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Bone grafts in maxillofacial surgery: A brief study of literature

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Abstract
Bone grafting is a surgical procedure of replacing and reconstruction of the lost bone and associated soft tissues with a motive of repair, regeneration and complete replacement of the bone which is missing either due to trauma or pathological reasons. Bone grafts acts as filler or scaffold which allows bone formation and supports wound healing. Also these induce bone regeneration due to rich source of mesenchymal cells, stem cells, progenitor cells and mineral reservoir.

Keywords: bone graft, allograft, autogenous, xenograft, reconstruction

Introduction

From the ancient times the surgeons were tirelessly devoted to restore what disease or trauma has taken away from man. Trauma and diseases that affect hard or soft tissues leave behind an area that is functionally compromised. Reconstruction is one of the basic principles of any surgical specialty. This certainly holds true even for the speciality of Oral and Maxillofacial Surgery. Among the various types of available tissues, bone is the most commonly used in Oral and Maxillofacial Surgical Reconstructive procedures. Bone grafts are helpful in the treatment of congenital bone defects, orthognathic deformities, in pre-prosthetic surgery, intemporomandibular joint deformities & in reconstruction of jaws after oncological surgery. Bone growth and bone healing involves multistep cascade consisting of chemotaxis of mesenchymal cells, proliferation of progenitor cells and formation of bone, cartilage and haematopoietic marrow [1].

Bone grafts can be classified as: autogenous grafts (autologous), homologous grafts (allografts), heterogeneous grafts (xenografts). Autologenous bone grafts are considered the 'gold standard'. It provides rapid, predictable results in reconstructed bone quality and quantity. They are widely used for augmentation before insertion of a dental implant and for raising the sinus floor and augmentation of the alveolar ridge. They do not cause any immunological reaction and have optimal biocompatible remodelling patterns. So, autologous bone is better over artificial bone substitutes in osteoinductive and osteogenic properties [2]. An autologous bone graft is best for small defects but in large defects, the homologous bone grafts and biomaterials are normally necessary. When harvesting an autogenous bone graft, there is considerable morbidity of donor site including deformity, pain, and haematoma.[3] The ideal characteristics which a bone graft should have are that it should be biocompatible, no risk of disease transmission, resistant to infection, dimensionally stable, amenable to skeletal fixation.

History of Bone Grafts

The history of bone graft is replete with controversies due to the radical nature of the procedure in earlier times. Understandably, the act of transferring bone from one person to another invited much public contention on social, ethical and religious grounds. Losses of bone, fractures or burn wounds in victims of the war compelled surgeons of their time to come up with methods to repair these defects (bone grafting and bone transplantation; Lancet, 1918). Indeed, necessity is the mother of invention. The history of bone grafting can be traced to Van Meekreen who in 1682 reported the use of canine calvarial bone to repair a cranial defect in a Russian soldier. Duhamel (1742) was given credit for the earliest scientific approach to osteogenesis. Von Haller (1763) regarded the periosteum with the chief support of blood vessels, as an agent for osteogenesis in the healing of fractures. Ollier (1867) believed that viable bone with attached periosteum was the best form of graft to use. Barth (1893-1898) and Marchand were the first to use the term "creeping substitution" to describe the invasion of old bone by bud-like masses of new bone without previous resorption of old bone. Axhausen (1907 and 1909) made a major contribution to the problem of osteogenesis and bone transplantation and concluded that all transplanted bone died, although most of the periosteum survived to become a source of osteogenesis.

Phemister (1914) described that cellular survival in bone grafts is dependent on diffusion from surrounding tissue [4]. Cancellous bone graft survival was superior to cortical grafts due to increased porosity of the graft, thereby increasing the surface area and facilitating osteoblast survival through diffusion (Gallie and Robertson, 1918). Mowlen (1944) was credited for popularising the use of cancellous bone grafting in a wide variety of clinical scenarios and stated that bone graft was no longer inorganic bridge which is to be completely resorbed and slowly replaced. Instead it is only the scaffold to carry these cells which can rapidly envelop it with new bone

and incorporate it the new repair [5].

