABLE I.—*Step by step treatment, instrumentations and settings used in the MAINST protocol.*

Step	Powder	Handpiece	Settings	Power & water	Time for site	Position	Photo
1) Chlorhexidine rinsing (0.12%/ min)	–	–	–	–	–	–	
2) Plaque disclosing + oral decontamination (gingiva, hard palate, buccal mucosa, vestibule, tongue dorsum)	Erythritol	Supragingival	PERIO 1.5 bar	Power: 50% Irrigation: 100%	5 s	Distance: 5 mm Angle: 45°	
3) Supragingival decontamination (biofilm and stains removal)	Erythritol	Supragingival	PERIO 1.5 bar	Power: 50% Irrigation: 100%	5 s	Distance: 5 mm Angle: 30°-45° Direction: apical to coronal	
4) Subgingival decontamination of pockets with probing depth up to 5 mm	Erythritol	Supragingival	PERIO 1.5 bar	Power: 50% Irrigation: 100%	5 s	Distance: 5 mm Angle: 30°-45° Direction: coronal to apical	
5) Subgingival decontamination of pockets with probing depth greater than 5 mm	Erythritol	Subgingival with Perioflow	PERIO 1.5 bar	Power: 50% Irrigation: 100%	5 s	Perio nozzle that reaches the bottom of the pocket	
6) Mechanical debridement	–	Ultrasonic handpiece, poly ether-ether ketone PEEK tip	–	Power: 70% Irrigation: 100%	No limit of time	–	
7) Manual debridement	–	Mini curettes	–	–	No limit of time	Cutting side directed to the soft tissue wall of the pocket	
8) Washing of the pocket	Chlorhexidine 0.20%	–	–	–	–	–	
9) Application of topical antibiotic	Doxycycline 14%	Flexible nozzle	–	–	–	–	

and then moved for 5 seconds apically-coronally and mesio-distally in order to remove as much biofilm from the implant surface as possible at every pathological site.

After that, supra and sub-gingival debridement and calculus removal was performed using a piezo-electric device (Air-flow® Master Piezon®, EMS Electro Medical Systems S.A.) with a Poly-ether-ether-ketone (PEEK) tip (PI tip, EMS Electro Medical Systems S.A.). The tool was set at 70% power with maximum irrigation and discontinued when the surface was judged as clean.

Mini curettes (Hu-Friedy, Chicago, IL, USA) were used to manually curette the granulation tissue, by directing the cutting side of the blade towards the soft tissue wall of the pocket.

The pockets were then rinsed with a 0.2% Chlorhexidine solution (Corsodyl®, GlaxoSmithKline).

The pockets were then filled with a 14% doxycycline controlled-release topical antibiotic (Ligosan®, Heraeus Kulzer GmbH, Hanau, Germany) following the manufacturer instructions. The tested product is a biodegradable and highly viscous gel for topical subgingival placement composed of a carrier gel (polyethylene glycol lactide/glycolide copolymers) containing doxycycline hyclate as an active ingredient.

Patients were instructed in oral hygiene procedures and advised not to brush the affected site for 12 hours and not to use interdental cleaning devices for 7 days on the treated area. During the follow-up visit, additional oral hygiene advice was given to patients.

Patients were recalled after 1, 3, and 6 weeks and then every 3 months for clinical evaluation and supra- and sub-gingival FM-EPAP.

Data management and statistical analysis

All continuous outcomes (PPD, REC and RAL) were modelled using a multilevel model fitted by linear mixed models [31] where the site was considered the statistical unit. All models account for different baseline values at patient, element and site levels for the variable of interest as well as a within patient different time effect (change).

A global element index was calculated for binary outcomes, sites bleeding on probing and harboring plaque (respectively called BOP-I and PI-I), by adding up within-implant individual site measurements (coded as 0/1); therefore, in these models the implant was the statistical unit. Counts were then modelled as number of sites affected per implant using two levels (patient and implant) generalized linear mixed models (GLMM) [32] with Poisson error distribution and *log* link function, and number of sites within implant as offset.

Moreover, the deepest probing site of each implant was also used as an unit for a secondary analysis (labelled as PPD-L, REC-L, RAL-L, BOP-L). Given that in these analyses we reduced the implant to a single site, the models did not include the site level.

