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Clinical Report

Two-year Follow-up of Treatment of Intrabony Periodontal Defect with Enamel Matrix Derivative

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Abstract

The aim of this retrospective clinical study was to evaluate 2-year follow-up results following regenerative periodontal surgery for intrabony defects using enamel matrix derivative (EMD). Thirteen patients (mean age: 53 years) with a clinical diagnosis of chronic periodontitis were subjected to data analysis. A total of 25 sites with intrabony defects received regenerative therapy with EMD. Follow-up continued for a minimum of 2 years. Treatment of intrabony defects with EMD yielded a statistically significant improvement in the mean values of probing depth and gains in clinical attachment level (CAL) at 2 years compared with those at baseline ($p<0.001$). Sites treated with EMD demonstrated a mean CAL gain of 3.4 mm and 3.2 mm at 6 months and 2 years, respectively. No statistically significant difference in gain in CAL was found between the 6-month and 2-year results. A gain in CAL of ≥3 mm from at baseline was found in 17 sites at 2 years. This gain was achieved with minimal recession of gingival margin and was sustained over a given period of time. A trend toward a progressive increase in radiopacity, suggestive of bone-fill, was observed. In summary, treatment of intrabony defects with EMD resulted in clinically favorable outcomes. The clinical improvements obtained with regenerative therapy with EMD were maintained over a period of 2 years.

Key words: Periodontal regeneration—Periodontitis—Enamel matrix derivative (EMD)—Intrabony defects

Introduction

The goal of regenerative periodontal therapy is to restore periodontal tissue, lost due to inflammatory periodontal disease and it is characterized by the formation of new

cementum with inserting collagen fibers, new periodontal ligament, and new alveolar bone[8]. An attractive way of promoting periodontal regeneration is to try to mimic the events that take place during the development of periodontal tissues[2]. One example of this is in treatment using an enamel matrix derivative (EMD). Enamel matrix derivative is derived from porcine tooth buds and is currently available in a commercial formulation (Emdogain® Gel, Biora AB, Malmö, Sweden)[3]. Since its introduction, extensive research regarding EMD has been carried out, and the results have demonstrated its ability to encourage periodontal regeneration[4,6,7,17,22]. There was, however, a substantial degree of variability in treatment outcome with a pronounced center effect[4,13]. Furthermore, most long-term study has dealt with the forerunner of the currently available gel, Emdogain®. Therefore, longitudinal data regarding the current product, Emdogain® Gel, is limited.

In order to further clarify the efficacy of these therapies, it is necessary to analyze the longevity of the clinical values observed after surgical treatment and healing, at one's own clinical setting. In an earlier study, we evaluated treatment of intrabony periodontal defects with EMD during the early stages of healing[14] and found that it was capable of inducing favorable periodontal healing with a high level of predictability. Based on this finding, we have extended our observations. The aim of this retrospective clinical study was to evaluate 2-year follow-up results following regenerative periodontal surgery for intrabony defects using EMD.

Methods

1. Patients

The study participants were selected from the patient population at the Suidobashi Hospital of Tokyo Dental College. A clinical diagnosis of moderate to advanced chronic periodontitis was made in all patients selected[11]. Written informed consent was obtained from all patients. The following criteria were used: 1) no serious (uncontrolled) systemic complications or history of allergies, 2) periodontal pockets with a probing depth (PD) of ≥6 mm, and 3) osseous defects estimated to be at least 4 mm deep and 2 mm wide (largest width). A total of 13 patients (9 women and 4 men) with a mean age of 53 years (range; 35 to 77 years) were included in the data analysis. Among the participants, two were smokers.

2. Initial periodontal therapy

After systemic and oral assessments, a periodontal treatment plan was formulated for each patient. Initial periodontal therapy consisting mainly of oral hygiene instructions, full-mouth scaling and root planing, and occlusal adjustment (if trauma from occlusion was present) was performed by three clinicians. For the smokers, attempts were made to provide smoking cessation care.

