Regenerative Treatment of Peri-Implantitis Bone Defects with a Combination of Autologous Bone and a Demineralized Xenogenic Bone Graft: A Series of 36 Defects

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ABSTRACT

Aim: As the treatment of peri-implantitis–induced bone loss is still a problem, we studied the regenerative treatment of these defects with a mix of autologous bone and a new type of bone graft substitute (demineralized xenogenic bone graft) including growth factors.

Material and Methods: In a prospective manner, 36 cases of peri-implantitis–induced bone loss (depth >4 mm) in 22 patients were followed for 1 year. After resolving the acute infection by local rinsing, granulation tissue was removed. The implants were decontaminated with etching gel and the defects were filled with autologous bone mixed 1:1 with a xenogenic bone graft. The prosthetic reconstructions did not have to be removed. Values of probing depths as well as bone defects were analyzed.

Results: The radiologic evaluation of the bone defects after regenerative treatment revealed a mean reduction of 3.5 mm comparing the values from 5.1 mm prior to surgery to 1.6 mm 1 year after treatment. Average reduction of the probing depth was 4 mm. The remaining bone defects were larger than 3 mm in 4 out of 36 implants 1 year after treatment. Probing depths of more than 4 mm were present in seven implants.

Conclusion: Within the limits of the study, we conclude that for bone defects larger than 4 mm in case of peri-implantitis, this single surgical intervention provided a reliable method to reduce bone defects.

KEY WORDS: bone defects, peri-implantitis, xenogenic bone graft

INTRODUCTION

The treatment of peri-implantitis–induced bone loss is a challenge for every oral surgeon that deals with dental implants. It has to be expected that this is increasingly a problem as in our collective after several years of observation,[1] as well as in other patient groups,[2] prevalence rates of peri-implantitis were around 28–56% of subjects and 12–43% of implant sites.[3] These prevalence rates may not represent community-based prevalence rates. These rates are unknown but are probably higher than success rates given by earlier studies that did not use the same criteria in their definitions. So it is essential to explore suitable therapeutic options for peri-implantitis.

While the lesions of peri-implant mucositis reside in the soft tissue, peri-implantitis also affects the supporting bone.[4,5] To date, treatment protocols for peri-implantitis-induced bone defects are under discussion: In the case of supracrestal bone defects, decontamination of the affected implant as well as implantoplasty may be sufficient,[6–8] while several authors recommend surgical treatment for larger defects.[2] The outcome of nonsurgical treatment of peri-implantitis is at least unpredictable.[4] Others even claim that in

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peri-implantitis lesions, nonsurgical therapy was not found to be effective.[9] Owing to prosthetic reasons, it is often impossible to perform submerged healing.[10]

Surgical treatment usually starts with the removal of granulation tissue und decontamination of the implant surface. The defects are then filled with bone or substitutes[11] and are often covered with membranes.[10,12,13] Comparisons of the treatment outcomes in studies involving humans and animals are difficult because of differences in implant type, graft type, and evaluation protocols. Therefore, further long-term studies in humans involving sufficient numbers of subjects are needed to provide a solid basis for recommendations regarding the surgical treatment of peri-implantitis.[14]

As autologous bone grafts combined with bovine hydroxyapatite revealed good results in sinus floor augmentations,[15] the combination of autologous bone with a xenogenic bone graft may also offer good results in peri-implantitis treatment. Colloss (Ossacur, Obersten-feld, Germany) is a resorbable lyophilized complex of extracellular matrix proteins extracted from diaphyseal equine bone, containing native bone morphogenetic proteins (BMPs) and vascular endothelial growth factor.[16,17] The main component is reconstituted Collagen type I. It has been proven to be effective in enhancing bone formation.[16] Several studies report, that Colloss apparently influenced the bone formation process, especially in initial phases,[18] and improves early osseointegration of allografted implants.[19] It should not be used in patients with known protein allergy, in children and in pregnant subjects, in joint regions and in cases of general infections. In certain cases reactions because of collagen protein intolerance may occur and a local swelling two to three days after application. No case of disease transmission is reported.

The aim of this study was to clinically evaluate the defect fill of peri-implantitis–induced bone defects after treatment with a mix of autologous bone and a demineralized xenogenic bone graft including growth factors.