In all models, time was modelled as a categorical variable representing visit 0 (basal) to visit 4 (1 year).

Statistical analysis

All results were reported as estimated and with 95% confidence intervals. For binary data, time effect was reported as proportional reduction (*e.g.* BOP $\Delta_{T2vsT0} = (1 - BOP_{T2} / BOP_{T0}) \times 100$). A P value <0.05 was considered statistically significant and all P values and confidence intervals were adjusted for multiple comparisons using Westfall procedure.[33] All analysis were performed using R [34] v. 3.3.1 and package lme4.[35]

Results

All 15 patients referred for peri-implantitis, contributing in total 27 osseointegrated implants, were included in the study and were followed for 12 months. The demographic characteristics of these 15 subjects are summarized in Table II. No patient smoked. Nine subjects contributed with one implant each, four with 2 implants, one with 4 implants and one patient with 6 implants. The type of implant was not known, but all the implants were threaded with a rough or moderately-rough surface.

TABLE II.—*Baseline demographic characteristics of the subjects enrolled in the study.*

Characteristics	N.
Subjects	15
Mean age	51±12.3
M/F ratio	7/8
Implants	32
Implants affected	27

There were no cases of implant failure, complications or adverse effects or recurrence of the disease for up to one-year and therefore no retreatments were needed. No patient took antibiotics for other reasons. Two supra-structures were removed for cleaning. The survival rate was 100% during the 12 months.

The estimated mean, proportions and local changes over time in the peri-implant clinical parameters of the 27 implants enrolled in the study are presented in Table III.

Implant plaque scores (PI-I) decreased significantly compared to baseline (T0=100% [95% CI: 82.8 to 100]; T4=13.9% [95% CI: 8.4 to 23.0]). Compared to baseline levels the changes in PI-I were always highly statistically significant (P<0.01).

Both the BOP score (BOP-I) and the BOP score for the deepest implant site (BOP-L) decreased significantly when compared to baseline. BOP-I reduced from 98.5% (95% CI: 79.8 to 100) at baseline to 4.5% (95% CI: 2.0 to 11.0) at T4. Simultaneously, the BOP-L decreased from 81.0% (95% CI: 46.0 to 100) at baseline to 3.0% (95% CI: 0.4 to 22.3) at T4.

Mean probing pocket depths at baseline, adjusted for plaque index, were 7.89 mm (95% CI: 6.91 to 8.86) and 8.00 mm (95% CI: 6.85 to 9.15), respectively, for the PPD-I and for deepest implant site (PPD-L). After the first step of the treatment (T1), these values already decreased to 5.87 mm (95% CI: 4.94 to 6.80) for PPD-I and to 6.30 mm (95% CI: 5.33 to 7.27) for the PPD-L. Following completion of active treatment both PPD-I and PPD-L showed an increased reduction during follow-up, and were 3.16 mm (95% CI: 2.70 to 3.63) and 3.46 mm (95% CI: 2.95 to 3.98), respectively, after 1 year. It is worth mentioning that at baseline, 95.4% of the peri-implant pockets had a PPD>5 mm, whereas after a follow-up of 3 months only 4 out of the 108 implant sites (3.7%) still had a PPD>5 mm,

TABLE III.—*Mean changes and 95% confidence interval (CI) of the clinical parameters analyzed for the average implant value (-I) and for the deepest implant site (-L) at different time points.*

