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Healing of intra-bony defects following treatment with a composite bovine-derived xenograft (Bio-Oss Collagen) in combination with a collagen membrane (Bio-Gide PERIO)

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Abstract

Aim: The purpose of the present study was to compare clinically the treatment of deep intra-bony defects with a combination of a composite bovine-derived xenograft (BDX Coll) and a bioresorbable collagen membrane [guided tissue regeneration (GTR)] to access flap surgery only.

Methods: Thirty-two patients, each of whom displayed one intra-bony defect, were treated either with BDX Coll+GTR (test) or with access flap surgery (control). The results were evaluated at 1 year following therapy.

Results: No differences in any of the investigated parameters were observed at baseline between the two groups. Healing was uneventful in all patients. At 1 year after therapy, the test group showed a reduction in the mean probing depth (PD) from 8.3 ± 1.5 to 2.9 ± 1.3 mm ($p < 0.001$) and a change in the mean clinical attachment level (CAL) from 9.4 ± 1.3 to 5.3 ± 1.5 mm ($p < 0.0001$). In the control group, the mean PD was reduced from 8.0 ± 1.2 to 4.4 ± 1.7 mm ($p < 0.001$) and the mean CAL changed from 9.6 ± 1.3 to 7.9 ± 1.6 mm ($p < 0.01$). The test treatment resulted in statistically higher PD reductions ($p \leqslant 0.05$) and CAL gains ($p < 0.001$) than the control one. In the test group, all sites (100%) gained at least 3 mm of CAL. In this group, a CAL gain of 3 or 4 mm was measured at 10 sites (62%), whereas at six sites (38%), the CAL gain was 5 or 6 mm. In the control group, no CAL gain occurred at three sites (19%), whereas at 10 sites (62%), the CAL gain was only 1 or 2 mm. A CAL gain of 3 mm was measured in three defects (19%).

Conclusions: Within the limits of the present study, it can be concluded that the combination of BDX Coll+GTR resulted in significantly higher CAL gains than treatment with access flap surgery alone, and thus appears to be a suitable alternative for treating intra-bony periodontal defects.

Key words: collagen membrane; composite bovine-derived xenograft; controlled clinical study; guided tissue regeneration; regenerative periodontal therapy

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Recent results from human histological studies have provided evidence that treatment of intra-bony defects with a bovine-derived xenograft (BDX) alone or in combination with either autogenous bone, guided tissue regeneration (GTR) or enamel matrix protein derivative (EMD) may result in periodontal regeneration (i.e. formation of new

cementum, new periodontal ligament and new alveolar bone) (Camelo et al. 1998, 2001, Mellonig 2000, Sculean et al. 2003a, 2004). BDX possesses good osteoconductive properties and is well integrated into bone tissue (Berglundh & Lindhe 1997, Skoglund et al. 1997, Camelo et al. 1998, 2001, Hämmerle et al. 1998, Mellonig 2000, Zitzmann et al. 2001, Sculean et al. 2003a, 2004). The material is very well tolerated and, until now, no allergic reactions related to the material have been reported (Camelo et al. 1998, 2001, Richardson et al. 1999, Camargo et al. 2000, Mellonig 2000, Zitzmann et al. 2001, Sculean et al. 2002, 2003a, b, 2004, Tonetti et al. 2004). Findings from clinical studies have indicated that treatment of intra-bony defects with BDX+collagen membrane may result in significantly higher clinical attachment level (CAL) gains and osseous fill compared with that obtained following access flap surgery (Camargo et al. 2000, Sculean et al. 2003b, Tonetti et al. 2004). The clinical results following treatment of intra-bony defects with BDX were comparable with those obtained with demineralized freeze dried bone allograft (DFDBA) (Richardson et al. 1999). The combination of an EMD and BDX did not additionally enhance the histological and clinical results compared with treatment with BDX alone (Scheyer et al. 2002, Sculean et al. 2002, 2003a).

A composite bovine-derived xenograft (BDX Coll) consisting of approximately 90% deproteinized cancellous bone particles, embedded in a biodegradable collagen matrix of porcine origin (10%), has been introduced in regenerative periodontal therapy. Histological results from dogs have indicated an enhanced healing potential on applying this composite graft material in periodontal intra-bony defects (Clergeau et al. 1996). Human histological studies have shown regeneration of cementum, periodontal ligament and bone following filling of intra-bony periodontal defects with this material alone or combined with a bioresorbable collagen membrane (GTR) (Nevins et al. 2003, Sculean et al. 2004). Findings from a recent case series have indicated that treatment of intra-bony defects with BDX Coll+GTR may result in substantial probing depth (PD) reduction and CAL gain (Zitzmann et al. 2003).

