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Original Article

Enamel Matrix Derivative (Emdogain®) for Wound Healing and Bone Regeneration: A Short-Review

Marwa Tamzini[1], Rawan Albeshti[2*] and Ahmed Abdesalam[1]

[1]*Department of Oral and Maxillofacial Surgery, faculty of Dentistry, University of Zawia, Zawia, Libya*
[2]*Department of Prosthodontics and Dental Materials, faculty of Dentistry, University of Zawia, Zawia, Libya*
**Corresponding Email: r.albeshti@zu.edu.ly*

ABSTRACT

Emdogain® is a unique gel containing an enamel matrix derivative of protein origin. This mixture of natural proteins can induce biological processes; that usually take place during development/regeneration of periodontium by stimulating certain cells involved in the healing process of soft/hard tissues. This agent is intended to improve the quality of patient's life by reducing pain, swelling and systemic inflammation after completing treatment procedures. Therefore, the aim of this short-review was to understand the rationale behind the use of Emdogain® as a smart biomaterial for periodontal and peri-implant regenerations; and further to provide a clinical perspective for Oral Surgeons and Periodontists in Libya.

Keywords: Enamel Matrix Derivative (Emdogain®); Implantology; Periodontology; Wound Healing; Regeneration.

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BACKGROUND

Emdogain® is the commercial name for a synthetic gel containing an enamel matrix derivative (EMD) [1]. The EMD is an extracted protein from porcine enamel matrix of developing premolars and molars [2, 3]. The major component of Emdogain® is enamel matrix proteins (amelogenins); they are a family of hydrophobic proteins that account for more than 90% of the organic constituents of the enamel matrix [4]. The other main components of the enamel matrix proteins are non-amelogenins consisting of; ameloblastin, enamelin, and amelotin [2-4].

Well known that the EMD influences a number of different cells and healing procedures, which certainly helps the wound healing and wound closure in the oral cavity [5]. The EMD is intended to be used for a topical application in conjunction with periodontal/peri-implant surgery in order to improve healing, reduce pain and swelling

and also to minimise the risk of infections and wound complications [6]. Moreover, the EMD can be used to support early soft tissue wound healing in oral surgical procedures [7]. Particularly, it can be used as a part of flap surgeries in general comprising dental implantation, peri-implant procedures and for soft tissue grafting and gingivectomy [7-9]. The application of EMD is quite easy, even if the defect is difficult to access and does not require any adaptation during the surgical procedure [10]; brief information about Emdogain® is listed in Table 1.

Table 1: Brief information about Emdogain®

Attributes	Description
Origin	Porcine Enamel
Composition	Enamel Matrix Derivative; Propylene Glycol Alginate; Water
Application	Wound Healing & Bone Regeneration
Availability	Ready to Use Gel

The mechanism of EMD has not been fully understood. However, it is proven that when amelogenin is applied on the target surface, the regeneration process will be initiated via amelogenin interactions with the surrounding cells [11]. The EMD stimulates various cell types and cellular processes that are crucial for the healing of oral tissues [12]. Consequently, the stimulated cells will migrate, proliferate and then produce extracellular matrix and growth factors; like collagen, transforming growth factor or/and vascular endothelial growth factor; all are essential for wound healing and regeneration procedures [13, 14].

On the other hand, the protein matrix in EMD mimics the natural environment of the developing tissue which evidently stimulates cell differentiation and cell maturation as well as tissue regeneration [15]. Accordingly, the EMD stimulates osteoprotegerin; leading to trigger the osteoblasts activity and indirectly inhibit the osteoclastogenesis process [15, 16].

Commercially, EMD is supplied in pre-filled, ready-to-use sterile syringes, as seen in Figure 1. It is manufactured in three different sizes by Straumann®. Each pre-filled syringe is for single use/one patient [17]; it is available as follows:

- 0.15 ml for procedures with single implants or isolated gingival recessions.
- 0.3 ml for procedures with single to multiple (2 to 3) implants, peri-implant

procedures, soft tissue grafting procedures and even can be used in combination with graft materials or membranes.

