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Two-year clinical results following treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane

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Abstract

Objectives: The aim of the present case series was to evaluate the 2-year results obtained following treatment of peri-implantitis lesions using either a nanocrystalline hydroxyapatite (NHA) or a natural bone mineral in combination with a collagen membrane (NBM+CM).

Material and Methods: Twenty-two patients suffering from moderate peri-implantitis ($n = 22$ intra-bony defects) were randomly treated with (i) access flap surgery (AFS) and the application of NHA, or with AFS and the application of NBM+CM. Clinical parameters were recorded at baseline and after 12, 18, and 24 months of non-submerged healing.

Results: Two patients from the NHA group were excluded from the study due to severe pus formation at 12 months. At 24 months, both groups revealed clinically important probing depth (PD) reductions (NHA: 1.5 ± 0.6 mm; NBM+CM: 2.4 ± 0.8 mm) and clinical attachment level (CAL) gains (NHA: 1.0 ± 0.4 mm; NBM+CM: 2.0 ± 0.8 mm). However, these clinical improvements seemed to be better in the NBM+CM group (difference between groups: PD reduction: 0.9 ± 0.2 mm; CAL gain: 1.0 ± 0.3 mm).

Conclusion: Both treatment procedures have shown efficacy over a period of 24 months, however, the application of NBM+CM may result in an improved outcome of healing.

Key words: bone graft; clinical study; collagen membrane; nanocrystalline hydroxyapatite; peri-implantitis

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Conflict of interests and source of funding statement

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Nowadays, there is considerable evidence supporting the cause-and-effect relationship between microbial plaque colonization and the pathogenesis of peri-implant infections (Mombelli et al. 1988, Becker et al. 1990, Alcoforado et al. 1991). While peri-implant mucositis describes reversible inflammatory reactions in the mucosa adjacent to an implant, peri-implantitis is defined as a series of inflammatory reactions affecting the tissues around an osseointegrated implant in function, resulting in the loss of the supporting alveolar bone (Albrektsson & Isidor 1994). Meanwhile, additional risk factors such as a previous history of periodontitis, cigarette smoking, polymorphisms of the interleukin-1 gene cluster, or occlusal overload were also identified to be

associated with an increased risk for peri-implant bone loss (Isidor 1996, 1997, Feloutzis et al. 2003, Gruica et al. 2004, Roos-Jansåker et al. 2006a, b). According to a cause-related concept, several treatment procedures have been recommended for the management of inflammatory processes affecting the tissues around an osseointegrated implant in function. In particular, mechanical and ultrasonic debridement, the adjunctive use of chemical agents (i.e. irrigation with local disinfectants, local, or systemic antibiotic therapy), or laser application have been reported to be clinically effective in controlling disease progression (Mombelli & Lang 1992, Tang et al. 2002, Büchter et al. 2004, Karring et al. 2005, Romeo et al. 2005, Schwarz et al. 2005, 2006a). So far, however, there is no reliable evidence suggesting which could be the most effective interventions for initially treating peri-implantitis (Esposito et al. 2006). A recent study, assessing the configurations and sizes of naturally occurring peri-implantitis lesions in humans, revealed that most of the defects (55.3%) showed a circumferential bone loss without dehiscence of the adjacent alveolar crest. However, circumferential bone loss was generally associated with a horizontal loss of the supporting alveolar bone (Schwarz et al. 2007). Because non-surgical treatment approaches failed to promote the re-osseointegration at exposed implant sites (Schwarz et al. 2006c), additional surgical interventions may be required in order to minimize the risk for a re-infection of the peri-implant pocket. This might be achieved either with resective surgery (i.e. elimination of pathological peri-implant pockets in combination with implantoplasty) or with bone augmentation procedures. So far, however, only very few clinical data are available reporting on the therapy of peri-implantitis with resective surgery (Romeo et al. 2005, 2007). While regenerative treatment procedures have been extensively investigated using an experimental peri-implantitis model in animals (Persson et al. 1996, Hürzeler et al. 1997, Nociti et al. 2001, Schou et al. 2003a–c), there are also only few data available evaluating the clinical outcomes of this concept of treatment (Hämmerle et al. 1995, Mattout et al. 1995, Behneke et al. 2000, Haas et al. 2000, Khoury & Buchmann 2001, Schwarz et al. 2006b, Roos-Jansåker et al. 2007a, b). In particular, most of these studies used the concept of guided bone regeneration (Dahlin et al. 1988), combined with the implantation of bone grafts or bone graft substitutes into the defect to support the barrier membrane preserving its original position. Recently, Schwarz et al. (2006b) reported on comparable clinical outcomes at 6 months following treatment of moderate intra-bony peri-implantitis defects using either a natural bone mineral (NBM) in combination with a collagen membrane (CM) or nanoscopic apatite particles (35%) in aqueous dispersion (65%). The latter material is provided as a ready-to-use paste in a syringe, that, due to its physicochemical properties, might be used without the additional application of a barrier membrane. So far, however, no investigations are yet available evaluating the long-term clinical results of both treatment procedures.