MATERIALS AND METHODS

In a prospective manner, 36 cases of peri-implantitis–induced bone loss in 22 consecutive patients of the departments of Oral and Maxillofacial Surgery of the Universities of Kiel and Erlangen were followed (male = 10; female = 12; aged 24–83 years) as a case series. The protocol was in accordance with the World Medical Association Declaration of Helsinki and was approved by the local ethics committee (B275/05). Fourteen defects were present in the left mandible, 12 in the right mandible, 7 in the left, and 3 cases in the right maxilla. Only implants showing a vertical bone loss amounting a minimum of 4 mm with circumferential crater defects with loss of oral and vestibular bone at least 1 year after implant insertion were included. Bone loss was evaluated by panoramic x-rays. Smaller bone defects and implants with mobility at presentation were excluded. Different titanium implant types, 1.5–9 years (mean 5.25 years) after insertion were included.

Treatment Protocol

Our treatment protocol is described in Figure 1. Before inclusion, bleeding on probing, mucosal recessions, and the probing depth were measured at four positions (distal, vestibular, lingual/palatinal, and mesial) as a

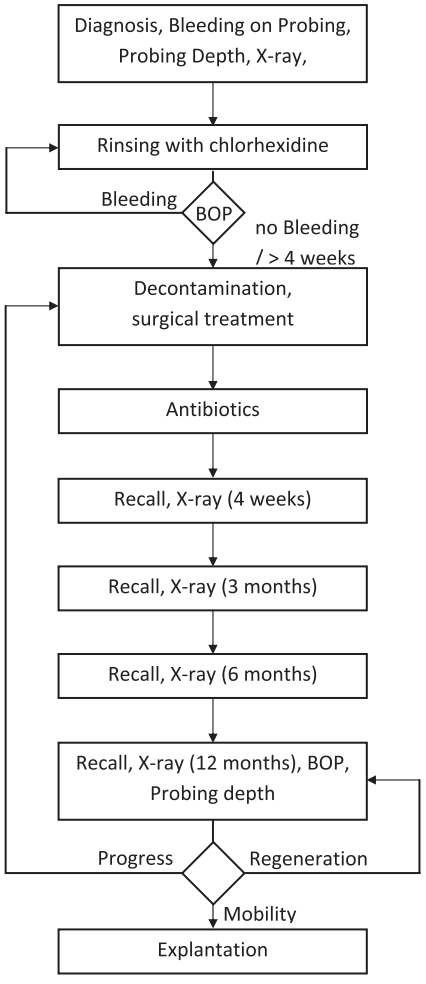

Figure 1 Kiel peri-implantitis treatment scheme. BOP = bleeding on probing.

measure for inflammation of the peri-implant mucosa[5] and a panoramic x-ray was taken to determine bone defects mesial and distal of the implant. To estimate magnification factors, the implant with known length served as reference. Evaluation was done by masked examiners (E.B. and O.Z.): Pre- and postoperative images were coded and evaluated together after the end of the study. Inter-observer differences were at a maximum of ±1 mm.

Prior to the surgical therapy, all patients received a decontamination treatment by rinsing infected peri-implant pockets (supra- and subgingivally) with chlorhexidine 0.12% (three times a week with 2 mL per implant) to resolve the acute inflammation to a chronic stage. Additionally, the implant was cleaned mechanically. Every week, bleeding on probing was tested. Patients were advised to use Durimplant (implant care gel, lege artis Pharma, Dettenhausen, Germany) starting 2 weeks after surgery: for 1 week daily, then once per week.

Surgical Treatment

Via marginal incision and after elevation of a mucoperiosteal flap, infected granulation tissue was removed carefully with curettes and diamonds under local anesthesia to gain access to the implant surface. The complete implant surface below the prosthetic reconstructions (which were not removed) was smoothed with rotating diamond grindings (see Figure 2A). Afterwards, the implant surface was decontaminated with etching gel (Gluma Etch 20 Gel, Heraeus Kulzer, Hanau, Germany; see Figure 2B). After raising a mucoperiosteal flap, a small amount of bone was harvested with a trephine from the mandible in the chin region or in another area with no infection. It was particulated with a bone mill and mixed 1:1 with 10 mg Colloss E (Ossacur, Oberstenfeld, Germany) in a bowl for each implant site treated. Osseous defects were filled to 1–2 mm above the alveolar crest (see Figure 2C). The wound was sutured without tension afterwards (see Figure 2D). All surgical interventions were performed by three experienced surgeons (J.W., A.S., and O.Z.).

