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Editorial

Biologics in Periodontal Practice-An Evidence-Based Perspective

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The ultimate objective of periodontal and implant related therapy is to preserve, improve, reconstruct, and maintain the tissues that provide support to teeth and dental implants to achieve predictable, successful, and long-lasting health, comfort, function, and aesthetics [1]. The immediate past decades have witnessed a beginning of a paradigm shift in implant dentistry adopting concepts from regenerative medicine for bioengineering with expectation of a more predictable, strategic and idealized soft and hard tissue reconstruction. Prosthetic rehabilitation of completely or partially edentulous atrophic maxillae often meets considerable clinical, technical and biologic challenges. Alveolar ridge aberrations as a sequel to bone loss after tooth extraction, periodontal disease, resective surgery, trauma and congenital conditions commonly require augmentation to allow prosthetic rehabilitation. Thus access flap procedures for horizontal and or vertical augmentation [2,3]. as well as modified Caldwell Luc and transalveolar osteotomy protocols to augment the subantral space [4,5] combined with implantable autogenous bone preparations, cadaver sourced (allogenic or xenogenic) or alloplastic biomaterials and devices for guided tissue/bone regeneration procedures have been used as standalone therapies or in combination protocols. According to the Food and Drug Administration (FDA), a "biological product" (biologic) is defined as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound) applicable to the prevention, treatment, or cure of a disease or condition of human beings [6].

In the field of oral tissue regeneration, the term "biologic" can be more narrowly defined as a therapeutic agent with biological activity that is administered to achieve an enhanced regenerative or reparative effect [7]. The use of biologics has progressively become a core component of contemporary periodontal practice. Biologics can be subclassified into stem cells, gene therapy agents, autologous blood-derived products (ABPs), and bioactive factors, such as enamel matrix derivative (EMD), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), bone morphogenetic proteins (BMPs), growth and differentiation factor 5 (GDF-5), and teriparatide (PTH 1-34) [8]. However, some questions remain about their safety, indications, and effectiveness in specific clinical scenario. The American Academy of Periodontology (AAP) best evidence consensus (BEC) has given a state-of-the-art, evidence-based perspective on the therapeutic application of autologous blood-derived products (ABPs), enamel matrix derivative (EMD), recombinant human platelet-derived growth factor BB (rhPDGF-BB), and recombinant human bone morphogenetic protein 2 (rhBMP-2). Evidence about root coverage from frequentist mixed-modeling approach to network meta-analysis showed that biologics (i.e., ABPs, EMD, and rhPDGF-BB) used in conjunction with coronally advanced flaps (CAFs) for root coverage purposes promote statistically and clinically significant improvements respective to baseline clinical parameters, specifically in terms of recession depth (RD) reduction, clinical attachment level gain, and keratinized tissue width (KTW) gain. Notably, KTW gains were more evident in sites treated with ABPs or rhPDGF-BB. The adjunctive use of ABPs and EMD does not provide substantial additional improvement in terms of clinical and patient-reported outcome measures (PROMs) to those achieved by CAFs alone when baseline KTW is >2 mm. Both platelet-rich fibrin (PRF) + CAF and EMD + CAF rendered inferior mean root coverage (MRC%), complete root coverage (CRC%), RD reduction, and KTW gain compared to subepithelial connective tissue graft (SCTG) + CAF, which should still be considered the "gold standard" in root coverage therapy. Regarding the use of rhPDGF-BB + CAF, although available studies have reported equivalent results compared to the gold standard intervention, limited evidence precludes formal comparisons with CAFs or SCTG+ CAF.[9] Evidence in infrabony defects from frequentist mixed-modeling approach to network meta-analysis revealed that the use of biologics (i.e., ABPs, EMD, and rhPDGF-BB) may significantly enhance the clinical and radiographic outcomes after the surgical treatment of infrabony defects. rhPDGF-BB and PRF are associated with superior clinical and radiographic outcomes compared to EMD and platelet-rich plasma (PRP). Combination therapies involving bone grafts, either with a biologic or barrier membrane, are the most effective strategies for the treatment of infrabony defects. However, the use of

membranes with biologics should be avoided when graft containment is feasible since their combined use may prevent some of the benefits associated with the use of biologics (i.e., chemotaxis for pluripotential mesenchymal cell migration from soft tissue niches). Allogeneic and xenogeneic bone grafts are associated with greater clinical benefits regarding clinical outcomes than autogenous and synthetic bone grafts. Xenogeneic bone grafts with rhPDGF-BB or PRF are the best combination therapy to maintain the stability of the gingival margin following regenerative treatment of periodontal infrabony defects [10]. Based on an analysis of the current evidence and expert opinion, American Academy of Periodontology (AAP) panel concluded that the appropriate use of biologics in periodontal practice is generally safe and provides added benefits to conventional treatment approaches. However, therapeutic benefits and risks range based on the specific biologics used as well as patient-related local and systemic factors. Given the limited evidence available for some indications (e.g., gingival augmentation therapy, alveolar ridge preservation/reconstruction, and implant site development), future clinical studies that can expand the knowledge base on the clinical use of biologics in periodontal practice are warranted [11].

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