Therefore, the aim of this case series was to evaluate the 2-year results obtained following treatment of moderate intra-bony peri-implantitis defects using either a nanocrystalline hydroxyapatite (NHA) or a NBM in combination with a CM (NBM+CM).

Material and Methods

Study population

The study population ($n = 22$ patients) and the short-term results (6-month data) have been described in detail previously (Schwarz et al. 2006b).

Briefly, the present parallel-design study reports on a total of 22 partially edentulous patients suffering from moderate peri-implantitis (Mombelli & Lang 1994) attending the Department of Oral Surgery, Heinrich Heine University, Düsseldorf, Germany, for peri-implant bone augmentation procedures (i.e. 11 patients in each group). Each patient was given a detailed description of the procedure and was required to sign an informed consent before participation. The study was in accordance with the Helsinki Declaration of 1975, as revised in 2000, and all participants signed informed consent forms. The study protocol was approved by the ethical committee of the Heinrich Heine University. The patient population consisted of eight men and 14 women (mean age 54.4 ± 12.5 years) exhibiting a total of $n = 22$ implants (Table 1).

Patient selection

Patients who reported smoking more than 10 cigarettes/day were defined as smokers (Tonetti et al. 1995). Patients who reported smoking only occasionally were not considered as smokers. According to the given definition, there were no smokers included in the present study. All patients had been treated previously by a single course of non-surgical instrumentation of respective titanium implants using plastic curettes (Straumann, Waldenburg, Switzerland), followed by pocket irrigation with a 0.2% chlorhexidine digluconate solution (Corsodyl®, GlaxoSmithKline Consumer Healthcare, Bühl, Germany) (CHX) and subgingival application of CHX gel 0.2% (Corsodyl® Gel, GlaxoSmithKline Consumer Healthcare). The criteria needed for inclusion were: (1) the presence of at least one screw-type implant exhibiting an intra-bony defect with a probing depth (PD) of >6 mm and an intra-bony component of >3 mm as detected on radiographs, (2) no implant mobility, (3) single tooth and bridgework re-saturations without overhangings or margins, (4) no evidence of occlusal overload, (5) the presence of keratinized peri-implant mucosa to facilitate a repositioning of the mucoperiosteal flap at the augmented areas, (6) no signs of acute periodontitis, (7) a good level of oral hygiene (plaque index <1) (Löe 1967), and (8) no systemic diseases that could influence the outcome of the therapy (i.e. diabetes, osteoporosis, and bisphosphonate medication). Hollow cylinder implants were excluded from the study. The distribution, mean age, and position of different implant systems in both groups have been described in detail previously (Schwarz et al. 2006b).

Clinical measurements

The following clinical parameters were measured immediately before, and 12, 18, and 24 months after treatment using a periodontal probe (PCP 12, Hu-Friedy, Leimen, Germany): (1) plaque index (PI) (Löe 1967), (2) bleeding on probing (BOP), evaluated as present if bleeding was evident within 30 s after probing, or absent if no bleeding was noticed within 30 s after probing, (3) PD measured from the mucosal margin to the bottom of the probeable pocket, (4) gingival recession (GR) measured from the implant neck (IN) to the mucosal

Table 1. Distribution and mean age (years ± SD) of different implant systems in both groups

Group	BRA	CAM	ITI	KSI	MTX	TSV	ZL	Age
NHA ($n = 11$)	1	1	2*	1	4	1	1	3.6 ± 1.9
NBM+CM ($n = 11$)	1	1	2†	1	3	2	1	4.0 ± 0.9

