Inflammatory reaction post implantation of bone graft materials

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ABSTRACT: In the dentistry field there are some clinical procedures that force the professional to use bone graft materials, namely in the areas of Implantology and Oral Surgery. Bone filler materials can be derived from the person being treated (autogenous bone), obtained from another individual within the same species (allografts), obtained from another species (xenografts) or synthetically derived (alloplastic materials). Each of these alternatives has advantages and drawbacks, depending on multiple factors, for example physico-chemical characteristics. One of the differences noticed is the inflammatory reaction. As the bone graft materials are so antagonistic in some parameters, they tend to produce different patterns in what concerns the inflammatory reaction, both acute and chronic processes. To further improve decision making regarding which bone substitute graft to use to treat bone defects, more standardized research is urgent to explore the full potential of the available alternatives.

KEYWORDS: bone graft materials, inflammatory reaction

Bone grafts are widely used in surgical procedures in Dentistry, particularly in Periodontology (1-5), Implantology (2, 6, 7), Endodontics (3, 5, 8-10) and Oral Surgery (11, 12).

Although autogenous bone continues to be the “gold standard” in bone substitution (13-20), numerous biomaterials have successfully been used as alternatives, like allografts, xenografts and synthetic materials (15-17, 20, 21). All of these have disadvantages: autogenous bone has to be harvested in a surgical procedure (with donor site morbidity), that can curse with some possible major and minor complications (15), increased operative time and blood loss, and often, limited quantity. If we think about harvesting bone in the oral cavity, complications can include altered sensation of the lower anterior teeth, discoloration of the lower incisors from pulpal injury and deposition of secondary dentin, mental nerve paresthesia, meteorotropism of the chin, fracture of the mandible and postoperative pain, in cases of mandibular symphysis procedure. Complications associated with the harvesting procedure in the mandibular ramus include the potential for damage to the inferior alveolar and buccal nerves and trismus after surgery, that oblige to the prescription of postoperative glucocorticoids and non-steroidal anti-inflammatory medication to help reduce dysfunction. Patients seek for alternatives that do not have the drawbacks of the autogenous bone.

Allografts can be mineralized or demineralized. Mineralized allograft is available in several forms, namely fresh, frozen and freeze-dried. Fresh allograft is rarely used because the speed with which the grafting transfers need to be performed leaves little time to test for disease or sterility and because they evoke an intense immune response, compromising the ability to incorporate. Frozen allografts are maintained at temperatures below -60°C to diminish degradation by enzymes, affording decreased immunogenicity and the process of freezing does not seem to adversely affect mechanical properties. Freeze-drying (lyophilization) involves the removal of water from the frozen tissue. These grafts become more brittle and undergo biomechanical alteration with loss of compressive, bending and torsional strength. Demineralized allograft is formed by acid demineralization of allograft bone, that leaves behind a composite of noncollagenous proteins, bone growth factors, and collagen. It is believed that processing chemicals and additives may be potentially toxic if very large doses of DBM are used. Allografts may transmit viruses (e.g. Hepatitis, HIV) and other diseases, biologic and mechanical properties can be lost secondary to its processing, are expensive, are not available in certain countries because of religious concerns and are quickly reabsorbed.

Xenografts consist of bone mineral derived from animals or bonelike minerals derived...
from calcifying corals or algae from which the organic component has been removed to eliminate the risk of immunogenic reactions or transmission of diseases. Xenografts can induce unfavorable immune response and also infectivity (13). Coral and algae derived bonelike minerals have less osteoconductive potential than other bone substitute materials. Coraline HA has a high rate of late complications. When used as a particulate, the granules tend to migrate, and the ones that stay in place become encapsulated by fibrous tissue. The blocks are prone to develop late dehiscences. Xenografts derived from natural bone sources have been extensively investigated, in particular cancellous bovine bone because of its similarity to human bone.

Alloplastic materials bear no risk of disease transmission, because of their completely synthetic nature and have the theoretic possibility of designing material characteristics for specific clinical indications. Chemical composition can be controlled to the molecular level, size and interconnectivity of macropores can be optimized for vascularization, ratios between crystalline and amorphous material can be varied, and the morphology of blocks and granules can be tailored. However not all characteristics of the ideal alloplastic bone substitute have been identified, and that is the aim to the future.

Therefore, it’s urgent to develop a material that matches the properties of bone without the drawbacks of autografts or allografts, being available any time, in any amount and at lower cost (19). A more future-oriented approach is to look for synthetic bone graft substitutes (22), but to date no synthetic material has been able to meet all desirable characteristics (35): to match biological and mechanical properties of human bone (18).

Inflammation is an expected consequence after implantation of any biomaterial in a living host. The process of implantation of biomaterials in subcutaneous or intramuscular sites in a model results in injury to tissues. The sequence of host reactions is: injury, blood-material interactions, provisional matrix formation, acute inflammation, chronic inflammation, granulation tissue, foreign body reaction and fibrosis/fibrous capsule development (Anderson 2001).

Acute inflammation is of relatively short duration, lasting from minutes to days, depending on the extent of injury. The main characteristics of acute inflammation are the exudation of fluid and plasma proteins (edema) and the emigration of leukocytes (predominantly neutrophils). Neutrophils and other motile white cells emigrate or move from the blood vessels to the perivascular tissues and the injury (implant) site.

Chronic inflammation is less uniform histologically than is acute inflammation. In general, chronic inflammation is characterized by the presence of macrophages, monocytes, and lymphocytes, with the proliferation of blood vessels and connective tissue (3, 4, 35, 36). It must be noted that many factors modify the course and histological appearance of chronic inflammation. Persistent inflammatory stimuli lead to chronic inflammation. Although the chemical and physical properties of the biomaterial may lead to chronic inflammation, motion in the implant site by the biomaterial may also produce chronic inflammation. The chronic inflammatory response to biomaterials is confined to the implant site. Inflammation with the presence of mononuclear cells, including lymphocytes and plasma cells, is given the designation chronic inflammation; whereas the foreign body reaction with granulation tissue development is considered the normal wound healing response to implanted biomaterials (i.e. the normal foreign body reaction).

The foreign body reaction composed of macrophages and foreign body giant cells is the end-stage response of the inflammatory and wound healing responses following implantation of a medical device, prosthesis, or biomaterial.

Biomaterial surface properties play an important role in modulating the foreign body reaction in the first two to four weeks following implantation of a medical device, even though the foreign body reaction at the tissue/material interface is present for the in vivo lifetime of the medical device. An understanding of the foreign body reaction is important as the foreign body reaction may impact the biocompatibility (safety) of the medical device, prosthesis, or implanted biomaterial and may significantly

Figure 1. Examples of an alloplastic (Bonelike®) and a xenogenous (Osteobiol®) material. SEM photographs, with magnification of 40x.
impact short- and long-term tissue responses with tissue-engineered constructs containing proteins, cells, and other biological components for use in tissue engineering and regenerative medicine.

In the daily practice of dentistry, these materials are used with many clinical indications, namely alveolar regeneration, treatment of dehiscences and fenestrations, crestal access sinus lift, lateral access sinus lift, periodontal regeneration, horizontal augmentation and vertical augmentation.

Determining which material to use for different clinical indications is based on many factors, including the size and location of the bone tissue defect as well as the structural, biological and biomechanical properties of the graft itself (21). The large number of alternatives available and the relative lack of quality information regarding their indications and effectiveness leave the surgeon desiring to use the products with a daunting task (16). To further improve decision making regarding which bone substitute graft to use to treat bone defects, more standardized research is recommended to explore the full potential of the available alternatives (21).

REFERENCES
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