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Papilla Preservation Technique combined with Emdogain® in the treatment of intrabony defects: a novel treatment regimen for chronic periodontitis

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SUMMARY

Background. Regenerative therapy with enamel matrix proteins derivative (EMD) was shown to induce periodontal regeneration in intrabony defects. However, the contribution of papilla preservation technique (PPT), to the clinical outcome of regenerative therapy is still not clarified. Therefore, we conducted the present study to evaluate clinically measurable results of a combined therapy by PPT and EMD in the treatment of isolated intrabony defects.

Methods. Sixty isolated intrabony defects in 25 patients were surgically assessed with EMD and PPT. The clinical parameters: clinical attachment level (CAL), probing depth (PD) and gingival recession (GR) were evaluated at baseline and at three years.

Results. The primary outcome variable was CAL. The sites treated with enamel matrix proteins demonstrated mean CAL change from 6.6±1.2 mm to 3.4±1.3 mm ($p<0.001$) and the mean PD was reduced from 5.9±1.0 mm to 2.7±0.8 mm ($p<0.001$) after three years. The mean GR decreased from 0.71±1.2 mm to 0.64±1.1 mm ($p<0.821$).

Conclusions. The results of the present case cohort study indicate that PPT combined with EMD resulted in significant improvement of the clinical parameters in the treatment of intrabony defects in chronic periodontitis.

Key words: regenerative periodontal therapy, enamel matrix derivative, intrabony periodontal defects, minimal invasive surgical technique.

INTRODUCTION

Periodontitis is a mostly chronic disease of the periodontal tissue, caused by pathogenic bacterial strains present in the dental plaque that induce an inflammatory response of the alveolar bone and soft periodontal tissue. The inflammation cascade causes breakdown of periodontal connective soft and hard tissue and represents one cause of tooth loss. Periodontal diseases affect up to 90% of the worldwide population [1] and are considered as the sixth complication of diabetes mellitus among other systemic diseases [2]. Additionally to the main cause of periodontitis, the pathogenic microorganisms, genetic, dermatological, haematological, granulomatous, immunosuppressive and neoplastic disorders also show periodontal manifestations. In this context, a recently published work about the molecular mechanisms in melanoma therapy revealed for the first time the involvement of the inflammatory associated protein UCP2 in carcinogenic inductional processes on molecular level [3]. Associations with cardiovascular disease, stroke, pulmonary disease and diabetes have been made by different groups, although the causal relations have not been established until now. In the last three decades we got new understanding about the development of periodontal tissue and its ability to regenerate. Bosshardt & Schroeder showed that the root cementum plays an essential role in the preservation of teeth [4]. Another study has proposed that enamel related proteins from epithelial root sheath are involved in the formation of acellular cementum [5, 6].

Since that timepoint, regeneration got to be an ultimative goal of periodontal treatment.

Different therapeutic regimen have been developed to achieve regeneration of intrabony defects: these include barrier membranes [7, 8], demineralized freeze-dried

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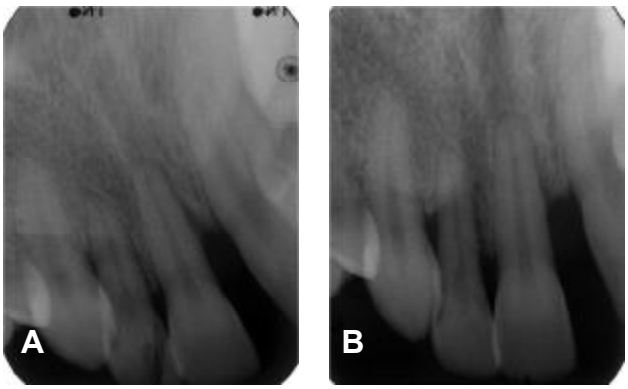

Fig. 1. X-ray of the defect tooth 8, 9: A – at baseline; B – treated with PPT and enamel matrix proteins 3 years after.

