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Primary flap closure combined with Emdogain® alone or Emdogain® and Cerasorb® in the treatment of intra-bony defects

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Abstract

Objectives: To compare clinical outcomes of three different modalities of treatment for deep intra-bony defects.

Material and methods: Fifty-six patients were paralleled for clinical parameters and randomly assigned to treatment. They displayed one angular defect each with an intra-bony component $\geqslant 3$ mm, probing pocket depth (PPD) and probing attachment level (PAL) $\geqslant 7$ mm, and plaque index (PI) <1. Nineteen defects were treated, respectively, with enamel matrix derivative (EMD)+tricalcium phosphate (TCP) or EMD alone and 18 defects with modified Widman flap (MWF). Primary flap closure was used in all three groups. PI, gingival index, bleeding on probing, PPD, PAL, and recession (REC) were measured before and 12 months after treatment.

Results: Treatment with EMD alone yielded a 3.9 ± 1.3 mm PPD decrease and a 3.7 ± 1.0 mm PAL gain ($p<0.001$), whereas EMD+β-TCP produced a 4.1 ± 1.2 mm PPD reduction and a 4.0 ± 1.0 mm PAL gain ($p<0.001$). These outcome parameters did not differ between the two groups. REC increased by 0.7 ± 1.3 mm. After MWF treatment, attachment gain was 2.1 ± 1.4 mm ($p<0.001$) and PPD reduction was 3.8 ± 1.8 mm, whereas REC increased by 1.5 ± 0.7 mm ($p = 0.042$ *versus* EMD).

Conclusion: Both EMD treatments showed similar clinical effects, with significant PAL gain and a significantly lower REC increase in comparison with MWF treatment.

Key words: β-tricalcium phosphate; enamel matrix derivatives; microsurgery; periodontal bony defects; regenerative therapy

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Periodontal regeneration in animals and humans can be enhanced by use of enamel matrix derivative (EMD) (Hammarström et al. 1997, Sculean et al. 1999, 2000). EMD is an extract of the enamel matrix that contains amelogenins of different molecular weight, which contribute to the formation of acellular cementum during dentogenesis (Hammarström 1997). Animal studies showed that EMD applied to the denuded root surface leads to regeneration of all periodontal structures (Hammarström et al. 1997, Hammarström 1997). Such ''biomimicry'' (Gestrelius et al. 2000) after EMD treatment of periodontal defects was also observed in humans. Various histological studies showed the new formation of both acellular and cellular cementum in most cases within 6 months after treatment (Heijl 1997, Mellonig 1999, Sculean et al. 1999). Yukna & Mellonig (2000) observed true regeneration showing new bone, new cementum, and new ligament and, in some cases, the formation of new connective tissue attachment or long junction epithelium. Similar findings have been reported recently by McGuire& Cochran (2003).

Schwartz et al. (2000), who studied osteoblast responses to EMD application, found that EMD supported cell-specific proliferation in early stages and cell differentiation in later stages of osteoblast development. Moreover, EMD was also found to prevent epithelial vertical growth by intra-cellular cAMP signalling and stimulates proliferation and attachment of desmodontal fibroblasts and their autocrine production of growth factors, such as transforming growth factor β1, IL-6, and platelet-derived growth factor AB (Gestrelius et al. 1997, Van der Pauw et al. 2000, Lyngstadaas et al. 2001).

EMD treatment of deep defects results in a reduction of probing depth and a 3–4 mm gain in clinical attachment (Cardaropoli & Leonhardt 2002, Kalpidis & Ruben 2002, Tonetti et al. 2002, Esposito et al. 2003, Sculean et al. 2003a). These results slightly exceed those of conventional open flap curettage and are similar to the results of guided tissue regeneration (Pontoriero et al. 1999, Minabe et al. 2002, Tonetti et al. 2002, Esposito et al. 2003, Yilmaz et al. 2003). As in other regenerative procedures, smoking is the most important factor influencing the EMD treatment outcome (Tonetti et al. 1996, 2002). The clinical advantages of EMD treatment over conventional flap surgery or non-surgical scaling and root planing have not been consistently confirmed (Hammarström et al. 1997, Dragoo 1999, Gutierrez et al. 2003), and have been found to be slight in most cases (Tonetti et al. 2002).

