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Review Article

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The Application of an Enamel Matrix Protein Derivative (Emdogain) in Furcations: A Review of Literature

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ABSTRACT

Periodontal disease results in the loss of the attachment apparatus. The search for techniques and products to encourage the regeneration of this tissue has received more attention over the past three decades. The results from basic research have shown that although there are not many studies on the use of EMD in the treatment of furcations, it is an essential option in the difficult management of furcations, and more research in periodontal regeneration is required. This paper aims to evaluate the effect of enamel matrix derivative (EMD) in the treatment of furcations.

Key Words: Enamel matrix protein derivative, Emdogain, Furcations, Regenerative periodontal therapy, Class I furcations, Class II furcations, Mandibular furcations, Maxillary furcatio

INTRODUCTION

Periodontal disease is an inflammatory disorder that damages the tooth's supporting tissues, including the gingiva, the periodontal ligament (PDL), and the alveolar bone.[1] According to a survey released by The Economist Intelligence Unit in June 2021, periodontal disease is regarded as the sixth most widespread disease in the world, with a number that has remained constant over the past 25 years. It also relates to systemic diseases like diabetes or cardiovascular disease,[2] which, if left untreated, are among the major causes of tooth loss.[3] Resorption of the alveolar bone from a multirooted tooth's bifurcation and trifurcation zones as a result of the development of periodontal disease known as furcation involvement.[4] Changes in the vertical and horizontal plane at the site of the root separation area are used clinically to determine the degree of furcation involvement. [5] In situations of periodontitis, the prevalence of furcations ranges from 30% to 50%.[6] Furcation defects are classified as class I, class II, or class III depending on the amount of horizontal bone loss.[7] Although nonsurgical procedures including scaling, root planing, photodynamic therapy, laser therapy, and other techniques are frequently used to furcations defects,[8] surgical treatment is usually required to manage class II and class III furcation defects. Moreover, additional periodontal treatments including periodontal or adjunctive therapies, like regenerative materials and antimicrobials, are required to boost the effectiveness of periodontal therapy in the treatment of furcation.[9] The main goal of this therapy is to arrest the disease progression, reconstitution of the lost periodontal structures (new formation of root cementum, periodontal ligament, and alveolar bone), and prevent the progression of the disease.[10] In recent years, important advances have been made in terms of tissue regeneration procedures. Enamel matrix derivatives (EMDs) have played a significant role in these latest innovations.[11,12] Emdogain® is a special gel that contains a protein-derived enamel matrix derivative. By activating particular cells involved in the healing process of soft and hard tissues, this mixture of natural proteins can stimulate biological processes that typically take place during periodontium development and regeneration.[13] According to findings from basic research, the enamel matrix protein derivative (EMD) plays a significant role in the healing of periodontal wounds.[14] Histological findings from research on both animals and humans have demonstrated that EMD therapy encourages periodontal repair.[14] Additionally, clinical research has shown that EMD therapy promotes periodontal wound healing in people through effects on various growth factors, cement formation, and angiogenesis.[12,15]

MATERIALS AND METHODS

An electronic literature search includes in *vitro* and in *vivo* studies, human case reports, and clinical comparative trials.

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The selected studies were pooled from MEDLINE, Scopus, and Cochrane Library up to August 2022. Articles in which the main objective was to evaluate the effect of Emdogain in furcations' treatment were selected.

The first search was done with Medline and Cochrane Library using the following keywords: 'enamel matrix derivatives–furcation' and 'enamel matrix derivatives–periodontology'. The majority of those do relate to the treatment of periodontal disease, and only a few articles discuss the use of EMD in furcations.

Inclusion criteria: Only randomized trials that included a sample of patients with furcation defects in upper or lower molar teeth were included. The proposed treatment for furcation lesions should include the use of EMD associated or not with other biomaterials.

Exclusion criteria: All studies that proposed treatment for furcation lesions without the use of EMD were excluded.

DISCUSSION

Mandibular furcations

In 2003, a clinical investigation involving 10 patients and evaluations at six, twelve, and thirty-six months following the application of an EMD in class II mandibular furcation defect was reported to be the first published clinical study using EMD for surgical therapy of furcations. [16] Both the probing attachment level in the center of the lingual/buccal furcation area on a vertical axis and the probing attachment level in the lingual and/or buccal furcation area on a horizontal axis (PAL-H) were evaluated as clinical parameters (PAL-V).

The results of the study showed that the clinical parameters improved at 6 months, however, at 12 and 36 months the numbers remained the same. When compared to lingual defects, buccal defects showed a higher reduction of the average values PAL-H, and PAL-V showed approximately equivalent average reductions for these two types of defects.[16]

EMD versus GTR

Three split-mouth comparative studies compared the efficacy of EMD versus the GTR by bioabsorbable membranes in the treatment of mandibular class II furcation defects.

