EDITORIAL

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Growth factors in oral and maxillofacial surgery: potentials and challenges

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A growth factor (GF) is a naturally occurring substance capable of stimulating cellular growth, proliferation, and cellular differentiation, one of the key factors for tissue regeneration. Usually, it is a protein or a steroid hormone, with unique functions according to the need of the body. For example, bone morphogenic proteins (BMPs) stimulate bone cell differentiation, whereas fibroblast GFs and vascular endothelial GFs trigger blood vessel differentiation (angiogenesis)[1]. Various GFs have been tested in the field of oral and maxillofacial surgery to regenerate defective tissues and to enhance the therapeutic effect of conventional treatment. Among GFs, BMP-2, and BMP-7 have been predominantly studied for clinical applications and used in combination with collagen/collagen composite scaffolds[2-5]. To date, it has been possible to reconstruct mandibular defect measuring 4 to 8 cm, maxillary sinus augmentation, and cleft alveolus using BMP-2 or BMP-7 combined with collagen sponge as carrier[2-5]. Based on previous controlled studies, in the United States, BMP-2, BMP-7 are now commercially available for clinical use; the use of BMPs is approved by the Food and Drug Administration (FDA) for sinus augmentation and alveolar ridge augmentation associated with extraction sockets[5]. Nowadays, beyond these approved applications, the use of BMPs to treat several refractory diseases--including bisphosphonate-related osteonecrosis of the jaw (BRONJ)--is being attempted in the field of oral and maxillofacial surgery[6]. As another popular GF in our field, platelet-derived growth factor (PDGF) is known as a 'starter' of wound healing process when a tissue needs regeneration. Therefore, it is known to be effective for both soft and hard tissues. So far, periodontal defect and alveolar bone defect have been successfully regenerated using PDGF, which is also commercially available. Transforming growth factor (TGF)-β and insulin-like growth factor (IGF) may be the next candidates of commercially available products following BMPs and PDGF. TGF-β and IGF play an important role in cartilage regeneration in the temporomandibular joint, although those are somehow effective for a variety of cells[2].

Despite such promising clinical successes of GFs for tissue regeneration, controversies still hound their clinical use for tissue regeneration of the oral and maxillofacial area. The biggest debate deals with the oncogenic potential of GFs. Many tumors including malignancies developing in the oral and maxillofacial area have already been proven to over-express the aforementioned GFs such as TGF-β, BMPs, etc., which are ironically beneficial for tissue regeneration when expressed in adequate amount in tissue. For the clinical trial of GF, supraphysiological doses are required for effective tissue regeneration but increase the risk of tumor development. Unfortunately, the optimum concentration and appropriate timing for administering GF are not fully established, which may be crucial for successful clinical outcome without side effects such as tumor development. Biologically, GFs usually react to each other in a very delicate and sophisticated manner, exchanging feedbacks from the responding cells and tissues. Therefore, GFs often have biphasic feature depending on the condition of the tissue. For example, unexpected delayed tissue regeneration may be happening due to the upregulation of GF inhibitor when exogenous GF is too much for the tissue condition. Therefore, in figuring out the proper dose and timing of GFs, more studies are needed to understand the exact mechanisms of the cascades of GFs when the target tissue is regenerated. In addition, a single dose of exogenous protein is well known not to induce a biological response adequately in compromised tissue conditions[1,2]. As discussed by Ripamonti et al.[7], there is much to discover about growth-signaling molecules in tissue, with unexplained differences between animal and human models. Therefore, blind faith in using GFs for target tissue regeneration should be avoided, and more meticulous considerations should consequently be endorsed prior to GF use.

Ongoing research studies on GFs including BMPs and GF delivery strategies such as gene therapy continue to generate promising therapies for the enhancement of therapeutic effect sans possible side effects. Up to now, the progress is quite promising. Therefore, I hope the application of GF will be one of the most powerful and safe modalities for tissue regeneration in the oral and maxillofacial area in the near future.

References

1. Lee K, Silva EA, Mooney DJ. Growth factor delivery-based tissue engineering: general approaches and a review of recent developments. J R Soc Interface 2011;8:153-70.
2. Payne KF, Balasundaram I, Deb S, Di Silvio L, Fan KF. Tissue engineering technology and its possible applications in oral and maxillofacial surgery. Br J Oral Maxillofac Surg 2013. pii: S0266-4356(13)00094-6.
3. Chanchareonsook N, Junker R, Jongpaiboonkit L, Jansen JA. Tissue-engineered mandibular bone reconstruction for continuity defects: a systematic approach to the literature. Tissue Eng Part B Rev 2013. [Epub ahead of print]
4. Cicciù M, Herford AS, Juodžbalys G, Stoffella E. Recombinant human bone morphogenetic protein type 2 application for a possible treatment of bisphosphonates-related osteonecrosis of the jaw. J Craniofac Surg 2012;23:784-8.
5. Spagnoli DB, Marx RE. Dental implants and the use of rhBMP-2. Oral Maxillofac Surg Clin North Am 2011;23:347-61.
6. Janssen NG, Weijs WL, Koole R, Rosenberg AJ, Meijer GJ. Tissue engineering strategies for alveolar cleft reconstruction: a systematic review of the literature. Clin Oral Investig 2013. [Epub ahead of print]
7. Ripamonti U, Tsiridis E, Ferretti C, Kerawala CJ, Mantalaris A, Heliotis M. Perspectives in regenerative medicine and tissue engineering of bone. Br J Oral Maxillofac Surg 2011;49:507-9.