Anton Sculean, Alice Kiss, Asta Miliauskaite, Nicole Birgit Arweiler, Matthias Hannig, Frank Schwarz

Ten-year results after treatment of intrabony defects with an enamel protein derivative (Emdogain®)

Anton Sculean
Department of Periodontology, Radboud University Medical Center, P.O. Box 9101, Internal Postal Code 117, Philips van Leydenlaan 25, 6500 Nijmegen, The Netherlands
Email: a.sculean@dent.umcn.nl

Alice Kiss

Asta Miliauskaite

Nicole Birgit Arweiler

All three:
Saarland University Clinic, Clinic for Restorative Dentistry, Periodontology and Preventive Dentistry, Building 73
66421 Homburg/Saar

Matthias Hannig
University Clinic of Dentistry, Department of Restorative Dentistry and Periodontology, Hugstetter Straße 55, 79106 Freiburg/Br.

Frank Schwarz
Centre for Dentistry, Polyclinic for Dental Surgery and Admission, Moorenstraße 5, 40225 Düsseldorf

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Treatment of intrabony periodontal defects with an enamel matrix derivative (EMD) promotes periodontal regeneration, i.e. regeneration of cementum, desmodontium and bone, resulting in significant reduction of probing depth and also in clinical attachment gain. There is, however, at present only limited information available on long-term results of this regenerative form of therapy. The aim of the present study was to evaluate clinical results 10 years after treatment of intrabony defects with the enamel matrix derivative Emdogain® (Straumann, Basel, Switzerland). Twenty-one patients who each had one intrabony defect with a probing depth ≥ 6 mm were treated with enamel matrix proteins. The following clinical parameters were investigated before treatment as well as 1 year and 10 years after treatment: probing depth (PD), gingival recession (GR) and clinical attachment level (CAL). After one year, the average probing depth PD had been reduced from 8.1 ± 1.7 mm to 3.5 ± 1.0 mm ($p < 0.0001$). After 10 years, PD was 4.0 ± 1.2 mm, i.e. significantly increased in comparison with the 1-year results ($p > 0.05$). Compared with baseline there was, however, still a significant improvement in probing depth ($p < 0.0001$). After 1 year, GR had increased from 1.9 ± 1.5 mm to 3.2 ± 1.9 mm ($p < 0.001$). After ten years, GR was 2.8 ± 1.5 mm. At this point in time, GR showed significant improvement compared with the 1-year results, but was still significantly greater than at baseline ($p < 0.001$). Average CAL changed from 10.0 ± 2.3 mm to 6.8 ± 2.3 mm ($p < 0.0001$) after 1 year, and subsequently to 7.0 ± 1.9 mm after 10 years. The change in CAL between 1 and 10 years was not statistically significant. The results suggest that clinical improvements that have been achieved after treatment with enamel matrix proteins can be maintained over a period of 10 years.

■ Introduction

Results of basic research have highlighted the role played by different kinds of radicular cementum in fixing the tooth in the alveolus and in repairing the periodontium[1]. Radicular cementum is necessary for the insertion of periodontal collagen fibres and therefore essential for fixing the tooth in the socket[1]. Enamel matrix proteins (EMP) form the largest part of the enamel matrix. They are 90% amelogenin; the

remaining 10% is made up of proline-rich non-amelogenins such as tuftelin, as well as other serum proteins[1]. The chemical structure of amelogenin has changed little in the course of evolution, and even between different animal species few changes have been detected[1]. *In vitro* and *in vivo* studies have been able to demonstrate that EMP influence the activity of desmodontal and gingival fibroblasts as well as epithelial cells in a variety of ways. For example, EMP led to an increased concentration of cAMP as well as increased synthesis and secretion of TGF-ß and IL-6 in desmodontal and gingival fibroblasts; furthermore, they led to increased stimulation of preosteoblast proliferation and also to differentiation of immature osteoblasts[2-7]. EMP can prevent or at least retard proliferation of epithelial cells[8,9]. Recent data have indicated that EMP even contain certain mitogenic factors, such as TGF-ß and bone morphogenic protein (BMP)-like growth factors, which can influence proliferation of desmodontal fibroblasts as well as biomineralisation in periodontal wound healing[2-6].

