REVIEW ARTICLE

Biomimetic Materials in Implantology

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ABSTRACT

The current strategies for healing bone defects are numerous and varied. At the core of each bone, healing therapy is a biomimetic mechanism, which works to enhance bone growth. These range from porous scaffolds, bone mineral usage, collagen, and glycosaminoglycan substitutes to transplanted cell populations. Bone defects face a range of difficulty in their healing, given the composite of dense outer compact bone and blood-rich inner trabecular bone. As such, the tissue possesses a number of inherent characteristics, which may be clinically harnessed as promoters of bone healing. These include mechanical characteristics, mineral composition, native collagen content, and cellular fraction of bone. This review charts multiple biomimetic strategies to help heal bony defects in large and small osseous injury sites, with a special focus on cell transplantation.

Keywords: Biomimetic, Bone graft, Implant, Osteoconduction, Osteoinduction, Stem cell.

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INTRODUCTION

Implant dentistry had made a stellar role in the field of dentistry. The goal of modern dentistry is to restore the patient to normal contour, function, comfort, esthetics, speech, and health, whether by removing caries from a tooth or replacing several teeth. Uniqueness of implant dentistry is to achieve this goal, regardless of the atrophy, and disease or injury of the stomatognathic system. The increased need and use of implant-related treatment result from the combined effect of several factors including aging population living longer, tooth loss related to age consequences of fixed prosthesis failure, anatomical consequences of edentulism, poor performance, and consequences of removable prosthesis. Psychological aspects of tooth loss and needs and desires of aging may be boomers, predictable long-term results of implant supported prosthesis; advantages of implant-supported prosthesis and increased public awareness.[1,2]

The social recognition of implants in dentistry has shown a dramatic increase in recent years. The history of dental implants goes back to 3000BC to the period when the ancient Egyptians civilization prospered. The major breakthrough in the history of dental implants came up with the discovery by Branemark in Europe 1950 that the Titanium can be integrated with the bone. The experiment was serendipity while Branemark was working with his thesis studying bone regeneration in the rabbit. He developed a titanium chamber to study wound healing, and this device was implanted into the bone of a rabbit. At the end of the study, the chamber could not be removed because the bone had fused (osseointegrated) to the titanium surface. He conducted several other experiments to confirm that titanium could indeed integrate and becomes part of the bone and it came up with the revolutionary concept of "osseointegration" in dental field.[1]

According to Branemark Osseointegration is defined as "the direct contact between living bone and a functionally loaded implant surface without interpose soft tissue at the light microscope level."[3,4]

Osseointegration is defined as "the apparent direct attachment or connection of osseous tissue to an inert, alloplastic material without intervening connective tissue."[5]

The implant design and surface condition influence the dynamics of osseointegration. Once an implant is inserted in a bone site, a cascade of biological events is initiated, and it is important to emphasize that the surface conditions of implant play a major role. Various scientific studies have been conducted on the surface characteristics and its modification to improve the bone-implant contact and the effect of osseointegration.

To enhance the bioactivity of the implant surface and to provide a higher osteoconductivity to the bulk material various approaches have been focused on coating titanium and its alloys with various biomimetic materials. Coating implants with factors known to induce endothelial cell differentiation and proliferation may promote greater vascularity in higher cortical bone thereby improving conditions for early and long-term bone remodeling.[6]

Biomimetic dental implants may be the next development in the field. The variety of biomimetic coatings

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may prove helpful for application in individual patients. Biomimetics is a term coined by Otto Schmitt in 1950's. It literally means to mimic life.

Biomimetic agents are that "materials that have been designed to elicit specified cellular responses mediated by interactions with scaffold-tethered peptides from extracellular matrix (ECM) proteins; essentially, by the incorporation of cell binding peptides into biomaterials through chemical or physical notification. According to Glossary of implant dentistry, a biomimetic agent is an "agent/material able to replicate or imitate a body structure (anatomy) and/or function (physiology)."[5]

Biomimetic agents applied to the implant surface should possess the following characteristics: [7]

1. Ability to induce differentiation of the appropriate cells for enhancing new bone formation;
2. Easy synthesis or production, avoiding extraction from allograft to eliminate the risk of transmission of infectious contagious diseases;
3. Resorbability in response to osteogenic action, avoiding problems of implant loss due to delamination of the coating;
4. No production of immune reactions in the receptor;
5. A good cost-effectiveness ratio.

BIOMIMETIC AGENTS[7]

- Bioceramics
  - Hydroxyapatite (HA)
  - Calcium phosphate phases.
- Bioactive proteins
  - Bone morphogenic proteins (BMP)
  - Type 1 collagen
  - RGD peptide sequence.
- Ions
  - Fluoride.
- Polymers
  - Chitosan.

