TREATMENT OF PERI-IMPLANTITIS: DESCRIPTION OF A TECHNIQUE OF SURGICAL DETOXIFICATION OF THE IMPLANT. A PROSPECTIVE CLINICAL CASE SERIES WITH 3-YEAR FOLLOW-UP

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SUMMARY
Objective. This prospective clinical case series on peri-implantitis therapy reports on clinical and radiographic changes occurring after the use of an innovative technique of surgical degranulation combined with a thorough detoxification of the implant and local antibiotics application.
Methods. In 14 partially edentulous patients, 18 implants diagnosed with peri-implantitis were treated. Implant detoxification was performed mechanically and chemically with citric acid at pH 1. Thereafter, tetracycline powder and chlorexidine gel by way of a collagen sponge carrier were applied on the implant surface, filling the bone defect. Neither resective nor regenerative surgery were performed. Clinical and radiographic parameters were recorded prior to and three years after treatment.
Results. Clinical parameters improved after three years observation period. A statistically significant ($p<0.001$) reduction of probing pocket depth (PPD) was found. Bone recovery was 35% in respect to baseline (prosthesis loading). The bone variation expressed in millimetres at time of surgical treatment and 3-year follow up was statistically significant ($p<0.001$). No implant was lost in the observation period.
Conclusion. Surgical degranulation combined with mechanical and chemical detoxification of the implant and local antibiotic therapy seems to be a reliable method for stopping and controlling peri-implantitis.

Key words: peri-implantitis, chemical detoxification, surgical degranulation.

Introduction

Infective peri-implantitis is a destructive inflammatory process of bacterial origin at attacks hard and soft tissues surrounding an osteointegrated implant causing the formation of peri-implant pockets and the resorption of the surrounding bone (1).The occurrence of peri-implantitis seems to be correlated to the number of years of smoking and the presence of periodontal disease (2), while there seems to be no correlation with the presence of systemic diseases like diabetes and osteoporosis (3).The estimated prevalence of peri-implantitis is between 5 and 10%, but its frequency is bound to increase (4). There are numerous surgical procedures used for the treatment of peri-implantitis. These procedures require various types of treatment. often combined such as: removal of inflamed tissues with or

without the surgical flap; pharmacological therapy (local and/or systemic); resective therapy; regenerative therapy; decontamination and detoxification of implant surfaces using chemical agents or laser irradiation. Some reviews have established that there is a lack of sufficient clinical evidence to recommend the use of a specific protocol for the treatment of peri-implant lesions (5). A scientifically-recognized protocol accepted on an international level during the fourth European Periodontology Workshop is Cumulative Interceptive Supportive Therapy (CIST) presented by Mombelli in 1999 to prevent and/or block peri-implantitis lesions (1). CIST is a cumulative protocol made up of five specific protocols performed in order which provides increasing antibacterial potential proportional to the severity and extension of the lesion (6). In the case of evident peri-implantitis with bone resorption >2mm the protocol foresees the use of antibiotic therapy systemic or local associated with resective or regenerative surgery. Regenerative surgery employing covering membranes has a high risk for complications such as the exposure or infection of the membranes themselves (7, 8). Resective surgery does not guarantee optimal aesthetic results (9).The aim of the present prospective clinical case series presentation is to evaluate a new protocol of surgical detoxification combined with local antibiotics for the treatment of peri-implantitis. The protocol makes use of a carrier for the local antibiotic. This carrier is made up of a collagen sponge soaked in chlorexidine gel and tetracycline powder. No regenerative surgery (8) or respective (9) is used in order to reduce possible treatment complications and guarantee positive aesthetic results given that resective therapies are not performed.