In 2004 Jepsen *et al. published a randomized clinical trial (part 1)in which the* enamel matrix derivative (EMD; test) was compared to the barrier membranes (control) for the treatment of mandibular buccal Class II furcation defects. 8 It was concluded that when compared to membrane therapy, enamel matrix derivative significantly reduced the horizontal furcation depth and had a relatively lower incidence of postoperative discomfort and swelling.[17]

In 2004 Meyle *et al.*, in a randomized clinical trial (part 2) compared EMD and barrier membranes for the treatment of class II furcations. Even though equivalent outcomes were obtained, a larger probability of gingival retractions was seen in the mid-furcation region in the case of the membrane-based treatment. In the areas where EMD was applied, no detectable bone resorption was found; however, membrane treatment led to marginal bone resorption. Additionally, the study demonstrated that regardless of the treatment, the furcation morphology was not related to clinical results at the time of surgery.[18]

In 2006 Hoffmann *et al.,* compared enamel matrix derivative and membrane in the treatment of buccal class II furcation defects in mandibular molars regarding patients' factors and treatment outcomes. Results showed a higher median reduction of the parameters for sites treated with EMD compared with sites treated by the membrane.[19]

EMD + OFD

In a split-mouth trial IN 2007, Chitsazi et al. assessed the efficacy of open flap debridement (OFD) using or not EMD in the treatment of class II furcation involvement in 10 non-smokers with 20 comparable bilateral class II furcation defects.[20]

Clinical measurements were taken at baseline and during the reentry procedure six months later. These measurements included clinical probing depth, vertical clinical attachment level, horizontal clinical attachment level, the location of the gingival margin, horizontal probing depth of the bony defect (E-HPD), the vertical depth of the bone crest, the vertical depth of the base of the bony defect (V-DBD), and length of the intrabony defect. [20]

The findings showed that the studied indices improved more in the EMD group than in the OFD group, with a 13% increase in VCAL compared to an 8.3% increase in the OFD group, but no statistically significant differences between the two groups after six months. According to the analysis of soft tissue parameters, the inclusion of EMD considerably increased the horizontal attachment gain by 1.2 mm (30%) for EMD more than for OFD.[20]

It was concluded that the adjunctive use of EMD enhances the efficiency of OFD in the management of mandibular class II furcation involvements.[20]

EMD + Autologous bone graft

In 2007, Aimetti *et al.* published a study on eleven patients, that aimed to assess the outcomes of treating buccal mandibular Class II furcation defects over 24 months with an enamel matrix derivative and autologous bone graft combination. The results were evaluated clinically and radiologically and showed the reduction of defects from class II to

class I in seven patients and complete closure of the defect in four patients.[21]

EMD + Allogenic bone graft + GTR

Jaiswal & Deo (2013) in a randomized controlled trial investigated the efficiency of EMD in combination with freeze-dried demineralized bone allograft (BGS) but also with bioresorbable membranes (BioMesh®) in the treatment of mandibular class II involvements.[22]

The authors described better outcomes by combining EMD with GTR by offering room for cell regeneration, support, and wound protection at the point of furcation during the healing process.[22]

Conclusions of this study showed that EMD + BGS + GTR and BGS + GTR both demonstrated statistically significant increased results in terms of vertical relative attachment level V-RAL gain, HPD reduction, and PPD. In addition, EMD + BGS + GTR caused a statistically significant reduction in V-RAL, PPD, and a non-significantly important reduction in HPD compared to BGS + GTR.[22]

EMD + HA/β-TCP

There were three studies done by Queiroz et al. between 2015 and 2017 that examined the combination of EMD with beta-Tricalcium phosphate/Hydroxyapatite (β-TCP/HA) in class II mandibular furcations.

In 2015, Queiroz *et al.* published a study on 13 patients; in this study EMD (Emdogain®) and -TCP/HA were used for the treatment of mandibular molar furcations with pockets >4 mm and retraction 2 mm 30 days after professional hygiene, along with scaling, scaling, and root planning. Full thickness flap was applied after the horizontal incision, without vertical releasing incisions, and sutured. [23] The PD, relative VCAL (RVCAL), relative gingival margin position (RGMP), and relative HCAL (RHCAL) parameters were reassessed six months after the intervention. As a result, an improvement was obtained in all situations, in 76.92% of patients, the furcation involvement changed to class I. Only 23.08% of the furcation remained as class II, primarily due to the gain of horizontal AL.[23]

