

Treatment of Class II Furcation Defects with Guided Tissue Regeneration or Enamel Matrix Derivative Proteins – A 12-Month Comparative Clinical Study

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Recently the use of enamel matrix derivative proteins (EMD) has been introduced as a treatment alternative for periodontal regeneration. However, its clinical effects in human Class II furcations are still poorly investigated.

The aim of this study was to compare the clinical results obtained for Class II furcations treated with guided tissue regeneration (GTR) to those obtained with the application of EMD.

Twenty paired Class II mandibular furcations were treated in 10 non-smoker patients included in this study. Each defect was randomly treated with an e-PTFE membrane (GTR) or with EMD. Following basic therapy, baseline measurements were recorded, including probing depth (PD) and relative clinical attachment level (CAL-R). Hard-tissue measurements were performed during surgery to determine vertical (BDL-V) and horizontal bone defect level (BDL-H). At the 12-month re-entry procedures soft and hard-tissue measurements were reevaluated.

Both procedures resulted in statistically significant PD reduction and gain in CAL-R with no significant differences between the groups. BDL-V resolution was statistically significant in both groups (GTR: 2.5 ± 1.14 mm and EMD: 1.5 ± 0.77 mm), as well as BDL-H resolution (GTR: 3.3 ± 1.82 mm and EMD: 2.2 ± 1.75 mm), without significant differences between the groups.

Based on this, GTR and EMD therapies may be recommended for the treatment of Class II furcations, producing similar soft and hard-tissue improvements. However, once the GTR technique achieved numerically better results in hard-tissue parameters, it seems to provide a slight advantage for this procedure when dealing with these defects.

Key words: guided tissue regeneration, enamel matrix derivative proteins, furcation lesions, randomized clinical study

INTRODUCTION

Furcation lesions are associated with increased risk of progressive loss of connective tissue attachment, alveolar bone resorption, and tooth mortality (Bjorn and Hjort, 1982; Becker et al, 1984; Wang et al, 1994; Wood et al, 1989; Hirshfield and Wasserman, 1978; McFall, 1982; Carranza and Jolkovsky, 1991), representing one of the greatest challenges in periodontal therapy. Surgical management permits access for root de-

bridement and decontamination, odontoplasty, osseous recontouring and periodontal regeneration. These procedures aim at the interruption of the disease process, the preservation of the remaining periodontal attachment and - most importantly - in the case of regenerative therapy the formation of new alveolar bone, new cementum and functionally inserted new periodontal ligament fibres. Successful outcome of furcation defects treatment is clinically defined by the elimination of horizontal and vertical defect components by bone fill.

Histologic evaluation, however, is the only way to verify periodontal regeneration, which means the formation of new periodontal tissues over previously contaminated root surfaces. As histologic evidence for successful furcation defect treatment is not viable for controlled clinical trials, any change in direct bone measurements (at surgery and at re-entry) has been understood as a primary variable to evaluate clinical success. Bone fill observed at re-entry procedures suggests a periodontal regeneration of the involved area, as well as changes in clinical attachment level, probing depth reductions and radiographic improvements.

Guided tissue regeneration (GTR), using expanded polytetrafluorethylene (e-PTFE) membranes, has become accepted as a successful procedure for the treatment of moderate (Class II) furcation defects (Gottlow et al, 1984; Gottlow et al, 1986; Becker et al, 1987; Becker et al 1988; Caffesse, 1990; Lekovic et al, 1989; Mellonig et al, 1994). Histological observations following the use of these barrier materials proved their ability to allow the periodontal ligament and bone cells to selectively repopulate the isolated space, resulting in new attachment apparatus formation (Gottlow et al, 1986; Nyman et al, 1982; Cortellini et al, 1993; Vincenzi et al, 1997). Clinical studies also support the effectiveness of the GTR therapy in the treatment of Class II furcation defects by means of pocket reduction, gain in clinical attachment level and bone defect fill (Becker et al 1988; Caffesse, 1990; Lekovic et al, 1989; Villaça et al, 2004).

However, the procedure has shortcomings: it is technique sensitive and requires a good degree of surgical skill (Parodi et al, 2000). In addition it may have problems associated to the bacterial colonization of exposed membranes that may adversely affect the outcome of the regenerative therapy (Bowers et al, 2003).