Materials and methods

Fourteen partially edentulous patients with 18 Calcitek (Sulzer Dental Inc.; Carlsbad, CA) osteointegrated oral implants were included in the study. The criteria for inclusion of patients were: (1) clinical signs: bleeding on probing; probing pocket depth ≥ 5 mm; presence of suppuration; absence of implant mobility; (2) radiographic signs: evidence of marginal bone through periapical radiographs. The work was conducted in accordance with the Declaration of Helsinki. Treatments were conducted with the understanding and the consent of the human subjects, and with the approval of the Director of the local Institution. All patients were asked for their medical histories including questions on their smoking habits, and their previous periodontal history. The percentage of patients who smoke corresponded to 57%. Patients with previous periodontal problems who had been treated and monitored in the same dental facilities in which the peri-implantitis surgery was performed, accounted for 80%. The peri-implantitis diagnosis was always performed by the same operator evaluating clinical and radiographic parameters. Considering both these parameters the diagnosis for all patients was of severe grade of peri-implantitis. Clinical parameters used were those proposed by Salvi in 2004 (10): plaque index, modified sulcus bleeding index (mBI) (11), perimplant probing pocket depth (PPD), mucosal recession (REC) (12), and presence of suppuration upon application of pressure (PUS). Probing pocket depth was recorded in 6 points around the implant (mesial; central; distal – both bucally and lingually/palatally). Clinical parameters were recorded prior to the treatment and 3 years after treatment. At least 4 conventional periapical radiographs were taken of each patient: upon placing of the implant, at prosthetic loading, at time of surgical treatment and at the 3-year follow-up. The periapical radiographs were taken with a parallel technique, using a centring device and individual mask from the time that the patients were enrolled in the study. The radiographs were developed manually with fresh chemical solutions. Mesial and distal marginal bone loss was measured considering the distance between the implant shoulder (IS) and the first visible bone to implant contact (B), as seen on periapical radi-

ographs. Dimensional distortion due to the intraoral radiograph was corrected by comparing the dimensions of the implant with the image on the radiograph. A comparison between radiographs taken at time of surgical treatment with those taken after the third year of follow-up was made. All the measurements were taken by the same operator, after converting the conventional radiographs in digital images and using a measurement software (ImageJ, NIH, Bethesda, MD). "Bone recovery" was calculated considering the radiographic mesial and distal bone to implant contact (IS-B) as seen on periapical radiographs, and expressed in percentage of absence of bone in contact with the implant. For this parameter a comparison was made between time of surgical treatment and three-year post operatory data. Calculations were made considering the actual length of implant contacting the surrounding bone, for each implant mesially and distally. As regards the surgical procedures, two weeks prior to surgery all patients were given instruction in oral hygiene manual removal of bacterial plaque with carbon fibre curettes, and subgingival irrigation with 0.2% chlorexidine, followed by H_2O_2 (12 volumes) and sterile physiological solution. Systemic therapy with amoxicillin (500 mg x 3 per diem) and metronidazole (250 mg x 3 per diem) or, in case of allergy to penicillin, with roxitromicina (150 mg x 2 per diem), was started the day before surgery and continued for 7 days. At time of surgery, the prosthetic component was removed in order to expose the peri-implant lesion. Surgeries were conducted following a previously described sedation protocol and in local anaesthesia (13). The prosthesis was cleaned with ultrasound and conserved in chlorexidine 0.2% solution until repositioning. An intrasulcus incision with thinning of the flap was made around the neck of the implant, and the epithelium and granulation tissue inside the peri-implant pocket were then removed. After exposure of the peri-implant area, tartar and plaque were removed from the peri-implant surface with a hyposonic instrument or ultrasonic teflon tips. Detoxification of the implant surface was performed using a cotton ball soaked in citric acid at pH 1 (40%) for at least 1-3 minutes or until the surface was shiny and clean. It was checked with magnifying glasses for tartar remains which, if any, were removed with mechanical instruments. The hydroxiapatite was removed with a diamond cutter and then polished with a rubber polishing tip. A collagen carrier sponge (Antema, Molteni Dental, Scandicci, FI, Italy) was applied around each implant. This carrier was divided in 4 parts and soaked in a mix of chlorexidine 0.2% (Corsodyl gel, GlaxoSmithKline, Verona Italy) and a half capsule of tetracycline powder (Ambramicina Scharper, Sesto San Giovanni MI, Italy). Modified internal vertical mattress sutures were applied using a non-reabsorbable 4-0 nylon suture around the implant (Ethicon Inc. Somerville, NJ, USA). The prosthesis was repositioned immediately following suturing (Figure 1). Sutures were removed after 14 days from surgery. Post-operatively, patients rinsed twice daily with chlorexidine 0.2% for 14 days and took anti-inflammatory medication (ibuprofen 400 mg or sublingual piroxicam 20mg, both twice daily for 3-4 days) for the three days following surgery. Following an initial healing phase, patients were enrolled in a maintenance program which foresaw, for the entire follow-up period, a dental hygienist check-up every three months and, if necessary, renewed motivation and instructions on oral hygiene procedures.