*Sand blasted large grit and acid etched surface.
†Titanium plasma flamed surface.
BRA, Brånemark System®, (cylindrical screw, machined surface), Nobel Biocare, Göteborg, Sweden; CAM, Camlog Screw Line®, (cylindrical screw, sand blasted and acid etched surface), Camlog, Wimsheim, Germany; ITI, ITI®, Straumann, (cylindrical screw), Waldenburg, Switzerland; KSI, KSI Bauer Schraube®, (conical screw, machined surface), KSI GmbH, Bad Nauheim, Germany; MTX, Spline Twist (MTX)®, (cylindrical screw, grit blasted surface), Zimmer Dental, Freiburg, Germany; TSV, Tapered Screw Vent®, (tapered screw, grit blasted surface), Zimmer Dental; ZL, ZL-Duraplant (Ticer)®, (cylindrical screw, anodic oxidized surfaces), ZL Microdent, Breckerfeld, Germany.; NHA, nanocrystalline hydroxyapatite; NBM+CM, natural bone mineral in combination with a collagen membrane.

margin, and (5) clinical attachment level (CAL) measured from IN to the bottom of the probeable pocket. The primary outcome variable was CAL. All measurements were made at six aspects per implant: mesiovestibular (mv), midvestibular (v), distovestibular (dv), mesiooral (mo), midoral (o), and distooral (do) by one blinded and previously calibrated investigator (K. B.).

Pre- and post-operative radiographs at 6 and 24 months were taken with the long cone paralleling technique and evaluated by one blinded investigator (K. B.).

Configuration assessment of peri-implant bone defects

The supra-alveolar, circumferential, and intra-bony components of the defects were measured during open-flap surgery by one blinded and previously calibrated investigator (K. B.). The baseline defect characteristics in both groups have been described in detail previously (Schwarz et al. 2006b).

Intra-examiner reproducibility

Five patients, each showing two implants with PDs $\geqslant$ 4 mm on at least one aspect, were used to calibrate the examiner. The examiner evaluated the patients on two separate occasions, 48 h apart. Calibration was accepted if measurements at baseline and at 48 h were within a millimetre $>$ 90% of the time.

Randomization procedure

The defects were randomly assigned before surgery to the following test and control groups according to a computer-generated protocol (RandList®, DatInf GmbH, Tübingen, Germany): (i) access flap surgery (AFS) and the application of a NHA (test), or (ii) AFS and the application of a NBM+CM (control). For allowing randomization, supra- and intra-bony components were estimated before surgery on radiographs and by performing transgingival bone sounding. The randomization process led to comparable mean values of all investigated clinical parameters at baseline in both groups.

Treatments

All operative procedures have been described in detail previously (Schwarz et al. 2006b). Briefly, all treatments were performed under local anaesthesia by the same experienced surgeon (F. S.). Following intra-crevicular incisions, full-thickness mucoperiosteal flaps were raised vestibularly and orally. Vertical-releasing incisions were performed only if necessary for a better access or to achieve a better closure of the surgical site. All granulation tissue was removed from the defects and the implant surfaces were thoroughly debrided using plastic curettes (Straumann® Dental Implant System, Straumann AG, Basel, Switzerland). Following cleaning, the exposed implant and the bony surfaces were rinsed with sterile physiologic saline.

At the test sites, bleeding into the defects was reduced to a minimum and they were subsequently filled with a ready-to-use paste in a syringe, containing about 65% water and nanoscopic apatite particles (35%) in an aqueous dispersion (Ostim, Heraeus, Hanau, Germany) (NHA). Care was taken to obtain a direct contact between NHA and the adjacent alveolar bone, without inter-position of a blood clot. Defects were slightly overfilled, as NHA has a viscous, fluid-like consistence and tends to leak from the defect.

At the control sites, the defects were filled with a NBM (BioOss® spongiosa granules, particle size 0.25–1 mm, Geistlich, Wolhusen, Switzerland) (NBM). The graft material was moistened in sterile saline for 5 min. before placement into the defect. Following grafting, a bioresorbable CM of porcine origin (BioGide®, Geistlich) (CM) was trimmed and adapted over the entire defect so as to cover 2–3 mm of the surrounding alveolar bone and to ensure stability of the graft material. Neither sutures nor pins were used for membrane fixation or stabilization. Finally, the mucoperiosteal flaps were repositioned coronally and fixed with vertical or horizontal mattress sutures in such a way as to ensure a non-submerged healing procedure.

Post-operative care and long-term maintenance

Post-operative care consisted of rinsing with a 0.2% chlorhexidine digluconate solution (Corsodyl®) twice a day for 2 weeks. The sutures were removed 10 days after the surgery. Recall appointments were scheduled every second week during the first 2 months after surgery and monthly during the short-term observation period of 6 months. During the rest of the observation period of 24 months, the patients were recalled every 6 months. Neither probing nor subgingival instrumentation was performed during the first 6 months after the surgery. A supragingival professional implant/tooth cleaning and reinforcement of oral hygiene were performed at 1, 3, 6, 12, 18, and 24 months after treatment.