Prophylactic antibiotics (ampicillin/sulbactam, Unacid 1.5 g i.v., Pfizer Pharma GmbH, Karlsruhe, Germany; in case of allergy: Clindamycin 600 mg) were given perioperatively. After surgery, sufficient analgesia was achieved with Ibuprofen (600 mg three times a day for 3 days). To reduce postoperative swelling which was heavy in some cases, cooling pads for 12 hours were recommended. The first recall took place 3 days after surgery. After 2 weeks, the sutures were removed. Further clinical controls were performed every 3 months, radiologic controls once a year.

Statistical Evaluation

Radiologic bone defect values were defined as the distance from the surrounding alveolar crest to the apical end. Means and 95% confidence intervals (95% CI) of

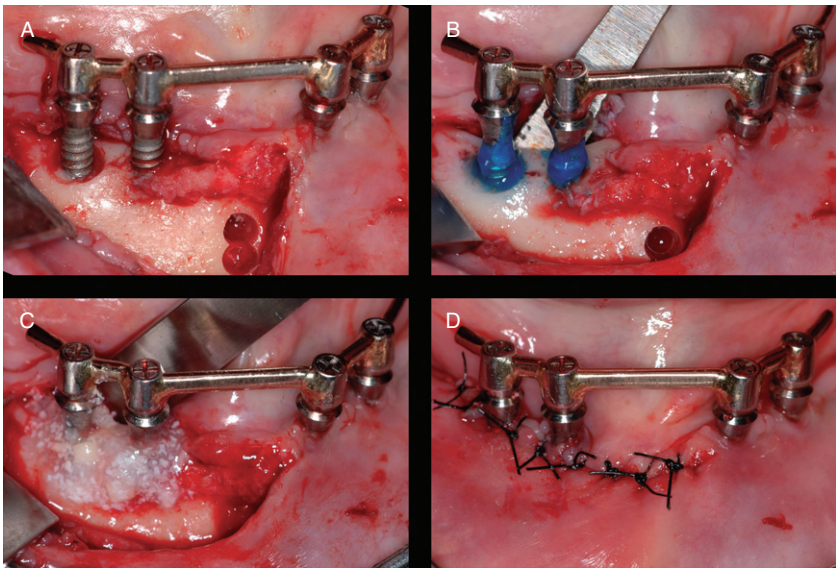

Figure 2 Intraoperative pictures. *A*, After removal of granulation tissue. Note the defects after bone harvesting. *B*, Decontamination with etching gel. *C*, Defect fill. *D*, After suturing. The prosthetic reconstruction was in situ during the whole procedure.

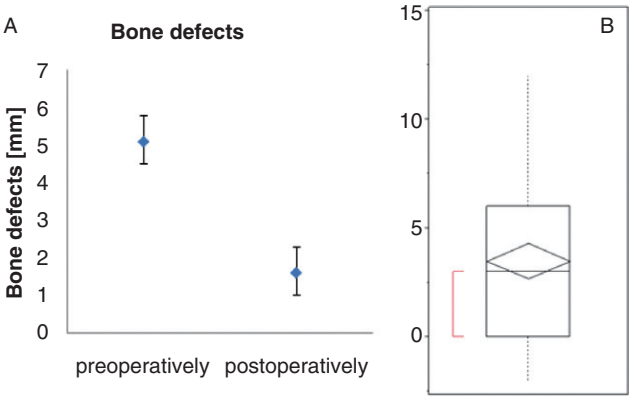

Figure 3 *A*, Bone defect sizes before and one year after surgery. Note the reduction of 3.5 mm. *B*, Box plot of bone defect reductions (in mm; minimum, maximum, quartiles, median, and mean).

the probing depth and bone defects as well as for the differences 1 year before and after the surgery was calculated. The locally infected site was included in the evaluation. Additionally, probing depth reduction and bone defect reduction frequencies are reported.

Bleeding on probing and suppuration frequencies as well as recessions per implant were calculated and reported directly before surgical intervention and after 12 months.

RESULTS

After surgery all patients developed a swelling visible extraorally that disappeared completely after 5 days. During the first days after surgery, pain could be controlled sufficiently with Ibuprofen. One implant (3%) of the 36 followed ones was lost 1 year after surgical therapy because of mobility.

Before surgical intervention, bleeding on probing was observed in 61% of the implants and in 25% after 1 year. The corresponding values for suppuration were 80% and 8%.

Recessions increased from 0.7 mm (SD 0.6 mm) before surgery to 2 mm (SD 1 mm) 1 year after surgery.

