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Using Enamel Matrix Derivative to Improve Treatment Efficacy in Periodontal Furcation Defects

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Abstract

Purpose

Furcations are complicated periodontal defects. Untreated furcations lead to loss of the involved teeth and supporting tissues. It has been demonstrated that regenerative biomaterials are beneficial in reconstruction of the bone surrounding furcation-affected teeth. These biomaterials range from bone grafts and nonresorbable/resorbable barrier membranes to biologics that are able to trigger inactive regenerative processes in periodontal tissues. Selection of appropriate material(s) to treat furcations is challenging. The aim of this article is to provide a comparative outlook on different biomaterials applicable in regeneration of furcations with a focus on enamel matrix derivative (EMD).

Methods

Scientific databases including PubMed/MEDLINE, ScienceDirect, and EMBASE were searched, and 28 articles were found primarily for this specific study. Full texts were studied to identify relevant studies; 17 studies were excluded because of irrelevancy, while 11 main studies were ultimately selected. Other references have been used for general statements.

Results

EMD is a protein complex widely used in the regeneration of different periodontal defects. To assess the effects of EMD for treatment of root furcations, clinical studies involving EMD with and without barrier membranes and bone grafts were selected and compared. Briefly, this study reveals that when EMD is combined with open flap debridement (OFD), guided tissue regeneration (GTR), or bone grafting (BG), the amount of class II furcations converted to class I increases significantly. EMD also reduces tissue swelling and patient discomfort after treatment.

Conclusions

This study provides evidence to find the best combination of biomaterials to treat furcation defects. The best results are obtained if EMD is combined with β-TCP/HA alloplastic bone grafts.

Furcation defects and treatments

Periodontitis is an inflammatory disease in which supporting tissues of the teeth, including gingiva, periodontal ligament (PDL), and alveolar bone, are destroyed. In multi-rooted teeth, bone destruction could spread to the separation zone of the roots. This condition is called furcation involvement (or simply, furcation).[1] The prevalence of furcations is about 30% to 50% in periodontitis cases.[2]

Based on the degree of horizontal bone loss, furcation defects are classified into class I, II, or III. In most instances of class II and III furcations, surgical treatment is needed to manage the resultant defects; however nonsurgical methods such as laser therapy, photodynamic therapy, scaling, and root planing using manual and power-driven scalers are routinely performed to treat furcations. Various regenerative therapies are also available for furcation defects, the more common among them being guided tissue regeneration (GTR) and regeneration using enamel matrix derivatives (EMD).[3] To compare outcomes of EMD therapy to other alternative approaches in the treatment of furcations, relevant comparative studies were reviewed and summarized as follows.

Methods

Scientific databases including PubMed/MEDLINE, ScienceDirect, and EMBASE were searched, and 28 articles were found primarily for this specific study. Full texts were studied to identify relevant studies; 17 studies were excluded because of irrelevancy, while 11 main studies were ultimately selected. Other references have been used for general statements.

Comparative studies of EMD treatment in combination with other methods for the treatment of periodontal furcations

EMD versus GTR

In 2004, Jespen et al[4] conducted a clinical study that compared the effectiveness of EMD to barrier membranes for treating mandibular buccal class II furcation defects. Forty-five patients with buccal class II furcation defects (probing depth >3 mm horizontally), full-mouth bleeding scores less than 25%, and full-mouth plaque scores were selected at baseline. In any of the following conditions patients were excluded from the study: (1) If they were involved in any other clinical trials; (2) had medical complications such as uncontrolled diabetes; (3) had been treated with antibiotics 3 months before surgery; (4) had molar restorations with buccal margins spreading out <1 mm from the entrance of the furcation; (5) had class II lingual furcation defects; or (6) had nonvital molars with posts or screw-retentive restorations or nonvital molars that had not undergone root canal therapy (RCT).

Of 45 defects treated with EMD, 35 showed reduction, 9 defects had no improvement, and 1 worsened. Clinical observations also revealed that in the group treated with barrier membrane, 30 defects reduced, 11 did not improve, and 4 worsened. The number of defects completely reduced were 8 and 3 after treatment with EMD and barrier membrane, respectively. Statistical analysis of data showed significant reduction in the horizontal depth of furcation defects in the EMD-treated group, compared to the group treated with GTR. The occurrence of pain/swelling after surgery was also lower in the EMD-treated group. Furthermore, it is noteworthy that antibiotics were prescribed four times less in the EMD-treated group compared to the membrane therapy group.[4]