Although these preliminary results are promising, there are still limited data from clinical studies evaluating the healing of intra-bony defects following treatment with BDX Coll+GTR. Furthermore, according to the best of our knowledge, for the time being, there are no data from controlled clinical studies comparing the treatment of intra-bony defects with BDX Coll+GTR with that with access flap surgery only.

Therefore, the aim of this controlled clinical study was to compare the treatment of intra-bony defects with BDX Coll+GTR (test) with access flap surgery alone (control).

Material and Methods

Thirty-two patients (17 females and 15 males) with one intra-bony periodontal defect each were included in this parallel design study (i.e. 16 patients in each group) after having signed an informed consent form. The study was performed according to the declaration of Helsinki as revised in 1983. The criteria needed for inclusion in the study were as follows: (1) no systemic diseases that could influence the outcome of the therapy; (2) a good level of oral hygiene, defined as a whole-mouth plaque index (PI) <1 (Löe 1967); (3) compliance with the maintenance programme and (4) presence of one intra-bony defect with a PD of at least 6 mm and an intra-bony component (INTRA) of at least 3 mm as detected on the radiographs. All patients received non-surgical periodontal treatment, including oral hygiene instructions and scaling and root planing under local anaesthesia at least 3 months prior to the start of the study.

The following clinical parameters were assessed 1 week prior to and 1 year after the surgical procedure using the same periodontal probe (PCP 12, Hu-Friedy, Chigago, IL, USA): PI, gingival index (GI) (Löe 1967), bleeding on probing (BOP), PD, gingival recession (GR) and CAL. Measurements were made at six sites per tooth: mesiovestibular (mv), midvestibular (v), distovestibular (dv), mesiooral (ml), midoral (l) and distooral (dl). The cementoenamel junction (CEJ) was used as the reference point. In cases where the CEJ was not visible, a restoration margin was used for these measurements. The study reports only measurements at the same deepest point of the selected defect. Pre- and postoperative radiographs were taken with the long cone paralleling technique.

Intra-examiner reproducibility

Five patients, each showing 10 teeth (single- and multi-rooted) with PDs >6 mm on at least one aspect of each tooth, 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 similar to the millimetre at $>90\%$ level. The examiner was not aware of the surgical procedure to be performed.

Surgical procedure

Following local anaesthesia and placement of intra-crevicular incisions, 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 roots were thoroughly scaled and planed using the hand and ultrasonic instruments. No root surface conditioning was performed. During surgery, the following measurements were made: distance from the CEJ to the bottom of the defect (CEJ–BD), and distance from the CEJ to the most coronal extension of the alveolar bone crest (CEJ–BC). The INTRA of the defects was defined as (CEJ–BD)–(CEJ–BC).

The defects were randomly assigned before surgery to the two treatment groups with the randomized block approach. Blocking to control for the effects of the prognostic variables INTRA and CAL was used to decrease outcome variability (Fleiss 1986). For allowing randomization, INTRA was estimated before surgery on radiographs and by performing transgingival bone sounding.

At the test sites, the defects were filled with a composite bovine-derived xenograft [BDX Coll (Bio-Oss Collagen®, Geistlich, Wolhusen, Switzerland)]. The graft material was moistened in sterile saline for 5 min. before placement into the defect. Following grafting, a bioresorbable collagen membrane of porcine origin (BioGide Perio®, Geistlich) 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 was re-posi-

tioned coronally and fixed with vertical or horizontal mattress sutures.

The same surgical protocol was also used for the control sites, however, without any additional procedure.

Postoperative care

The postoperative care consisted of 0.2% chlorhexidine rinses twice a day for 4 weeks. The sutures were removed 14 days after the surgery. Recall appointments were scheduled every second week during the first 2 months after surgery and monthly following the rest of the observation period. Neither probing nor subgingival instrumentation were performed during the first year after surgery.

Statistical analysis

The statistical analysis was performed using a commercially available software program (SPSS® for Windows, Chicago, 1997). The primary outcome variable was the CAL. In the calculations, the deepest site per tooth was included. For the statistical evaluation of the changes from baseline to 1 year, the paired *t*-test was used. For the comparisons between the groups, the unpaired *t*-test was used. The α error was set at 0.05. The power of the study, given 1 mm as a significant difference between the groups, was calculated to be 0.70.

Results

The postoperative healing was considered as generally uneventful. Minor complications were related to usual postoperative swelling and occurred within the first days after surgery. Neither allergic reactions nor suppuration or abscesses were observed in any of the patients. Membrane exposure occurred at four out of the 16 sites. The exposed parts of the membranes disintegrated without any side effects.

