APPLICATIONS OF BIOMATERIALS FOR BONE AUGMENTATION OF JAWS: CLINICAL OUTCOMES AND *IN VITRO* STUDIES

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SUMMARY

Partially or totally edentulous jaws frequently undergoes from moderate to severe bone atrophy with problems of prosthetic rehabilitation. The inability to make a prosthetic rehabilitation on implants may led to the use of a partial or total removable denture with difficulties in eating and speech, ulcerations of the oral mucosa and loss of facial vertical dimension. These problems may be solved performing bone augmentation procedures.

Bone grafts and distraction osteogenesis brought implant dentistry from an experimental practice to become a consolidate dental procedure. Bone grafts, in particular, are currently a valuable treatment modality for the prosthetic rehabilitation. Numerous biomaterials have been developed for the rehabilitation of partially or totally edentulous jaws with fixed or removable dentures. The aim of this paper is to describe biomaterials for bone augmentation. Biomaterials are gradually resorbed by the osteoclasts and replaced by new bone formed through osteoblastic activity. Many biomaterials have been studied, but the most common are as follows: Allogro®, Algipore®, Osteobiol®, Peptide-15, Engipore®, Medpore®, Osteoplant®, Calcium sulfate, Perioglass®, Bio-Oss®, Calcium phosphate.

Key words: dental implant, bone augmentation, bone grafts, biomaterials, denture problems.

Introduction

Totally or partially edentulous jaws may induce bone atrophy with problems of prosthetic rehabilitation. The inability to make a prosthetic rehabilitation on implants may led to the use of a partial or total removable denture with difficulties in eating and speech, ulcerations of the oral mucosa for trauma and loss of facial vertical dimension. These problems may be solved by bone augmentation of edentulous jaws. Before the era of implant dentistry, many surgical techniques were adopted to perform bone augmentation of the jaws. The main techniques were sulcoplasties and grafting procedures. Although these techniques were largely used, the long-term therapeutic success was poor, since the increase of bone was temporary and not durable. In addition, a considerable rate of morbidity had to be dealt with.

Since the implant dentistry has changed the way to approach the totally or partially edentulous arches (1-3), pre-prosthetic surgery has varied its objectives. It was not intended to reconstruct more bone sufficient to ensure the prosthesis stability, but to allow the correct positioning of the dental implants (4-6). This treatment is generally accepted for the partially or totally edentulous jaws (PTEJs). Although the use of dental implants for rehabilitations of partially or totally edentulous arches is widely accepted, the selection of a reconstructive surgical procedure to facilitate reliable placement of implants in such a PTEJs are still subjects of discussion in the literature. Bone augmentation in PTEJs is undergo-

ing a major shift from autologous and allogenic bone grafts to synthetic bone graft substitutes (7, 8). Biomaterials for bone augmentation in PTEJs are gradually resorbed by the osteoclasts and replaced by new bone formed through osteoblastic activity. Large bone defects still represent a major problem in oral and maxillofacial surgery. Traditional bone-repair treatments are based on two principles: graft transplant and distraction osteogenesis. Thus far, none of these strategies have proven to be always resolving. As an alternative, a tissue engineering approach has been proposed for PTEJs treatment, where osteogenic cells, hydroxyapatite scaffolds, growth factors and physical forces are involved in the bone defect repair. For bone augmentation, different sources of osteoprogenitor cells have been suggested, and in most cases bone marrow stromal cells have being the first choice. For optimal bone regeneration of PTEJs bone, scaffolds need to fit anatomically into the bone defects and, ideally, augment cell growth and differentiation.
The aim of this paper is to describe biomaterials for bone augmentation of the PTEJs. The biomaterials we describe are as follows: Allogro®, Algipore®, Osteobiol®, Peptide-15, Engipore®, Medpore®, Osteoplant®, Calcium sulfate, PerioGlass®, Bio-Oss®, Calcium phosphate.