The combination of EMD with bone replacement materials is aimed at enhancing wound stability and gain sufficient space for the regenerative process. Combining graft material with EMD has a synergistic effect in terms of promoting periodontal regeneration. In most studies on treatment of intra-bony bony defects in humans, EMD was used in combination with xenogenous bone grafts (Lekovic et al. 2000, 2001, Camargo et al. 2001, Rosen & Reynolds 2002, Scheyer et al. 2002, Sculean et al. 2002, Velasquez-Plata et al. 2002, Zucchelli et al. 2003); however, the results were inconsistent.

Today, β-tricalcium phosphate (β-TCP) provides an implantable granulate material for filling and re-construction of osseous defects, allowing for ''remodelling'' of the original bony structure. Physicochemically, β-TCP is a resorbable material with $\geqslant$99% phase purity (Tadic & Epple 2004), total microporosity, and a homogeneous ceramic sinter structure. Thus, optimal matrix for the formation of new bone is available immediately after implantation. The inter-granular spaces provide a scaffold for in-growths of blood vessels for nutrition of the newly formed bony structures. From the initial stage of bone regeneration, the material is dissolved due to biochemical conditions of the implant bed. Within 24 months, the material is completely metabolized, and the damaged bone is completely restored (Ellinger et al. 1986, Artzi et al. 2004). Gera et al. (2002) studied the regenerative–reparative potential of β-TCP in the treatment of two-/three-walled bony defects. After 6 months, wound healing was very variable, but after 1 year, a substantial gain of bone and attachment was observed, unless sequestration occurred. The largest bone filling was observed radiographically in three-wall defects.

Table 1. Patient characteristics and tooth and defect features in three treatment groups at baseline

Patient characteristic	Treatment groups (no. of patients)			p^*
	EMD ($n = 19$)	EMD+C ($n = 19$)	MWF ($n = 18$)	
Age (years, mean ± SD)	56.6 ± 9.4	59.7 ± 7.6	55.0 ± 8.4	
Sex (m/f)	9/10	8/11	9/9	0.95
Smoking habit	5	4	4	
Defect location				
Upper jaw	8	8	13	0.11
Lower jaw	11	11	5	
Tooth type				
Incisor	1	1	4	0.14
Canine	5	6	2	
Premolar	7	6	2	
Molar	6	6	10	
Type of defect				
One-/two-walled	11	9	10	0.65
Two-/three-walled	8	10	8	
Depth of defect (mm)				
3–4	9	9	10	0.78
5–8	9	9	8	
10–12	1	1	0	

EMD, Emdogain®; EMD+C, Emdogain®+Cerasorb®; MWF, modified Widman flap technique; SD, standard deviation.

All the above-mentioned studies, except the study by Zucchelli et al. (2003), used open-flap debridement. Inter-proximal tissue maintenance and primary flap closure were often reported as important factors of wound healing and improved treatment outcomes (Cortellini et al. 1995, 1999, Murphy 1996, Zucchelli et al. 1997, Zucchelli et al. 2003, Francetti et al. 2004, Trombelli et al. 2005, Linares et al. 2006). These observations had already been reported by Ramfjord & Nissle (1974), who introduced modified Widman flap (MWF) surgery as a technique for primary flap closure in intra-bony defect repair.

One of the regenerative treatment techniques, using microsurgery for primary flap closure and aiming at maximum tissue preservation, was described by Cortellini & Tonetti (2001). Similarly, Wachtel et al. (2003) reported significant improvement of clinical outcomes using microsurgical access flap for primary flap closure according to the principle of the modified papilla preservation technique in EMD treatment of intra-bony defects.

The aim of our study was to compare regenerative treatment modalities using primary flap closure combined with EMD alone or in combination with β-TCP and conventional reparative MWF technique for the treatment of intra-bony defects in terms of their clinical outcomes, including pocket depth reduction, probing attachment gain, and improvement of gingival recession.

Material and Methods

Fifty-six patients (29 females and 27 males) with at least one intra-bony defect were enrolled in the parallel-group clinical trial (Table 1). After radiographic determination of the intra-osseous component by use of a calibrated periodontal probe (PCPUNC 15, Hu Friedy Mfg. Co. Inc., Chicago, IL, USA), the patients were randomly assigned to one of the three different treatment groups according to a random number table.