3. Clinical parameters

At least 4 weeks after the initial therapy, re-evaluation was performed. The following baseline clinical parameters were recorded prior to surgery. Probing depth was measured using a Williams probe with a force of 0.25 N and rounded to the nearest millimeter. Clinical attachment level (CAL) was measured from the cemento-enamel junction to the apical depth of periodontal probe penetration. Probing depth, CAL and gingival recession were registered at 6 sites. Tooth mobility was recorded using the Miller index[9]. The presence or absence of supragingival dental plaque was recorded by the O'Leary Plaque Control Record[10]. Postoperative re-evaluations were performed at 6, 12 and 24 months after surgery.

4. Radiographic examination

Intraoral radiographs were obtained by the paralleling cone technique. Subjective evaluation was used to detect potential changes in radiographical images.

5. Periodontal regenerative therapy

An individualized treatment plan, with

alternatives, was presented, and informed consent to the proposed surgical intervention obtained from each patient. If other dental pathologies or conditions were present, they were treated prior to or concurrently with the regenerative therapy. Surgical interventions were implemented between January 2008 and June 2009. Interventions ranged from localized to quadrant surgery, with at least one tooth in the quadrant having intrabony defects matching the above-mentioned criteria. Regenerative therapy with EMD was performed at 25 sites (17 molars, 3 premolars, 3 canines, and 2 incisors) in 13 patients by the standard procedure as described previously[15]. Briefly, a full-thickness periodontal flap (papilla preservation technique) was employed to gain access to the root surface for scaling and root planing. In localized procedures, a vertical, releasing incision was made on the buccal aspect, at least one tooth distant from the lesion. Following debridement, sites were acid-etched with 36% orthophosphoric acid for 15 sec in order to remove smear layers. After the sites were thoroughly rinsed with sterile saline, 0.3 ml or 0.7 ml EMD solution (Emdogain® Gel) was applied, in accordance with the manufacturer's instructions. No attempt was made to use bone graft or other supplementary modalities. The flaps were immediately replaced and sutured with monofilament, non-resorbable sutures. Either modified vertical mattress or interrupted sutures were used to obtain complete closure of the inter-dental soft tissues.

Postoperative instructions were given to each patient. Patients received an oral antibiotic (typically 300 mg/d cefdinir) and a non-steroidal anti-inflammatory drug for 3 to 5 days. They were advised to use a mouth rinse twice daily. The sutures were removed after 10 to 14 days. After suture removal, patient plaque control was resumed at the surgically treated sites with the roll brushing technique utilizing an ultra-soft toothbrush. Any adverse reactions or patient perceptions (*i.e.*, pain, bleeding, or swelling, as obtained by interview) during the first week postsurgically were assessed and recorded.

6. Supportive periodontal therapy

Meticulous supragingival professional tooth cleaning was also performed biweekly for the first 6 weeks postsurgery. Thereafter, patients were recalled once a month. They received supportive periodontal therapy, consisting mainly of oral hygiene instruction and professional plaque control.

7. Data management and statistical analysis

Each patient contributed one to multiple defects. Therefore, each individual site was regarded as a statistical unit. The primary outcome variable was CAL. The aspect of the tooth (topographically related to the intrabony defect) presenting the largest CAL value at the time of presurgical recordings was used for further comparison and statistical analysis of outcome variables.

A non-parametric Friedman test was used to analyze changes in quantitative data over time. The Spearman rank correlation was calculated to assess correlations between data. A software package (InStat version 3.10 for Windows, GraphPad Software, La Jolla, CA, USA) was used for the statistical analysis. A p-value of less than 0.01 was considered statistically significant.

Results

None of the patients showed any healing complications after the initial periodontal therapy. During initial therapy, an effort was made to obtain an optimal level of oral hygiene by patient self-care, as well as professional care. The two smokers, however, declined such care and continued smoking throughout the course of treatment.

The mean PD of the treated sites at baseline was 7.1 ± 2.8 mm, and the defect type included 1 to 3-wall intrabony defects (1-wall: 5 sites, 2-wall: 14 sites, 3-wall: 6 sites). The majority of defects treated demonstrated good flap closure during the first and second postoperative week. Complications were related to the usual minor post-operative pain and occurred within the first days after surgery.

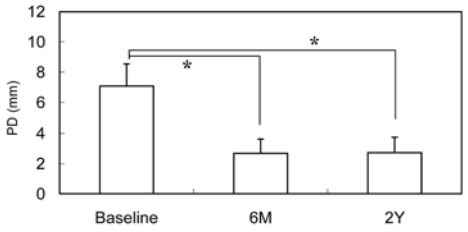


Fig. 1 PD values (mean ± SD) of treated sites at each observation period
n = 25, *p<0.001, Friedman test with Dunn post test.