Allogro®

Allogro® (*Ceramed*, Lakewood, CO) a demineralized freeze-dried bone allograft is useful as scaffold to fill bone defects and to restore bone loss in PTEJs. Thanks to its osteoinductivity, Allogro® is used to fill bone defects in case of non unions, delayed unions, spinal fusions, augmenting procedures for implant placement and in periodontal regeneration. Dental pulp represents an ideal source of stem cells for PTEJs therapy, because easily accessible (pulpectomy itself is a therapy in some cases) and containing a high number of stem cells compared to equal volumes with the bone marrow. Furthermore Allogro® induces osteoblast phenotype expression and extracellular matrix deposition and mineralization in dental pulp stem cells as demonstrated by the activation of osteoblast related genes SPP1 and FOSL1. The differentiation potential of this biomaterial on stem cells behaviour was also demonstrated by the disappearance of the staminal marker ENG. Allogro® has high potential used as bone scaffold in bone tissue engineering (9-11).

Algipore®

Algipore® is a marine derived highly porous carbonated red alga, chemically converted into hydroxyapatite. Due to its porosity, Algipore adsorbs physiologic fluids so that cytokines and growth factors permeate in full thickness the material, allowing bone forming cells to colonize and differentiate inside. However, how this material alters osteoblast activity to promote bone formation is currently under research. Algipore seems to act reducing bone resorption processes in the early stages of cell differentiation (12-14).

Osteobiol®

OsteoBiol® (Tecnoss Dental, Turin, Italy) is a cortical collagenated porcine bone largely employed as substitute for bone grafting. In animal model porcine bone showed good biocompatibility and osteoconductive properties. OsteoBiol® is actively resorbed by human osteoclasts (15-17). OsteoBiol® has been demonstrated specific properties as a scaffold favouring natural bone regeneration of atrophic jaws.

Peptide-15

Peptide-15 (P-15) (Ceramed, Lakewood, CO) is a bone augmentation material for PTEJs treatment analogue to the cell binding domain of col-

lagen. When used for PTEJs bone augmentation, P-15 competes for cell surface sites for attachment of collagen and, when immobilized on surfaces, it promotes adhesion of cells and facilitates physiological process like cells binding, migration and differentiation of cells. In addiction it may influence the behaviour of dental pulp stem cells *in vitro* by enhancing proliferation, differentiation and deposition of matrix. P-15 has demonstrated high potential for use in bone tissue engineering (18-22).

Engipore®

Engipore® (Finceramica, Faenza, Italy) is a new bioactive material used for PTEJs rehabilitation, with architecture very similar to the natural bone. It is largely employed in bone regeneration in oral and maxillofacial surgery because it's gradually resorbed by the osteoclast and replaced by new bone through osteoblastic activity. The molecular mechanism by which this material influences the behaviour of osteoblast inducing proliferation and bone formation is poorly understood. This biomaterial influences the differentiation of adipose derived stem cells by the activation of osteoblast (23, 24).

Medpor®

Medpor® (Porex Corporation, Fairburn, Georgia, USA) is an alloplastic biomaterial extensively used for PTEJs bone augmentation. Medpor® fixed in PTEJs bone is flexible, stable, and exhibit rapid soft-tissue growth. It has the particularity of being able to be shaped in various ways in order to obtain the ideal form (25-27). Medpor® has the characteristic of not being easily absorbed demonstrates long-term stability, high tensile strength, and doesn't show surrounding soft-tissue reaction. Medpor® scaffolds have high potential for use as bone tissue scaffold in bone tissue engineering (28, 29).

Osteoplant®

Osteoplant® (Bioteck, Arcugnano, Vicenza, Italy), is derived from equine bone. It is formed by flexible cortical and spongy bone tissue, it's a promising material for bone grafting in PTEJs rehabilitation. This biomaterial is completely resorbable, inducing osteoclast activation and promoting the substitution of the scaffold with new bone augmentation in PTEJs (30, 31). Osteoplant® induces osteogenesis on human stem cells, as showed by the activation of bone related genes ALPL, SPP1 and RUNX2, and by the down-regulation of the mesenchyme stem cells marker ENG (32, 33).