	T0 (95% CI)	T1 (95% CI)	T2 (95% CI)	ΔT2 *vs.* T0 (95% CI)	T3 (95% CI)	T4 (95% CI)	ΔT4 *vs.* T0 (95% CI)
PI-I, %	100 (82.8;100)	45.4 (34.3;60.0)	14.8 (9.1;24.2)	85.2 (71.2;92.4) [a]	6.5 (3.1;13.6)	13.9 (8.4;23.0)	86.1 (72.4;93.7) [a]
BOP-I, %	98.5 (79.8;100)	23.0 (15.3;34.3)	12.0 (7.0;20.8)	87.9 (74.8;94.2) [a]	1.0 (0.3;6.5)	4.5 (2.0;11.0)	95.3 (85.4;98.5) [a]
PPD-I, mm	7.89 (6.91;8.86)	5.87 (4.94;6.80)	4.08 (3.67;4.49)	-3.81 (-4.73;-2.88) [a]	3.09 (2.63;3.55) [b]	3.16 (2.70;3.63) [b]	-4.72 (-5.67;-3.77) [a]
REC-I, mm	0.01 (-0.43;0.46)	0.70 (0.26;1.14)	1.66 (1.14;2.19)	1.65 (1.13;2.17) [a]	1.75 (1.13;2.36)	1.68 (1.08;2.29)	1.67 (1.04;2.30) [a]
RAL-I, mm	7.90 (6.85;8.94)	6.57 (5.53;7.62)	5.78 (5.07;6.49)	-2.12 (-2.72;-1.52) [a]	4.85 (4.07;5.62)	4.85 (4.06;5.65)	-3.05 (-3.66;-2.43) [a]
BOP-L, %	81.0 (46.0;100)	27.0 (12.4;58.7)	18.0 (7.3;44.4)	77.8 (14.2;94.3) [c]	0 (–)	3.0 (0.4;22.3)	96.3 (48.1;99.7) [c]
PPD-L, mm	8.00 (6.85;9.15)	6.30 (5.33;7.27)	4.47 (3.96;4.97)	-3.54 (-4.92;-2.16) [c]	3.40 (2.85;3.96) [d]	3.46 (2.95;3.98) [d]	-4.54 (-5.90;-3.19) [c]
REC-L, mm	0.22 (-0.41;0.85)	1.12 (0.68;1.55)	1.99 (1.48;2.50)	1.77 (0.92;2.62) [c]	2.17 (1.58;2.77)	2.14 (1.54;2.75)	1.92 (0.97;2.88) [c]
RAL-L, mm	8.10 (6.83;9.37)	7.42 (6.32;8.51)	6.61 (5.837;0.40)	-1.48 (-2.74;-0.23) [c]	5.69 (4.80;6.58)	5.66 (4.77;6.54)	-2.44 (-3.75;-1.14) [c]

PI: plaque index; BOP: bleeding on probing; PPD: probing pocket depth; REC: recession of the mucosal margin; RAL: relative attachment level.
[a] P<0.01; [b] significantly lower than 4 mm, P value <0.01; [c] P<0.02; [d] significantly lower than 4mm, P value <0.05.

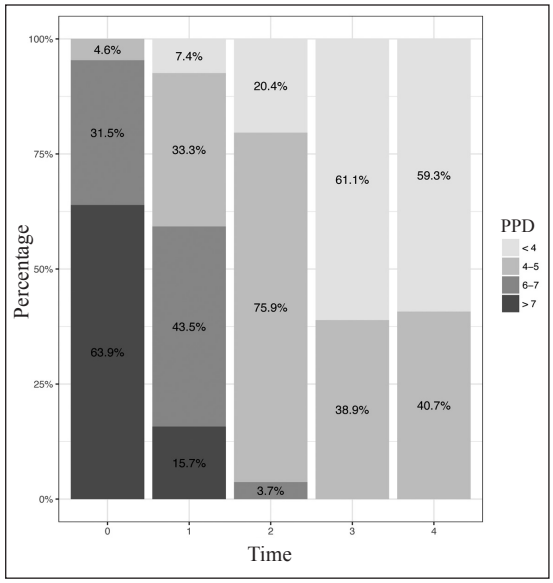


Figure 1.—Frequency distributions of the probing pocket depths and number of pockets around all implants treated at the various time intervals, for different depths categories.

and none at 6 and 12 months. The frequency distributions of the probing pocket depths around all implants treated at the various time intervals are shown in Figure 1.

Similarly, the mucosal margin around the treated implants showed a statistically significant recession (REC-I) compared to baseline values 0.01 mm (95% CI: -0.43 to 0.46). The mean values for the implant averaged score (REC-I) were 0.70 mm (95% CI: 0.26 to 1.14) after the first active part of the treatment (T1) and 1.66 mm (95% CI: 1.14 to 2.19) after 3 months of follow-up (T2), whereas, at the same time intervals (baseline values REC-L=0.22 mm [95% CI: -0.41 to 0.85]), the estimated deepest site score (REC L) was 1.12 mm (0.68 to 1.55) at T1 and 1.99 mm (95% CI: 1.48 to 2.50) at T2. Afterwards, the levels of mucosal margins remained almost stable over time both for REC-I and REC-L.