Statistical analysis

Clinical and radiographic values were reported both as individual data, as well as mean and standard deviation. To test for significant differences, analysis was performed by two-sample Student's t-test. Comparisons between results at 3 years and at time of surgical treatment conditions within the same treatment group were performed with a Student's t-test for paired data. The value $p<0.05$ was considered as the limit of statistical significance.

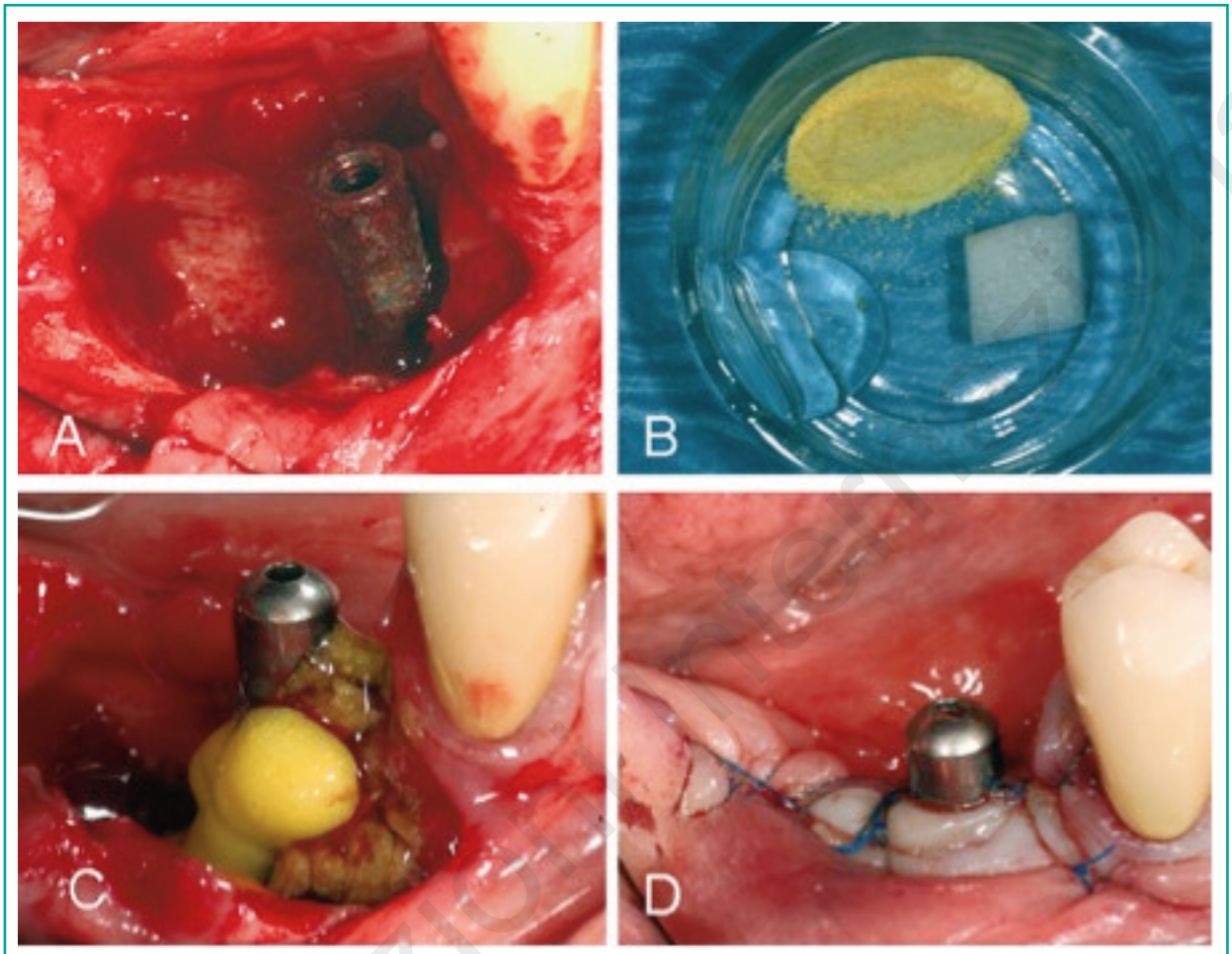

Figure 1
(A) Peri-implant defect after raising of the flap. (B) Collagen sponge (carrier), tetracycline powder and chlorhexidine gel 0.2%. (C) Collagen sponge and tetracycline/chlorhexidin mix in place. (D) Suture.