To be included in the study, the patients had to meet the following criteria: (1) absence of systemic diseases with possible impact on treatment outcome, (2) adequate oral hygiene (plaque index <1) (Löe 1967), and (3) existence of a radiologically proven bony defect with the probing depth of $\geqslant 7$ mm and an intra-osseous component of $\geqslant 3$ mm. Each patient had a single periodontal bony defect. All patients gave their informed consent before being enrolled in the study.

Defects in 19 patients were surgically treated with enamel matrix proteins alone (Emdogain®, Biora, Malmö, Sweden), defects in 19 patients were treated with Emdogain® combined with commercially available resorbable β-TCP (Cerasorb®, Curasan, Kleinostheim, Germany), whereas defects in 18 patients were treated with MWF surgery (Ramfjord & Nissle 1974). Primary flap closure was used in all three treatment modalities. The three study groups were comparable in terms of age, sex, smoking behaviour, teeth involved, and the type and depth of bony defects (Table 1).

Baseline measurements

One week before surgery, an independent and calibrated examiner, blinded for group membership, performed the following baseline measurements in each patient, using a stiff periodontal probe (PCPUNC 15): probing pocket depth (distance between the gingival margin and bottom of the pocket), probing attachment level (distance between the cementoenamel junction and bottom of the pocket), gingival recession (distance between the cementoenamel junction and gingival margin) as an aesthetic parameter, full-mouth plaque index, gingival index (Löe 1967), and bleeding on probing after 30 s. The measurements of probing pocket depth, probing attachment level, and gingival recession were recorded to the nearest millimetre at the deepest point of the inter-dental site.

The calibration of examiner was performed according to Glavind & Löe (1967). The difference between duplicate measurements of probing pocket depth and probing attachment level was used to assess the accuracy and reproducibility of measurements (method error). All measurements were performed by a single examiner. The method errors in measured reduction of pocket depth and loss of attachment ranged from ± 0.30 to ± 0.50 mm and from ± 0.54 to ± 0.78 mm, respectively, and were comparable with the error reported by Glavind & Löe (1967).

Six tooth measurements (mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual) were performed, with the cementoenamel junction serving as the reference point. The deepest measuring site defined by the inter-dental line angles of the affected tooth was used for analysis.

The depth of the intra-bony component was determined during surgery as the difference between the distance from the cementoenamel junction to the bottom of the defect and the distance from the cementoenamel junction to the most coronal portion of the bone crest.

The pre-surgical protocol involved an initial 3-week interval with professional tooth cleaning, patient motivation, scaling, root planing, and oral hygiene instructions. The overhanging filling margins were removed where necessary and rough grinding was performed.

Surgical procedures

All surgical procedures were performed under local anaesthesia. For surgical mobilization of the mucoperiosteal flap, either a simplified papilla preservation technique (Cortellini et al. 1999, Zucchelli et al. 2003) or a microsurgical approach was used according to the modified papilla preservation technique (Cortellini et al. 1995), as suggested by Wachtel et al. (2003). The simplified variant as described by Zucchelli et al. (2003) was chosen if the width of the inter-dental space was <2 mm, whereas the modified variant with the microsurgical approach (Wachtel et al. 2003) was used if the inter-dental space was wide and gingival thickness sufficient.

In case of a narrow inter-dental space, an oblique incision according to the original technique (Cortellini et al. 1999) and buccal and lingual intra-sulcular incisions were made with microsurgical blades.

In case of a wide inter-dental space, a horizontal incision on the base of the papilla was performed according to the original technique (Cortellini et al. 1995). In accordance with the Wachtel et al. (2003) technique, buccal and lingual intra-sulcular incisions were performed with microsurgical blades (Hu Friedy Mfg. Co. Inc.). The mucoperiosteal flap was elevated buccally and palatally with fine papilla and periosteal elevators. Loupes (magnification factor 5.0, Carl Zeiss, Oberkochen, Germany) were used for better visual control of the *surgical* area. To provide a better access to the buccally located defects, a slightly modified flap design was used (Figs 1 and 2). In contrast to the original techniques (Cortellini et al. 1999, Wachtel et al. 2003), the papilla flap was designed by use of microsurgical blades (Figs 1b and 2b) and extended beyond the defect border, thus providing better access to the defect area. The underlying bone around the defect was exposed (Figs 1c and 2b) to provide better healing conditions after suturing of the flap (Figs 1e and 2d).

