The use of Enamel Matrix Derivative (Emd) for Treatment of Combined Apicomarginal Lesions in Apical Surgery: A Retrospective Analysis

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ABSTRACT

Objective: The outcome of apical surgery using modern techniques is favourable. However, the presence of a combined apicomarginal defect may negatively affect the postsurgical healing. The objective of this retrospective analysis was to assess the healing of teeth with apicomarginal defects treated with apical surgery and enamel matrix derivative (EMD).

Methods: This retrospective study evaluated the application of EMD in apical surgery of 17 teeth with apicomarginal defects. Cases were followed for at least 1 year, and healing was classified based on established clinical and radiographic criteria.

Results: The patient sample included nine females and eight males with a mean age of 50±18.2 years. Maxillary incisors (six lateral and four central) were the most frequently treated teeth. The majority of apicomarginal defects was located on the facial aspect of the root (70.6%) and belonged to defect class I (76.5%). Follow-up periods ranged from 1 to 5 years. Healing was successful in 14 teeth (82.4%).

Conclusion: The application of EMD resulted in a similar outcome as in previously published clinical studies related to regenerative techniques for the treatment of apicomarginal defects in conjunction with apical surgery.

Keywords: Apical surgery, enamel matrix derivative, endo-perio lesion

INTRODUCTION

Apical surgery using microsurgical principles is a well-established treatment option in endodontics. Modern techniques of apical surgery have shown high success rates, and 1-year results are reasonably suggestive of the long-term prognosis (1). However, periapical healing may be compromised in situations, in which the apical lesion has extended along the root surface to the marginal periodontium. Such a combined endo-perio lesion, or apicomarginal defect, carries the risk of epithelial downgrowth along the denuded root surface following apical surgery (2). The apical extension of the junctional epithelium may result in the establishment or recurrence of the communication between the marginal periodontium and apical area, thus jeopardizing the healing outcome but also carrying the risk of gingival recession with aesthetic concern (3).

Several papers have proposed classifications for the location and extent of periradicular lesions in conjunction with apical surgery (4–6). Such classifications are helpful to categorise lesions, treatment selection, and reported outcome. Following the establishment of (guided) tissue regeneration techniques in periodontology and implant dentistry, there has been a growing interest in using this treatment option also in apical surgery (3). Regenerative techniques include the use of barrier membranes, bone replacement/filler materials, growth factors, or combinations thereof.

In the early 1990s, a Swedish team of researchers demonstrated the biologic capability of enamel matrix proteins (EMP) for periodontal regeneration. The major component of EMP is amelogenin that constitutes about 90% of the matrix. EMP were found to be involved in the development and prere-
generation of root cementum (7). In the very first animal experiment about EMP, its positive effect on periodontal regeneration was demonstrated in a buccal dehiscence model in monkeys (8). The purified fraction of EMP, derived from the enamel layer of developing porcine teeth, was subsequently given the working name “enamel matrix derivative” (EMD) and was marketed as Emdogain® (Straumann, Basel, Switzerland) (9).

Clinical applications of EMD in dentistry have been reported in periodontology, dental traumatology, and endodontics. Indications for EMD in periodontology include angular intrabony defects, class II furcation defects, and recession defects (9, 10). In dental traumatology, EMD has been used adjunctively for replantation of avulsed teeth, but without convincing results (11, 12). The treatment of teeth with posttraumatic external replacement resorption using EMD in conjunction with intentional replantation has shown a recurrence rate of ankylosis in 53% (13). In endodontics, case reports have documented the application of EMD for treatment of buccal or palatal radicular grooves, in conjunction with tooth autotransplantation, and for the management of large endodontic lesions around dental implants (14–17).

The objective of this retrospective analysis was to assess the healing profile of teeth with apicomarginal defects treated with apical surgery and EMD.

MATERIALS AND METHODS

Our database of teeth treated with apical surgery was screened for the following criteria:

- apicomarginal defect,
- adjunctive use of EMD during apical surgery,
- minimum follow-up of 1 year.

All cases were treated by the same surgeon using a surgical microscope (Möller Denta 300; Haag-Streit International, Köniz, Switzerland). Full mucoperiosteal flaps were raised. Osteotomy and 3-mm root-end resection were done with rotary instruments under irrigation with saline. Root-ends were prepared with ultrasonic microtips (Endo success apical kit; Sat-elec Acteon, Mérignac, France) for root-end filling with mineral trioxide aggregate [MTA, ProRoot®; Dentsply Tulsa Dental, Tulsa, USA] or bioceramic root repair material [BC RRM, Total Fill®; Brasseler BUSA, Savannah, USA]) or alternatively with round diamond burs (for root-end sealing with composite, Retroplast; Retroplast trading, Rorvig, Denmark). The apicomarginal defects were thoroughly cleaned with hand instruments. Denuded root surfaces were conditioned with 24% EDTA (PrefGel®, Straumann, Basel, Switzerland) for 1 minute and subsequently rinsed with saline. Immediately before flap repositioning, the EMD (Emdogain®, Straumann, Basel, Switzerland) was applied to the apicomarginal defect in order to cover the exposed root surface. Wound margins were reapproximated using single interrupted sutures (Seralon®; Ser-ag-Wiessner GmbH, Naila, Germany). Patients were prescribed nonsteroidal analgesics and chlorhexidine mouthwash. Sutures were removed 5–7 days postoperatively.