Recently, the use of enamel matrix derivative proteins (EMD) – which is easily applied as a gel – was introduced as a new treatment alternative for periodontal regeneration (Hammarström, 1997). It has been suggested that the application of these proteins on a previously contaminated root surface promotes periodontal regeneration, mimicking events that take place during the development of the periodontal tissues. Morphological studies have shown that cells of Hertwig's epithelial root sheath, which is an extension of the enamel-form-

ing dental organ, have a secretory phase during which enamel-related matrix proteins are secreted and temporarily deposited onto the root surfaces providing an initial and, as it appears, essential step in the formation of acellular cementum (Hammarström, 1997). Furthermore, the cells close to the root surface seem to carry the message not only to form acellular cementum but also an associated periodontal ligament and alveolar bone (Andreasen, 1981; Hoffman, 1960; Ten Cate et al, 1971). Histological analysis of interproximal defects in monkeys (Sculean et al, 2000), as well as of human biopsies (Heijl, 1997; Sculean et al, 1999; Mellonig, 1999), following the application of EMD revealed the formation of new cementum with inserting collagen fibers on previously diseased root surfaces. The application of EMD in the treatment of intrabony defects in clinical trials also resulted in significant new attachment (Heijl et al, 1997; Heden et al, 1999; Heden, 2000; Okuda et al, 2000). Unfortunately, its clinical effect in degree II furcation involvements still requires investigation. Therefore, the aim of the present study was to compare the clinical results obtained for Class II furcations treated with GTR therapy, using e-PTFE membranes, to those obtained with the application of the EMD.

MATERIALS AND METHODS

In this controlled randomized clinical trial, a total of 20 defects comprised the study group. Ten patients with moderate to advanced chronic periodontitis (seven females and three males; mean age 46.5 ± 6.29 years; range 39 to 58 years) participated in this study. The patients were recruited following the inclusion criteria of: 1) at least one pair of contralateral mandibular molars with similar Class II furcation involvement as determined by clinical evaluation and standard radiographs; 2) no contributory medical history; 3) non-smokers; 4) no systemic antibiotics or chemotherapeutic agents used in the previous six months; and 5) no endodontic or periapical pathology. The Institution's Human Research Committee approved the study protocol and informed consents were obtained after explanation of the procedures, the associated risks and benefits to the patients, and the need for appropriate documentation and re-entry surgery.

Pre-surgical procedures

Initial therapy was performed on all patients, consisting of full-mouth scaling and root planing, detailed oral hygiene instructions and occlusal adjustment when indicated. Four weeks later, the baseline examination was performed, including probing depth (PD), relative clinical attachment level (CAL-R) – which differs from the commonly utilized measure (clinical attachment level), once the fixed point is not the cementum-enamel junction but a reference point on the acrylic stent – and gingival recession (GR). These soft-tissue measurements were assessed using an automated probe (Florida Probe Corporation, Gainesville, FL, U.S.A) and an acrylic stent with reference marks at the vestibular or lingual surfaces of the involved teeth to determine the exact site of measurement at the baseline and 12 months after surgery. Radiographic examination was also done as part of the documentation. Standard radiographs were taken with a customized stent to allow an accurate evaluation between the examinations, using the extension cone paralleling technique.

Surgical procedures

Following administration of local anesthesia, intrasulcular and releasing incisions at the proximal line angles of the adjacent teeth were performed and mucoperiosteal flaps were reflected. After complete removal of inflammatory granulation tissue, the root surfaces were thoroughly scaled and root planed using Gracey curets and ultrasonic points. After hemostasis, intrasurgical hard tissue measurements were recorded. The vertical components of the furcation defects (BDL-V) were assessed using the acrylic stent at the presurgical midline reference point and were obtained through the difference between the measurements recorded from the cementum-enamel junction to the top of the alveolar crest to those obtained from the cementum-enamel junction to the bottom of the osseous defect. Likewise, in order to measure the horizontal depth of the defect (BDL-H), a wire and tube assembly was previously adapted to the acrylic stent as described by Simonpietri-C et al (2000), and the distance from the deepest horizontal point of the furcation to the assembly was recorded (Fig 1). Therefore, the BDL-H was a relative measurement, once the outside surface of the tube assembly was determined as the fixed point of evaluation during the probing act.



Fig 1 Intrasurgical hard tissue parameter. In order to measure the horizontal depth of the defect (BDL-H) the distance from the deepest horizontal point of the furcation to the assembly was recorded.