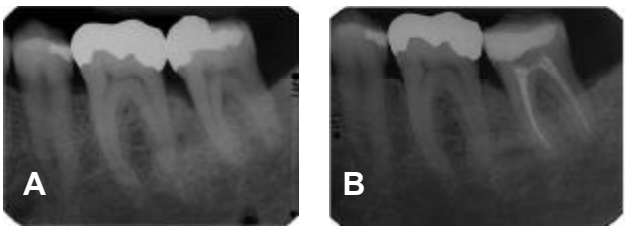

Fig. 2. X-ray of the defect tooth 18, 19: A – at baseline; B – treated with PPT and enamel matrix proteins 3 years after.

bone allograft (DFDBA) [8], combination of barrier membranes and grafts [10, 11], and enamel matrix derivative (EMD) [12, 13]. One of them is periodontal regeneration mediated by enamel matrix proteins (Emdogain®, Institut Straumann AG, Waldenburg, Switzerland).

Results of experimental studies have shown that a preparation of crude porcine enamel matrix could initiate the formation of tissue in monkeys that was histologically identical to acellular, extrinsic fiber cementum [14].

EMD is a composition of mainly amelogenin and related proteins. It is commercially available in Europe since end of 1995 and is already established as a resorbable, implantable material that implies also the potential to induce angiogenic effects in *in-vitro* models [15, 16].

Various results from available studies on enamel matrix proteins showed that enamel matrix proteins may lead to significant probing depth reduction and gain of clinical attachment level [17-26].

A recently published case report showed that even in aggressive periodontitis that is normally refractive to therapy such successful clinical management could be gained and maintained over a period of 3 years [27].

The results from Zetterström et al. [17] are corroborating to those of a split-mouth, randomized, controlled multicenter study involving 33 subjects [19]. These data indicated that the topical application of enamel matrix proteins onto diseased root surfaces associated with intrabony defects promote an increased gain of radiographic bone formation and clinical attachment level compared to control treatment.

On the other hand, a key to successful healing events in the periodontal wound is flap management and

Table 1. Mean PD, GR, CAL at baseline and three years after treatment with PPT and enamel matrix proteins.

	Papilla Preservation Technique + EMD®		
	Baseline	3 Years	P Value
PD	5.9 ± 1.0 mm	2.7 ± 0.8 mm	<0.001
GR	0.71 ± 1.2 mm	0.64 ± 1.1 mm	<0.821
CAL	6.6 ± 1.2 mm	3.4 ± 1.3 mm	<0.001

Table 2. Mean Plaque/Gingival Index and BoP scores at baseline and 3 years after treatment with PPT and enamel matrix proteins

	Papilla Preservation Technique +EMD®	
	Baseline	3 Years
PI	0.9	0.1
GI	1.2	0.2
BoP	31%	5%

primary flap closure. This technique was described by Takei et al. [28] for the first time.

It has been shown that, minimally invasive or microsurgery combined with enamel matrix proteins improves clinical outcome and decreases gingival recession [29-31].

Until now, there are only few clinical data [32, 33] evaluating the outcome after treatment with enamel matrix proteins combined with PPT in intrabony defects.

Aim of the Study

The aim of the present study was to evaluate clinically measurable results of a combined therapy by minimal invasive surgical technique papilla preservation techniques (PPT) and enamel matrix derivative (EMD) in the treatment of isolated intrabony defects.

MATERIALS AND METHODS

Twenty five patients (14 females and 11 males) aged between 28 and 68 years with a total number of 60 periodontal intrabony defects took part in this study. Sixty intrabony defects were treated with papilla preservation technique in combination with enamel matrix proteins. The number of defects per patient varied between 1 to 5. The study was performed according to the declaration of Helsinki as revised in 1983.

Inclusion criteria were: 1) no systemic diseases; 2) a good level of oral hygiene after initial therapy (Plaque control record <1); 3) Probing pocket depth ≥6 mm; 4) 2-3 wall intrabony defects; 5) non-smokers; 6) no use of antibiotics during the previous 6 months; 7) no periodontal treatment during the last 2 years.

The following clinical parameters were evaluated prior to and at three years after the surgical treatment with the same periodontal probe (PCP 12, Hu-Friedy, Chicago, IL, USA) with a tip diameter of 0.5 mm:

1) plaque index (PI) according to Silness & Löe 1964 [32],

2) gingiva index (GI) according to Löe & Silness 1963 [33],

3) bleeding on probing (BoP),

4) probing depth (PD),

5) clinical attachment level (CAL),

6) gingival recession (GR).