Results

The configuration of the defects has been described in detail previously (Schwarz et al. 2006b). Briefly, surgical defect examination revealed that all implants in the test and control groups exhibited a semi-/or circumferential bone loss without dehiscence or fenestration of the adjacent vestibular and oral alveolar bone. However, in all cases, semi-/or circumferential bone loss was also associated with a horizontal loss of the supporting alveolar bone.

At 12 months following treatment, two patients of the test group, exhibiting

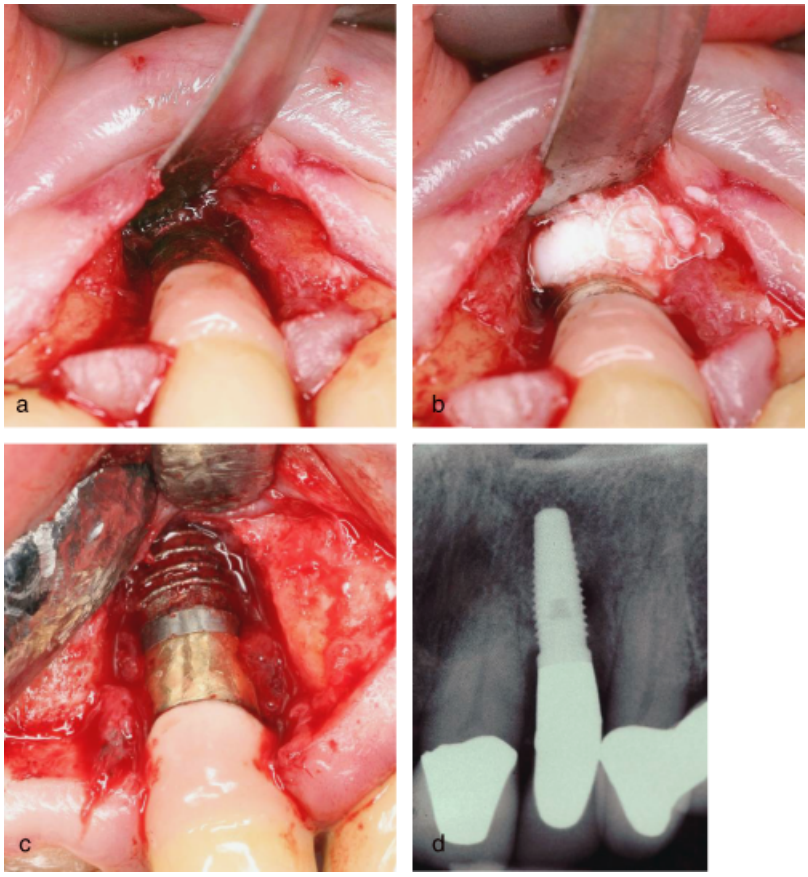

Fig. 1. (a) Semi-circumferential intra-bony defect. (b) Situation following application of nanocrystalline hydroxyapatite (NHA). (c) Situation at re-entry after 12 months due to severe pus formation revealing a loose fibrous tissue, poorly attached to the implant surface. There were no signs of any new bone formation. NHA residues were clinically not detectable. (d) Corresponding radiograph showing no decrease in radiolucency at the mesial aspect of the defect compared with 6 months (see Schwarz et al. 2006a – Figs 4a and b).

Table 2. Clinical parameters (mean ± SD) at baseline and 12 months for the test (NHA; $n = 9$ patients) and control (NBM+CM; $n = 11$ patients) groups

	Baseline	12 months	Difference
Plaque index			
Test	0.6 ± 0.5	0.8 ± 0.6	0.2 ± 0.4
Control	0.8 ± 0.4	0.9 ± 0.5	0.1 ± 0.3
Bleeding on probing (%)			
Test	80	36	44
Control	78	29	49
Probing depth (mm)			
Test	6.9 ± 0.6	4.9 ± 0.8	2.0 ± 0.5
Control	7.1 ± 0.8	4.4 ± 0.6	2.7 ± 0.6
Gingival recession (mm)			
Test	0.4 ± 0.2	0.8 ± 0.4	0.4 ± 0.2
Control	0.4 ± 0.3	0.7 ± 0.5	0.3 ± 0.4
Clinical attachment level (mm)			
Test	7.3 ± 0.8	5.7 ± 0.9	1.6 ± 0.3
Control	7.5 ± 1.0	5.1 ± 0.7	2.4 ± 0.7

NHA, nanocrystalline hydroxyapatite; NBM+CM, natural bone mineral in combination with a collagen membrane.