Bioceramics

Widely used bioceramic in dentistry is calcium phosphate salts. The addition of HA to the surface of titanium implants can be regarded as the first improvement in implant surface condition that favors quick osseointegration. HA was first added by electrophoresis and then by other methods including plasma spraying or ion beam-assisted deposition. At present, physiologic deposition method is used, these include electrolytic deposition or implant-immersion in simulated body fluids. Stimulated body fluids are rich in calcium, phosphorous, and other elements are prepared under specific conditions to obtain 30 to 50 mm layer of phosphate crystals by gradual precipitation. Bioceramic coated dental implants are a valid therapeutic option. This type of coating shows high biocompatibility and long-term success rates.[8]

BIOACTIVE PROTEINS

BMP

Urist was the first to report (mid-1960) on the group of proteins that, because of their osteoconductive potential, came to be known as the BMP's. These proteins act on undifferentiated, primarily mesenchymal cells, inducing them to differentiate into osteoblasts and, in some situations, chondroblasts. *De novo* bone formation can be achieved anywhere that these proteins are implanted, including extra-osseous sites such as muscle or subcutaneous tissue. This property of BMPs has been shown experimentally to be highly effective in the management of compromised sites intended for future implants. Experimental investigation with recombinant human BMP-2 (rhBMP-2) in animal models has shown that it promotes the initial integration of dental implants and "rescues" implants affected by the experimentally induced peri-implant bone loss. To date, 20 types and subtypes of BMP's have been reported except for BMP 1 that is classified as metalloproteinase; all BMP belong to the transforming growth factor β.[9-12]

GROWTH FACTORS (GF'S)

Cytokines are polypeptide protein factors of low molecular weight (<80 KDa) with pleiotropic action. They behave as mediators of complex interactions among different cell types. The cytokine group includes growth factors, a heterogeneous family of proteins involved in a wide variety of biological processes related to proliferation, differentiation, and chemotactism of cells.[13-16]

Platelet-rich protein (PRP) was proposed due to its high content of GF's. PRP can enhance regeneration mediated by the releasing of GF's such as TGF-β, platelet-derived growth factor, and insulin-like growth factor -1. However, there are various challenges regarding the coating of PRP on implant surface including the short half-life of GF's, which is contradictory to the basic requirements of the biomimetic agents.[11]

Type 1 collagen: Collagen is the major protein of the human body and plays an essential role in tissue repair and regeneration because of its high dimensional stability, and its presence in all hard and soft tissues, it has been considered for implant surface coating. Type 1 collagen, produced by osteoblasts serves as a scaffold for bone formation. Hence, type 1 collagen was considered to be a biomimetic agent for implant surface coating.[12]

RGD peptide, RGD, or arginine- glycine-aspartic acid is expressed in several of these ECM proteins. It

has been known that this sequence has a high affinity for some proteins of the integrin family and is of great importance in the binding cells to the ECM. It has been observed that early adhesion of human osteoblast-like cells to the homogeneous surface of RGD peptide is determined by integrins with an affinity for collagen. This has led to the developmentof RGD peptides as a potential biomimetic agent for implant surface coating. It improves selective osteoblasts binding to the implant thus favoring early osseointegration. Xiang *et al*. found an increased binding of animal osteoblasts to titanium surface pretreated with RGD peptides.[12]

IONS-FLUORIDE

Few researchers used Chemical modification that binds the essential elements (fluoride) to bone to an implant surface to promote osteogenesis. There are implants treated with fluorine as biomimetic agents. The mechanism is based on the formation of fluorapatite, promotion of osteoblast proliferation, and stimulation of alkaline phosphates active.

Fluoride is the halogen family member with the lowest atomic number and weight. IN aqueous solution, it appears in the form of fluoride ion, a highly reactive ion with considerable capacity to form very stable compounds with other elements. This allows fluoride to interact with HA with improved crystallinity and lower dissolution rate in comparison with HA.[17]

POLYMERS CHITOSAN

It is a polymer of the polysaccharide of natural origin that is formed of copolymers of glucosamine and N–acetyl glucosamine. With regard to bone tissue, it has been reported that chitosan can act as an effective scaffold for osteoblasts, permitting apposition of ECM and can enhance differentiation of the preosteoblastic cell into osteoconductive properties with moderate osteoconductive potential. Chitosan can enhance biological bone regeneration processes paving the true potential of chitosan as a biomimetic agent for coating titanium implants.[18]

CONCLUSION

Implants with biomimetic properties, whose surface has been treated with bioceramics or ions are commercially available and shown faster speed of osseointegration. Other promising, bioactive agents such as BMPs, chitosan or hormones, whose true potential for application as the biomimetic agent has yet to be established. Research and development in this field will require attention to 3 main aspects: Selecting the appropriate surface texture, developing efficient carrier vehicles or surface pre-coating agents for initial retention of the biomimetic substances and their subsequent controlled release, and identifying the appropriate biomimetic agents for achieving the desired outcome in a particular clinical scenario (e.g., better vascularization, better osteoinduction, accelerated healing time, or enhanced bone density). Combining the concepts of biomimetics and dental implants may change the world of implant dentistry as we know it today. Understanding implant geometry, chemistry, and bioactivity and the interactions between these factors is the key to future improvements in implant design and to ensuring progress in this exciting and rewarding field of dentistry.

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