In 2016, Queiroz *et al.* published a study on 41 patients, three study groups were included as the following: EMD alone (13 patients), -TCP/HA alone (14 cases), and EMD in combination with TCP/HA. 2[4] Plaque index (PI), PPD, RVCAL and RHCAL, gingival index (GI), and RGMP were the clinical parameters that were assessed at baseline and after six and twelve months of treatment, respectively. At 12 months, there were no variations in the levels of the free GM across the groups, but there were substantial disparities between the PDs and the levels of vertical and horizontal attachment.[24] Between groups, there were no appreciable changes in the horizontal attachment gain: 2.64 0.93 mm for -TCP/HA, 2.77 0.93 mm for EMD, and 2.93 0.83 mm for EMD + -TCP/HA. After the investigation, 85.3% of the locations were only partially closed.[24]

In 2017, Queiroz *et al.* published a study on 39 patients, EMD and *β*-TCP/HA were used together in the furcation defects to evaluate their effect on the microbiocenosis of the furcations. Patients were divided into three study groups: EMD alone, EMD in association with a BGS composed of β-TCP/HA, or bone substitute alone.[25]The study's findings indicated that there are differences in the microbial flora composition in the approximate areas and furcations, with the furcation's complex microbiome consisting of more diverse sites than interproximal ones. More importantly, despite the presence of species including *Porphyromonas* (*P. gingivalis*) and *Treponema (T. denticola*) in the furcation defects, this important finding revealed that they made up just a small portion of the furcations' microbiome core. Although similar outcomes were shown in the repair of furcation defects, individuals with EMD who were receiving therapy had their microbiomes remain stable for longer as commensal abundance increased and pathogen richness decreased.[25]

Maxillary furcations

There has been less research done on treating maxillary furcations.

In 2008, Casarin et al. published a randomized, double-blind clinical trial that examined the clinical response of class II proximal furcations treated with enamel matrix derivative proteins (EMD). The patients were divided randomly into control group (open flap debridement (OFD)+24% ethylenediaminetetraacetic acid (EDTA) conditioning), and test group (OFD+24% EDTA conditioning application).[26] The following parameters: Plaque index (PI), bleeding on probing (BOP), pocket depth (PD), gingival margin position (GMP), vertical and horizontal bone levels (VBL and HBL), and furcation closure were assessed before and two, four, and six months after the procedures. The results of the study showed that the use of EMD in proximal furcations led to a higher rate of class-II to class-I furcation conversion rather than a better reduction in PD or an increase in clinical and osseous attachment levels.[26]

In 2010, Casarin et al. published a continuation of their 2008 study with a two-year follow-up instead of a 2,4- and 6-month follow-up. At two years, there was a greater improvement in the bone support in the proximal furcation area in the group treated with EMD compared with that treated with OFD therapy.[27]

In 2013, Peres *et al. published* a prospective double-blind, controlled, parallel, and randomized clinical study, to clinically evaluate proximal furcations treated with hydroxyapatite/β-tricalcium phosphate (HA/β-TCP) alone or in combination

with enamel matrix derivative (EMD).[28] A number of parameters were evaluated at baseline followed by a follow-up evaluation after six months which included: gingival index (GI), plaque index (PI), relative gingival margin position (RGMP), relative vertical attachment level (RVAL), relevant horizontal attachment levels (RHAL), relative vertical bone level (RVBL), relative horizontal bone level (RHBL) and furcation diagnosis parameters.[28] The study showed that both treatments lead to improvements in all the clinical parameters measured. But still, the closure of proximal class II furcation defects is unpredictable.[28]

CONCLUSION

Although the role of EMD in the regenerative treatment of bony defects has been extensively studied, there are only a few studies that evaluated the use of EMD in the treatment of furcation defects. Most of these studies evaluated its use in mandibular class II furcations, and only a few studies were about maxillary furcation defects. Moreover, the analysis of the research revealed a variety of EMD uses, not only individually but also in conjunction with resorbable membranes, BGS, and -TCP/HA. However, only a small number of studies (three) monitored the effectiveness of the treatment after a year. Additionally, the microbiome at these defects was different from the microbiome found in periodontal pockets. Compared to surgical treatments using resorbable membranes, the use of EMD has resulted in a larger reduction in the depth of grade II furcations. When treating grade II maxillary furcations, the clinical outcomes with the use of EMD were less favorable than when treating mandibular furcations.

The results show that although there are not many studies on the use of EMD in the treatment of furcations, it is an essential option in the difficult management of furcations, and more research in periodontal regeneration is required.

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Conflicts of interest

There are no conflicts of interest.

Authors' Contribution:

Rawia Karameh – Study conception and design, collection of data, statistical analysis and interpretation of results, drafting the manuscript.

Mahmoud Abu-Ta'a – Critical revision of the manuscript.

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