The radiologic evaluation of the bone defects resulted in a regeneration from 5.1 mm (95% CI: 4.4–5.9 mm) prior to surgery to 1.6 mm (95% CI: 1.1–2.2 mm) 1 year after surgical treatment, a mean reduction of 3.5 mm (95% CI: 2.7–4.3 mm, $n = 36$ implants, see Figures 3 and 4).

Average reduction of the probing depth was 4 mm (95% CI: 3.3–4.6 mm, $n = 36$ implants, see Figure 5). Pockets could be reduced from an average of 7.5 mm (95% CI: 6.8–8.1 mm) to 3.5 mm 1 year after treatment (95% CI: 3.1–3.9 mm). Twenty-one defects gained more than 3 mm of clinical attachment level.

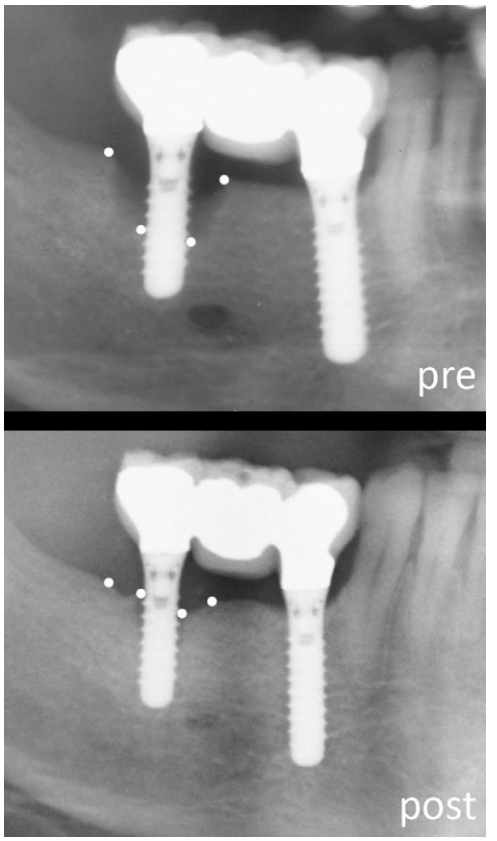

Figure 4 Magnification of a section of panoramic x-rays before (pre) and 12 months after (post) surgical intervention. The lateral points indicate the surrounding bone level, the medial ones the deepest point of the pockets beside the implant.

Probing depth reduction and bone defect reduction frequencies are presented in Table 1. The remaining

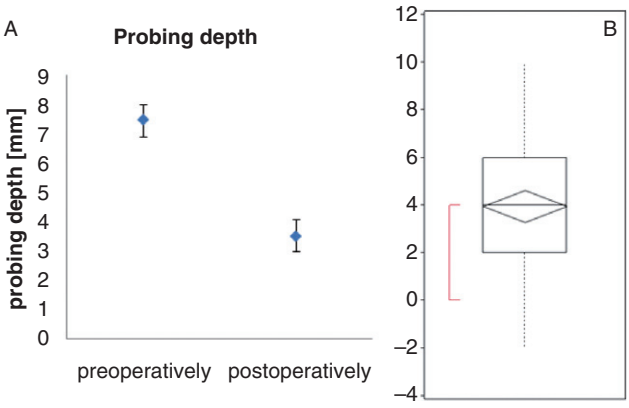

Figure 5 *A*, Probing depth before and 1 year after surgery. Average reduction was 4 mm. *B*, box plot of probing depth reductions (in mm; minimum, maximum, quartiles, median, and mean).

TABLE 1 Probing Depth Reduction and Bone Defect Reduction Frequencies (Number of Implants)

(mm)	Bone Defect Reduction	Probing Depth Reduction
<1	9	4
1–2	10	9
3–4	6	6
>4	11	17

bone defects were larger than 3 mm in 4 out of 36 implants 1 year after treatment. Probing depths of more than 4 mm were present in seven implants.

One local infection occurred 1 week after surgery causing loss of the augmentation material without loss of the implant. No further therapy was necessary in this case and the site was included in the statistical evaluation. No patients withdrew from the study.