- 0.7 ml for large wound areas and implant procedures with several implants.

Therefore, the goal of the current short-review was to understand the rationale behind the use of Emdogain® for wound healing and bone regeneration; and further to provide a clinical perspective for Oral Surgeons and Periodontists.

Figure 1: Ready-to-use syringe of Emdogain® [17]

Emdogain® in Relation to Implantology

Obviously, the first days after implant placement are always associated with increasing in the risk of wound healing complications as post-surgical pain, redness, inflammation or/and swelling [18]. However, the complication-free healing period helps improving the patient acceptance for the surgical treatments [18, 19]. Thus, the use of Emdogain® is extremely recommended in dental implant procedures and in other situations, where the stimulation of healing is indicated [19].

It should be highlighted that, EMD stimulates the early wound healing process and supports the success of the implantation procedure by; stimulating/accelerating soft tissue formation/maturation, stimulating keratinised gingiva formation, protecting against oral pathogens, reducing early post-surgical inflammation (peri-implant mucositis & peri-implantitis) and reducing the risk for post-surgical pain [20-23]; all will aid in:

(1) Reducing the risk of wound complications;
(2) Improving the aesthetic result and;
(3) Improving patient comfort simultaneous.

Villa, O., *et al.* 2015 stated that the EMD promotes the re-epithelialisation and neovascularisation process in full-thickness surgical wounds on the oral mucosa. They reported that the amount of re-epithelialisation was 70% higher at day one and 25% higher at day three after the surgical procedure [24]. A randomised controlled trial for peri-implantitis treatment proved that the

adjunctive use of EMD has a significant influence on improving the implant survival in the long-term [25]. Furthermore, previous studies showed that the application of EMD can enhance the proliferation and osteogenic differentiation of human periodontal ligament stem cells on titanium implant surface [26, 27].

Emdogain® in Relation to Periodontology

It is well known that periodontitis is a multifactorial inflammatory disease of the dental attachment apparatus [28]. If the condition is untreated, this may cause breakdown of the periodontium (periodontal ligament, alveolar bone & cementum) and eventually leads to tooth loss [29]. One of the treatment lines for loss of periodontal support is the periodontium regeneration [28, 29]. Consequently, the modern approach that accepted by periodontists is the application of Emdogain®; especially during flap surgeries to facilitate the process of wound healing [30].

Soft tissue wound healing is a dynamic process composed of a series of overlapping cellular and molecular actions; including hemostasis and blood clot formation, inflammation, fibroplasia, re-epithelialisation, granulation tissue formation, and remodelling of the connective tissue [30]. Many studies emphasised that, the EMD has a mitogenic effect on gingival fibroblasts and stimulates production of extracellular matrix [30-33]. Moreover, *in vitro* and *in vivo* experiments verified that the EMD plays a remarkable role in wound healing favouring soft tissue regeneration and angiogenic activity [34, 35]. All of these effects could clearly explain the ability of EMD for promoting the periodontal regeneration and soft tissue wound healing; in association with improving the clinical attachment level and reducing probing depth [35].

On the basis of many findings, it has demonstrated that nearly all patients are free from post-surgical wound healing complications after EMD application compared to patients who treated using guided tissue regeneration (GTR) [36, 37]. This helps the fast healing process after the periodontal managements; via:

(1) Reducing the risk of wound healing complications as a part of regenerative procedures compared to membrane technologies; using GTR.

(2) Reducing patient discomfort and minimising pain, inflammation,

redness and swelling during the recovery period.

(3) Improving the aesthetic outcome and increasing the soft tissue volume by formation of keratinised gingiva.

CONCLUSION

In this era, the complication-free healing process is increasingly demanded by patients in dental clinics. The EMD (Emdogain®) is the best choice to accelerate healing and minimise discomfort for patients by providing less swelling, less pain and faster recovery after the surgical treatments were done. The EMD initiates and promotes the natural healing process of soft/hard tissues in the oral cavity which leads to patient satisfactions.

Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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