Table 3. Clinical parameters (mean ± SD) at baseline and 18 months for the test (NHA; $n = 9$ patients) and control (NBM+CM; $n = 11$ patients) groups

	Baseline	18 months	Difference
Plaque index			
Test	0.6 ± 0.5	0.8 ± 0.6	0.2 ± 0.3
Control	0.8 ± 0.4	1.0 ± 0.9	0.2 ± 0.4
Bleeding on probing (%)			
Test	80	34	46
Control	78	30	48
Probing depth (mm)			
Test	6.9 ± 0.6	5.1 ± 0.6	1.8 ± 0.5
Control	7.1 ± 0.8	4.4 ± 0.8	2.7 ± 0.6
Gingival recession (mm)			
Test	0.4 ± 0.2	0.8 ± 0.6	0.4 ± 0.4
Control	0.4 ± 0.3	0.7 ± 0.6	0.3 ± 0.4
Clinical attachment level (mm)			
Test	7.3 ± 0.8	5.9 ± 1.0	1.4 ± 0.3
Control	7.5 ± 1.0	5.1 ± 1.0	2.4 ± 0.7

NHA, nanocrystalline hydroxyapatite; NBM+CM, natural bone mineral in combination with a collagen membrane.

a total of $n = 2$ implants, were excluded from the study due to severe pus formation (Fig. 1). Both patients received further peri-implantitis treatment procedures (i.e. Er:YAG laser decontamination and bone augmentation procedures using NBM+CM), revealing that the implants seemed to be surrounded by a poorly attached, loose fibrous tissue of slightly varying degrees of thickness. There were no clinical signs of any NHA residues. Following treatment, both implants remained inconspicuous with respect to pus formation throughout the study period of 24 months. Thus, in the following, only the data of the 20 available patients are presented. In all other cases, the post-operative healing was considered to be generally uneventful, and all patients reported a high degree of satisfaction with the provided treatment, which was related to the possibility of maintaining the implants.

The mean PI and BOP values for each of the groups at baseline and after 12, 18, and 24 months are summarized in Tables 2–6.

In both groups, the mean PI values remained low throughout the study period. However, a slight increase was observed in both treatment groups when comparing either the baseline or 18-month PI values with the 24-month values, respectively (Tables 4 and 6).

Similarly, the mean BOP scores improved compared with baseline in both groups. However, a slight increase was also observed in both treatment groups when comparing either the baseline or the 18-month BOP values with the 24-month values, respectively (Tables 4 and 6).

The mean PD, GR, and CAL in both groups at baseline and after 12, 18, and 24 months are summarized in Tables 2–6.

In particular, at 24 months after therapy, the test group showed a reduction in mean PD from 6.9 ± 0.6 at baseline to 5.4 ± 0.7 mm and a change in mean CAL from 7.3 ± 0.8 at baseline to 6.3 ± 0.9 mm. In the control group, the mean PD was reduced from 7.1 ± 0.8 at baseline to 4.7 ± 0.7 mm and the mean CAL changed from 7.5 ± 1.0 at baseline to 5.5 ± 1.0 mm (Table 4).

However, when comparing the 12-month clinical parameters with the 18-month values, the test group showed a slight increase in mean PD and CAL of 0.2 ± 0.2 and 0.2 ± 0.3 mm, respectively. In the control group, the mean PD and CAL values remained nearly unchanged at 4.4 ± 0.8 and 5.1 ± 1.0 mm, respectively (Table 5).

Table 4. Clinical parameters (mean ± SD) at baseline and 24 months for the test (NHA; $n = 9$ patients) and control (NBM+CM; $n = 11$ patients) groups

	Baseline	24 months	Difference
Plaque index			
Test	0.6 ± 0.5	1.3 ± 0.5	0.7 ± 0.5
Control	0.8 ± 0.4	1.2 ± 0.9	0.4 ± 0.5
Bleeding on probing (%)			
Test	80	44	36
Control	78	34	44
Probing depth (mm)			
Test	6.9 ± 0.6	5.4 ± 0.7	1.5 ± 0.6
Control	7.1 ± 0.8	4.7 ± 0.7	2.4 ± 0.8
Gingival recession (mm)			
Test	0.4 ± 0.2	0.9 ± 0.7	0.5 ± 0.5
Control	0.4 ± 0.3	0.8 ± 0.7	0.4 ± 0.4
Clinical attachment level (mm)			
Test	7.3 ± 0.8	6.3 ± 0.9	1.0 ± 0.4
Control	7.5 ± 1.0	5.5 ± 1.0	2.0 ± 0.8

NHA, nanocrystalline hydroxyapatite; NBM+CM, natural bone mineral in combination with a collagen membrane.