Seventeen patients fulfilled the inclusion criteria, and their charts and radiographs were retrospectively evaluated. Healing was determined clinically (absence or presence of signs and/or symptoms) and radiographically, i.e., complete, incomplete, uncertain, or unsatisfactory resolution of radiolucency according to the criteria defined by Molven et al. (18):

- Successful: Absence of clinical signs/symptoms and complete/incomplete radiographic healing,
- Doubtful: Absence of clinical signs/symptoms and uncertain radiographic healing,
- Failed: Presence of clinical signs/symptoms or unsatisfactory radiographic healing.

Apicomarginal defects were categorized into three classes (Fig. 1) by visualization after flap reflection:

- Class I: Complete denudation of facial root surface,
- Class II: Complete apicomarginal defect with thin buccal bone plate,
- Class III: Incomplete denudation of facial root surface with (a) marginal bony bridge of ≤2 mm width, or (b) para-marginal bony bridge of ≤2 mm width.

Periodontal probing was evaluated preoperatively and at the follow-ups using a periodontal probe (Colorvue Tip, Hu-Friedy, Leimen, Germany). Pocket depths and levels of gingival margin were assessed to the nearest 0.5 mm at four aspects: mesiobuccal, midbuccal, distobuccal, and oral (midpalatal/midlingual). The probing force amounted to approximately 0.2–0.3 N.
**RESULTS**

Details of patients’ sex and age, treated teeth, defect types, as well as clinical and radiographic healing outcomes are presented in Table 1. The study samples included nine females.
and eight males with a mean age of 50.0±18.2 years (median age, 55 years; age range, 9–72 years). Maxillary incisors (six lateral and four central incisors) were the most frequently treated teeth. The majority of apicomarginal defects was located on the facial aspect of the root (n=12, 70.6%) and belonged to defect class I (n=13, 76.5%) (Fig. 2–8). Nine of the evaluated cases had a follow-up period of 1 year. For the other cases, follow-up periods ranged from 14 months to 5 years. Healing was successful in 14 patients (82.4%).

**DISCUSSION**

While there is abundant evidence on the use of EMD in periodontal surgery, this is the first clinical report that describes the use of EMD in apical surgery. Previous clinical studies evaluated other regenerative techniques for the treatment of

**TABLE 1.** Details of the treated cases (n=16)

| Case # | Gender | Age  | Tooth/root | Defect type/site | REF          | Follow-up | Radio-graphic healing | Clinical findings | Outcome   |
|--------|--------|------|------------|-----------------|--------------|-----------|----------------------|------------------|-----------|
| 1      | Male   | 57   | 22         | I/facial        | BC RRM       | 1 y       | Complete             | -                | Success   |
| 2      | Male   | 38   | 22         | IIIb/facial     | BC RRM       | 1 y       | Incomplete           | -                | Success   |
| 3      | Female | 67   | 21         | I/facial-distal | BC RRM       | 1 y       | Uncertain            | Gingival recession | Doubtful  |
| 4      | Female | 63   | 26 mb      | I/distal        | BC RRM       | 1 y       | Complete             | -                | Success   |
| 5      | Male   | 61   | 26 mb      | I/facial        | MTA          | 1 y       | Complete             | -                | Success   |
| 6      | Female | 49   | 12         | I/facial        | BC RRM       | 1 y       | Incomplete           | -                | Success   |
| 7      | Female | 67   | 12         | I/facial        | MTA          | 1 y       | Complete             | -                | Success   |
| 8      | Female | 72   | 13         | I/facial        | MTA          | 2 y       | Complete             | -                | Success   |
| 9      | Male   | 51   | 21         | IIIa/facial     | MTA          | 1 y       | Complete             | -                | Success   |
| 10     | Female | 22   | 22         | I/facial        | MTA          | 1 y 2 m   | Complete             | -                | Success   |
| 11     | Male   | 24   | 16 mb      | I/facial        | MTA          | 3 y       | Uncertain            | Soft tissue recession and fenestration | Failure   |

mb: Mesiobuccal; BC RRM: Bioceramic root repair material; MTA: Mineral trioxide aggregate; REF: Root-end filling

