The use of enamel matrix derivative alone versus in combination with bone grafts to treat patients with periodontal intrabony defects

A meta-analysis

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ABSTRACT

Background. The authors performed a meta-analysis to compare the clinical outcomes of enamel matrix derivative (EMD) used in combination with various bone grafts with EMD alone in patients with intrabony defects.

Types of Studies Reviewed. The authors retrieved relevant studies through Sept. 30, 2011, from MEDLINE, PubMed, Embase and Cochrane Central Register of Controlled Trials. The main clinical outcomes were probing pocket depth (PPD) reduction, clinical attachment level (CAL) gain, gingival recession (REC) increase and defect fill gain. The authors performed two separate meta-analyses, according to the length of follow-up. They also conducted subgroup analyses regarding the study designs and surgical procedures used.

Results. The authors included 11 studies in their meta-analysis. At six to eight months' follow-up, pooled estimates showed that there was no significant difference regarding PPD reduction (P = .62) and CAL gain (P = .23) among the treatment groups, but there was a significant difference regarding defect fill gain and REC increase. At 12 months' follow-up, pooled estimates revealed no significant differences regarding PPD reduction (P = .29), CAL gain (P = .15) and REC increase (P = .30) between the groups, but the authors still detected a significant difference for defect fill gain.

Clinical Implications. In trials with a short-term follow-up, the combination therapies yielded better clinical outcomes regarding defect fill gain and REC increase compared with EMD alone, whereas most clinical outcomes were not significantly different between the two groups in the long run. The additional benefits from using combination therapies to promote periodontal tissue regeneration need to be confirmed.

Key Words. Enamel matrix derivative; bone grafts; intrabony defects; meta-analysis; randomized controlled trials.
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The goal of periodontal therapy is to regenerate lost supporting structures for the tooth that have been destroyed by periodontal disease.[1] Treatment procedures such as various bone grafts,[2] guided tissue regeneration,[3] use of enamel matrix derivative (EMD)[4] or combinations of the aforementioned[5] have been suggested as regenerative periodontal therapies to achieve this goal. Among these procedures, one well-established method to enhance periodontal tissue regeneration is the application of EMD to a previously debrided and conditioned tooth root surface.[6] However, one of the limitations inherent in EMD is related to its gellike consistency after it has been reconstituted, which may affect its regenerative potential.[7]

Overcoming this limitation, using EMD with various bone biomaterials may limit soft-tissue collapse and maintain the space.[8] The results of several controlled clinical trials have shown that using porcine EMD in combination with bovine porous bone mineral may enhance the regenerative outcome with regard to the clinical attachment level (CAL) gain compared with using EMD alone.[9,10] However, controversy

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exists regarding the benefit of using EMD in combination with different types of bone biomaterials. The results of one controlled clinical study whose investigators compared the use of EMD and autogenous bone graft combined with EMD alone showed comparable outcomes of CAL gain but less gingival recession (REC) for the combined treatment.[11]

The rationale behind combining EMD with various bone biomaterials is the potential synergistic effect of both materials. EMD promotes cell attachment and proliferation; expression of growth factors, cytokines and extracellular matrix; and mineralization of human periodontal ligament while causing apoptosis of epithelial cells.[12,13] On the other hand, bone biomaterials may enhance the osteoinductive potential at the site of intrabony defects and act as an effective space-maintaining scaffold for bone regeneration, as well as prevent the collapse of supracrestal soft tissues into the defects.[10] This rationale has been supported partially by a more favorable clinical outcome when using combined therapies to treat deep vertical bony defects.[14]

Although investigators in many randomized trials have compared the clinical outcomes of EMD used with various bone grafts with EMD alone to treat intrabony defects,[9-11,15-22] none of the trials was large enough to confirm the outcomes within subgroups. Therefore, a meta-analysis that allows for the pooling and quantification of results from different studies is needed to overcome this shortcoming. Despite the initial enthusiasm regarding the use combined therapies, there still is disagreement regarding the benefit of using EMD in combination with different types of bone biomaterials. For this reason, we conducted a meta-analysis of randomized controlled trials to compare the clinical outcomes of EMD used in combination with different types of bone grafts with EMD alone in patients with periodontal intrabony defects.

METHODS

Search strategy. We searched databases, including MEDLINE (1950 to Sept. 30, 2011), PubMed (1966 to Sept. 30, 2011), Embase (1984 to Sept. 30, 2011), Cochrane Central Register of Controlled Trials (third quarter 2011), Cochrane Database of Systematic Reviews (2005 to Sept. 30, 2011), Web of Science (1900 to Sept. 30, 2011), ClinicalTrials.gov and Google Scholar. We searched the literature by using combinations of the terms "enamel matrix proteins," "enamel matrix derivative," "Emdogain" and "intra-bony defects." (**Editor's note:** Emdogain is manufactured by Straumann, Basel, Switzerland.) We limited our search to articles that included the terms "humans," "clinical trial," "review" and "meta-analysis." In addition, we hand searched the reference lists of potentially relevant articles found as a result of the database searches to identify any additional studies that we may have missed.

Study selection. Using a predefined protocol, two reviewers (W.L., L.X.) independently selected studies for evaluation if the articles met the following criteria: studies that compared the clinical outcomes of EMD used in combination with various bone grafts with EMD alone in patients with periodontal intrabony defects; studies that were prospective, randomized and controlled; clinical outcomes that were measured at baseline and six months or more after treatment; data that were available and not published in another article.

Data extraction and quality assessment. The two independent reviewers (W.L., L.X.) performed data extraction and quality assessment. For each trial, they collected the following information: name of the first author, year of publication, study design, patient demographics (mean age and sex ratio), total number of intrabony defects in each group, types of intrabony defects, types of bone grafts in the treatment group and length of the follow-up. They assessed the methodological quality of each study by evaluating generation of randomization, patient and examiner masking, description of follow-up and allocation concealment (Table 1). However, the participants knew what regenerative materials they received because the appearance of bone grafts was different from that of EMD, and it was difficult for investigators to make these materials look alike in appearance. Because masking and allocation concealment could not be performed easily, the reviewers considered the trials with adequate randomization and clear descriptions of follow-up to be high quality.

Statistical analysis. We conducted a meta-analysis by using statistical software (Revman

ABBREVIATION KEY. AB: Autogenous bone. **BDX:** Bovine derived xenograft. **BG:** Bioactive glass. **BPBM:** Bovine porous bone mineral. **CAL:** Clinical attachment level. **DFDBA:** Demineralized freeze-dried bone allograft. **EMD:** Enamel matrix derivative. **EMP:** Enamel matrix proteins. **GTR:** Guided tissue regeneration. **PPD:** Probing pocket depth. **RCT:** Randomized controlled trial. **REC:** Gingival recession. **TCP:** Tricalcium phosphate.