The cemento – enamel junction (CEJ) was used as reference point. In cases where the CEJ was not visible, a restoration margin was used for these measurements.

All measurements were made at six sites per tooth: mesiofacial, facial, distofacial, mesiolingual, lingual and distolingual.

Every patient received initial periodontal therapy and oral hygiene instructions. Full-mouth scaling and root planing was performed within 24 hours under local anaesthesia. Re-evaluation of the clinical parameters and planing of surgical therapy took place after 6 weeks. Periapical radiographs were taken with the long cone parallel technique prior to and at 3 years after surgery (Fig. 1a, b; 2a, b). In this study only the data for the deepest point of the selected defects were reported. The intrabony component was ≥3 mm.

Examiner reproducibility

Six patients, each displaying 10 teeth (single-rooted or multi-rooted) with probing depths >6 mm on one aspect of each tooth, were used to calibrate the examiner. The examiner evaluated the patients at two separate timepoints, 48 h apart.

Calibration was accepted if measurements at baseline and at 48 h were similar to the millimeter at more than 90%. Trained examiner performed the clinical measurements after the treatment and he was not informed about the surgical procedure that has been performed. They were allocated to concealment of their data towards the examiner.

Surgical procedure

All surgical procedures were performed under local anaesthesia. A modified (sites with interdental width >2 mm) and simplified (sites with interdental width ≤2 mm) papillary preservation flap was created. All granulation tissue was removed from the defects and root surfaces were scaled and planed using hand and ultrasonic instruments (SONICflex 2003 KaVo, Bieberach, Germany). Measurement of intrabony defects was performed by use of periodontal probe. After that, root surfaces were conditioned for 2 min with 24% EDTA gel (PrefGel, Institut Straumann AG, Waldenburg, Switzerland) to remove the smear layer and the defects were thoroughly rinsed with sterile saline to remove all EDTA residues. Following root conditioning, enamel matrix proteins were applied onto the root surfaces and into the defects with a sterile syringe. Finally, the flap was coronally repositioned and closed with crossed horizontal and vertical internal mattress sutures.

The patients were advised to rinse twice a day for 4 weeks with rinsing solution (Chlorhexamed Fluid 0.2 %, Glaxo SmithKline, Germany). Only after this period of time tooth brushing was allowed in the treated areas. The sutures were removed 14 days after surgical treatment. Recall appointments were determined every 2 weeks during the first two months, and once monthly for the next four months. After six months and during the rest of observation period of 3 years, the patients were recalled on a 3-month's basis.

Statistical analysis

The statistical unit was the intrabony defect. The statistical analysis was performed using a commercially available software program (SPSS for Windows 95, SPSS Inc., Chicago, IL). The deepest defect per tooth was included in the calculations. The paired *t*-test was used for the statistical evaluations of the changes from baseline to 3 years after treatment.

RESULTS

No postoperative complications such as allergic reactions, suppuration or abscesses were postoperatively observed and during the complete study period.

Table 1 illustrates the mean PD, CAL, GR at baseline and after three years. Pre-operative probing depth varied between 6 and 9 mm. Table 2 shows mean plaque and gingival index, BoP scores at baseline and three years after treatment.

The sites treated with papilla preservation technique combined with enamel matrix proteins demonstrated mean CAL change from 6.6±1.2 mm to 3.4±1.3 mm ($p<0.001$) at three years.

PD of the sites treated with papilla preservation technique combined with enamel matrix protein decreased from 5.9±1.0 mm to 2.7±0.8 mm ($p<0.001$) at three years.

Three years after treatment, the mean GR decreased from 0.71±1.2 mm to 0.64±1.1 mm ($p<0.821$) in the sites treated with papilla preservation technique combined with enamel matrix proteins.

DISCUSSION

It is well established that the pathophysiological effects of periodontitis are not only limited to the oral cavity. Here exists a bidirectional interrelationship between systemic diseases and periodontitis because of destructive inflammatory cascades induced by different kinds of pathogens [2, 36, 37].

