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Bone Graft in Dentistry- review

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Abstract:
Background: *The bone graft serving as a scaffolds for the in-growth of vessels, perivascular tissue and mesenchymal cells forms the host bed exhibits the characteristic of osteoinduction. This scaffold allows gradual replacement of bone graft over time by resorption of old bone trebecule and formation of new bone. Each grafts type has its own healing and incopration mechanism. Replacement of bone is a complex and demanding undertaking. Bone formation occurs when osteoblasts secrete collagen molecules and ground substances. The collagen molecules polymerize to form collagen fibers. Calcium salts precipitate in the ground substance along the collagen fibers to form osteoid. Osteoblast become trapped in the osteoid and then are called osteocyes.*
Mature compact bone is composed of approximately 30% organic matrix and 70% calcium salts. 90% to 95% of the organic matrix is collagen fibers and the remainder is the gelatinuous medium calld ground substance, which is composed of chondroitin sulfate and hyaluronic acid.
Keywords: *bone graft,corticalbone ,cancellous bone, bone regeneration*
Material and methods: *over 103 article where selected for review following a comprehensive search of the literature from pubmed central.*
Results: *The factors have been shown to have a high influence on induction of osteoblast to proliferation and differentiation in vitro and also to stimulate bone formation when administered in vivo . Some of the factors have been implicated not only in the initiation of induction but also in the promotion, maintenance and was termination of bone formation*
Conclusion: *The goal is to configure these materials as competent carriers of the biomolecular pro-osteogenics or as supportive scaffolds for cellular proliferation and bone formation. One technique that is showing more promise is three-dimensional printing technology. Three-dimensional complex shapes or structures can be computer generated, constructed in a three dimensional printer and then used as protein or cellular carriers for custom implantable bone graft substitutes.*

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I. Introduction:

Bone is a natural composite material, which by weight contains about 60% of mineral, 30% of matrix and 10% of water. Bone is also living tissue, with about 15% of its weight being due to its cellular content. The matrix of bone is comprised of Type 1 collagen that is highly aligned, yielding a very anisotropic structure. This component of bone is predominantly responsible for its tesile strength. The mineral component is in the form of calcium phosphate know as hydroxyl appatite (HA).

In the body, bone serves a number of functions, such as functions such a providing the cells. Found in marrow, that differentiate into blood cells and also acting as a calcium reservior. There are 2 types of bone, compact or cortical bone and cancellous or trabecular (also know as spongy bone). Compact bone is very dense, consisting of parallel cylindrical units (osteon) found in the shaft of long bones as well as on the outer surface of smaller bone in the body.

Trabecular bone is less dense and is made up of an array of rods and struts that form an open-cell foam, the pores of which are filled in by marrow. This type of bone is found at the ends of long bones and inside smaller bones.

Bone formation in grafting is characterized by three types of bone growth :

1. Osteogenesis

Is the formation of a new bone by osteoblast derived from the graft material itself.

2. Osteoinduction
Is the ability of material to induce the formation of osteoblast from the surrounding tissue at the graft gost site. Which results bone growth.

3. Ostoconduction
Is the ability of a material to support the growth of bone over a surface**.**

II. Materials And Method

over 103 article where selected for review following a comprehensive search of the literature from pubmed central.

III. Discussion

As recent ago as the 1970's and 80's, before the renaissance of "dental implants", muchof pre-prosthetic oral surgery was aimed at simply building a stable base for a denture in patients who had experienced severe atrophy of their jaws.

Tissue grafting attempts above all was made by Hunter (1728-1793). Much of Hunter's acquaintance might be attributed to his military practice and his experience with animals. He explained how to assess muscle power in a weak muscle.

Bone grafting was followed later by Louis Xavie3 Eduard Leopold Ollier (1830-1900). Ollier was born in Vans in Ardeche and studied at Lyons and Ontpellier. Ollier performed pioneering bone grafts. Although he was successful, his methods and the theories behind them were in fierce opposition. In 1877, Ollier suggested that bone growth may be inhibited in order to correct certain deformities by resecting the epiphyseal plate. In 1899, Ollier for the first time described dyschondroplasia or Ollier's Disease.

Sir William Macewen (1848-1924) acted upon many bone grafting afterward. In term of his orthopedic contributions, he completed many osteotomies and developd a one-piece osteotome.

Macewen's key research interest was bone growth and in 1879 he performed the first of his pioneering bone grafts. Probably the most significant figures in bone grafting at turn of the century is Sir Robert Jones (1855-1933). Willis Campbell (1880-1941) was also a major figure in bone grafting and performed inlay full thickness grafts for non-union fixed with screws of beef bone.

Bone grafts have been used to augment orthopedic repairs in veterinary as well as human surgery for several decades and sill being researched to look for new approaches to improve bone healing (Fox, 1984(22); Griffon, 2002)(23).