Bertelsen (1944) repeated the work and compared the potency of extracts obtained from corticalis, total bone, marrow, periosteum and epiphysis. In his experiments, marrow extract proved most potent. Levander (1945) later extended the specific osteogenic hormone theory to cover many similar cases of tissue induction. *Lacroix* (1945) had also produced an alcoholic extract of cartilage capable of inducing osteogenesis on injection [6]. In 1965, Urist demonstrated that an extract of demineralized bone matrix could cause invading mesenchymal cells from the host to become osteoblasts and make new bone in a heterotopic site [7].

Classification of bone grafts

Table 1: Bone grafts can be classified based on

Based on Nature of Bone:	Source of Donor
a) Cancellous bone grafts b) Cortical bone grafts c) Corticocancellous grafts • Blocks • Chips • Powder • Marrow grafts	a) same individual b) Allogenic bone graft- from another individual of same species c) Isogenic bone graft- from genetically related individual d) Xenografts from different species e) Composite grafts
Extraoral Donor Site	**Intraoral Donor Site**
a) Calvarial graft • Full thickness • Split thickness b) Rib graft c) Iliac crest graft • anterior ilium • posterior ilium d) Trephine grafts e) Tibia	a) Mandible b) Mandibular symphysis c) Retromolar area d) Mandibular ramus e) Coronoid process f) Palate g) Zygomatic bone h) Nasal aperture
Depending on The Vascularity	**Depending on Function**
a) Non vascularised bone graft b) Vascularised bone graft c) Pedicled & microvascular free flaps	a) Bridging graft or inlay graft b) Reconstruction graft c) Contour graft-onlay graft

Pathophysiology of bone grafts

The hallmark of reconstruction of the jaws is the grafting of bone into sites of loss or need. Advances in the understanding of bone physiology, immunologic concepts and technology have made successful reconstruction of the jaws possible. Bone reconstruction on a physiologic level is accomplished by combinations of three processes: osteogenesis, osteoconduction and osteoinduction [8].

Osteogenesis

Osteogenesisis defined as the formation of new bone. Osteogenesis was first discovered by Mowlem. This process occurs when viable osteoblasts and/or osteoblast precursors (stem cells) are transplanted with the bone graft. Osteoblast precursors differentiate into mature osteoblasts under appropriate host conditions. Osteoblast precursors are found in bone, bone marrow, periosteum and other tissues.

Osteoconduction

Osteoconduction refers to a bone graft or implant's ability to provide a structural framework on which host cells reconstitute. This scaffold enables the in growth of vessels, osteoblasts and stem cells so that union occurs with the host skeleton. Both viable and nonviable materials may possess osteoconductive properties. The process of osteoclastic resorption followed by osteoblastic deposition is termed creeping substitution Creeping substitution is referred to as osteoconduction. Osteoconductive properties are found in cancellous autografts and allografts, demineralised bone matrix, hydroxyapatite, collagen and calcium phosphate, ceramics.

Osteoinduction

Osteoinductionis the recruitment of stem cells from the host bed into the graft site, where they differentiate into osteoblasts. Several growth factors which influence this process are bone morphogenic proteins (BMPs), platelet-derived growth factors, insulin-like growth factors, fibroblast growth factors (acidic and basic), epidermal growth factor, TGF-B (B1 and B2) and retinoic acid.

Bone morphogenic proteins

BMPs are part of a large, multi-functional growth factor family with diverse effects on cell activity in both development and regeneration. In 1965, Urist was first to describe osteoinductive capacity of demineralized bone matrix. So far more than 20 BMPs have been discovered.

Mechanism of BMP Signalling

The BMP binds to two types of serine/ threoninekinase receptors: type I and II receptors. Seven type I and five type II receptors are present in mammals. A complex of type I receptor and type II receptor interact with BMP ligand. The ligand/receptor complex results in the activation of

serine/threoninekinase of BMP receptor I (BMPR-I), resulting in the phosphorylation of members of R-Smad family of signal transducers (Smad 1, Smad 5 or Smad 8).Receptor regulated Smad (R-Smad), common mediator Smad(co Smad) and inhibitory Smad (I-Smad) are three types of Smad. The phosphorylated R-Smad binds with C Smad 4 and translocates in the nucleus where R-Smad/C Smad complex interacts with the core binding factor (CBF). The activated CBF activates osteoblast specific element 2 and leads to the transcription of osteocalcin gene [12].