Table 5. Clinical parameters (mean ± SD) at 12 and 18 months for the test (NHA; $n = 9$ patients) and control (NBM+CM; $n = 11$ patients) groups

	12 months	18 months	Difference
Plaque index			
Test	0.8 ± 0.6	0.8 ± 0.6	0
Control	0.9 ± 0.5	1.0 ± 0.9	0.1 ± 0.3
Bleeding on probing (%)			
Test	36	34	2
Control	29	30	1
Probing depth (mm)			
Test	4.9 ± 0.8	5.1 ± 0.6	0.2 ± 0.2
Control	4.4 ± 0.6	4.4 ± 0.8	0.1 ± 0.4
Gingival recession (mm)			
Test	0.8 ± 0.4	0.8 ± 0.6	0.0 ± 0.3
Control	0.7 ± 0.5	0.7 ± 0.6	0.0 ± 0.2
Clinical attachment level (mm)			
Test	5.7 ± 0.9	5.9 ± 1.0	0.2 ± 0.3
Control	5.1 ± 0.7	5.1 ± 1.0	0.1 ± 0.5

NHA, nanocrystalline hydroxyapatite; NBM+CM, natural bone mineral in combination with a collagen membrane.

When comparing the 18-month clinical parameters with the 24-month values, the test group showed an increase in mean PD and CAL of 0.3 ± 0.5 and 0.4 ± 0.5 mm, respectively. In the control group, the mean PD and CAL values also revealed an increase of 0.3 ± 0.5 and 0.4 ± 0.3 mm, respectively (Table 6).

The frequency distribution of CAL gains after 24 months in both treatment groups is shown in Table 6. In particular, in the test group 22.2% of the sites ($n = 2$ defects) gained at least 2 mm of CAL. In contrast, a CAL gain of at least 2 mm was measured in five defects (45.5%) in the control group (Table 7).

Table 6. Clinical parameters (mean ± SD) at 18 and 24 months for the test (NHA; $n = 9$ patients) and control (NBM+CM; $n = 11$ patients) groups

	18 months	24 months	Difference
Plaque index			
Test	0.8 ± 0.6	1.3 ± 0.5	0.5 ± 0.4
Control	1.0 ± 0.9	1.2 ± 0.9	0.2 ± 0.3
Bleeding on probing (%)			
Test	34	44	10
Control	30	34	4
Probing depth (mm)			
Test	5.1 ± 0.6	5.4 ± 0.7	0.3 ± 0.5
Control	4.4 ± 0.8	4.7 ± 0.7	0.3 ± 0.5
Gingival recession (mm)			
Test	0.8 ± 0.6	0.9 ± 0.7	0.1 ± 0.2
Control	0.7 ± 0.6	0.8 ± 0.7	0.1 ± 0.2
Clinical attachment level (mm)			
Test	5.9 ± 1.0	6.3 ± 0.9	0.4 ± 0.5
Control	5.1 ± 1.0	5.5 ± 1.0	0.4 ± 0.3

NHA, nanocrystalline hydroxyapatite; NBM+CM, natural bone mineral in combination with a collagen membrane.

Table 7. Frequency distribution of CAL gain after 24 months in the test (NHA; $n = 9$ patients) and control (NBM+CM; $n = 11$ patients) groups

CAL gain (mm)	Test		Control	
	N°	*%*	*N°*	*%*
0	2	22.2	1	9.1
1	5	55.5	2	18.2
2	2	22.2	5	45.5
3	0	–	2	18.2
4	0	–	1	9.1

NHA, nanocrystalline hydroxyapatite; NBM+CM, natural bone mineral in combination with a collagen membrane; CAL, clinical attachment level.

In both treatment groups, radiological observation at 24 months revealed a decreased translucency within the intra-bony component of the respective peri-implant bone defects. Compared with the radiographs obtained at 6 months, however, there was no difference in the peri-implant translucency noted within groups.