DISCUSSION

Beside reasonable pain for the patient, progressive peri-implantitis leads to implant loss. So, adequate therapeutic regimens are required to at least stop irreversible bone loss. When a peri-implantitis is diagnosed, it has to be decided which way to go; following a "wait and see" strategy may complicate the course as after an implant removal, often, augmentations are necessary causing additional costs and time consumption. While a conservative therapy for smaller defects may be sufficient,[6,8] regenerative procedures are said to be necessary for bone defects larger than 4 mm in depth to avoid implant loss.[2] In animal studies, open debridement and surface decontamination was more effective than closed debridement.[4]

Regenerative procedures do not address disease resolution but rather attempt to fill the osseus defect.[4] Although the main goal of the treatment of peri-implant disease is to control the infection and to prevent disease progression,[20] other aspects seem to make regenerative methods more favorable than purely resective strategies: While the implant may remain in function, the esthetic outcome may be compromised by mucosal recessions.[20] In our study, before surgery, recessions were smaller than 1 year after surgery, but the swelling before surgery was considerable.

This is the first report about the clinical application of an autologous bone graft mixed with an osteoinductive material for regenerative treatment of bone defects because of peri-implantitis. Hanisch[21] reported that rhBMP-2 has the potential to promote bone formation and re-osseointegration in advanced peri-implantitis defects in a nonhuman primate model. Vertical bone gain in rhBMP-2 defects is significantly greater than in controls. RhBMP-2 can induce bone regenerative treatment in close neighborhood to the implant surface in an animal model.[22] Implant surfaces coated with recombinant human BMPs show a clinically significant potential to stimulate local bone formation.[23] Colloss is a demineralized xenogenic bone graft material. Beside Collagen Type I, it contains osteoinductive signal proteins so our aim was to improve regeneration by the help of these proteins.

The radiologic evaluation of the bone defects resulted in a defect fill of the bone defects of 3.5 mm on average 1 year after regenerative therapy, while probing depths could be reduced from an average of 7.5 mm to 3.5 mm. It is important to mention that only 1 out of 36 implants had to be removed. In all other cases, the treatment had lead to a stable implant surrounding. Most patients (23 out of 36) had probing depth reductions of at least 3 mm 1 year after treatment. Bone regenerative treatment was only assessed by x-ray, not by histologic analyses, as a reoperation for histological evaluation would not be ethical in patients. This procedure should be reserved for animal experiments. While a panoramic tomography allows the entire implant to be visualized, limitations including image resolution and distorsion are well known.[5] There is said to be an underestimation of bone loss in conventional radiography.

Decontamination of the infected area is essential. In the literature, several procedures are described, ranging from chemicals like chlorhexidine[24,25] or organic acids[26] to Er : YAG-Laser,[27,28] as well as mechanical purge and implant sleeking.[29,30] In a review, no single method of surface decontamination (chemical agents, air abrasives, and lasers) was found to be superior.[31] For decontamination of the implant surface, we have chosen etching gel, which is used, in general, for etching teeth before filling therapy. Etching gel has the great advantage of being precisely applicable without touching the surrounding bone or connective tissue but also reaching nonvisible areas. It has been used in our department for more than 4 years for such cases without any complication. Microbiological tests (not published) of implants

in situ have revealed complete elimination of the bacterial flora after decontamination with etching gel.

Jovanovic[32] reported about bone regenerative treatment in peri-implant defects simply covered with expanded polytetrafluoroethylene membranes in humans. The percentage of bone fill at reentry ranged from 28.4% to 100% in 19 implants after about 6 months. The use of autologous bone grafts alone in 12 implant sites[11] resulted in a bone level regenerative treatment of 3.2 mm on average after 3 years. Another study in eight cynomolgus monkeys with 64 implants[33] revealed an average bone gain of 4.7 mm for the combination of autologous bone and a nonresorbable membrane, as well as 4 mm for bone only and 3 mm for membrane only. The best results are thereby reported for the combination of autologous bone and membranes. Nonresorbable membranes have the disadvantage that they have to be removed in a second surgical approach and often cause soft tissue defects. To avoid these problems, we have omitted the membrane. This decision was justified by the observation that it is possible to treat peri-implant defects with a bone substitute, with or without a resorbable membrane.[10]

It has to be mentioned that we only observed one treatment group and that we did not compare the results with a control group. Ibuprofen has an analgesic compound effect but also an anti-inflammatory one. As we did not observe a control group without ibuprofen, we cannot determine the influence of this anti-inflammatory effect. Nevertheless the patients suffered from an extraorally visible swelling for a few days after surgery.

Within the limits of the study, we can conclude that for bone defects with a depth of more than 4 mm in case of peri-implantitis, this single surgical intervention provides a reliable method to reduce these defects sufficiently under local anesthesia.

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