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Effects of different growth factors and carriers on bone regeneration: a systematic review

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Objective. The application and subsequent investigations in the use of varied osteogenic growth factors in bone regeneration procedures have grown dramatically over the past several years. Owing to this rapid gain in popularity and documentation, a review was undertaken to evaluate the in vivo effects of growth factors on bone regeneration.
Study Design. Using related key words, electronic databases (Medline, Embase, and Cochrane) were searched for articles published from 1999 to April 2010 to find growth factor application in bone regeneration in human or animal models.
Results. A total of 63 articles were matched with the inclusion criteria of this study. Bone morphogenetic protein 2 (BMP-2) was the most studied growth factor. Carriers for the delivery, experimental sites, and methods of evaluation were different, and therefore articles did not come to a general agreement.
Conclusions. Within the limitations of this review, BMP-2 may be an appropriate growth factor for osteogenesis. (Oral Surg Oral Med Oral Pathol Oral Radiol 2012;xx:xxx)

Reconstruction and healing of critical-sized bone defects continue to challenge the orthopedic and maxillofacial surgeons.[1] The United Nations and the World Health Organization specifically addressed this topic during the past decade, dedicating to it the subject of "Bone and Joint."[2] The current options in bone regenerating procedures represent a broad spectrum. The present choices include placement of autograft, allograft, xenograft, alloplast, or various combinations of each in the defect area. Autogenous bone grafting is still widely held as the gold standard for the treatment of osseous defects.[3] Inherent disadvantages of autogenous bone grafts include graft accessibility, prolonged operation time, donor site morbidity, and overall costs. Therefore, the development of alternative methods for bone regeneration and repair continues.[4,5] Three new strategies are currently undergoing vigorous explorations.[6] First is transduction of genes encoding cytokines with osteogenic capacity into cells at the repair sites (gene therapy).[7] Second is the transplant of culturally expanded stem cells derived from various host tissues, including bone marrow and adipose tissue, into the area of interest (stem cell therapy). This option is building a valuable animal model base of research for analysis, but it is not enthusiastically applied yet and is in its infancy regarding universal acceptance. The third approach is the application of osteoinductive growth factors, such as bone morphogenetic proteins (BMPs),[8,9] vascular endothelial growth factor (VEGF),[10] platelet-derived growth factor (PDGF),[11] and transforming growth factor beta (TGF-β)[12] (protein therapy), which has become a mainstay. Protein therapy and the incorporation of osteoinductive morphogens have demonstrated an appreciable promise in clinical practice.[13] The combination or synergistic effects of ≥2 growth factors has also been evaluated and has shown predictable results.[14,15] The multiplicity of applied factors, carriers, and methods throughout the literature, however, has made it difficult to assess the most predictable therapy. The present paper attempts to compile a com-

Statement of Clinical Relevance

The multiplicity of applied growth factors in bone regeneration, carriers, and methods throughout the literature has made it difficult to assess the most predictable therapy; these proteins may have varied effect in different animal models. Finding an appropriate growth factor with an appropriate carrier may lead to enhance bone regeneration in dento-maxillofacial defects.

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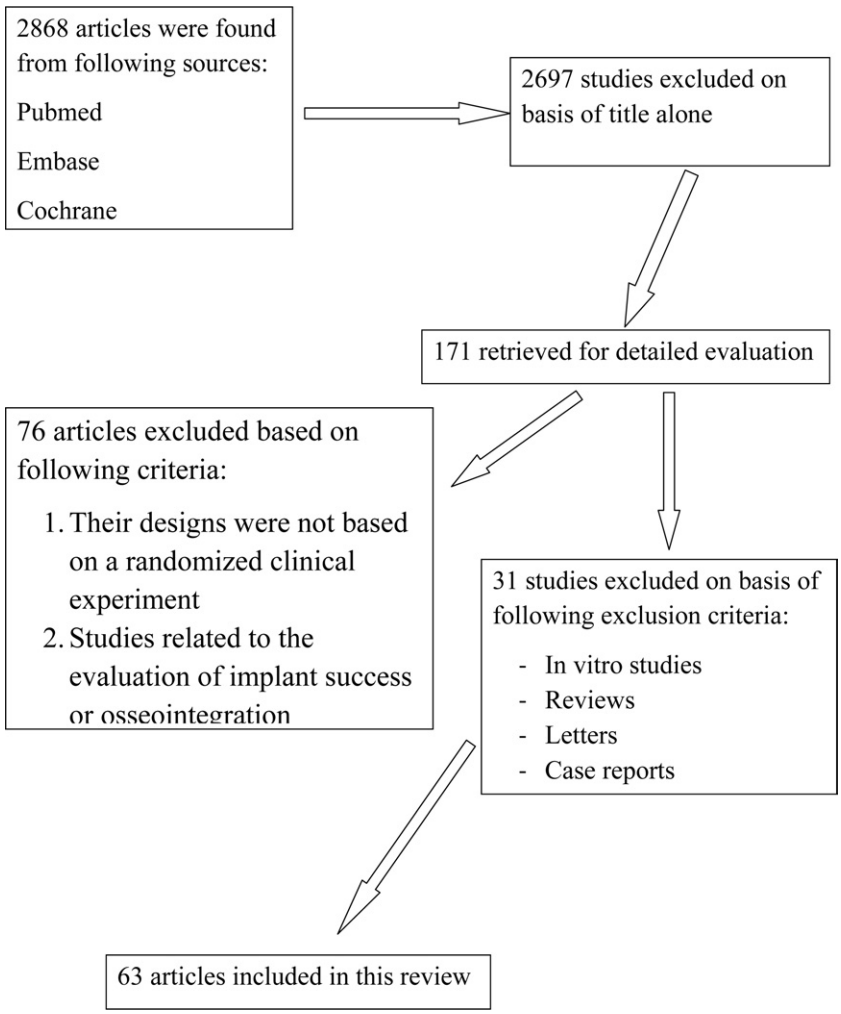

Fig. 1. Information flow diagram.

prehensive review on protein therapy and subsequently provide a better understanding and insight into its role in bone healing and osteogenesis.

MATERIALS AND METHODS

Data sources

Electronic databases (Medline, Embase, and Cochrane) were searched by the authors for articles published from 1999 to April 2010. The search terms included words related to the formation of bones, such as "bone regeneration" OR "bone formation" OR "bone reconstruction" AND key words related to growth factors including "osteogenic factors" OR "growth factors."

Study selection

All titles and abstracts were retrieved and assessed as to their relevance to the desired subject. Papers assessed in this analysis were in vivo studies performed either on human models or on animals. After examining the full texts, papers that reported bone regeneration through the application of a specific growth factor were selected. All in vitro studies, review articles, and case reports were omitted. Those articles that contained references to implant survival and/or osseointegration percentage were also excluded. Distraction osteogenesis or free vascularized tissue transfer were also excluded (Figure 1).

Data extraction

Identification information, such as journal name, publishing date and authors' names were blocked out during the assessment to prevent possible reviewer bias. Data regarding the assessed model, applied growth factor, carrier, evaluated site, duration of the study, and method of assessment and reporting the results of each study were extracted from the articles and organized in a table (Table I). A quick review of Table I reveals taht the studies differ in all of these criteria. To be able compare the studies, articles were