OFD + EMD

Chitsazi et al[5] conducted a clinical study in 2007 to examine the efficacy of open flap debridement (OFD) with EMD for treating mandibular class II furcation defects. The selected patients for the study were 10 healthy nonsmokers, both men and women, having bilateral class II furcation defects. There were 20 total defects. Based on initial radiographic examinations, horizontal probing depth (HPD) of defects were >3 mm in all instances. In test groups, OFD was performed in combination with EMD, whereas in control groups, only OFD was completed. Several tissue parameters were investigated to assess the effectiveness of treatments, including the following soft tissue parameters: clinical probing depth (CPD) and vertical and horizontal clinical attachment level (V-CAL and H-CAL). Hard tissue parameters consisted of exposed horizontal probing depth of bony defects (E-HPD), vertical depth of bone crest (V-DBC), vertical depth of the base of bony defects (V-DBD), and length of the intrabony defect (LID). These parameters were measured before, during, and 6 months after surgery.

After 6 months, results showed the same improvement of V-CAL in control and test groups. CPD was also not statistically different in test groups compared with controls. Conversely, in the EMD-treated

group, horizontal attachment gain was approximately 30% more than that of OFD. EMD improved both E-HPD and V-DBD resolution of the bony defects. The authors concluded that EMD enhances the efficacy of OFD in treating mandibular class II furcations.[5]

In 2008, Casarin et al[6] evaluated EMD-induced effects on proximal class II furcation defects. Fifteen patients with proximal class II furcations presenting bleeding on probing (BOP) were included in the study. Probing depths (PDs) were >5 mm. In the control group (n = 15), conditioning with 24% ethylenediaminetetraacetic acid (EDTA) was performed, followed by open flap debridement (OFD). In the test group (n = 15) EMD was applied after conditioning and OFD. Clinical parameters such as BOP, PD, plaque index (PI), furcation closure, gingival margin position (GMP), relative vertical and horizontal clinical attachment level (RVCAL and RHCAL), and, lastly, vertical and horizontal bone level (VBL and HBL) were assessed before surgery, along with 2, 4, and 6 months postsurgery.

After 6 months, both groups displayed reduction of gingival recession and PD, but results showed no significant differences between the two groups. The RHCAL gains improved in the test group (2.28 ± 1.21 mm) compared to the control (1.36 ± 1.26 mm). The measured RVCAL improvements were 1.00 ± 0.39 mm in the test group and 0.95 ± 0.54 mm in the control. The HBL gain was 1.79 ± 1.00 mm and 1.38 ± 1.17 mm in the control and test groups, respectively. The gain in VBL was 1.12 ± 1.04 mm in the control and 1.82 ± 0.82 mm in the test group; however, there were no statistically significant differences ($p > 0.05$) observed for the RHCAL, RVCAL, VBL, and HBL gains between the test and control. In contrast, the number of class II furcations converted to class I was quite different in the control and test group ($p < 0.05$). While 9 furcations were converted in the test group, and 2 were completely closed, conversion occurred only in 5 furcations of the control group. Based on the results, the authors concluded that EMD does not improve the clinical attachment levels or PD reductions obtained by OFD; however, a higher rate of class II to class I furcation conversions could be gained by EMD treatment.[6]

Two years follow-up of the last study was also performed by Casarin et al.[7] Twenty-four months after treatment, the amount of PD reduction was 1.9 ± 1.6 mm and 1.0 ± 1.3 mm in the test group and control, respectively ($p > 0.05$). RHCAL was 1.4 ± 0.9 mm in the test group and 1.3 ± 0.7 mm in control ($p > 0.05$). Despite there being no statistically significant differences among the test and control groups in PD reduction and RHCAL gains after 24 months, the number of remaining class II furcations were obviously different. The nonconverted class II furcations observed in the test and control groups were 5 versus 10 ($p< 0.05$), respectively. Two-year follow-up results indicated that, compared to OFD, using EMD increases the conversion rate of class II furcation defects to class I.[7]

EMD + autologous bone graft

In a study conducted by Aimetti et al[8] in 2007, the efficacy of a combination of EMD and autologous bone graft for treatment of class II furcation defects was evaluated. The patients selected for the study were 11 patients with at least one mandibular facial class II furcation defect. Only vital teeth with a minimum of 2 mm of keratinized tissue were included in the study. Two years after treatment with EMD and autologous bone graft, clinical and radiographic observations revealed statistically significant improvements at the defect sites; 7 of 11 class II furcation defects changed into class I defects, and 4 defects showed complete clinical closure. The authors determined that combination of EMD and autologous bone graft could be an efficient treatment for furcation-involved mandibular molars.[8]