Implant attachment levels (RAL) showed the same tendency, although the gain in RAL continued up to the 6 months' follow-up (T3) and remained stable for up to 1 year. RAL-I changed from 7.90 mm (95% CI: 6.85 to 8.94) at baseline to 4.85 mm (95% CI: 4.06 to 5.65) after 1 year, whereas the RAL-L score went from 8.10 mm (95% CI: 6.83 to 9.37) to 5.66 mm (95% CI: 4.77 to 6.54) after 1 year.

Figures 2 and 3 show the clinical outcomes over time of PPD, REC, and RAL.

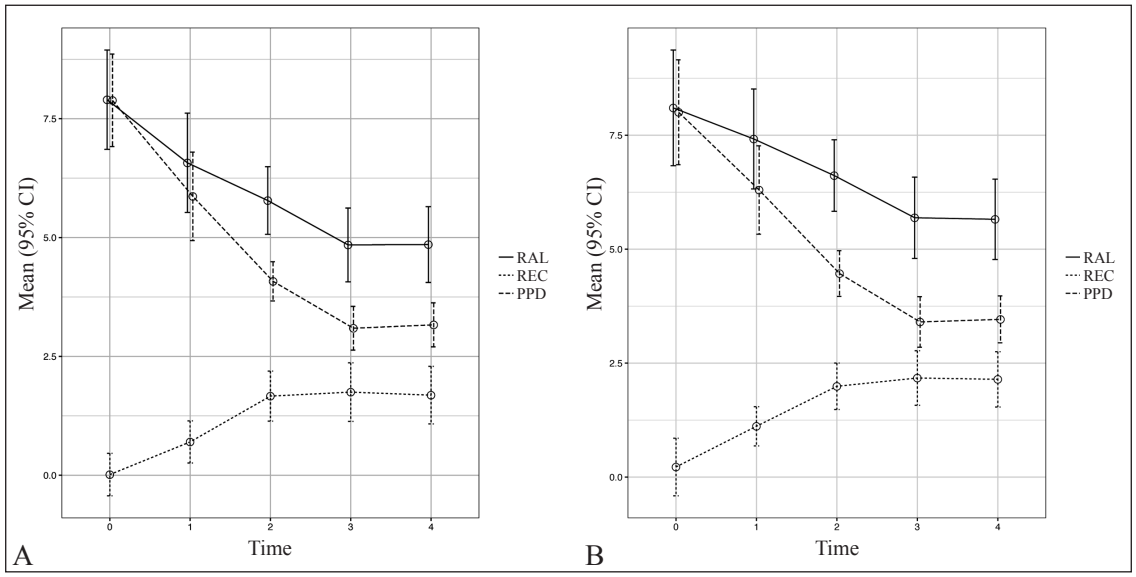


Figure 2.—A) Outcomes of the averaged clinical parameters over time with 95% confidence intervals (error bars); B) outcomes of the clinical parameters at the deepest implant site over time with 95% confidence intervals (error bars).
PPD: probing pocket depth; RAL: clinical attachment level; REC: recession of the mucosal margin.