Data derived from histological studies on animals and humans have shown that surgical periodontal therapy of intrabony defects with EMP can result in regeneration of radicular cementum, desmodontium and bone[10-16]. Results of controlled clinical studies have furthermore shown that surgical therapy of intrabony defects with application of EMP leads to statistically significant increases in clinical attachment in comparison with baseline or with conventional periodontal surgery[17-24]. Comparative histological and clinical studies were not able to demonstrate any difference between regenerative therapy with EMP and guided tissue regeneration (GTR)[18,20,22-24].

There are, however, at present only limited data on long-term results after regenerative treatment with EMP[17,25-29]. Consequently, the aim of the present study was to analyse clinical results 10 years after regenerative therapy of intrabony periodontal defects with EMP.

■ Study design

Twenty-one patients aged between 34 and 60 years who each had one deep intrabony periodontal defect were treated with EMP. Subgingival curettage under local anaesthesia was performed 3 months before surgery in all patients. Positive motivation and a cooperative attitude were requirements for taking part in the study. The criterion for a sufficient standard of oral hygiene was a reduction of periodontal index (PI) to a value <130. The following clinical parameters were recorded before surgery as well as 1 year and 10 years later: probing depth (PD), gingival recession (GR) and clinical attachment loss (CAL). All measurements were performed with a rigid periodontal probe (PCP 12, Hu-Friedy) at six points per tooth (buccal: mesiobuccal, central, distobuccal; lingual: mesiolingual, central, distolingual). Bone regeneration was assessed using conventional X-rays, which were taken using parallel angle and right-angle techniques respectively (Figs 1 and 2). Statistical analysis was performed by first computing the average values for PD, GR and CAL, where the maximum value for each patient was included in the analysis, and the same point of measurement was reassessed in the follow-up examinations. As the data showed normal distribution (when submitted to the Kolmogorov-Smirnov-Test), the Student *t*-test for paired samples was applied to detect differences between the baseline value and 1-year and 10-year values.

■ Surgical procedure

After local anaesthesia and performance of sulcus incisions, a fully mobilised mucoperiostal flap was formed on the buccal as well as on the oral side of the defect. No vertical incisions were made. After removal of granulation tissue, root smoothing was performed using manual and ultrasonic instruments (Fig 3). The bone was not modified. In order to remove the smear layer, the root surfaces were conditioned by exposing them either to 37% phosphoric acid for 15 seconds or to 24 % EDTA gel (Emdogain®, Straumann, Basel, Switzerland; formerly BIORA AB, Malmö, Sweden) for 2 minutes. This was followed by thorough rinsing of the defect as well as the surrounding soft tissue with sterile saline solution. EMP (Emdogain®, Straumann, Basel, Switzerland; formerly BIORA AB, Malmö, Sweden) were then applied onto the blood-free root surface and afterwards also into the defect using a sterile syringe (Fig 4). The flaps were then immediately fixed with vertical or horizontal mattress sutures.

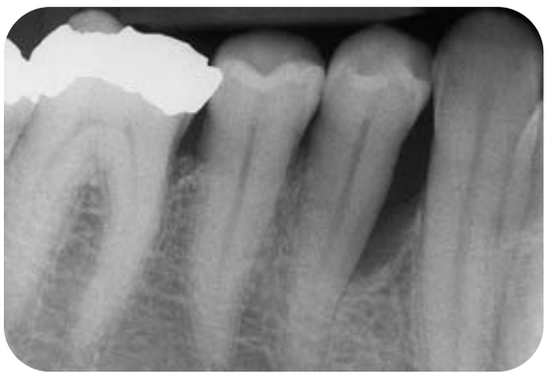

Fig 1 Pre-operative X-ray: deep intrabony defect mesial of tooth 44.

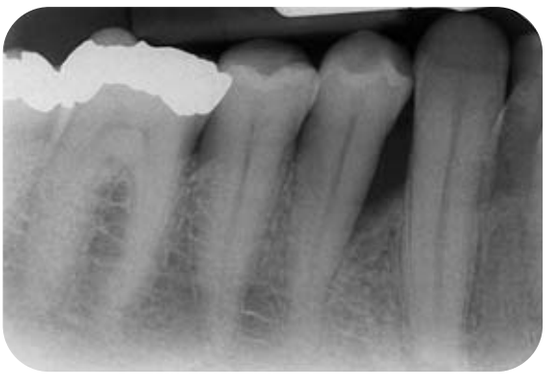

Fig 2 Filling of the intrabony defect visible 10 years after regenerative therapy with Emdogain®.