Bone is the second most common transplantation in human and as estimation between 5,00,000-6,00,000 bone grafting procedures are performed annually in the United States (Bauer and Muschler, 2000(24); Betz, 2002(25). Laurencin et al. (2006)(26) stated that in 1998, only 3,00,000 bone grafting procedures were performed in the United Stated and 9 of 10 was involved in autograft. The bone grafting number had been reached to 5,00,000 in the US and 2.2 million worldwide in 2006 (Laurencin et al. 2006(27).

Grafts also have been reported to be used to replace bone lost of bone cysts or neoplasia (Alexander, 1987(26); Brinker, 1997(28).

Bone grafts are also being used in neurosurgeries, maxillofacial surgeries as well as dental procedures (Zamprogno, 2004)(29).

Autogenous bone graft is defines as the bone harvested from one site and transplanted in other site in the same individual and include cancellous, cortical, corticocancellous and vascularized bone grafts (Fox, 1984(23); Bauer and Muschler, 2000(24); Zamprogno, 2004)(29).

Xenogenous bone graft is described as the bone harvested from an individual and implanted into another from different species. Synthetic bone grafts such as ceramics, coral derives ceramics, ceramic combined with collagen, bio active glass (Ladd, 1999(30); Linovitz, 2002(31); Muschler, 1996) have different characteristics in structural strength rate of resorption or replacement by host, mechanism of action, osteoinductive potential, osteoconductive properties and handling capability (Ladd, 1999)(30).

Some of disadvantages of these graft materials include cost, poor handling, poor resorbability and presence of animal tissue in composition of the grafts (Vaccaro, 2002) (32).

Many still remain unproven to enhance bone healing and implantation of autogenous and allogenous graft materials stay the most common methods used to boost the bone healing and bone formation (Zamprogno, 2004)(29).

Bone graft incorporation which defines as the rate of graft resorption and replacement by host bone depends on contact between the recipient bed and the donot tissue along with initiation of several independent processes such as osteogenesis, osteoinduction, osteoconduction and osteopromotion (Zamprogno, 2004)(29).

The incorporation of a bone graft is defined as theprocess of envelopment and interdigitation of the donor bone tissue with new bone deposited by the recipient (Morone et al. 1998(33); Gregory et al. 2009)(34).

Finally, bone production from the osteoblasts onto the graft's three-dimensional framework occurs, followed by bone remodeling in response to mechanical stress (Goldeberg and Stevenson, 1993)(35).

This ideal graft would posses the following potentials; an osteoconductive matrix that provide a nonviable three-dimensional framework acquiescent to the in growth of blood vessels and osteoprogenitor cells requires for bone formation, osteoinductive factors that recruit the recipient's mesenchymal cells through chemotaxis and then induce or modulate bone formation, osteogenic cells that are osteoblast cells or graft cells with the potential to differentiate into osteoblasts and structural integrity that provides mechanical support and a porous, well-developed surface to let the bone forming cells and osteoinductive factors walk on that to lay down the new bone (Gazdag et al. 1995)(36).

Fresh autogenous bone graft bone mineral and collagen which provide a scaffold for osteoconduction mean (Betz, 2002; Keating and McQueen, 2001a,b; Ladd, 1999; Linovitz, 2002).

After transplantation autogenous bone graft become thoroughly incorporated into the grafted spot with neither initiation of immune reaction nor potential for disease transmission (Keating and McQueen, 2001a,b(37); MacNeil, 1999).

Survival of the cells in the autograft is necessary for graft success and any damage to the graft cells, while transplantation cause delayed bone healing (Burchardt and Enneking, 1978)(38).

to the graft cells (Fox, 1984)(22). Antibiotic application is contraindicated as well. Predominantly some antibiotics such as kanamycin and neomycin are not only bactericidal but also cellucidal and should be avoided in bone grafting procedures (Fox, 984 (22)); Hulse, 1980; Zamprogno, 2004)(29).

Fibrous tissue is produced when mesenchymal cells are positioned under tension with adequate level of oxygen (Zamprogno, 2004)(29).

The potential sources of viable cells in autogenous bone graft are the periosteal cells, the endosteal cell, the bone marrow cells and the cells of the bone (Hulse, 1980)(39).

Other studies showed that the osteocytes of the grafted bone were only responsible for only 10% of newly formed bone (Vassenur, 1987)(41) and the heamatopoietic marrow cells had insignificant role in bone regeneration (Gray and Elves, 1979)(40).

Some studies suggested that the cells of the bone marrow are beneficial to new bone regeneration because it provides a great source of osteogenic factors contains osteoblastic progenitor cells and cytokines and also contains a biodegradable fibrin scaffold that rapidly would be revasuclarized (Fleming et al., 2000; Zamprogno, 2004)(29).