Figure 6. Postoperative periapical radiograph

Figure 7. Clinical situation one year after surgery. Gingival recession amounted to 1.5 mm on the facial root aspect but pocket probing depth were ≤2 mm
The management of apicomarginal defects should consider the defect configuration as well as the characteristics of the denuded root surface. With regards to the defect configuration, the apicomarginal communication is often limited to the facial root aspect. However, it may extend to the proximal (mesial and/or distal) root surfaces. The latter configuration is problematic, particularly in multiroot teeth, given that the apicomarginal defect may include the bifurcation area. With respect to the surface characteristics of the exposed root, absence of bone does not necessarily mean complete absence of periodontal tissue on the root surface. If preoperative probing is within normal range, connective tissue attachment may still be present. Following flap elevation, such periodontal tissue remnants on an apparently denuded root surface can be visualized by intraoperative staining (methylene blue). In such a situation, the root surface should not be curetted in order to preserve periodontal tissue remnants.

Most of cases in this report were maxillary incisors (n=10) or mesiobuccal roots of maxillary molars (n=5). The facial bone over these roots is usually very thin (26, 27), and therefore, bone dehiscences may facilitate the development of an apicomarginal lesion on the facial root aspect. In fact, 12 out of 16 apicomarginal defects were located on the facial aspect.

While the traditional GTR technique implies the application of a barrier membrane to exclude an undesired propagation of soft tissue into the defect, the use of growth factors for healing of bone defects has rather a biologic than a mechanical rationale. So far, only one experimental study on dogs has evaluated the effects of EMD in apical surgery (28). The authors reported that the healing of the former periapical defect was better when EMD was applied, and new cementum was dom-

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**TABLE 2. Clinical studies on regenerative techniques in apical surgery for treatment of combined apicomarginal lesions**

| Author(s) year        | Study type       | Regenerative technique | N technique | N initial | Follow-up | Success rate | Statistics     |
|-----------------------|------------------|------------------------|-------------|-----------|-----------|--------------|----------------|
| Dietrich et al. 2003  | Prospective cohort study | ABBM+collagen membrane | 25          | 23        | 1 year    | 83%          | NA             |
| Marin-Botero et al. 2006 | Randomized clinical trial | Periosteal graft Polyglycolic membrane | 15          | 15        | 1 year    | 87%          | No significant difference |
| Kim et al. 2008       | Retrospective cohort study | Calciumsulfate+ collagen membrane | NA          | 19        | 1–5 years | 74%          | NA             |
| Goyal et al. 2011     | Randomized clinical trial | Collagen membrane PRP PRP+collagen sponge | 10          | 10        | 1 year    | 80%          | No significant difference |
| Dhiman et al. 2015    | Randomized controlled trial | PRF | 10          | 9         | 1 year    | 89%          | No significant difference |
| von Arx & Bosshardt (present study) | Retrospective cohort study | Control | 15          | 15        | 1–5 years | 82.4%        | NA             |

ABBM: Anorganic bovine bone mineral; EMD: Enamel matrix derivative; NA: Not applicable; PRF: Platelet-rich fibrin; PRP: Platelet-rich plasma
inantly achieved in the EMD group compared to the control group. They also detected new collagen fibers bridging the area from new cementum to new alveolar bone only in the EMD group. Currently, no data are available on the combined use of EMD and barrier membranes for the treatment of apico-marginal lesions in apical surgery.

The effects of EMD on tissue regeneration at the cellular and molecular levels have been extensively analyzed experimentally and clinically. Characteristic properties of EMD have been summarized by Bosshardt (29) as follows:

- It acts as a cytostatic rather than cytotoxic agent on epithelial cells.
- It stimulates the proliferation of gingival and periodontal ligament (PDL) fibroblasts.
- It increases PDL cell attachment.
- It stimulates total protein synthesis by human fibroblasts.
- It positively influences wound healing and angiogenesis.
- It has antibacterial properties (particularly its carrier propylene glycol alginate).

These multifaceted effects of EMD may explain its successful application for periodontal tissue regeneration. If root-end filling blocks bacterial leakage from the root-canal system, and no lateral canals are present, one may expect healing of apico-marginal defects providing that epithelial downgrowth along the denuded root surface can be prevented. In this respect, EMD may be superior to other regenerative techniques since it has a cytostatic effect on epithelial cells (29).

Considering the data from previous clinical studies on the treatment of apicomarginal defects in conjunction with apical surgery (Table 2), each study has analyzed a different treatment approach, but interestingly, reported similar success rates. This observation may point to the fact that the sealing of the root end is the decisive factor irrespective of the applied regenerative technique. Since only one study had a control group, no definitive conclusions can be made at this stage. Due to the retrospective nature of the present analysis and limited sample size, the results must be interpreted with caution. More studies are warranted to examine this clinically relevant issue in apical surgery.

CONCLUSION

The application of EMD resulted in a similar outcome compared to previously published clinical studies related to the use of regenerative techniques for the treatment of apico-marginal defects in conjunction with apical surgery.

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