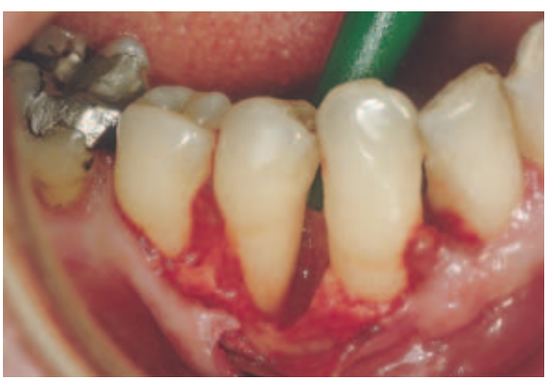

Fig 3 Intrabony defect exposed after removal of granulation tissue and thorough scaling and root planing.

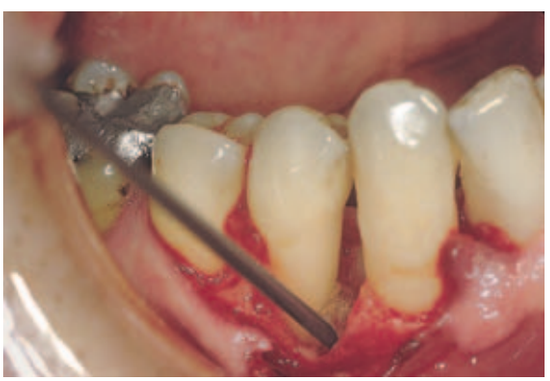

Fig 4 Application of Emdogain®.

Post-surgery

After surgery, antibiotics were administered for 1 week (1 g amoxicillin/day), and twice daily rinsing with 0.2% chlorhexidin gluconate solution (Corsodyl®, SmithKline Beecham, Bühl) was prescribed for the ensuing 6 weeks. During this period, the patients themselves did not perform mechanical cleaning of the areas affected by surgery. Two weeks after surgery, the sutures were removed. Only after 6 weeks were the patients allowed to clean the areas affected by surgery cautiously with a soft toothbrush.

During the first 2 months after surgery, follow up examinations were conducted every 2 weeks, including professional dental cleaning without subgingival instrumentation in the area affected by surgery. During the first year after surgery, follow up sessions which also included professional dental cleaning were conducted on a monthly basis. After the first year, the patients were integrated into an intensive follow-up programme (follow up examinations and professional dental cleaning every 3 to 6 months).

Results

The distribution of the defects and their characteristics are presented in Tables 1 and 2. Most of the defects showed a two-walled configuration. Average PI values were 0.7 ± 0.4 at start of treatment, 0.8 ± 0.4 after 1 year and 1.0 ± 0.9 after 10 years. No statistically significant differences were found between the baseline value and the results after 1 and 10 years. Average values of gingival index (GI) were 1.8 ± 0.6 at start of treatment, 0.5 ± 0.5 after 1 year and 1.2 ± 0.5 after 10 years. A statistically significant difference was found between the baseline value and the 1- and 10-year results respectively ($p < 0.001$). No

Table 1 Distribution of teeth with respect to maxilla/mandible and type of tooth

Type of tooth	Maxilla (n)	Mandible (n)	Total (n)
Incisors/canines	8	8	16
Premolars	0	2	2
Molars	2	1	3
Total	10	11	21

Table 2 Defect configuration

Defect type	Number
Single-wall	2
One- to two-walled	3
Two-walled	14
Three-walled	2
Total	21

Table 3 Clinical parameters at start of treatment, after 1 year and after 10 years (average ± standard deviation)

Parameter	Baseline situation	Mandible (n)	p-value	10 years	p-value
Probing depth	8.1 ± 1.7	3.5 ± 1.0	<0.0001	4.0 ± 1.2	<0.05
Gingival recession	1.9 ± 1.5	3.2 ± 1.9	<0.001	2.8 ± 1.5	<0.05
Clinical attachment level	10.0 ± 2.3	6.8 ± 2.3	<0.0001	7.0 ± 1.9	n.s.

statistically significant differences were found between the 1-year and the 10-year results. Average values of bleeding on probing (BOP) were 56% at start of treatment, 30% after 1 year and 39% after 10 years. A statistically significant difference was found between the baseline values and the 1- and 10-year results respectively ($p < 0.001$). No statistically significant differences were found between the 1-year and the 10-year results.

The clinical parameters found at start of treatment as well as after 1 and after 10 years are presented in Table 3.