Discussion

The results of the present case series demonstrated that the treatment of intra-bony peri-implantitis defects with both NHA and NBM+CM resulted in clinically important reductions of BOP and PD as well as gains of CAL. The clinical results measured at 12 months were maintained in both groups over a period of 24 months. In the present study, the mean PD reduction and CAL gain obtained at 12 months was 1.5 ± 0.6 and 1.0 ± 0.4 mm, respectively, in the NHA group, and 2.4 ± 0.8 and 2.0 ± 0.8 mm, respectively, in the NBM+CM group. Even though the mean PD reductions and CAL gains appeared to be the highest in the NBM+CM group, it must be emphasized that the present case series does not have the statistical power to rule out the possibility of a difference between both treatment groups. Therefore, further studies enrolling a higher number of patients and defects are needed in order to clarify this issue (Gunsolley et al. 1998). Recently, Schwarz et al. (2006b) reported on the short-term clinical outcomes following treatment of peri-implantitis lesions using NHA and NBM+CM. In particular, at 6 months after therapy, the NHA group showed a reduction in mean PD from 7.0 ± 0.6 to 4.9 ± 0.6 mm and a change in mean CAL from 7.5 ± 0.8 to 5.7 ± 1.0 mm. In the NBM+CM group, the mean PD was reduced from 7.1 ± 0.8 to 4.5 ± 0.7 mm and the mean CAL changed from 7.5 ± 1.0 to 5.2 ± 0.8 mm (Schwarz et al. 2006b). These short-term results are in agreement with the 12- and 18-month clinical outcomes, as observed in the present study. However, when comparing the 18-month with the 24-month results, it has to be noted that both groups revealed slight increases of mean PD and CAL values. These changes may probably be explained in both treatment groups by the slightly higher mean values of PI after 24 months of healing compared with those values measured at baseline or at 18 months. Because the mean BOP values also increased in both groups at 24 months, it might be speculated that plaque accumulation has caused an inflammation and subsequently a loss of CAL. In this context, it is important to point to the results of controlled clinical studies that have shown that the stability of CAL gain following conventional and regenerative periodontal treatment is dependent on stringent oral hygiene and compliance with a supportive periodontal care programme (Tonetti et al. 1996, Cortellini & Tonetti 2004). As described above, currently, there are only very limited data on the clinical outcome of bone augmentation procedures at intra-bony peri-implantitis

