

The Use of Emdogain in Endodontic Procedures

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ABSTRACT

The interrelationship between pulpal and periodontal disease occur by way of intimate anatomic and vascular connections between pulp and periodontium. Pulpal and periodontal problems are responsible for more than 50% of tooth mortality. A clinician must be able to treat both the pulpal component and also maintain the health of the supporting structures. Emdogain has a significant roles in regeneration by the stimulation of the periodontal ligament (PDL), cementum, bone and vascular components enamel matrix derivative (EMD) proteins are secreted by the Hertwig's epithelial root sheath (HERS) during the tooth development which play a key role in the development of tooth-supporting tissues. The aim of this review is innumerate various uses of emdogain in various endodontic procedures.

Keywords: Emdogain, Endo-perio lesion, Reimplantation, Resorption, Direct pulp capping.

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INTRODUCTION

The endodontic-periodontal lesion has great influence on periradicular tissues and can cause localized inflammatory bone resorption. Sanders JJ et al suggested that endodontically treated teeth may not respond as well as untreated teeth to periodontal procedures.¹ Bergenkoltz et al suggested that the presence of an intact cementum layer is important for the protection of pulp from toxic element produced by plaque microbiota, so periodontal disease and periodontal treatments should be regarded as potential cause of pulpitis and pulpal necrosis.²

Enamel matrix derivative (EMD) proteins are secreted by the Hertwig's epithelial root sheath (HERS)

during tooth development and may be critical in the formation of cementum. Emdogain® (Straumann) appears to play a very important roles in regeneration by the stimulation of the periodontal ligament (PDL), cementum, bone and vascular component. Not only endo- perio lesions but Emdogain is also helpful in procedures, like reimplantation of tooth, tooth transplantation and osseous formation in infrabony defects.

Emdogain

Composition of Emdogain

Slavkin (1989) suggested that enamel matrix proteins (EMPs) are expressed along the forming root and have pivotal role in the differentiation of progenitor cells into cementoblasts.³

According to Bosshardt (2008), commercial Emdogain consist of enamel matrix derivate, water and a carrier, i.e. propylene glycol alginate.⁴ The exact composition of enamel matrix derivative is not completely clear but it contains, at least in part, the same proteins as those secreted by Hertwig's epithelial cells. In addition, EMD contains non-amelogenin proteins including enamelin, tufelin and ameloblastin (Zeichner-David 2001).⁵ It is generally assumed that EMD also contains other biologically active factors beside enamel proteins detected TGF- β 1- or TGF- β -(transforming growth factor), like substances in EMD, and suggested that they are the main functional components of the product. In addition, EMD has been documented to contain a BMP-like growth factor (bone morphogenic protein), which belongs to the TGF- β family, and also BSP-like molecules (bone sialoprotein). EMD is widely used for periodontal regeneration of a teeth affected by periodontitis.⁶

Effects of Emdogain on Mesenchymal Cells

Emdogain and Bone-derived Cells

Alveolar bone cells, e.g. osteoblasts, osteoclasts and their precursors, are crucial in periodontal regeneration. In osteoblastogenesis, EMD has been shown to promote osteogenic differentiation of pluripotential mesenchymal cell lines into the osteoblast and/or chondroblast lineage and to stimulate transcription factors related to osteogenesis and chondrogenesis.⁷ Keila et al (2004) states that

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EMD enhances the proliferation and osteogenic potential of bone marrow stromal cells (BMSCs) which has been observed to increase the ability of BMSCs to differentiate into cementoblasts.

Emdogain and Fibroblasts

Gestrelus et al stated that EMD enhances the proliferation, migration and *in vitro* wound healing of periodontal ligament fibroblasts and gingival fibroblasts.⁸ EMD induces matrix and total protein synthesis.

Effects of Emdogain on Epithelial Cells

During periodontal development, molecules from Hertwig's epithelial root sheath can induce differentiation of mesenchymal precursors to form periodontal tissues. It is assumed that EMD can mimic this process.^{3,8} The proliferation of epithelial cell rests of Malassez (ERM) is enhanced by EMD.

Clinical Applications of Emdogain®

Pulp Therapy

It is an important regulator of enamel mineralization and plays an important role during periodontal tissue formation. EMD contains BMP like molecules and BMP expressing cells. BMP like molecules in EMD promote odontoblast differentiation and reparative dentin formation. EMD suppresses the inflammatory cytokine production by immunocytes and contains TGF- β like molecules which creates favorable environment for promoting wound healing in the injured pulp tissues.⁹

Nakamura Y et al concluded that amount of hard tissue formed in EMD treated teeth was more than twice that of the calcium hydroxide treated control teeth.¹⁰ Al-Hezaimi K stated MTA produced a better quality reparative hard tissue response with the adjunctive use of EMD compared with calcium hydroxide.¹¹