Carrier Materials for Bmp

Biocompatibility, biodegradability, malleability and sufficient compressive strength are the characteristics for carrier materials. They can be classified into four groups: natural polymers, inorganic materials, synthetic polymers and composites. Type I absorbable collagen sponge, type I collagen matrix and combination of rhBMP 7 with carboxymethyl cellulose are the approved carrier materials. Collagen carriers are better due to their biocompatible nature and release of physiological products [13, 14, 15].

Table 2: Biological Actions of BMP

▪ **BMP-1 activates BMPs and may be involved with Langergiedion Syndrome.**
▪ BMP-2 is osteoinductive and plays a role in embryogenesis, differentiation of osteoblasts, adipocytes,chondrocytes, inhibiting bone healing, repair of long bone and in augmentation of maxillary sinus.
▪ BMP-3 is osteoinductive and promotes chondrogenic phenotype.
▪ BMP-4 is osteoinductive, promotes embryogenesis and fracture healing.
▪ BMP-5 is osteoinductive and promotes embryogenesis.
▪ BMP-6 regulates chondrocyte differentiation and neuronal maturation.
▪ BMP-7 is osteoinductive and plays a role in differentiation of osteoblasts, chondroblasts, adipocytes.
▪ BMP-8 is osteoinductive
▪ BMP-9 is osteoinductive, stimulates hepatocyte proliferation, growth and function.
▪ BMP-12 and BMP-13 inhibit terminal differentiation of myoblasts.[14]

Healing of bone grafts

Gabriele Stringa discussed the historical evolution of healing of autogenous bone grafts. Marchand (1901) studied the vessels in transplanted bone; Lawen (1909) described the vessels in a human tibial graft. Nemilow (1914) investigated the part played by the periosteum in the early vascular penetration of the graft; the experiments performed in rabbits to show that in the first six days the transplanted periosteum vascularised, whereas no vessels were found in the bone without periosteum. Bertini (1926) used only autogenous bone to study the behaviour of the vessels near and in the holes made by him in the bone of rabbits. Hancox (1947) observed the direct vascularisation of small transplanted grafts and noted functioning vessels in a graft after five hours from its implantation; Nemilow (quoted by Petrow 1914) found the injected substance in the vessels of periosteum which was transplanted two days previously and Gallie and Robertson (1919) after the time saw new capillaries in the opened Haversian canals. Bertini (1926) and Urist (1953) observed the earliest signs of saw evidence of vascularization of the homogenous graft after thirty-five days and the greatest penetration after sixty to ninety days. Siffert (1955) could not see any vascular invasion after six weeks. Wilson (1951) reported good vascular penetration in twelve weeks. Kiehn *et al*. (1952) working with very small fragments, could not find vessels inside the graft before the eleventh day but found almost complete vascular penetration after two weeks. Kreuz *et al.* (1951) of autogenous cancellous or cortical bone grafts is essentially same during the first two weeks. In the first week, the graft is in a focus of an inflammatory response characterised by infiltration of vascular buds into the transplant bed. The necrotic tissues are removed by the macrophages. In the second week, the inflammatory response subsides with continued fibro vascular proliferation and increasing osteoclastic activity with necrosis of cellular elements. Some peripheral cells remain viable by passive diffusion of nutrients. In the later stages of healing, cancellous and cortical bone grafts can be distinguished by differences in the rate of revascularisation, by creeping substitution and by the completeness of the repair [9].

In cancellous grafts, the numerous vascular spaces surrounding the bone are primed for invasion by new blood vessels. Revascularisation of the cancellous bone graft may occur within hours of the transplantation and is completed within 2 weeks. In cortical bone grafts revascularization requires 1 or 2months or even longer. The cortical architecture delays revascularisation because the new vessels must follow pre-existing Volkman and Haversian canals from the periphery of the graft into its interior.