Results

The clinical characteristics of patients prior to treatment are reported in Tables 1 and 2. The majority of patients were smokers and showed periodontal-type problems. Before surgical treatment plaque and bleeding index were positive and the average depth of periodontal pockets was 6.8 mm (Table 3). The clinical results after three years are reported in Table 4. At the three year follow up, bleeding on probing (mBI) and suppuration (PUS) were no longer present in all the patients. Gingival recession (REC) was absent. Mean probing pocket depth (PPD) reduction was statistically significant ($P<0.001$). Radiological characteristics are reported in Table 5. Marginal bone recovery was calculated in relation to bone loss at time of surgical treatment and after three years. Average mesial and distal bone resorption was 5.1 (± 1.9) mm and 5.7 (± 2.0) mm at time of surgical treatment, and 3.3 (± 1.8) mm and 3.2 (± 2.1) mm three years after treatment. The variation of these parameters over 3 years was 1.9mm (± 2.4) and 2.5mm (± 2.6) mm, mesially and distally, respectively.

Table 1 - Characteristics of patients included in the study.

Patient	Age	Gender	Smoker	Periodontal problems
1	46	F	No	Yes
2	54	F	No	Yes
3	54	F	No	Yes
4	51	M	Yes	Yes
5	43	F	Yes	Yes
6	63	F	No	No
7	77	F	Yes	No
8	66	F	Yes	No
9	79	F	Yes	Yes
10	66	F	Yes	Yes
11	61	F	No	Yes
12	87	F	Yes	Yes
13	62	F	Yes	Yes
14	88	F	No	Yes
mean	64.1			
SD	14.3			

Table 2 - Type of implant used in the patients (Calcitek).

Patient	Site	Length mm	Diameter mm
1	35	10	3.25
2	46	10	3.25
3	26	10	4
4	22	13	3.25
5	45	10	5.25
	46	8	3.25
6	25	15	4
7	36	10	4
	37	8	4
8	45	13	4
9	43	15	3.25
10	44	13	3.15
	45	13	3.15
11	36	10	4
	37	10	4
12	36	10	4
13	26	10	4
14	15	10	3.5

Table 3 - Clinical parameters prior to treatment (time of surgical treatment) (mBI: modified bleeding index; PUS: presence of pus; REC: recession; probing mb-cb-db/ml-cl-dl: mesio/central/disto buccal and lingual).

Patient	Site	Plaque	mBI	PUS	REC	PPD (mm)							
						mb	cb	db	ml	cl	dl	mean	±St.Dev.
1	35	+	+	+	-	5	6	8	4	7	8	6.3	1.6
2	46	+	+	+	-	5	4	4	5	6	6	5	0.9
3	26	+	+	+	-	6	8	8	7	9	9	7.8	1.2
4	22	+	+	+	-	6	8	8	7	8	9	7.7	1
5	45	+	+	+	-	8	8	8	9	8	8	8.2	0.4
	46	+	+	+	-	7	6	6	6	6	7	6.3	0.5
6	25	+	+	+	-	7	8	7	5	6	5	6.3	1.2
7	36	+	+	+	-	5	7	7	7	7	7	6.7	0.8
	37	+	+	+	-	8	7	7	7	8	6	7.2	0.8
8	45	+	+	+	-	5	8	7	6	8	8	7	1.3

To be continued →

Continued from Table 3

9	43	+	+	+	-	6	6	8	8	7	5	6.7	1.2
10	44	+	+	+	-	5	5	8	6	8	7	6.5	1.4
	45	+	+	+	-	8	8	7	7	6	6	7	0.9
11	36	+	+	+	-	8	8	8	6	7	7	7.3	0.8
	37	+	+	+	-	8	7	7	6	6	7	6.8	0.8
12	36	+	+	+	-	5	7	7	6	7	7	6.5	0.8
13	26	+	+	+	-	6	7	5	5	7	6	6	0.9
14	15	+	+	+	-	6	5	6	7	8	8	6.7	1.2
											Average	6.8	0.3

Table 4 - Clinical parameters after three years of follow-up (for the legend, see Table 3).