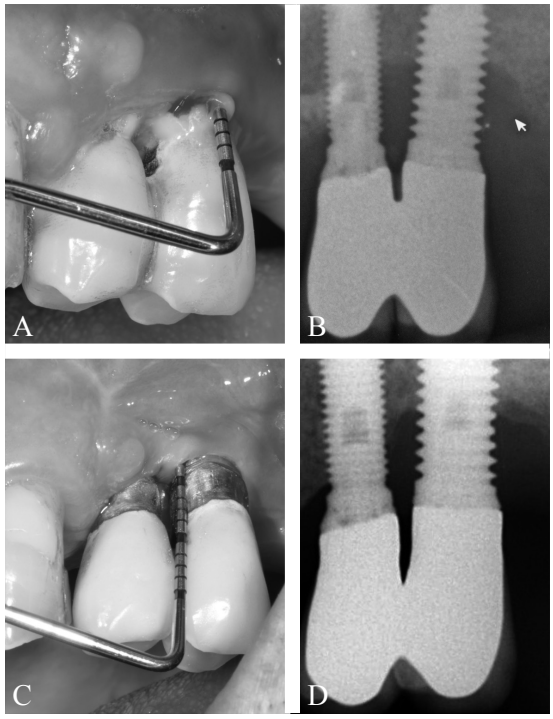


Figure 3.—Clinical case: A) clinical baseline; B) baseline X-ray; C) clinical control at 1 year; D) 1-year post-treatment X-ray.

Discussion

This case series describes the results of a multiple anti-infective non-surgical therapy (MAINST) in the treatment of the acute phase of peri-implantits. The general positive improvements obtained on baseline clinical parameters were maintained for over 12 months. All the patients recruited in this study had a history of periodontitis and were previously included in a maintenance program with their respective dental professionals.

Non-surgical treatment of peri-implantitis seems to have limited and non-durable clinical efficacy on peri-implantitis lesions.[12] The reduction of bacterial load and resolution of inflammation can be incomplete since many factors could prevent an efficient decontamination of the implant surface: the design of the supra-structure,[36] different types of abutment connections, the roughness of the implant surface [37] and the shape and the design of the implant.[10, 12]

Different manual and power driven instruments have been used in non-surgical treatment, including plastic, carbon fiber and titanium curettes,[38] as well as ultrasonic instrumentation.[38, 15] A recent review [12] on the treatment of peri-implantitis stated that the use of an air abrasive device could improve the outcome of a non-surgical approach, compared to other protocols. If correct time and pressure settings are selected, air polishing can be safely used both for supra- and sub-mucosal debridement at mucositis and peri-implantitis sites, without the occurrence of adverse events (*e.g.* emphysema formation).[23]

This study used a erythritol-chlorhexidine (0.3%) based powder, a low abrasive powder delivered in pockets >4 mm by a special flexible nozzle (Perio Flow nozzle). The device allows the operator to modulate air pressure and water settings in order to reduce the risk of emphysema formation, by limiting the pressure below 1.5 bar, when used sub-gingivally. The perio-nozzle has 3 lateral air powder exits and also one apically for water which, accordingly to the manufacturer, further reduces the risk of emphysema even if no study have been conducted on this aspect.

The air-abrasive system is used to mechanically remove as much biofilm as possible from the implant surface. Since detoxification of the affected surface is not possible with a mechanical device, a highly concentrated (14%) local antibiotic is chosen as adjunctive therapy. The effectiveness of this specific controlled-release doxycycline has been shown to be highest in the first 7 days,[29] so sub-gingival application of the topical antibiotic is repeated after one week. Topical antibiotics delivered by controlled release systems can reach a local concentration up to 1000 times higher than the Minimum Inhibitory Concentration (MIC90, concentration at which the bacteria inside a biofilm are affected. A local antibiotic which was able to maintain a concentration 1000 times superior to MIC90 for 10 days [39] was used. Clinically, we obtained a clear reduction of the signs of inflammation in a few days.

Non-surgical instrumentation in the peri-implant pocket was performed only after one

week because the rapid demineralization of the bone does not necessarily involve the destruction of the collagen fibers. Therefore, there might be a high healing and regeneration potential if no mechanical instrumentation is performed before this potential healing occurs in the first week of the antibiotic application.[40] In addition, the use of sub-mucosal air-polishing is not recommended in an highly inflamed tissue. Subsequently, a second local application was applied in the peri-implant pocket at the end of the instrumentation at T1.

Several adjunctive therapies to the mechanical treatment of peri-implant diseases have been investigated over time, including lasers,[41] systemic antibiotics [42] and different topical antimicrobials.[13, 18-20] The application of chlorhexidine in different formulations and regimens, in addition to mechanical debridement resulted in poor outcomes, suggesting that it may have limited antimicrobial effects in peri-implant lesions.[19, 20, 43] In this study, chlorhexidine was used as an irrigant.