EMD + allogenic bone graft + GTR

In 2013, Jaiswal and Deo[9] conducted a clinical study to assess the use of EMD combined with demineralized freeze-dried bone allograft (BG) and GTR using bio-resorbable membrane for treating class II furcations. Thirty healthy patients diagnosed with chronic periodontitis having a mandibular class II buccal or lingual furcation were selected. Horizontal probing depth of furcations was not less than 3 mm. Several clinical parameters, including horizontal probing depth (HPD), vertical probing pocket depth (PPD), vertical relative attachment level (V-RAL), and relative gingival margin level (RGML), were measured at baseline level, along with 6 and 12 months after surgery.

Treatment was given in three groups: (1) EMD + BG + GTR, (2) BG + GTR, and (3) open flap debridement (OFD). The results showed significant reduction in the mean HPD after 12 months in the EMD + BG + GTR group (2.10 ± 0.99 mm) and the BG + GTR group (1.50 ± 0.52 mm), while HPD reduction was not significant in the OFD group (0.50 ± 0.70 mm). PPD was reduced significantly in all three groups. The amount of PPD reduction was significantly greater in EMD + BG + GTR (1.74 ± 1.00 mm) compared to BG + GTR (0.81 ± 0.31 mm), as well as OFD (0.46 ± 0.52 mm). Similarly, V-RAL gain in EMD + BG + GTR (2.12 ± 1.07 mm) was statistically significant compared to BG + GTR (0.85 ± 0.31 mm) and OFD (0.34 ± 0.74 mm). Finally, the number of class II furcations that clinically closed or converted to class I was much more in EMD + GTR + BG group (10 defects) than in BG + GTR (8 defects) and OFD (2 defects).[9]

HA/β-TCP + EMD

To evaluate the treatment of proximal furcation defects using hydroxyapatite/β-tricalcium phosphate (HA/β-TCP) combined with EMD, Peres et al[10] conducted a randomized clinical trial in 2013. Thirty patients with chronic periodontitis having one or more proximal class II furcation(s) were selected, with probing pocket depth (PPD) ≥5 mm and plaque index (PI) ≤20%. All patients presented bleeding on probing (BOP). Next was random assignment of these patients to one of the following two study groups: (1) open flap debridement (OFD) + HA/β-TCP filling (HA/β-TCP group) and (2) OFD + HA/β-TCP + EMD filling (HA/β-TCP-EMD group). Relevant clinical parameters including PPD, PI, gingival index (GI), relative gingival margin position (RGMP), relative vertical clinical attachment level (RVCAL), relative horizontal clinical attachment level (RHCAL), relative vertical bone level (RVBL), and relative horizontal bone level (RHBL) were documented at baseline, along with 6 months after surgery.

Six months after treatment, improvements were observed in both groups ($p < 0.05$). In the HA/β-TCP-EMD and HA/β-TCP groups RVCAL gains were 2.10 ± 0.87 mm and 1.47 ± 0.99 mm; RHCAL gains were 1.57 ± 1.58 mm and 1.47 ± 1.46 mm, respectively. Similarly, the gains in RVBL were 1.70 ± 1.26 mm and 1.47 ± 1.13 mm; gains in RHBL were 1.70 ± 1.37 mm and 1.90 ± 1.11 mm, respectively. The results of RVCAL, RHCAL, RVBL, and RHBL showed no significant differences between HA/β-TCP-EMD and HA/β-TCP groups; however, the number of furcation closures were significantly different: 7 versus 4 closed furcations were observed in HA/β-TCP-EMD and HA/β-TCP groups, respectively. The authors concluded that both treatments resulted in improvements of clinical parameters and could be considered as interchangeable therapeutic choices for the treatment of proximal class II furcations.[10]

In a similar study, Queiroz et al[11] evaluated the therapeutic outcomes of EMD and/or HA/β-TCP for treating mandibular class II buccal furcations. Forty-one patients were included in the study, all having a buccal class II furcation involvement on a mandibular molar. Probing pocket depth (PPD) was not less than 4 mm, and bleeding on probing (BOP) was observed in all selected cases. Three study groups were

formed including: (1) EMD (n = 13); (2) HA/β-TCP (n = 14); and (3) EMD + HA/β-TCP (n = 14). Clinical parameters measured at baseline and 6 and 12 months after treatment were PPD, plaque index (PI), gingival index (GI), relative vertical and horizontal attachment level (RVCAL and RHCAL), and relative gingival margin position (RGMP).