After 1 year, the average probing depth PD had been reduced from 8.1 ± 1.7 mm to 3.5 ± 1.0 mm ($p < 0.0001$). After 10 years, PD was 4.0 ± 1.2 mm, i.e. significantly increased in comparison with the 1-year results ($p > 0.05$). Compared to baseline there was, however, still a significant improvement in PD ($p < 0.0001$). After 1 year, GR had increased from 1.9 ± 1.5 to 3.2 ± 1.9 mm ($p < 0.001$). After 10 years, GR was 2.8 ± 1.5 mm. At this point in time, GR showed significant improvement compared to the 1-year results, but was still significantly greater than at baseline ($p < 0.001$). Average CAL had decreased from 10.0 ± 2.3 mm to 6.8 ± 2.3 mm ($p < 0.0001$) after 1 year and 7.0 ± 1.9 mm after 10 years. The change in CAL between 1 and 10 years was statistically not significant.

■ Discussion

The results of the present case study have shown that treatment of intrabony defects with EMP leads to statistically significant reductions of probing depths and to gains of clinical attachment that can both be maintained over a period of 10 years. After 10 years, the average PD-values were still significantly better than the pre-operative values (baseline situation). Average PD-values were, however, significantly higher after 10 years than after 1 year.

On the other hand, average GR-values showed statistically significant improvements after a period of 10 years compared with the data after 1 year. It should be noted that a minor, statistically not significant loss of CAL (average values) was found when comparing the analysis results after 1 year with those after 10 years. This observation could be taken to

suggest that remodelling of the soft tissues over a longer period of time can take place without great losses of clinical attachment. Long-term studies after conventional and regenerative periodontal therapy also gave rise to similar observations[26-28].

The finding that treatment of intrabony defects with EMP over a short period of time, i.e. up to a year, can result in significant PD-reductions and CAL-gains is in agreement with the results of earlier studies[17-24]. In these studies, average CAL-gains ranging from 2.1 mm to 4.6 mm were reported, while in the present study, an average CAL-gain of 3.2 mm was measured after 1 year. This difference could be explained in terms of factors such as defect configuration and/or initial defect depth. It is known that two- and three-walled defects have a higher healing potential than single-wall defects[31].

Observations made in earlier studies, which included repeated surgery with reopening of the site, have shown that CAL-gain after treatment with EMP is often associated with osseous filling of the intrabony component[19,27]. It can furthermore be assumed, on the basis of results of histological studies in humans, that CAL-gains after application of this form of therapy actually represent, at least to a large extent, real periodontal regeneration[12-16].

The present 10-year results furthermore confirm the results of case report studies and controlled clinical studies in which this regenerative method was evaluated after 3, 4 and 5 years respectively[17,25-29]. In one controlled clinical study, Heijl et al[17] compared treatment of intrabony defects with flap surgery with and without application of EMP respectively. Eight months after therapy, average CAL-gain was 2.1 mm under treatment with flap surgery and EMP (test), and 1.5 mm after flap surgery alone (control). Thirty-six months after therapy, the average CAL-gain was 2.2 mm in the test group and 1.7 mm in the control group.

In a 4-year case report study, 33 patients with a total of 46 intrabony defects were treated consecutively with EMP[27]. Results after 4 years showed that the 1-year results had remained stable. In one case, reopening of the surgical site revealed near complete filling of the intrabony defect component. These results agree with a recently published long-term comparative study, in which it was shown that the results achieved after regenerative therapy with EMP and GTR can be maintained over a period of 5 years[28].

It should equally be pointed out that the plaque- and bleeding-parameters after 10 years did not show a statistically significant increase in comparison with 1-year values. This in turn suggests that optimal plaque control was ensured during the whole 10-year observation period.

Another important factor with a strong bearing on the results of regenerative periodontal therapy is smoking[32]. The patient population selected for the present study was, however, exclusively made up of non-smokers. The results presented are therefore probably also due to careful selection of patients and defects as well as good oral hygiene (patient compliance).

Findings of earlier studies that could demonstrate that results achieved after conventional periodontal therapy can be maintained over long periods of time should, however, equally be taken into consideration[28]. The top priority of regenerative therapy is therefore, from a clinical point of view, to gain more dental supportive tissue in order to prevent further progression of periodontitis.

The results presented here have shown, on the one hand, that improved clinical parameters after regenerative periodontal therapy with EMP can be maintained over a period of 10 years and, on the other hand, that this therapy presents a possibility of preserving teeth with deep intrabony defects.

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