The mean PI, GI and BOP at the treated sites for each of the two groups at baseline and after 1 year are summarized in Table 1.

The mean PI did not reveal a statistically significant difference in any of the two groups when compared with baseline or between the groups. In both groups, the GI and BOP improved significantly compared with baseline ($p<0.001$). However, at 1 year, the difference between the groups was not statistically significant.

Table 1. Mean (± SD) plaque, gingival and bleeding scores at the treated sites at baseline and the 1-year examination

	Test	Control
Plaque index scores		
Baseline	0.9 ± 0.3	0.8 ± 0.6
12 months	0.8 ± 0.5	0.9 ± 0.5
Gingival index scores		
Baseline	1.4 ± 0.5	1.6 ± 0.5
12 months	0.7 ± 0.4	0.8 ± 0.4
Bleeding scores		
Baseline	74%	72%
12 months	23%	25%

Table 2. Distribution and configuration of treated defects

	Test ($N=16$)	Control ($N=16$)
Maxilla	7	8
Mandible	9	8
Anterior teeth	7	6
Pre-molars	5	5
Molars	4	5
1–2 wall	5	4
2 wall	9	9
3 wall	2	3

Defect characteristics with respect to tooth type are presented in Table 2. No differences in the distribution of the defects were found between the two groups.

Baseline defect characteristics are presented in Table 3. At baseline, no differences in the depth of the INTRA were found between the two groups.

The clinical results at 1 year after treatment are presented in Table 4.

No differences in any of the investigated parameters were observed at baseline between the two groups. Healing was uneventful in all patients. At 1 year after therapy, the test group showed a reduction in the mean PD from 8.3 ± 1.5 to 2.9 ± 1.3 mm ($p<0.001$) and a change in the mean CAL from 9.4 ± 1.3 to 5.3 ± 1.5 mm ($p<0.0001$). In the control group, the mean PD was reduced from 8.0 ± 1.2 to 4.4 ± 1.7 mm ($p<0.001$), and the mean CAL changed from 9.6 ± 1.3 to 7.9 ± 1.6 mm ($p<0.01$). The test treatment resulted in statistically higher PD reductions ($p\leqslant0.05$) and CAL gains ($p<0.001$) than the control one.

The frequency distribution of CAL gain for both treatment groups is shown in Table 5. In the test group, all sites (100%) gained at least 3 mm of CAL. In this group, a CAL gain of 3 or 4 mm was measured at 10 sites (62%), whereas at six sites (38%) the CAL gain was 5 or 6 mm. In the control group, no CAL gain occurred at three sites (19%), whereas at 10 sites (62%) the CAL gain was 1 or 2 mm. A CAL gain of 3 mm was measured in three defects (19%).

Patients who reported smoking more than 10 cigarettes daily were defined as smokers (Tonetti et al. 1996). 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.

Discussion

The results of this study have shown that treatment of deep intra-bony defects with both the combination of BDX Coll+GTR and access flap surgery resulted in significant PD reductions and CAL gains. The test treatment has, however, led to statistically significantly higher PD reductions and CAL gains than the control one.

In a recent case series study, 12 patients with a total of 22 intra-bony defects were consecutively treated with BDX Coll+GTR (Zitzmann et al. 2003). At 24 months following therapy, the results revealed a mean CAL gain of 3.2 mm. On analysing the data in more detail, the authors found that the clinical improvements were greater at deep sites (i.e. INTRA > 3 mm) than at shallow ones (i.e. INTRA ⩽ 3 mm). These findings are consistent with the results of the present study where, at 1 year following therapy, the mean CAL gain measured 4.1 mm. However, when interpreting the results, it is important to point out that in the present study, all 16 defects treated with BDX Coll+GTR have gained at

Table 3. Baseline defect characteristics expressed in mm (mean ± SD)

Treatment	PD (mm)	GR (mm)	CAL (mm)	CEJ–BD (mm)	CEJ–BC (mm)	INTRA (mm)
Test ($n = 16$)	8.3 ± 1.5	1.1 ± 0.9	9.4 ± 1.3	10.6 ± 1.1	6.8 ± 1.2	3.8 ± 1.2
Control ($n = 16$)	8.0 ± 1.2	1.8 ± 1.1	9.6 ± 1.3	10.8 ± 1.2	7.1 ± 1.3	3.7 ± 1.3

PD, probing depth; GR, gingival recession; CAL, clinical attachment level; CEJ–BD, distance from the cemento-enamel junction (CEJ) to the bottom of the defect; CEJ–BC, distance from the CEJ to the most coronal extension of the alveolar bone crest; INTRA, intra-bony component.