Twelve months after treatment, clinical examinations revealed significant improvements in all parameters except RGMP. Although none of the defects were closed completely, 85.3% showed partial closure. The authors concluded that because of its regenerative potential, EMD could be promising for treatment of furcation defects.[11]

Conclusion

Enamel matrix derivative (EMD) is a protein complex mainly constituted of amelogenins. Amelogenins play a central role in the formation and maturation of enamel in developing teeth of mammals. Several manifestations indicate that EMD has the potential to induce cementum formation and angiogenesis, while modulating wound healing in periodontal tissues. These unique features are the rationale to exploit EMD in the treatment of periodontal defects including gingival recessions, intrabony defects, fenestrations, and furcations.

Use of EMD in conjunction with OFD improves therapeutic outcomes, especially horizontal attachment gain and number of class II to class I furcation conversions. Induction of osteogenesis by EMD promotes new bone formation both vertically and horizontally. EMD also stimulates the healing of soft tissues and accelerates tissue repair. When applied in combination with GTR, EMD significantly reduces pain and swelling and decreases the need for antibiotics because of its antibacterial and anti-inflammatory nature.

Autogeneous and allogenic bone grafts possess osteogenic and osteoconductive capabilities, respectively. On the other hand, due to its growth-like factor activities, EMD provides osteoinductivity. The combination of EMD and various types of bone grafts causes a synergic effect and boosts osteogenesis.

In β-TCP/HA alloplastic bone grafts, β-TCP provides the necessary minerals for tissue mineralization and osteogenesis, due to its fast rate of dissolution and resorption. In contrast to β-TCP, the slow resorption of HA results in volume preservation at the defect site and avoids tissue shrinkage and collapse. It can be concluded that best results are obtained if EMD is combined with β-TCP/HA alloplastic bone grafts.

References

1 Nibali, L, Zavattini, A, Nagata, K, et al: Tooth loss in molars with and without furcation involvement—a systematic review and meta-analysis. *J Clin Periodontol* 2016; **43**: 156- 166

2 Svärdström, G, Wennström, JL: Prevalence of furcation involvements in patients referred for periodontal treatment. *J Clin Periodontol* 1996; **23**: 1093- 1099

3 Zambon, JJ: Unanswered questions: can bone lost from furcations be regenerated? *Dent Clin North Am* 2015; **59**: 935- 950

4 Jepsen, S, Heinz, B, Jepsen, K, et al: A randomized clinical trial comparing enamel matrix derivative and membrane treatment of buccal Class II furcation involvement in mandibular molars. Part I: study design and results for primary outcomes. *J Periodontol* 2004; **75**: 1150- 1160

5 Chitsazi, MT, Farahani, RM, Pourabbas, M, et al: Efficacy of open flap debridement with and without enamel matrix derivatives in the treatment of mandibular degree II furcation involvement. *Clin Oral Investig* 2007; **11**: 385- 389

6 Casarin, RC, Del Peloso Ribeiro, É, Nociti, FH, et al: A double-blind randomized clinical evaluation of enamel matrix derivative proteins for the treatment of proximal class-II furcation involvements. *J Clin Periodontol* 2008; **35**: 429- 437

7 Casarin, RC, Del Peloso Ribeiro, É, Nociti, FH, et al: Enamel matrix derivative proteins for the treatment of proximal class II furcation involvements: a prospective 24-month randomized clinical trial. *J Clin Periodontol* 2010; **37**: 1100- 1109

8 Aimetti, M, Romano, F, Pigella, E, et al: Clinical evaluation of the effectiveness of enamel matrix proteins and autologous bone graft in the treatment of mandibular Class II furcation defects: a series of 11 patients. *Int J Periodont Restorative Dent* 2007; **27**: 441- 447

9 Jaiswal, R, Deo, V: Evaluation of the effectiveness of enamel matrix derivative, bone grafts, and membrane in the treatment of mandibular Class II furcation defects. *Int J Periodont Restorative Dent* 2013; **33**: e58- 64

10 Peres, MF, Ribeiro, ED, Casarin, RC, et al: Hydroxyapatite/β-tricalcium phosphate and enamel matrix derivative for treatment of proximal class II furcation defects: a randomized clinical trial. *J Clin Periodontol* 2013; **40**: 252- 259

11 Queiroz, LA, Santamaria, MP, Casati, MZ, et al: Enamel matrix protein derivative and/or synthetic bone substitute for the treatment of mandibular class II buccal furcation defects. A 12-month randomized clinical trial. *Clin Oral Investig* 2016; **20**: 1597- 1606