In sequence the root surfaces of all experimental teeth, irrespective of the treatment modality, were conditioned with 24% ethylenediaminetetraacetic acid (EDTA) containing gel (PrefGel, Biora AB, Malmö, Sweden) for two minutes according to the instructions given by the manufacturer. The EDTA remnants were removed with copious rinsing with sterile saline. At this moment the defects were randomly selected for the treatment with EMD or e-PTFE membrane. With root surfaces free of smear layer and without blood or saliva residue, regenerative periodontal procedures were begun with the application of EMD gel (Emdogain, Biora AB, Malmö, Sweden) on the entire root surface, beginning at the deepest area of one of the randomly selected bilateral defects. Subsequently, the full-thickness flaps were coronally positioned and sutured with 6.0 non-absorbable sutures (Gore-Tex® suture - ePTFE nonabsorbable monofilament, W.L. Gore & Associates, Arizona, USA) (Fig 2). At the contralateral defects, the membranes (Gore-Tex® Regenerative Material, W.L. Gore & Associates, Arizona, USA) were trimmed and adapted on the buccal or lingual surfaces of the experimental teeth, being adjusted 1 mm coronally to cover the entrance of the furcation area in order to avoid root concavities, which could lead to the formation of gaps between the membrane and tooth surface, and extended to the adjacent bone approximately 2 mm laterally and apically. The membranes were secured in this position with sling 6.0 non-absorbable sutures. The flaps were subsequently coronally displaced in order to com-

Fig 2a–d EMD group.



Fig 2a Pre-operative view of a mandibular right first molar with a Class II furcation defect.



Fig 2b Mucoperiosteal flap reflected and delimited by the releasing incisions at the proximal line angles of the involved tooth. Observe the furcation defect after removal of inflammatory granulation tissue.



Fig 2c Application of EMD gel.



Fig 2d Full-thickness flap coronally positioned and sutured. Then, one more application of EMD gel.

pletely cover the membranes and were retained with sling and simple interrupted sutures (Fig 3). All patients were instructed to rinse twice a day with a 0.12% chlorhexidine digluconate solution for 15 days, and amoxicillin plus clavulanic acid (500 mg, tid) was prescribed for 10 days, starting 24 hours before the procedures. After this period, in cases of exposure of the membranes, an initial dose of 200 mg of doxycycline followed by 100 mg of doxycycline once a day for 20 days was prescribed (Simonpietri-C et al, 2000). Discontinuation of tooth brushing and attention to avoid trauma or pressure at the surgical sites were also recommended during that period.

The sutures were removed after 14 days, and the patients were instructed to clean the surgical sites

with a cotton pellet soaked in 0.12% chlorhexidine digluconate solution twice a day for 15 days. Membranes remained in position for four weeks. The participants were recalled weekly during the first month and monthly from then on.

Twelve months postsurgically, the soft-tissue changes were evaluated at the same presurgical reference points following the same sequence. At this time, intrasulcular incisions and mucoperiosteal flaps were elevated to gain access to the treated furcations. Any changes in the vertical and horizontal morphology of the bony defects were assessed and osseous measurements were made as in the initial surgery (Fig 4). Furthermore, the standard radiographs were also repeated in this consultation as part of the documentation (Figs 5). The same examiner pre-

Fig 3a–d GTR group.



Fig 3a Pre-operative view of a mandibular left second molar with a Class II furcation defect.



Fig 3b Mucoperiosteal flap reflected and delimited by the releasing incisions at the proximal line angles of the involved tooth. Observe the furcation defect after removal of inflammatory granulation tissue.



Fig 3c The e-PTFE membrane trimmed and adapted on the lingual surface.



Fig 3d Full-thickness flap coronally positioned and sutured.

Fig 4a–b In order to illustrate the findings observed during initial and re-entry surgeries:



Fig 4a Pre-operative view of a Class II furcation defect in a mandibular left first molar.



Fig 4b The area treated with GTR therapy 12 months after surgery during the re-entry.

Fig 5a–b EMD group.



Fig 5a Initial radiograph of a mandibular right first molar with a Class II furcation defect.



Fig 5b 12-month radiograph of the treated area.

viously calibrated with 95% reproducibility recorded all measurements.

Statistical analysis

Quantitative data were recorded as mean ± standard deviation. The Mann-Whitney Test was used to determine if the two groups had similar-sized defects preoperatively, and if one surgical procedure produced a better clinical result after 12 months (between group analysis). The Wilcoxon test was used to analyse if the clinical and surgical measurements differed before and after treatment (intra-group analysis). For all statistical analyses the significance level of 5% was adopted.