Table 4. Clinical parameters at baseline and 1 year for the test and control groups

($n = 16$ for each group)	Baseline	1 Year	Difference	Significance (p)
Probing depth				
Test	8.3 ± 1.5	2.9 ± 1.3	5.4 ± 0.9	<0.001
Control	8.0 ± 1.2	4.4 ± 1.7	3.6 ± 1.3	<0.001
			$p \leqslant 0.05$	
Gingival recession				
Test	1.1 ± 0.9	2.4 ± 1.1	1.3 ± 1.0	<0.01
Control	1.8 ± 1.1	3.5 ± 1.4	1.6 ± 0.9	<0.01
			NS	
Clinical attachment level				
Test	9.4 ± 1.3	5.3 ± 1.5	4.1 ± 0.9	<0.0001
Control	9.6 ± 1.3	7.9 ± 1.6	1.9 ± 1.1	<0.01
			$p<0.001$	

NS, non-significant.

Table 5. Frequency distribution of CAL gain in the test and control groups ($n = 16$ for each group)

CAL gain (mm)	Test		Control	
	No.	%	No.	%
0	0	0	3	19
1	0	0	1	6
2	0	0	9	56
3	5	31	3	19
4	5	31	0	0
5	5	31	0	0
6	1	7	0	0
7	0	0	0	0

CAL, clinical attachment level.

least 3 mm or more CAL. Moreover, at six out of the 16 defects, a CAL gain of 5 or 6 mm was measured.

When interpreting the clinical results, it also needs to be pointed out that the PI, GI and BOP values measured in this study are somewhat higher than those reported by some of the previous clinical studies evaluating treatment of intra-bony defects with either GTR alone or BDX+GTR (Cortellini et al. 1996, Tonetti et al. 1996, 2004). Thus, it cannot be excluded that with further improvement of the plaque control, a higher CAL gain might have been obtained.

On the other hand, despite the fact that between the two groups there were neither differences in terms of initial defect depth and configuration nor were there any other factors such as postoperative infection or smoking that might have interfered with the healing process, it is most likely that the significantly higher CAL gains obtained in the test group are as a result of the type of treatment. Moreover, results from human histological studies have demonstrated that treatment of intra-bony defects with BDX Coll+GTR may predictably enhance periodontal regeneration characterized by formation of new cementum, new periodontal ligament and new bone (Nevins et al. 2003, Sculean et al. 2004). Thus, based on these histological findings, it may be assumed that the results obtained following this treatment modality do not only represent a clinical improvement but also, at least in part, periodontal regeneration.

Results from previous controlled clinical studies evaluating the healing of intra-bony defects with BDX+GTR have reported a mean CAL gain of 2.1, 4.0 and 3.3 mm, respectively (Camargo et al. 2000, Sculean et al. 2003b, Tonetti et al. 2004). The results are comparable with those obtained with BDX Coll+GTR by Zitzmann et al. (2003) and also to those from the present study. Therefore, it might be speculated that both grafting materials in combination with the used collagen membrane are suitable techniques for treating intra-bony periodontal defects (Camargo et al. 2000, Sculean et al. 2003b, Zitzmann et al. 2003, Tonetti et al. 2004). It is, however, important to point out that to date, there are no published data from controlled clinical studies comparing these treatment modalities directly and therefore, no conclusions can be drawn regarding the possible advantage of using BDX+GTR or BDX Coll+GTR for treating intra-bony periodontal defects. Prospective, randomized, controlled clinical studies are needed in order to clarify these issues.

The mean of 1.9 mm of CAL gain obtained in the control group is in agreement with most of the reported results (Cortellini et al. 1996, Camargo et al. 2000, Sculean et al., 2003b). Slight differences in the results may be explained with baseline defect depth and configuration. It is well documented that the postoperative PD reduction and CAL gain obtained after any type of regenerative or conventional periodontal treatment is dependent upon the initial defect depth (i.e. the deeper the defect, the higher the CAL gain) (Ramfjord et al. 1987, Kahldahl et al. 1996, Cortellini et al. 1998). When interpreting the results obtained following access flap surgery, it should be emphasized that out of 16 cases, a CAL gain of 3 mm was measured in only three defects (19%).

Taken together, all these data seem to indicate that regenerative therapy of intra-bony periodontal defects with BDX Coll+GTR may more predictably result in 3 mm or more CAL gain than treatment with access flap surgery. This issue in turn may become especially critical when the clinician needs to decide the type of treatment for predictably improving the outcome of periodontal surgery of deep intra-bony defects at strategically important teeth.

Within the limits of the present study, it can be concluded that the combination of BDX Coll+GTR resulted in significantly higher CAL gains than treatment with access flap surgery and thus appears to be a suitable alternative for treating intra-bony periodontal defects.

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