After the flap was elevated and the papilla flap pushed to the palatal site with a fine papilla elevator, the granulation tissue was removed from the defects with curettes and from the inner side of the flap by use of microsurgical scissors. The root surfaces were cleaned and planed by use of manual and ultrasound instruments (Piezon Master 400 – EMS SA, Nyon, Switzerland; (Figs 1c and 2b). After the defects were cleaned, the neighbouring root surfaces were conditioned for 2 min. with 24% ethylenediaminetetraacetic acid (EDTA, PrefGeL, Biora, Malmö, Sweden) to remove the smear layer and then thoroughly irrigated with sterile saline solution. In the Emdogain®-treated group, enamel matrix protein (Emdogain®) was applied to the root surfaces (Fig. 1d). The same procedure was used in the group treated with a combination of Emdogain® and Cerasorb® until the defects were completely filled (Fig. 2c).

After exact re-positioning, the buccal and palatal part of the flap were adapted to each other without tension by horizontal mattress sutures (Gore-Tex CV-5, RT-16, Gore-Tex W.L. Gore, Flagstaff, AZ, USA or Ethilon 4-0, Ethicon GmbH & Co. KG, Norderstedt, Germany) according to the simplified or modified papilla preservation technique, as suggested by Zucchelli et al. (2003) and Wachtel et al. (2003). Microsurgical suturing material (Vicryl 8/0 Ethicon, needle GS-9) was used for optimal primary flap closure. In our flap design, horizontal mattress sutures were not used (Figs 1e and 2d).

In the MWF-treated group, the mucoperiosteal flap was mobilized as originally described (Ramfjord & Nissle 1974). Paramarginal incisions were used to remove the pocket epithelium, while two vertical incisions were performed to improve flap flexibility. To achieve complete flap closure after coronal re-position of the flap, a periosteal incision was performed in the most apical portion of the buccal flap. Thorough scaling and root planing followed the removal of the granulation tissue from the defect. No additional agents were applied in these patients. All surgical procedures were performed by the same surgeon (I. B.).

An antibiotic regimen (Doxycyclin, 100 mg/day) was prescribed for one week after surgery, and 0.1% chlorhexidine digluconate solution (Chlorhexamed, Glaxo-Smith Kline Consumer Healthcare, Bühl, Germany) for wound care for 4 weeks. The patients were instructed to avoid mechanical cleaning of the surgical area for 4 weeks. Instead, professional tooth cleaning was carried out with a rubber cup. The sutures were removed 2 weeks after surgery.

Fig. 1. Microsurgical access flap for buccally located defects. (a) Site treated with Emdogain® alone and microsurgically modified ''papilla-preservation'' technique with 7 mm loss of attachment before surgery; (b) incision extended beyond the defect border in comparison with the original technique (Cortellini et al. 1995); (c) flap deflection with buccal one+two-wall bony defect; (d) application of Emdogain; (e) flap reposition and fixation with microsuture (Vicryl 8/0 Ethicon, needle GS-9); and (f) situation 1 year after surgery with improved papilla contour in comparison with pre-operative situation.

Appointments were made for plaque control every 4 weeks for half a year. After that, supportive therapy in terms of professional tooth cleaning was provided at 3-month intervals. During 1-year follow-up, neither probing nor subgingival instrumentation was performed.

The smokers avoided smoking 3 weeks before and 6 weeks after surgery. Thereafter, six smokers quit smoking, while three continued smoking <10 cigarettes/day. One patient dropped out of the study (MWF group) due to moving abroad and was thus excluded from the analysis.

One year after surgery, probing depth, attachment level, gingival recessions, plaque index, gingival index, and bleeding on probing were re-assessed.