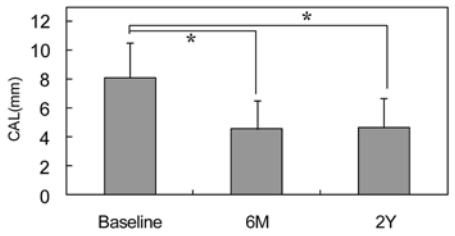


Fig. 2 CAL values (mean ± SD) of treated sites at each observation period
n = 25, *p<0.001, Friedman test with Dunn post test.

Table 1 Frequency distribution of gains in CAL at 2Y

CAL gain (mm)	Prevalence (%)
<2	16
2–3	44
4–5	28
≥6	12

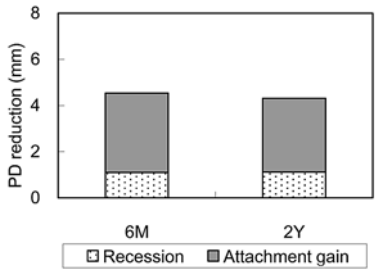


Fig. 3 Contribution of gingival recession and gain in CAL to reduction in PD
Mean values are shown.

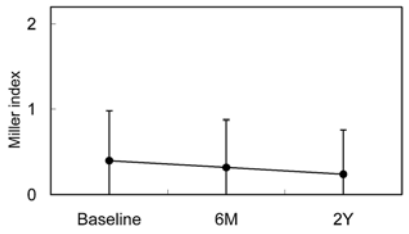


Fig. 4 Scores for tooth mobility (mean ± SD) of treated teeth at each observation period
n = 25. No significant change in tooth mobility was observed. p = 0.567, Friedman test with Dunn post test.

Observations on early post-operative healing have been described in detail elsewhere[14].

A statistically significant improvement in mean PD was already observed at 6 months postsurgically (Fig. 1). Mean reductions in PD at 6 and 24 months was 4.4 ± 1.4 mm (range 3 to 7 mm) and 4.4 ± 2.1 mm (range 2 to 8 mm), respectively. Reduction in PD was maintained over the 2-year observation period, with no significant change.

Sites treated with EMD demonstrated a mean change in CAL from at baseline (8.1 ± 2.4 mm) to 4.7 ± 2.0 mm and 4.9 ± 1.8 mm at 6 months and 2 years, respectively. A statistically significant change in CAL was also observed at 6 months postsurgically (Fig. 2). Mean gain in CAL in the recorded sites at 6 and 24 months was 3.4 ± 1.4 mm (range 1 to 7 mm) and 3.2 ± 1.6 mm (range 1 to 7 mm), respectively. The gain in CAL was maintained over the 2-year observation period, with no significant change. Table 1 shows the frequency distribution of gain in CAL at 2 years. Eleven sites demonstrated a gain in CAL of 2 to 3 mm and 7 sites a gain of 4 to 5 mm. In the 2 smokers, gain in CAL at 2 years was 2 mm and 3 mm.

A significant positive correlation was found between the baseline PD values and gains in CAL at 2 years ($r = 0.551$, $p = 0.004$, by Spearman rank correlation). The reduction in PD was achieved with minimal recession of the gingival margin (Fig. 3).

No significant change was observed in tooth mobility over the observation period (Fig. 4), although it was typical to find a tran-

sient increase in mobility immediately after surgery. No significant difference in gain in CAL was found between teeth without mobility and teeth with mobility (≥1, Miller index, $p = 0.157$, Mann-Whitney U test).

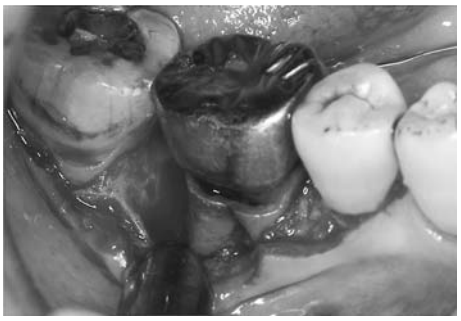
No apparent adverse reactions were recorded as a result of multiple applications of EMD within the same patient. The clinical and radiographic appearances of a representative case are shown in Fig. 5.