RESULTS

Both groups presented baseline similar size defects according to the clinical and surgical parameters summarized in Tables 1 and 3. After 12 months, statistically significant differences were achieved in the clinical parameters evaluated – PD and CAL-R – in both experimental groups (Table 1). The gingival recession reduction was statistically significant only in the GTR group. Analysis between the groups of all the related clinical parameters did not reveal statistically significant differences after the follow-up period (Table 2).

Re-entry procedures showed significant changes in vertical and horizontal components of the furcation defects in both groups. At the 12-month postoperative examination, statistically significant horizon-

tal and vertical defect resolutions were observed in both experimental groups when compared to baseline (Table 3). Although comparisons between the outcomes of the two therapeutic approaches revealed no statistically significant difference for the hard tissue parameters, the GTR group showed a slightly superior defect resolution, especially in terms of the vertical bone component as presented in Table 4.

DISCUSSION

The results of the present controlled randomised clinical trial indicate that the treatment of Class II furcation defects with GTR or EMD may result in statistically significant reduction in PD and gain in CAL-R at the one-year post-surgery examination. No statistically significant differences were found in these clinical parameters between the two groups after the period of evaluation.

Although disparity in soft-tissue improvements between different trials seems to be frequent in furcation defects, more than in intrabony defects (Simonpietri-C et al, 2000), the improvements seen in this study are in accordance with previous clinical data following GTR therapy (Becker et al, 1988; Anderegge et al, 1991; Schallhorn and McClain, 1988), confirming the well-documented regenerative results obtained with this procedure in the treatment of Class II mandibular furcation defects (Gottlow et al, 1984; Gottlow et al, 1986; Becker et al, 1987; Becker et al 1988; Caffesse, 1990; Lekovic et al, 1989; Mellonig et al,

Table 1 Mean values \pm SD (mm) of clinical parameters at baseline and 12-month examination

parameter	GTR group			EMD group			Between group analysis*	
	baseline	12 months	p value #	baseline	12 months	p value #	baseline	12 months
PD	2.6 \pm 1.28	1.1 \pm 0.92	0.007	3.0 \pm 0.83	1.4 \pm 0.64	0.005	NS	NS
RCAL	8.1 \pm 0.94	6.8 \pm 1.00	0.005	8.2 \pm 1.06	7.5 \pm 1.18	0.007	NS	NS
GR	1.9 \pm 0.94	0.7 \pm 0.64	0.007	1.7 \pm 0.70	1.1 \pm 0.80	0.046	NS	NS

#: Intra-group analysis – Wilcoxon Matched Pairs Test

*: Between group analysis – Mann-Whitney U Test

NS: no significant difference

Table 2 Mean changes \pm SD (mm) of clinical measurements between baseline and 12-month examinations within experimental groups

group	clinical parameters		
	PD	RCAL	GR
GTR	1.2 \pm 0.63	1.2 \pm 0.58	1.2 \pm 0.82
EMD	1.6 \pm 0.68	0.9 \pm 0.82	0.7 \pm 0.87
p value*	0.341	0.253	0.193

*: Between group analysis – Mann-Whitney U Test

Table 3 Mean values \pm SD (mm) of surgical parameters at baseline and 12-month examination

parameter	RTG group			EMD group			Between group analysis*	
	baseline	12 months	p value #	baseline	12 months	p value #	baseline	12 months
HDD	11.8 \pm 1.63	8.6 \pm 1.16	0.005	2.0 \pm 1.72	9.8 \pm 1.16	0.007	NS	NS
CEJ-AC	4.9 \pm 1.51	3.4 \pm 0.96	0.007	5.0 \pm 1.58	4.4 \pm 1.56	0.017	NS	NS
VDD	5.7 \pm 0.94	3.2 \pm 1.13	0.005	6.1 \pm 1.02	4.6 \pm 0.51	0.005	NS	NS

#: Intra-group analysis – Wilcoxon Matched Pairs Test

*: Between group analysis – Mann-Whitney U Test

NS: no significant difference

group	surgical parameters		
	HDD	CEJ-AC	VDD
GTR	3.3 ± 1.82	1.5 ± 1.41	2.5 ± 1.14
EMD	2.2 ± 1.75	0.7 ± 0.63	1.5 ± 0.77
p value*	0.181	0.098	0.066

*: Between group analysis – Mann-Whitney U Test

Table 4 Mean changes ± SD (mm) of surgical measurements between baseline and 12-month examinations within experimental groups

1994). In addition, the soft-tissue changes demonstrated here are also superior to those achieved with open flap debridement when used as the control group of GTR therapy studies, showing an additional benefit of both regenerative techniques used in the present study.