In cancellous bone graft following revascularisation, primitive mesenchymal cells lining the trabeculae differentiate into osteoblasts and deposit osteoid around the central core of necrotic bone. Initial repair of cancellous bone graft is by bone formation, whereas cortical graft repair is by osteoclastic activity with early resorption preferentially directed to the peripherally located Haversian system. Osteoblasts then appear and deposit osteoid, where resorption of bone has occurred. Ariyan S. (1980) said that the bone defect filled or bridged with bone graft healed through osteogenesis. The endosteal osteoblasts survived as long as 5 days after transplantation due to their ability to absorb nutrients from the surrounding tissues. Entrapped platelets inside the graft DE granulated, releasing potent growth factors.

In cancellous grafts the entrapped areas of necrotic bone are gradually resorbed by osteoclasts and in time the cancellous graft is completely replaced by viable new bone. Whereas, in cortical grafts the initiation of appositional phase takes place before the necrotic bone has been completely removed. The areas of non-vascularised bone become sealed off from further osteoclastic resorption, leaving the cortical graft as an

admixture of necrotic and viable bone. The mechanical strength of cancellous and cortical grafts is affected by healing. Cancellous grafts initially strengthen as repair is initiated by new bone formation and then the mechanical strength normalises as the necrotic bone is removed. Cortical grafts weaken to approximately 60% of normal strength for up to several months after grafting because repair is initiated by osteoclastic resorption, which increases the internal porosity of the graft [9].

Table 3: Factors Affecting Graft Healing

Graft Factors	Recipient Factors
▪ The embryonic origin of the graft. ▪ The histologic bone components (cancellous or Cortical). ▪ The graft viability (vascularised & non-vascularised) ▪ The role of revascularisation (early versus delayed). ▪ The presence or absence of periosteum. ▪ Graft dimensions (length, breadth, height & width).	▪ Age of patient (mature / immature cells). ▪ Implantation site (orthotopic or heterotopic). ▪ The condition of irradiated bed (Irradiated, scarred, soft tissue contracture, infection). ▪ The recipient location (resorptive or depository surface). ▪ The graft position in relation to mechanical stresses (Onlay, inlay, bridging). ▪ Type of fixation (rigid or non-rigid).

Summary and Conclusion

The successful management of a patient entails the restoration of form and function of the affected part. Reconstructive surgery or the ability to make a patient whole again is a basic principle of any surgical speciality. This certainly holds true for the specialty of oral and maxillofacial surgery. In maxillofacial region, the treatment of developmental and surgical defects requires recontouring both soft tissue and hard tissues. The hard tissue in the form of autogenous bone grafts is the gold standard for bony reconstruction in the maxillofacial region as it provides osteoconduction, osteogenicity and osteoinductivity. The ability to recruit fresh, autogenous bone for the repair of skeletal defects is at the centre of reconstructive oral, maxillofacial and craniofacial surgery. Contemporary surgical principles and technical refinements allow for the effective harvesting of bone from a number of different anatomic sites (e.g. - cranial vault, mandible, rib, anterior and posterior ilium, tibia). The proximity of the cranial vault to other surgical sites, availability of relatively large quantities of bone and favourable consistency make cranial bone harvest an extremely viable reconstructive manoeuvre within the surgeon's armamentarium.

Microvascular free bone flaps are modern means of restoring bone-Containing composite defects of the maxillofacial region. The techniques are simple and reliable. The results are reproducible and offer significant advantages over staged mandibular reconstruction. In particular, these techniques decrease costs and provide means of rapid definitive reconstruction. Patients avoid multiple surgical procedures with immediate reconstruction that allows them to return to productive lives in society. Proper selection of an appropriate donor site and appropriate preoperative planning facilitate application of these techniques in an expedient manner. Microvascular free bone flap reconstruction should be considered for all patients with composite bone-Containing defects of the maxillofacial region.

Every donor site has its inherent advantages and complications. Extra-oral site may leave the patient with an additional wound and the intra-oral donor site offer advantage of invisible scar and close by donor site but carries the disadvantage of limited amount of grafting material. Hence it can be concluded that autogenous bone grafts offer osteoinduction and should be the preferred choice for the grafting. The choice of donor site is always surgeon's prerogative.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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