Calcium sulphate

The ideal bone graft material for PTEJs bone augmentation, would be biocompatible, completely biodegradable, osteoconductive unexpensive, easy to handle, and able to support the defect area until bone growth is complete. Several bone graft materials are available for PTEJs, but none of them have thus far satisfied all of these requirements. The calcium sulphate is a material used for a long time for bone grafts and it's suitable to facilitate the healing process and regeneration of bone tissue (34-36). Calcium sulphate strongly influences the behaviour of adipose stem cells *in vitro* by enhancing proliferation, differentiation and deposition of matrix by increasing the activity of RUNX2, SP7 and SPPI (37-40).

PerioGlass®

Among the different type of alloplastic bone graft, PerioGlass® (PG) (US Biomaterials Corp., Alachua, FL) is used to fill periodontal defects and rehabilitation of PTEJs, thanks to biocompatibility and osteoconductive properties

(41-43). Moreover, promotes mineralized extracellular matrix deposition, enhancing bone formation. This biomaterial is actively resorbed by human osteoclasts and it could be used as bone tissue scaffold in bone tissue engineering (44, 45).

Bio-Oss®

Bio-Oss® (Geistlich, Wolhusen, Switzerland) is a deproteinized sterilized bovine bone used for bone grafts. This biomaterial promotes osteogenesis, has a very low resorption rate and a very little degradation. For this reason it is largely employed as scaffold for maxillary sinus floor elevation as confirmed in a long-term study and PTEJs bone augmentation (46-49).
Bio-Oss® is very similar to human bone, so it's used in bone grafts before implants insertion. When subjected to histological examination it's possible to observe this biomaterial surrounded by newly formed bone with well organized osteons. This biomaterials favours new angiogenesis and represents a scaffold for bone formation (50-52). Bio-Oss® leads to osteoblast phenotype expression and extracellular matrix deposition and mineralization in bone mesenchimal stem cells as demonstrated by the activation of osteoblast related genes ALPL, SPP1 and RUNX2.

Calcium phosphate

Calcium phosphate (CaP) is highly biocompatible and it is one of the synthetic grafts used for PTEJ with the longest clinical history. This biomaterial has been utilized as bone graft for treatment of alveolar bone loss and maxillary sinus augmentation. CaP has been used as a membrane to facilitate healing and to prevent the loss of other grafting materials. When associated with other bone grafts it seems to have a favourable effect on osteogenesis. CaP has an osteoinductive potential on dental pulp stem cells population and promotes osteogenic activity (53).

Discussion

Biomaterials for bone regeneration have made great progress over the last years. Many materials have appeared on the market, but only a few have been proven effective in maintaining the quantity and bone volume adequate for a correct placement of implants. In addiction, even if the main factor for survival rate of implants in PTEJs is the quality of bone of receiving sites, the presence of oral mucosal diseases may be the main cause of failure of bone augmentation and implant survival (54-64). It is of paramount importance since infection can happen with high frequencies in bone regeneration (65-68) also after cancer resection (69-73). In some pediatric conditions can be useful to have a low bacterial loading especially in syndromic conditions (74-82).
Biomaterials have allowed improving implant dentistry from an experimental to a consolidate dental procedure. It is currently a valuable treatment modality in the prosthetic treatment of PTEJs. Numerous techniques have been developed for the rehabilitation of PTEJs with fixed or removable prosthetics. Today, the options for the restoration of the PTEJs with implants can be categorized as follows: insertion of short and narrow implants and a fixed or removable prosthesis; augmentation of the bone with the use of distraction osteogenesis or grafting procedures in combination with the insertion of dental implants loaded with a fixed or removable prosthesis; placement of an intraosseous dental implants supporting a denture.

Conclusions

Nowadays bone autograft is still considered the best choice for bone augmentation, however tissue engineering may represent a new frontier. Tissue engineering can produce scaffolds that can encourage natural bone regeneration of atrophic jaws, and modulate the activity of osteoinductive factors, osteogenic cells, and their

extracellular environment. Bone regeneration for the correction of defects in PTEJs rehabilitation is an increasingly important issue, in fact bone cell activation by growth factors using synthetic resorbable scaffold is an useful and safe option. Synthetic and biological materials are increasingly used to provide temporary or permanent scaffolds for bone regeneration of PTEJs. Bone augmentation is frequently necessary before placement of dental implants in atrophic jaws. Beside bone autograft, various bone substitutes have been used, with favourable results.

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