Statistical analysis

Data analysis was performed with Statistical Package for Social Sciences 11.0 for Windows (SPSS Inc., Chicago, IL, USA) and was based on the value obtained at the same, deepest site of the respective defect. The differences between the baseline values and values obtained 1 year after treatment were presented as means $\pm$ standard deviation and analysed with Student's *t*-test for dependent samples and McNemar's test. The groups were compared by *t*-test for independent samples, χ^2 test, and Fisher's exact. The α error was set at 0.05.

Results

Tissue shrinkage was less pronounced in patients treated with Emdogain® alone or in combination with Cerasorb® than in MWF-treated patients. There was a slight, but still obvious aesthetic improvement after use of microsurgical

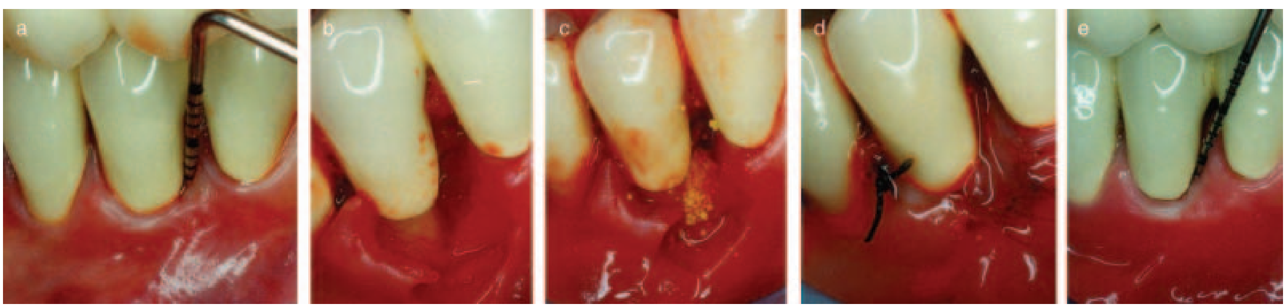

Fig. 2. Microsurgical access flap for buccally located defects. (a) Site treated with Emdogain® in combination with Cerasorb® and microsurgically modified ''papilla-preservation'' technique, with 7 mm loss of attachment before surgery; (b) flap deflection with buccal one+two-wall bony defect, (c) application of Emdogain® and Cerasorb®; (d) flap reposition and fixation with microsuture (Vicryl 8/0 Ethicon, needle GS-9); and (e) situation 1 year after surgery with unaltered gingival contour in comparison with the pre-operative situation.

Table 2. Mean plaque index, gingival index, and frequency of bleeding on probing in three treatment groups at baseline and 1 year after treatment

Parameter	Treatment groups			p
	EMD ($n = 19$)	EMD+C ($n = 19$)	MWF ($n = 18$)	
PI (mean ± SD)				
Baseline	0.7 ± 0.1	0.7 ± 0.1	0.8 ± 0.2	0.32
1 year	0.5 ± 0.1	0.5 ± 0.1	0.6 ± 0.2	
Difference	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.2	
GI (mean ± SD)				
Baseline	0.9 ± 0.2	1.1 ± 0.2	0.9 ± 0.2	0.15
1 year	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	
Difference	0.1 ± 0.1	0.3 ± 0.1	0.1 ± 0.2	
BOP (%)				
Baseline	43.8	42.1	50.0	0.05
1 year	18.8	21.1	22.0	
Difference	25.0	21.0	27.8	

EMD, Emdogain®; EMD+C, Emdogain®+Cerasorb®; MWF, modified Widman flap technique; PI, plaque index; SD, standard deviation; GI, gingival index; BOP, bleeding on probing.

Table 3. Probing pocket depth, probing attachment level, and gingival recession at baseline and 1 year after treatment