Patient	Site	Plaque	mBI	PUS	REC	PPD (mm)							
						mb	cb	db	ml	cl	dl	mean	±St.Dev.
1	35	-	-	-	-	3	3	4	4	3	3	3.3	0.5
2	46	-	-	-	-	3	4	4	3	3	4	3.5	0.5
3	26	+-	-	-	-	4	4	3	3	3	4	3.5	0.5
4	22	+-	-	-	-	3	3	3	4	4	3	3.3	0.5
5	45	-	-	-	-	3	4	4	3	3	3	3.3	0.5
	46	-	-	-	-	4	3	3	3	4	3	3.3	0.5
6	25	-	-	-	-	3	4	4	4	4	3	3.7	0.5
7	36	-	-	-	-	3	2	3	3	4	3	3.0	0.6
	37	-	-	-	-	3	4	3	3	2	3	3.0	0.6
8	45	-	-	-	-	4	4	3	3	4	3	3.5	0.5
9	43	-	-	-	-	4	3	3	3	3	4	3.3	0.5
10	44	-	-	-	-	3	3	3	3	4	4	3.3	0.5
	45	+-	-	-	-	4	3	4	4	3	4	3.7	0.5
11	36	-	-	-	-	3	3	3	3	3	3	3.0	0.0
	37	-	-	-	-	4	3	4	4	3	3	3.5	0.5
12	36	-	-	-	-	4	3	4	3	4	3	3.5	0.5
13	26	-	-	-	-	3	4	3	4	3	4	3.5	0.5
14	15	+-	-	-	-	4	3	2	4	4	3	3.3	0.8
											Average	3.4	0.1

Table 5 - Mesial (M) and distal (D) bone variations in millimeters at baseline and 3-year follow up as measured on endoral radiographs (IS= implant shoulder; B= first radiological bone to implant contact).

Patient	Site	IS-B (mm) baseline		IS-B (mm) 3ys f-u			Variation	
		M	D	M	D		M	D
1	35	1.2	3.8	0.4	0.0		0.8	3.8
2	46	3.1	3.1	3.6	3.3		-0.5	-0.2
3	26	4.8	7.3	4.6	5.4		0.2	1.9
4	22	4.5	4.5	1.4	2.3		3.1	2.2
5	45	4.7	5.6	2.8	4.0		1.9	1.6
	46	4.0	3.4	2.3	1.7		1.7	1.7
6	25	6.1	6.1	4.3	4.3		1.8	1.8
7	36	4.9	6.5	0.0	0.9		4.9	5.6
	37	4.7	4.9	2.2	2.2		2.5	2.7
8	45	5.6	9.6	5.7	8.2		-0.1	1.4
9	43	10.5	10.5	0.5	0.4		10.0	10.1
10	44	5.9	5.0	4.1	4.1		1.8	0.9
	45	5.7	5.3	5.3	3.9		0.4	1.4
11	36	4.2	4.8	3.8	4.4		0.4	0.4
	37	4.9	3.8	3.9	2.8		1.0	1.0
12	36	4.7	4.6	3.8	2.6		0.9	2.0
13	26	5.5	7.2	4.6	5.7		0.9	1.5
14	15	7.4	7.4	5.6	0.5		1.8	6.9
	Average	5.1	5.7	3.3	3.2	Average	1.9	2.6
	St. dev. (±)	1.9	2.0	1.8	2.1	St. dev. (±)	2.4	2.6
		Pre		3ys			var	
	Overall average	5.4		3.2		Overall average	2.2	
	St. dev. (±)	2.0		1.9		St. dev. (±)	2.5	

This variation was statistically significant ($p<0.001$). These data confirm the results related to PPD obtained after 3 years. None of the implants were removed during follow up. Bone recovery was 35 ± 30% (Table 6, Figures 2, 3).