Some studies have focused on local application of sustained release antimicrobials in addition to the mechanical treatment of peri-implantitis.[13, 18-21] Systemic administration of different antibiotic molecules is commonly used in emergency situation such as acute peri-implantitis, although there is no evidence on their efficacy [44] and the increased worldwide level of antibiotic resistance must be taken into consideration.[45] The application of topical antibiotics as an adjunct to mechanical debridement improves clinical outcomes.[13, 18-21] Nevertheless, it is quite difficult to compare the results of other studies with our case series. Different implant surface decontamination protocols, vehicles, molecules and recall strategies are used. Severe peri-implantitis cases are included in our case series (raw mean baseline measure was 7.96±1.86 mm), while less severe cases are treated in other studies (Mombelli *et al.*[18] mean PPD of 4.72±0.98 mm; Buchter *et al.*[21] 5.68±0.28 mm). This could partly explain the greater PPD reduction obtained in our study. Another possible reason could be the rigorous protocol of a multiple step anti-infective non-surgical treatment, that addressed not only the implant site but the entire oral cavity, including curettage of the peri-implant pocket. The patient's compliance in self-performed infection control is another important anti-infective measure. Plaque index dropped significantly from 100% at baseline to below the 20% threshold level at all other follow-up visits. Similar and significant reductions were seen also for BOP scores.

Another important factor could be the type of local antibiotic used and the protocol of application, timing and dosage. Buchter *et al.*[21] also used a doxycycline hyclate as a local antibiotic, but at a lower active drug concentration (8.5% *vs.* 14%) and with a different delivery vehicle.

The reduction in PPD was due both to soft tissue shrinkage and gain of clinical attachment from T0 to T1 and from T1 to T2. An average reduction in probing pocket depth at the deepest site of approximately 2 mm (7.77 to 5.57 mm) was recorded at T1 (7 days) and was due to about 1 mm gain in clinical attachment. During the acute phase, the periodontal probe was able to penetrate deeper in the inflamed connective tissue. This possibility had been shown by Fowler *et al.*[46] and it is probably even more pronounced in an abscess situation and around oral implants.[47] At T2, the PPD reduction from baseline was about 5 mm (7.77 to 2.83), with a 2-mm recession. This data is statistically significant and can be considered clinically important.

In this preliminary study we did not aim to evaluate the radiographical changes in the bone levels between baseline and end of the study. Nevertheless, the radiological information gathered indicated a general stabilization and in some cases also an improvement in bone levels and the data will be presented in further clinical trials.

Limitations of the study

The limits of this study were due to the small sample analyzed and the lack of a control group. This was the first step in analyzing the results of a protocol, therefore it was applied to a small cohort of patients. Due to the

promising results a randomized clinical trial is in progress, in order to better understand the potential effect of this treatment protocol. Another limitation was linked to the use of different non-surgical treatments at once, so it was difficult to assess if the promising results were due to one step in particular or to the sum of the singular steps. There are other on-going studies trying to answer this question, while the reason for using a multiple approach is explained in the text. The use of a local antibiotic together with the airflow therapy is also more expensive than using systemic antibiotic with traditional hand instruments.

These results were obtained by a clinician with experience in the use of air abrasive devices and in patients following the same maintenance program, therefore the generalizability of the study should be viewed in this perspective.

Conclusions

Within the limits of the study, we showed that the MAINST protocol — a combination of Erythritol Powder Air Polishing supra and sub gingival and topical Doxycycline — obtained good results in a non-surgical approach for treating acute peri-implantitis for up to 1 year. MAINST was associated with a strict quarterly supportive periodontal therapy. Further prospective randomized clinical trials will clarify if this protocol will be able to provide better outcomes compared to other non-surgical peri-implantitis treatments.

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Funding.—This study was partially supported by EMS and Hereus Kulzer by supplying the materials which were used.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Acknowledgements.—The authors wish to express their gratitude to A. Sordillo and G. Garzetti (University of Brescia) for their contributions in the clinical work related to this study.

Article first published online: October 3, 2017. - Manuscript accepted: September 26, 2017. - Manuscript revised: July 26, 2017. - Manuscript received: December 29, 2016.