Parameter	Treatment groups (mean ± SD)			p
	EMD ($n = 19$)	EMD+C ($n = 19$)	MWF ($n = 18$)	
PPD (mm)				
Baseline	8.6 ± 1.3	8.6 ± 1.4	9.8 ± 1.7	0.84
1 year	4.7 ± 0.9	4.5 ± 1.2	6.0 ± 1.2	
Difference	3.9 ± 1.3	4.1 ± 1.2	3.8 ± 1.8	
PAL (mm)				
Baseline	10.3 ± 1.8	9.8 ± 1.3	10.2 ± 1.7	<0.001
1 year	6.5 ± 1.4	5.8 ± 1.1	8.1 ± 1.2	
Difference	3.7 ± 1.0	4.0 ± 1.0	2.1 ± 1.4	
REC (mm)				
Baseline	2.4 ± 2.0	1.3 ± 1.2	1.1 ± 1.1	0.042
1 year	3.1 ± 2.2	1.9 ± 1.7	2.6 ± 1.6	
Difference	0.7 ± 1.3	0.7 ± 1.1	1.5 ± 0.7	

SD, standard deviation, EMD, Emdogain®; EMD+C, Emdogain®+Cerasorb®; MWF, modified Widman flap technique; PPD, probing pocket depth; PAL, probing attachment level; REC, gingival recession.

approach in comparison with the pre-surgical situation (Figs 1a, f and 2,a e). Wound healing and follow-up periods were free of complications in all cases. All patients showed good compliance during the study.

In comparison with baseline values, the plaque and gingival indices were significantly improved 1 year after treatment in all groups (t-test$_{dep}$, $p \leqslant 0.001$ for all). However, these indices did not significantly differ between the groups either before or 1 year after the treatment (Table 2). The number of bleedings on probing was significantly reduced 1 year after treatment (McNemar's test, $p \leqslant 0.02$). However, the difference in bleeding on probing between the groups was not highly significant (χ^2 test, $p = 0.05$).

One year after treatment, probing pocket depth was significantly reduced in comparison with baseline values in all groups (t-test$_{dep}$, $p < 0.001$). There was no significant difference in probing pocket depth between the groups (t-test$_{indep}$, $p = 0.84$; Table 3). Similarly, the probing attachment level was significantly improved in all groups (t-test$_{dep}$, $p < 0.001$). The attachment gain differed between the groups (t-test$_{indep}$, $p < 0.001$), with the MWF technique producing the lowest mean gain of attachment with a maximum variability (Table 3). The Emdogain®-treated group had more pronounced gingival recessions before the surgery than the other two groups ($p = 0.05$; Table 3). Gingival recession significantly increased after surgery in all three groups (t-test$_{dep}$, $p \leqslant 0.026$), with the mean increase in the MWF-treated group being twice as large as in the other groups ($p = 0.042$).

The analysis of the level of clinical attachment, i.e. of the classes of attachment gain, showed that the highest ($\geqslant 4$ mm) gain in clinical attachment was achieved in over half of patients treated with Emdogain® alone or in combination with Cerasorb® (Table 4), which was significantly more than in the MWF-treated group, where only one patient had the $\geqslant 4$ mm gain in clinical attachment (χ^2 test, $p < 0.001$). In the MWF-treated group, 11 patients had the lowest ($\leqslant 2$ mm) class of attachment gain, which was significantly more than in the other two groups (χ^2 test, $p < 0.001$). A reduction in pocket depth of > 3 mm was achieved in over half of the patients in each treatment group (Table 5).

Primary flap closure at baseline was achieved in all patients treated with Emdogain® alone or in combination with Cerasorb® and in 10 of 18 patients treated by the MWF procedure. At 2 weeks, complete coverage of the inter-dental space was present in 16 of 19 patients treated with Emdogain® alone, 17 of 19 patients treated with Emdogain® in combination with Cerasorb®, and six of 18 MWF-treated patients.

Discussion

We found that treatment of deep intra-bony defects with Emdogain® either alone or in combination with Cerasorb® led to a clinically and statistically significant reduction of probing pocket depth and gain in clinical attachment. The additional application of Cerasorb® showed no clear superiority to treatment with Emdogain® alone. Similar results were reported by Sculean et al. (2004) for bioactive glass combined with Emdogain®.

In terms of reduced pocket depth and attachment gain, our study results are within the range of similar clinical studies using Emdogain®. The extent of gain in clinical attachment 1 year after treatment in our study was comparable to that reported by Wachtel et al. (2003), who used Emdogain® in combination with a microsurgical tissue-protecting flap. Also, in our study, complete flap closure after 2 weeks was achieved in over four of five patients treated with

Table 4. Distribution of classified gain of attachment in three treatment groups

Attachment gain (mm)	Treatment group (no. of patients)			
	EMD ($n = 19$)	EMD+C ($n = 19$)	MWF ($n = 18$)	total
⩽2	1		11	12
3	7	7	6	20
>3	11	12	1	24

EMD, Emdogain®; EMD+C, Emdogain®+Cerasorb®; MWF, modified Widman flap.