defects (Behneke et al. 2000, Haas et al. 2000, Khoury & Buchmann 2001, Roos-Jansåker et al. 2007a, b). In particular, Behneke et al. (2000) evaluated open-flap surgery and autogenous bone (AB) (block or particulate) following implant surface decontamination using an air-powder abrasive. A total of 25 ITI screw implants in 17 patients with progressive peri-implant tissue destruction were included. Subsequent to a non-submerged healing procedure and supportive systemic antibiotics for 7 days, the mean PD decreased from 4.9 mm at baseline to 2.2 mm after 1 year, 1.8 mm after 2 years, and 1.6 mm after 3 years. The mean CAL changed from 6.1 mm at baseline to 3.9 mm after 1 and 2 years, and to 3.8 mm after 3 years. A total of five patients revealed a dehiscence of the mucoperiosteal flap at 9–30 days following surgery. However, the healing complications did not seem to have a negative influence on the amount of repair (Behneke et al. 2000). Haas et al. (2000) evaluated a combination of AB graft particles with an e-PTFE membrane in 17 patients exhibiting 24 IMZ implants. The mean defect depth at baseline was 5.5 ± 2.0 mm. Implant surface decontamination was performed using toluidine blue and soft laser irradiation at a wavelength of 906 nm. Subsequent to a submerged surgical procedure, and an uneventful primary wound healing, exposure of the membrane occurred in all patients after a mean of 3 weeks. One patient was excluded from the study due to premature removal of the membrane as a result of suppuration. After 9.5 months, radiographic evaluation demonstrated a mean bone gain of 2.0 ± 1.9 mm, merely corresponding to 36.4% of the previous defect height. Khoury & Buchmann (2001) reported on surgical treatment of 25 patients exhibiting a total of 41 peri-implant defects with supporting bone loss $>50\%$ of the implant length (IMZ and Friadent). Implant surface decontamination was performed using chlorhexidine, citric acid, and hydrogen peroxide. After 3 years of non-submerged healing, the mean PD reduction was 5.1 ± 2.7 mm for AB grafts alone, 2.6 ± 1.6 mm for AB+CM, and 5.4 ± 3.0 mm for AB+e-PTFE. The differences between AB and AB+CM as well as AB+ePTFE and AB+CM were statistically significant. Membrane exposure was observed in one patient of the CM group, and at five implant sites of the ePTFE group (Khoury & Buchmann 2001). Most recently, Roos-Jansåker et al. (2007a) evaluated the use of a phycogenic hydroxyapatite either alone or in combination with a resorbable polylactide/polyglycolide membrane for the treatment of advanced peri-implantitis defects (bone loss $\geqslant 3$ threads) in 36 patients exhibiting a total of 65 implants (i.e. 63 BRA and two Astra implants with a rough surface). Surface decontamination was performed using hydrogen peroxide (3%), and all patients received systemic antibiotics (amoxicillin+metronidazole) for 10 days. After 1 year of non-submerged healing, both treatment procedures resulted in comparable clinical and radiographic improvements as indicated by PD reductions (3.4 *versus* 2.9 mm) and defect fill (1.4 *versus* 1.5 mm) (Roos-Jansåker et al. 2007a). However, the results from a recent case series have pointed to an improved PD reduction (4.2 mm) and defect fill (2.3 mm), when the membrane-covered sites were left to heal in a submerged position (Roos-Jansåker et al. 2007b). All these data, taken together with the results from the present study, seem to indicate that a long-term clinical effect following surgical treatment of peri-implantitis lesions might be achievable using several types of bone augmentation procedures. From a clinical point of view, however, one must realize that a generalization of the above-reported outcomes of healing might be considered to be difficult due to differences in patient selection criteria, defect configurations, evaluation protocols, treatment procedures, including supportive anti-microbial therapy, implant surface decontamination, and bone augmentation procedures, as well as the mode of healing (i.e. submerged or non-submerged). While recently published data may point to an improved outcome of healing at submerged sites (Schwarz et al. 2006c, Roos-Jansåker et al. 2007a, b), the effect of post-surgical antibiotic medication, particularly at non-submerged peri-implantitis defects, is still rather unknown. In this context, it must be emphasized that the reason to pass on supportive anti-microbial therapy in the present study was based on the observation that the systemic administration of amoxicillin and metronidazole for the surgical treatment of intra-bony periodontal defects failed to improve the outcome of treatment additionally (Sculean et al. 2001). When interpreting the clinical outcome following surgical treatment of peri-implantitis, it must also be realized that true re-osseointegration can only be assessed histologically. While previous experimental animal studies indeed provide clear evidence that the application of NBM supported the process of re-osseointegration at ligature-induced peri-implantitis defects (Machado et al. 2000, Nociti et al. 2001, Schou et al. 2003a), there are currently no histological data available for NHA. However, a mineralization and even complete resorption of non-osseous-integrated NHA remnants was observed at 12 weeks following application in critical-size calvarial defects of pigs (Thorwarth et al. 2005). Similar results were also observed following application in acetabular bone of animals, as well as tibial, calcaneal, or distal radial fractures of humans (Chris Arts et al. 2006, Huber et al. 2006). Recent experimental data suggest that NHA may optimize the conditions for bone formation within the defect area by supporting a guided vascularization during biodegradation. In this study, NHA was implanted into dorsal skin-fold chambers of golden hamsters (Laschke et al. 2007). When interpreting these results, it must be kept in mind that the respective experimental conditions do not reflect the real situation encountered in the oral cavity. In particular, several periodontal pathogens might have an impact on the organization of NHA, particularly at non-submerged sites. Indeed, at 6 months following application of NHA in fresh extraction sockets of beagle dogs, histological analysis revealed a high variability of NHA resorption and its osteoconductive properties. In particular, while one-half of the specimens exhibited high resorption rates and subsequently small remnants of NHA, wound healing at the other sites was characterized by a very slow graft resorption. In these areas, NHA was partially separated from the surrounding alveolar bone by a gap of up to 0.2 mm (Rothamel et al. 2007). These findings might also be supported by the present results, because re-entry in two patients of the NHA group, excluded from the study at 12 months due to severe pus formation, revealed a loose fibrous tissue without any signs of new bone formation.

Within the limits of the present case series, it was concluded that both treatment procedures have shown efficacy

over a period of 2 years; however, the application of NBM+CM may result in an improved outcome of healing.

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Clinical Relevance

Scientific rationale for the study: The clinical application of a NHA or a NBM+CM has been shown to improve healing of intra-bony peri-implantitis defects on a short-term basis of 6 months. Till date, there are no data on the long-term clinical results following these treatment procedures.

Principal findings: The present results have indicated that both treatment procedures resulted in clinically important reductions of PD and gains of CAL at 24 months after surgery. However, the application of NBM+CM appeared to be associated with higher PD reductions and CAL gains. Moreover, two patients in the NHA group were excluded from the study due to severe pus formation at 12 months.

Practical implications: Over a period of 24 months, the application of NBM+CM may result in a more predictable and improved outcome of healing.