Studies on the Effect of Enamel Matrix Derivatives on Early Wound Healing. Which Applications are Evidence-Based?

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ABSTRACT

The goal of regenerative periodontal therapy is the reconstitution of the lost periodontal structures (i.e. the new formation of root cementum, periodontal ligament and alveolar bone). Results from basic research have pointed to the important role of the enamel matrix protein derivative (EMD) in periodontal wound healing. Histological results from animal and human studies have shown that treatment with EMD promotes periodontal regeneration. Moreover, clinical studies have indicated that treatment with EMD positively influences periodontal wound healing in humans. The goal of the current overview is to present, based on the existing evidence, the clinical indications for regenerative therapy with EMD.

Key Words: enamel matrix proteins, wound healing, postoperative complications

Results from basic research and histological results from animal and human studies which pointed to the important role of the enamel matrix protein derivative (EMD) in periodontal wound healing and promotion of periodontal regeneration have been mentioned in the previous three parts of this paper.¹³ Given the increasing importance of the patient’s acceptance of various current surgical procedures in periodontology, which is essentially related to the process of wound healing (swelling, tenderness, oedema, pain, suppuration, algereal reactions, maintenance of the primary wound closure etc.), the aspects associated with the wound healing are mentioned in almost all controlled clinical studies reports.

Primary wound closure maintained over time is especially important, as EMD, alone or in various combinations with bone grafts and/or membranes, has to be retained within the defect in order to become effective.

Several studies have attempted to evaluate the effect of EMD treatment on early wound healing.⁴⁵ In a double-masked, split-mouth, placebo-controlled, randomized study 28 patients with moderately advanced chronic periodontitis were scaled and root planed, and the soft tissue wall of the pocket was curetted to remove pocket epithelium and adjacent granulation tissue.⁴ All experimental sites were carefully irrigated with saline. When the bleeding from the pocket had ceased, a 24% EDTA gel was applied in the sites and retained for 2 min. The sites were then thoroughly irrigated with saline to remove EDTA remnants. Subsequently, left and right quadrants were randomized to subgingival application of EMD (test) or vehicle (control). All sites were re-examined clinically after 1, 2 and 3 weeks. In addition, a visual analogue scale (VAS) was used to score the degree of post-treatment discomfort. The results indicated that EMD topically applied in instrumented sulci enhance
the early healing of periodontal soft tissue wounds. Furthermore, at 1 week, the proportion of patients reporting a VAS score ≤ 20 was significantly higher for the EMD treated quadrants than for controls.

Another study has evaluated by clinical means and as patient perception of post-operative events, the effect of EMD on the healing of soft-tissue wounds following periodontal surgery. Patients scheduled for periodontal flap surgery were treated with either a modified Widman flap and application of EMD (test) or with modified Widman flap alone (control). Clinical measurements were taken at four different points in time, at surgery, 1, 4 and 8 weeks after surgery. The results revealed that of all parameters evaluated, none showed a significant difference between the control and EMD groups, except for gingival swelling at the one-week assessment where the EMD group exhibited a higher swelling score. It was concluded that the early wound healing of periodontal flap-surgeries in those sites treated with EMD is not different from control sites.

More recently, a series of studies were undertaken to describe a new surgical approach (minimally invasive surgical technique MIST, modified minimally invasive surgical technique M-MIST, respectively) and to evaluate preliminarily its clinical results (among them, the early wound healing) and the patient perception associated with the application of EMD in the treatment of either isolated or adjacent intrabony defects. In a study from 2007, thirteen deep isolated intrabony defects in 13 patients were surgically accessed with the MIST. The technique was designed to limit the mesio-distal flap extension and the corono-apical reflection in order to reduce the surgical trauma and increase flap stability. EMD was applied on the debrided root surfaces and stable primary closure of the flaps was obtained with internal modified mattress sutures, while surgery was performed with the aid of an operating microscope and microsurgical instruments. Beside clinical outcomes, the intraoperative and postoperative perception of the patient was recorded. The early wound healing was uneventful, primary wound closure was obtained and maintained in all sites with the exception of one site with a small wound dehiscence after one week. Patients did not report any pain, only three patients experienced a slight discomfort for two days post-operatively. The results indicated that MIST associated with EMD resulted in excellent clinical improvements while limiting patient morbidity.

In a similar study on forty deep isolated intrabony defects in 40 patients, primary closure was obtained in all treated sites and at 1-week follow-up visit, 95% of the sites were still closed. Only 12 subjects reported moderate post-operative pain (VAS 19 ± 10) that lasted for 26 ± 17 hours. The results indicated the very limited post-operative morbidity of the technique associated with EMD. Same results were obtained by the same authors when using the same technique (MIST associated with EMD) on multiple adjacent intrabony defects, or when using a modified MIST (M-MIST) for defects without a lingual intrabony component.

It is interesting to note that the wound healing of the injured pulp tissue, known as highly sensitive and with reduced healing capacities, was also studied in association with EMD. After animal-studies in rats demonstrating that different healing processes of the injured pulp existed for EMD and Calcium-hydroxyde preparations, and bone morphogenic proteins (BMP) – expressing macrophages might play important roles in reparative dentin formation, two clinical controlled studies compared and histologically evaluated EMD versus formocresol as pulpotomy agents in the primary dentition. These studies offered preliminary evidence that EMD is a promising material which may be used in pulpotomy procedures, especially in the primary dentition.

Guided Tissue Regeneration (GTR) is known to have complications due to postoperative infections, membrane exposure and delayed wound healing. Direct comparisons between GTR and EMD in treatment of intrabony defects showed that EMD leads to significantly less complications and patient morbidity. In some studies, the results of EMD treatment are at least the same, or even better than the results of GTR. In one study, the additional use of a membrane in regenerative therapy with EMD does not improve the result, but can even amplify the postoperative complications.

Based on the available data, EMD appear to have a beneficial effect on the early wound healing, both on periodontal and on pulpal wounds. However, at the current time it appears that no definitive conclusions can be drawn to what extent the additional application of EMD may additionally enhance early wound healing following conventional periodontal therapy.

REFERENCES

3. Stratul SI, Sculean A. The use of an enamel matrix protein derivative (Emdogain®) in regenerative periodontal therapy. Which applications