Table 5. Distribution of classified reduction of pocket depth in three treatment groups

Reduction of pocket depth (mm)	Treatment group (no. of patients)			
	EMD (n = 19)	EMD+C (n = 19)	MWF (n = 18)	total
⩽2	1	1	4	6
3	7	4	4	15
>3	11	14	10	35

EMD, Emdogain®; EMD+C, Emdogain®+Cerasorb®; MWF, modified Widman flap.

Emdogain® alone or in combination with Cerasorb®, which is comparable with the results reported by Wachtel et al. (2003).

A meta-analysis (Kalpidis & Ruben 2002) of controlled trials including 317 defects with a mean depth of 5.4 mm yielded an average 3.2 mm gain of clinical attachment (33% of original attachment level) and a 4 mm reduction (50% of original value) of probing pocket depth. Cardaropoli & Leonhardt (2002) followed 10 deep intra-bony defects treated with Emdogain® combined with open flap curettage and root planing for 1 year and observed a mean 6.5 mm gain of attachment and a 3.2 mm reduction in pocket depth. In a long-term study by Sculean et al. (2003a), Emdogain® treatment of defects with an initial probing depth similar to that in our study produced an average 4.3 mm reduction and a 3 mm gain in attachment. However, control group results were not reported.

The observed differences in clinical outcomes can easily be accounted for by the varying depth of defects, as deeper defects generally lead to a larger reduction of probing depth and gain of attachment (Tonetti et al. 1996). Sculean et al. (2003b) compared the outcomes of Bio-Oss® (BioOss, Geistlich Pharma AG, Wolhusen, Switzerland) with those of Bio-Oss® combined with Emdogain® in the treatment of a larger initial probing depth and obtained slightly larger improvements. In their study, plaque and gingival -indices decreased to the levels comparable with those obtained in our study, but the percentage of bleeding on probing was reduced by a third, whereas in our study, it was reduced by a half or more.

In our study, gingival recessions increased in both Emdogain®-treated groups by 0.7 mm on average, which is a satisfactory outcome from the aesthetic point of view and comparable with the 0.8 mm increase reported by Sculean et al. (2003b). However, the lack of difference between the two Emdogain®-treated groups in our study remains an unresolved question. It is not clear whether the applied bone replacement material (Sculean et al. 2003b) or rather a different flap design (i.e. simplified or modified papilla preservation technique) produced the relative stability, but the increase in gingival recessions in two Emdogain®-treated groups was half the increase in the MWF-treated group.

It should be emphasized that the placement of a paramarginal incision itself in the MWF technique may consequently lead to incomplete wound closure and, thus, to an increase in gingival recessions. However, to cover the inter-proximal area, we used paramarginal incisions 0.5–1.0 mm distant from the tooth and extended inter-proximally as far as the inter-dental papillae for the maximum possible preservation of the periodontal tissue (Flores-de-Jacoby & Mengel 1995). Moreover, the flexibility of the MWF may have been enhanced by two vertical-releasing incisions combined with a periosteal incision, thus allowing the coronal position of the flap and tension-free primary wound closure.

The absence of severe post-surgical complications indicates that both materials were well tolerated even when applied in combination. Moreover, by use of Emdogain® many problems arising from membrane implantation and retrieval during guided tissue regeneration may be avoided (Tonetti et al. 1996, Sculean et al. 1999, 2000).

The failure to show a treatment advantage of additional use of β-TCP supports the scepticism expressed by some clinicians as to what extent alloplastic materials can produce reparative or regenerative effects beyond simple fill-up. In comparison with MWF surgery, procedures using Emdogain® have been clinically proven to be an effective regenerative treatment of periodontal bony defects, even without additional use of bone replacement graft material. In our study, a larger gain of clinical attachment (⩾4 mm) was almost exclusively seen in the Emdogain®-treated groups, while most cases with a ⩽2 mm attachment gain were in the MWF-treated group.