Discussion

This study constitutes part of our continuing effort to delineate long-term outcomes in periodontal regenerative therapy with EMD. After 2 years, periodontal surgery with EMD resulted in a significant reductions in PD and gain in CAL.

The mean gain in CAL at 2 years was of clinical significance (3.2 mm; 39% of the baseline CAL). This gain was comparable with that observed in our earlier study in a private practice setting[15]. A meta analysis of clinical studies on the management of angular osseous defects with EMD[7] revealed a reduction in PD of 4.0 mm (50% of the baseline PD) and gain in CAL of 3.2 mm (33% of the original attachment level) in a total of 317 lesions over an observation period ranging from 6 to 12 months. In their international multi-center study, Tonetti *et al.*[21] reported a mean gain in CAL of 3.1 mm at 1 year. The 2-year results in the present study are also in agreement with other long-term data[4,18–20].

Heijl *et al.*[5] reported that distinct radiographical bone-fill was observed at as early as 5 months after surgery with EMD, and further bone gain may be expected for as long as 3 years. In some cases in the present study, a progressive improvement in bone defect as evidenced by change in radiopacity was observed from 1- to 2-year postoperatively. This suggests gain of functional attachment, which is considered to be the sign of true regeneration[5]. Radiographic imaging provides evidence of bone-fill rather than true regeneration, and the present report is based



a

b

c

d

Fig. 5 A representative case; 64-yr-old woman with generalized chronic periodontitis

a: Clinical appearance of tooth #46 during surgery with EMD. Note extensive intrabony defect extending from furcation to distal root area.

b: Radiographic view at initial visit, showing vertical bone loss as well as furcation involvement.

c: After 6 months, further resolution of intrabony component of defect was observed. No lamina dura reformation was observed.

d: After 2 years, lamina dura reformation was observed.

solely on clinical cases, with no histological evidence. However, considering the theoretical basis of this procedure and the cumulative evidence presented by many studies, it seems sound to assume that the results do demonstrate signs of regeneration.

While the majority of cases in the present study demonstrated clinically favorable outcomes, 4 sites (16%) demonstrated a gain in CAL of less than 2 mm at 2 years. It is also noteworthy that, after 2 years, 11 surgical sites subsequently lost 1.0 mm of the CAL gained at 6 months, while 2 sites gained a further 2.5 mm (data not shown). At this time, it is not clear whether this is a sign of a "downhill" prognosis. We intend to longitudinally monitor and evaluate the outcomes in these cases.

Although no significant adverse healing was noted in the two smokers, gain in CAL at 2 years in those patients was rather modest. Since smoking has been shown to have a negative effect on bone regeneration following periodontal treatment[12], we advised them that their smoking habit might result in poorer regeneration during the course of treatment. At Suidobashi Hospital, we have initiated a unique smoking cessation treatment program, in collaboration with other health care professionals[16]. We would like to effectively incorporate this program into our periodontal practice.

During the 2-year observation period, no significant change in tooth mobility was observed (Fig. 4). Moreover, no significant difference in gain in CAL was found in relation to tooth mobility. It has been suggested that mobile teeth are at greater risk of future attachment loss when compared to teeth without mobility[23]. Although it is not clear if this is the case for teeth with regenerative therapy, more attention should be paid to mobile teeth during the maintenance period.

This study had several limitations. Since the size of the patient sample was small, no attempts were made to differentiate location of surgical sites or defect types in the data analysis. Type of osseous defect has been shown to be an important determinant in EMD treatment[1]. Since this was not a prospective case-controlled study, no control (flap surgery only or with placebo) data were available. Furthermore, a standardized reproducible method or computer-assisted subtraction was not utilized for analysis of intraoral radiographs. No evaluation of subgingival microflora was performed. The effect of subgingival microflora on EMD treatment is another area that needs to be investigated in further study.

In summary, the current results demonstrate that periodontal surgery with EMD yields a clinically relevant gain in attachment with signs of bone-fill. Within the limitation of the present study, it was shown that the clinical improvements obtained with regenerative therapy with EMD were maintained over a period of 2 years.

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