Surgical exposure and re-entry is the only way to confirm the degree of defect closure, although regeneration can only be confirmed by histological evidence. Soft-tissue measurements alone can be misleading, once a tight connective tissue attachment rather than a furcation fill may prevent probe penetration. Re-entry measurements, as represented in the present study by the hard-tissue parameters, are a more reliable indication of treatment effectiveness.

At the 12-month postoperative examination, statistically significant horizontal and vertical defect resolutions were observed in both experimental groups corroborating the effectiveness of both regenerative procedures in the treatment of the defects. Statistically significant differences were not found between the groups in terms of hard-tissue defect resolution. The small sample size may have been a reason for the lack of significance. However, this is due to the strict inclusion criteria used in this study. Variables related to the patient (e.g. smoking), furcation (e.g. defect morphology and extent), tooth (e.g. root trunk length and presence of concavities), marginal gingiva (e.g. width of keratinized tissue) and treatment (e.g. membrane exposure) have been reported as factors that may influence the outcome of regenerative procedures (Machtei and Schallhorn, 1995; Karring and Cortellini, 1999; Garret, 1996; Mardam-Bey et al, 1991; Bowers et al, 2003), especially GTR therapy. In the present study, non-smoking patients presenting moderate bilateral fur-

cation defects (Class II) in teeth with a root trunk of adequate length and with a minimum width of 3 mm of keratinised tissue were scheduled for treatment. These criteria were adopted to increase the treatment predictability, to allow an adequate placement of the membranes, always positioned coronally to a possible root concavity, and a coronal displacement of the flaps in order to reduce membrane exposure and prevent gingival recessions in both groups.

Although the differences in hard parameters between the groups were not statistically significant, numerically better results were achieved with the GTR therapy (BDL-V: 2.5 ± 1.14 mm and BDL-H: 3.3 ± 1.82 mm) in comparison with the EMD procedure (BDL-V: 1.5 ± 0.77 mm and BDL-H: 2.2 ± 1.75 mm).

According to the clinical observations and the outcome of the present study it could be suggested that the EMD acts especially on root surfaces, modifying the healing process locally and creating an environment conducive to the formation of cementum. This event may lead to new attachment formation and consequently result in PD reduction and CAL-R gain, but may not always be related to new bone level improvement. Actually, Sculean et al (1999) investigating the healing of human intrabony defects following the treatment with either EMD or GTR found that the treatment with EMD led in six out of seven treated defects to a formation of a new connective tissue attachment and, to a certain extent, to bone regeneration, whereas the treatment with GTR resulted in all seven defects in new cementum and bone regeneration. The mean clinical attachment level gain in the EMD group was 3.2 mm and represented histologically a mean of 2.6 mm of new cementum and a mean of 0.9 mm of new bone. The mean clinical attachment level gain

in the GTR group was 3.6 mm and represented histologically a mean of 2.4 mm of new cementum and a mean of 2.1 mm of new bone.

Subtraction radiographic evaluation was not undertaken in the present study, however comparisons between initial and 12-month postoperative radiographs revealed a better radiographic bone level improvement in the GTR group, in which an increased radiopacity around the furcation area appeared as a pattern at the 12-month postoperative evaluation, when compared to the EMD group. Parodi et al (2000) treating deep intrabony defects with EMD application also observed that the good clinical results obtained after 12 months were not confirmed by the radiographic results, in which significant improvements in bone level were not detected. In surgical re-entry cases, new tissue with a rubbery consistency, well adherent and which could not be probed but was not mineralized was observed.

CONCLUSIONS

According to the results of the present study, GTR and EMD therapies were successful in the treatment of human Class II furcation lesions, producing similar soft and hard-tissue improvements. However, the GTR technique achieved numerically better results in hard tissue parameters after the 12-month evaluation, although the differences were not statistically significant. Thus, the use of both therapies may be recommended for the treatment of Class II furcation defects, with a slight advantage for GTR

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