Discussion

Osseointegrated implants have become a viable option for replacing missing teeth in totally and partially edentulous patients (14) and the peri-implantitis is one of the causes of failure of the dental implants. The aim of this prospective clinical case series was to evaluate a surgical procedure capable of ensuring thorough detoxification of the peri-implant lesion, in order to guarantee both elimination of the infected site and stability over time (3 years) of the clinical and radiographic results. The majority of the patients included in the study were smokers and were classified as patients with periodontal problems. These patients were defined as at risk

Table 6 - Bone recovery "% baseline" and "%3ys f-u" represents the percentage of absence of bone in contact with the implant, at time of surgical treatment (baseline) and 3-year post operatory. Calculations were made considering the actual length of implant contacting the surrounding bone, for each implant mesially and distally.

Patient	Site	% baseline		% 3ys f-u		% Bone recovery	
		M	D	M	D	M	D
1	35	11.5	38.5	4.2	0.0	63.9	100.0
2	46	30.6	30.6	36.1	33.3	-18.2	-9.1
3	26	48.5	72.7	46.4	53.6	4.2	26.3
4	22	34.9	34.9	11.1	17.5	68.2	50.0
5	45	47.2	55.6	27.8	40.3	41.2	27.5
	46	50.0	41.9	29.3	20.7	41.4	50.7
6	25	41.0	41.0	28.7	28.7	30.0	30.0
7	36	49.1	64.9	0.0	9.4	100.0	85.0
	37	58.9	61.5	27.1	27.1	54.0	56.0
8	45	42.8	73.4	43.9	63.4	-2.0	14.0
9	43	70.2	70.2	34.0	26.0	52.0	63.0
10	44	45.2	38.3	31.5	31.5	30.0	18.0
	45	43.8	41.1	41.1	30.1	6.0	27.0
11	36	42.8	48.0	38.0	44.0	4.0	1.0
	37	48.0	38.0	39.0	27.0	23.0	9.0
12	36	47.1	45.6	38.5	26.2	18.0	43.0
13	26	54.7	71.8	45.9	57.4	16.0	20.0
14	15	73.7	73.7	56.1	5.3	24.0	93.0
	Average	46.7	52.3	32.2	30.1	30.9	39.1
	St. dev. (±)	13.8	15.5	14.6	17.1	29.2	31.1
	Overall average	49.5		31.1		35.0	
	St. dev. (±)	14.7		15.7		30.1	

of peri-implantitis (4). In this procedure, detoxification of the peri-implant lesion was performed with both mechanical (degranulation) and chemical (citric acid) mechanisms. The use of 40% citric acid is probably the best method for removing lipopolysaccharides from implants (15), even those covered in hydroxiapatite (16). Its action is effective against both aerobic and anaerobic bacteria (17). Currently in the literature there is no data on acute and/or chronic toxicity regarding the use of citric acid in biological models, both *in vitro* and *in vivo*. *In vitro* studies have demonstrated that citric acid and the tetracycline solution are comparable in the detoxification of implants. In addition, the results do not suggest a possible toxic effect of citric acid, given that the fibroblasts cover a greater surface area on the implant detoxified with citric acid than with tetracycline solution (18). In the protocol utilized, the elimination of the infection is reinforced by local antibiotic therapy, combined with systemic therapy. Tetracycline is widely

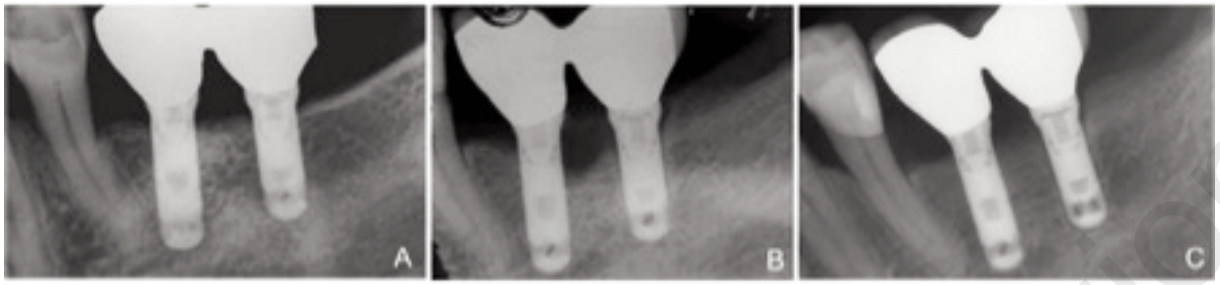

Figure 2
Radiographic follow up of patient n.1. (A) Prosthesis loading. (B) Time of surgical treatment (7 years after implant insertion). (C) After 3 years from treatment.