The treatment outcomes in the Emdogain®-treated groups in our study are in line with histologic findings confirming the ability of Emdogain® to promote epithelial migration, fibroblast proliferation, and true periodontal regeneration (Nyman et al. 1982, Hammarström 1997, Sculean et al. 2000, Rosen & Reynolds 2002, Scheyer et al. 2002). Only recently, the ability of Emdogain® to support proliferation and attachment of fibroblasts has been demonstrated in vitro (Dragoo 1999, Cochran et al. 2003). The regenerative potential of Emdogain® is controversial. The studies suggest that Emdogain® serves as a liquid jelly-like membrane barrier and emphasize the antibacterial effect of EMDs and their carrier substance (Arweiler et al. 2002, Spahr et al. 2002).

In the controlled multicentre study including 172 patients, Tonetti et al. (2002) obtained only 0.6 mm additional gain in attachment and reduction of pocket depth. In our study, the additional gain in attachment after use of Emdogain® (3.7 mm) or Emdogain® and β-TCP (4 mm) compared with the gain in the MWF-treated group (2.1 mm) was clearly more pronounced.

In contrast to the results reported by Lekovic et al. (2000) and Zucchelli et al. (2003) for bovine porous bone mineral, our study failed to confirm clear clinical improvement of periodontal regeneration by additional use of β-TCP as a bone substitute material. The similar clinical outcomes in both Emdogain®-treated groups in our study may be due to differences in defect morphology and flap designs. The majority of defects were combined two-/three-walled defects preventing a collapse of the flap and, thus, providing space conditions for healing similar to those with replacement bone materials (Sculean et al. 2004). However, the primary flap closure may also have played a role in the treatment outcome. Maximal preservation of inter-dental tissue and primary flap closure are among the highest priorities for optimal clinical results (Cortellini & Tonetti 2001, Wachtel et al. 2003, Francetti et al. 2004, Trombelli et al. 2005, Linares et al. 2006). Thus, defect configuration (two+three wall defects) and microsurgical access flap may have both influenced treatment outcomes in our study in favour of Emdogain®-treated groups, yielding similar results in both Emdogain®-treated groups.

The purpose of the present study was to compare the 12-month clinical results of two regenerative treatment methods using either Emdogain® alone or Emdogain® in combination with Cerasorb® with the results of conventional flap surgery (MWF procedure). Although a simplified papilla preservation technique without Emdogain® would make a more appropriate control method for the regenerative procedures in our study, the MWF surgery was preferred for several reasons. The MWF technique is often applied for treatment of intra-bony defects in periodontal practice. Furthermore, MWF is the only conventional surgical technique that uses post-operative primary closure of inter-dental space, similar to the papilla preservation technique. However, in the MWF technique, the gingival recession is always increased due to paramarginal incision. Therefore, the differences in soft tissue behaviour (gingival recession) should be interpreted with caution. In 10 of 18 MWF-treated patients, primary flap closure was not achieved post-operatively and flap vascularization may have been compromized by two vertical-releasing incisions. Owing to all these reasons, a comparison of the results was possible, but the interpretation of the differences was limited because the MWF-treated group may not have been a true control.

In conclusion, all three investigated treatment modalities led to a significant clinical improvement compared with the pre-operative situation. Within the limits of this study, data suggest that treatments with Emdogain® alone or in combination with β-TCP have similar clinical effects in terms of reduced probing depth, gain in probing attachment, and increased gingival recession, when a primary flap closure is used. Also, both treatment modalities using Emdogain® showed clear clinical advantages over modified flap surgery.

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Clinical Relevance

Scientific rationale for the study: Primary flap closure combined with enamel matrix derivative (EMD) or bovine porous bone mineral for treatment of intra-bony defects showed significantly better clinical outcomes than conventional flap technique. No such information is available for EMD combined with β-tricalcium phosphate (TCP).

Principal findings: No significant synergistic effects of EMD combined with β-TCP were observed in comparison with EMD alone, but both treatments produced significantly higher attachment gain in comparison with modified flap surgery.

Practical implications: Both EMD treatments deserve equal consideration if primary flap closure is used.