Destructive catabolic inflammatory cascades are the key mechanism to tooth loss in periodontitis. Stopping the inflammation response of the immune system as a direct reaction to the invasion of specific pathogenic bacteria onto and into periodontal tissue is one of the most important targets in periodontal therapy in our days.

Almost all modern therapeutic procedures are aimed at stopping the inflammation processes by conservative or surgical treatments in order to erase and suppress the growth of the pathogenic microbiotic flora.

These therapeutic regimen do not cover the genetically determined regenerative potential of the individuum.

In this context the individual patient could be helped by functional gene screening techniques for identification of target genes that imply the predisposition for the development of periodontitis [38].

The ability of different bacterial strains to manipulate the host response by for example abrogating angiogenic and/or pro-inflammatory responses contribute further to the complex machinery destroying periodontal tissue and making an effective therapy very difficult [39, 40, 41].

Therefore, early diagnosis and alternative therapy options based on the regenerative potential of the individual patient and the agents used are of utmost importance.

In the present study we investigated the possibility of using EMD combined with minimally invasive surgery, underscoring the well-known regenerative potential of EMD in the clinical treatment of periodontitis and in vitro studies, as well.

The angiogenic effects of EMD have been demonstrated recently in in-vitro cell culture models [15,16].

The molecular mechanism to the cells leading to angiogenesis after application of EMD is still unknown and needs to be elucidated further by many more molecular biologic experiments.

Clinically, the application of EMD to periodontic intrabony defects leads to improved tissue regeneration.

Thus, measuring clinical parameters to evaluate the outcome of treatment options is required.

Enamel matrix proteins seem to be safe and able to regenerate the periodontal tissue.

The results of the present study indicate that treatment of intrabony periodontal defects with papilla preservation technique and enamel matrix protein results in clinical and statistical significant reduction of PD and gain of CAL.

Most important aspect in periodontal surgery is soft tissue management. Careful preservation of interdental tissue, atraumatic flap management and primary closure of interdental space are of fundamental importance [42]. Papilla preservation technique compared to access flap fulfills the requirements mentioned above and results in uneventful wound healing and minimal gingiva recession.

No allergical reactions against enamel matrix proteins were observed in our study. The clinical safety of EMD was already proved by Zetterström et al. [17].

It is also well known that the effect of smoking has a negative influence on the regenerative process [43], therefore; smokers were excluded from this study.

Compliance of the patient and perfect oral hygiene play a fundamental role in the process of regeneration. In the present study plaque and bleeding scores were not significantly higher compared to baseline. The results from previously controlled clinical studies also reveal, that the stability of clinical attachment following regenerative therapy depends on perfect oral hygiene and compliance during recall program [44].

In the present study only II-III wall defects were included, since these defects have the highest potential for regeneration as shown previously [19, 45].

The use of enamel matrix proteins in combination with Access Flap is well documented [17, 19, 21, 22]. The sites treated with enamel matrix protein revealed reduction of PD from 3.3 mm to 3.1 mm at eight and thirty-six months postoperative recall, respectively [19].

These results corroborate to those reported by Okuda et al. [22]. Reduction of mean PD of

3 mm has been shown already after twelve months postoperatively. In a multicenter study, Zetterström et al. [17] reported the clinical outcome after enamel matrix protein or access flap surgery at eight months and three years postoperatively. At eight months, mean CAL gain of 3.1 mm was measured. In another study PD reduction of 5.2 mm was reported twelve months postoperatively by Heden et al. [21].

There are few data available on the treatment of intrabony defects using papilla preservation technique and EMD [31, 32, 33, 46]. The sites treated with papilla preservation technique and EMD showed gain of CAL of 3.1 mm at twelve months after surgical treatment [32]. Another report showed a mean CAL gain of 5.9 mm after 12 months postoperatively [46]. Tonetti et al. showed a mean CAL gain of 3.1 mm at twelve months [33]. Our study showed the gain of CAL of 3.2 mm after three years. The results of these previous studies corroborate to the data of the present study using papilla preservation technique and enamel matrix proteins.

CONCLUSIONS

The following conclusions can be made from this investigation:

1. Papilla preservation technique in combination with enamel matrix proteins showed a significant gain of CAL and reduction of PD.
2. Microsurgical approach preserved gingival tissue and showed minimal recession of gingiva (GR) in the present study.

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