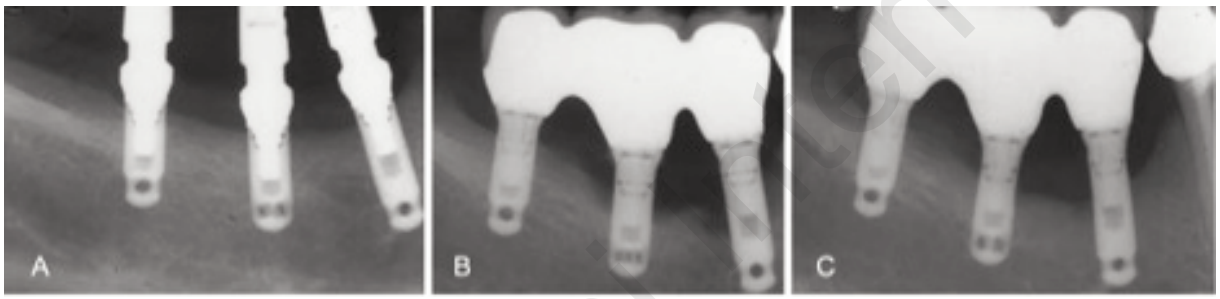

Figure 3
Radiographic follow up of patient n 5. (A) Radiography taken just before prosthesis loading. (B) Radiography taken at time of surgical treatment (9 years after implant placement). (C) Radiography taken after 3 years.

used as local therapy in regeneration procedures owing to its positive effect with bone graft material, regeneration of extraction socket bone (19). Van Winkelhoff reported that, for the treatment of peri-implantitis with moderate deep lesions, local application of minocycline or doxycycline as an adjunct to mechanical debridement and irrigation with an antimicrobial agent may be effective (20). In regard to tetracycline, its use has been indicated to reduce the bacterial contamination of the treated area in case of infection due to the exposure of non resorbable membranes (21). Resective therapy associated with implantoplasty seemed to influence positively the survival of oral implants affected by inflammatory processes, but no specific comments were expressed about the effect of this topical antibiotic (9). A carrier was used for the local antibiotic therapy in the form of a collagen sponge soaked in tetracycline granules and chlorexidine gel. The collagen sponge is needed to keep the tetracycline fixed in the peri-implant site. The bacteriostatic action of the tetracycline controls the infection, contributes to the detoxification of the implant, and probably slows the migration of fibroblasts (9). Moreover, the sponge functions as a space maintainer and prevents flap invagination. Histological studies have demonstrated that the sponge, positioned *in vivo* inside the tissues is reabsorbed by enzymatic deterioration after 3-5 weeks, a period of time during which it can be hypothesized that the treated area remains "isolated" from the surrounding environment. The peri-implant bone defects treated in this study were characterized by having 2 or 3 residual bony walls. In such a

defect, the sponge may stay in place during healing. In case of absence of a residual wall, the stability of the antibiotic carrier may be compromised, or even not achievable. The results obtained with this procedure are encouraging. The clinical parameters, and in particular the probing depth, improved in a statistically significant manner following treatment. The absence of bacterial plaque is consequent to more attentive oral hygiene that patients implemented as a result of the maintenance program in which they were enrolled throughout the whole follow-up period. The absence of bleeding on probing and suppuration following treatment confirms the resolution of active inflammation in the treated sites and, consequently, significantly improved oral health compared to prior to the treatment. Radiological results confirmed such clinical data. The surgical method described in this prospective clinical case series does not make use of membranes thus reducing the risk of complications. No implant was lost in the follow up period. The absence of gingival recession following treatment contributes to the aesthetic results. In conclusion, the described surgical method allowed for stable clinical and radiographic results over time, and for maintenance in a functional condition of the treated implants.

Disclosure

Funding: none.
Competing interests: none.
Ethical approval: not required.
Patient permission: not required.

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