Oslon et al experimentally exposed human pulp of nine pairs of premolars and registered postoperative symptoms. He stated that postoperative symptoms were less frequent in the EMD gel-treated than in the calcium hydroxide treated teeth. In the EMD gel-treated teeth, new tissue partly filled the gel initially which was later occupied by hard tissue formed alongside the exposed dentine surfaces. EMD was detected in the areas where new hard tissue had been formed. Thus, he concluded that a considerable amounts of hard tissue were formed in the pulp tissue after the capping with EMD gel.¹² EMD is released from the PGA-gel and precipitates when the acidity is neutralized and the temperature is increased, e.g. by tissue fluids.⁸

Ahmed A Mohamed et al conducted a study in which he compared the clinical, radiographical and histological effect of enamel matrix derivative (Emdogain®) versus formocresol on pulpotomized human primary teeth. A clinical follow-up of formocresol and emdogain treated teeth was done at 2,4 and 6 months. Emdogain® showed an overall clinical success rate of 100% at 2 and 4 months whereas a success rate of 86.7% at 4 months was observed in formocresol pulpotomized teeth.¹³

An immunohistochemical study by Nakamura et al (2004),¹⁴ demonstrated that enamel matrix proteins were present as an insoluble protein matrix in detectable amounts at the application site for about 4 weeks. These findings demonstrate that enamel matrix molecules have the capacity to induce rapid pulpal wound healing in pulpotomized teeth, and suggest that presence of enamel matrix nanospheres at the application site stimulates growth and repair of dentin.

The formation of dentine islands and dentine bridge below amputation site and along dentine walls suggests that EMD treatment not only stimulates pre-existing odontoblasts, but also recruits new odontoblasts of unknown origin from the central part of the pulp through mimicking biological mediators normally active during early dentinogenesis. The PDGF-BB secreted by macrophages at the wound site is also reported to stimulate reparative dentinogenesis after surgical pulp exposure and direct pulp capping in rat incisor model.¹⁵

However, it has recently been reported that EMD induces an intracellular cyclic-AMP signal in mesenchymal cells. This intracellular signal is followed by secretion of autocrine growth factors and other transcription factors that subsequently increase proliferation and maturation of extracellular matrix secreting cells.¹⁶

Treatment of Endo-perio Lesion

The endodontic-periodontal lesion has great influence on periradicular tissues and can cause localized inflammatory bone resorption. A combined periodontal and endodontic lesion is very difficult to treat. Keng-ting Chu et al reports a case with combined endo-perio lesion and was treated by periodontal surgery using the connective tissue graft, Emdogain® and Freeze-dried bone, after endodontic treatment. He concluded that a connective tissue graft, combined with a bone graft and Emdogain®, can be used as a barrier to treat a combined periodontal and endodontic lesion of the thin-gingival type. Emdogain® was approved by the FDA for the topical application to diseased root surfaces to treat intrabony and furcation type of defects.¹⁷



Use of Emdogain in Avulsion and Reimplantation of Tooth

Emdogain[®] may play a role in reducing external root resorption following avulsion and subsequent reimplantation. The primary causes of extraction was ankylosis in a growing child and severe external root resorption at any age and are discernible by six months and definitive by 1 year. Kenny et al reported a case of 14-year-old boy who presented with an avulsed maxillary right lateral incisor that was stored dry for 1 hour and then in Hank's balanced salt solution for 30 minutes. Endodontic treatment was performed extraorally and then periodontal surface was prepared. Emdogain was mixed according to the manufacturer's directions and applied to the root and clot-free socket according to protocol, and the incisor was replanted. This incisor has been replanted for over 3 months and there are no early signs of rejection, root resorption or ankylosis.

In vitro studies have demonstrated that it influences the migration, attachment, proliferative capacity and bio-synthetic activity of PL cells.⁸ Emdogain has been shown to enhance PL cell proliferation and protein production in addition to promoting mineral nodule formation by PL cells. Emdogain may act as a matrix for cells responsible for regenerating PL at a wound site.¹⁸

Schmidlin PR reported with chronic periapical periodontitis on tooth 45. The root canal was treated and a wide apical perforation was closed with MTA[®] as an apical plug. Nine months later, the tooth presented with increased mobility, bleeding on probing and probing pocket depths of 9 mm. Despite good periapical healing radiographically, the tooth showed signs of localized marginal bone loss that was diagnosed as being due to a cemental fracture. The tooth was splinted, a mucoperiosteal flap was raised and the fragment of cementum was removed. The defect was treated in a regenerative approach, using EMD. Six months after therapy, the probing pocket depths decreased to values of 3 mm and a defect fill was radiographically visible. The 10-year follow-up showed a stable situation.²⁰

De Oliveira MT et al performs a histometric assessment of root surface resorption in reimplanted teeth with use of Emdogain in rats. He concluded that if Emdogain is used as root canal filling, has properties capable of showing a lower percentage of resorption in reimplanted teeth.²¹

SUMMARY

Emdogain promotes the regrowth lost hard and soft tissues. Studies have shown that it has a significant roles in regeneration by the stimulation of the periodontal ligament (PDL), cementum, bone and vascular components and application of it can give more appreciable results.

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