Autogenous bone graft (bone autograft) as stated earlier includes cancellous, cortical, corticocancellous and vascularized bone grafts. Cancellous bone autograft is the first constituent to be described in this study.this graft is the most common graft material used in practice and is considered an ideal graft material (Alexander, 1987; Damien and Parsons, 1991; Fox, 1984(22); Griffon, 2002(23); Ladd, 1999(30); MacNeil, 1999; Vaccaro, 2002)(32).

It can be used for all indication that requires graft but it could be most effective in conditions where osteoblast cell population and as the consequent new bone formation is scare such as long bone defefts, pre-traumatized tissues; infection affected sites and highly vascular damaged bones (Fleming et al., 2000).

The most common harvesting site for autogenous cancellous bone graft is the iliac crest, tibial crest, humeral greater tubercle and greater trochanter of femur (Alexander, 19887; Damine and Parsons, 1991; Fox, 1984(22); Griffon, 2002)(23).

Right away after graft implantation, heamatoma forms at the transplant-host site, attracting cytokines and growth factor to the area. Heamatoma formation indicates the first step of graft incorporation and also prevents blood loss (Abbott et al., 1947(42); Bauer and Muschler, 2000)(24).the granulation tissue becomes dominant, the graft become revascularized and the graft replaced by new host bone in which osteoclast activity starts and multiplies (Burchardt and Eneeking,1 978). The graft-host site develops a layer of cartilage (Enneking, 1957)(43) and later after that fibroblast influenced by growth factors and interleukins manufacture collagen (Bauer and Muschler, 2000(24); Zamprogno, 2004)(29).

Strength of the grafted site would be gradually increase as the old bone is reported new bone is laid down and cancellous bone is replaced by cortical bone (Burchardt and Enneking, 1978). It is reported that after 100 days grafted site is indistinguishable from the normal bone (Abbott et al., 1947(42); Zamprogno, 2004)(29).

Another weak spot of autogenous cancellous grafts is limited graft material obtained from the patients (Betz, 2002(25); Fleming et al., 2000; Griffon, 2002(23); Linovitz, 2002(31); Vaccaro, 2002)(32).the posterior aspect of iliac crest which could be harvested very easily. It is also believed that cancellous bone autograft harvesting increases the time and cost of surgery (Betz, 2002(25); Fleming et al., 2000; Griffon, 2002(23); Linovitz, 2002(31); Vaccaro, 2002)(32)

Greenwald et al. (2001) stated either cancellous bone autograft or an osteoi9nductive agent is necessary for critical sized defects.

allogenous cortical bone graft (Bauer and Muschler, 2000), the clinical use of cortical bone autograft is such scarce. The sites of graft material harvesting are fibula, ribs, distal ulna and iliac wing (Fleming et al., 2000).

Bone material takes place slowly. The new bone primarily develops from the graft bed en route for the graft via granulation tissue (Abbott et al., 1947)(42).

The resorption process gradually declines after a year to the normal level (Enneking, 1957)(43) and dissimilar to cancellous bone autograft which will be completely healed and repaired over the time, the cortical bone autograft would be remain unaltered once the catabolic and anabolic stages of repair have been completed and they are remain as a mixture necrotic and viable cell (Burchardt and Enneking, 1978)(45).

protein and nucleic acid synthesis is launched to prepare for the following cellular proliferation and further amplification of the osteoinduction cascade occurs through the release of additional growth factors (Prolo and Rodrigo, 1985; Gregory et al., 2009).

This is seen histologically and is also accompanied by the detection of Type-IV collagen, laminin and factor VIII (all common in blood vessel components) (Prolo and Rodrigo, 1985).

The vascular invasion indicates the transition from the cartilage differentiation phase to the final phase of bone induction osteogenic precursor differentiation into bone (Gregory et al., 2009).

McKibbin (1987)(50) described a two-callus response in a natural fracture healing experimental model. The primary callus involved the direct production of bone through membranous ossification, whereas the inductive callus involved indirect bone production through endochondral bone formation.

The cartilage – specific proteoglycans have long glycoasminoglycan chains with negatively charged chondroitin sulfate and keratin sulfate. These result in large aqueous domains that provide mechanical stability to a developing callus by increasing its intrinsic pressure (Ross et al., 1986)(51).

It therefore appears that this cartilage is not only an intermediary in the process of new bone formation on bone healing but also supplies an important structural function to the ongoing fusion mass (Gregory et al., 2009).

Allogenous bone graft materials have osteoinduction potential owing to the presence of growth factor in the graft material which include insulin-like growth factor type II, transforming growth factor-β, platelet derived growth factor, fibroblast growth factor and bone morphogenic proteins. These growth factors are in the matrix and are being released by osteoclastic resorption (Bauer and Muschler, 2000; Fleming et al. 2000; Ladd, 1999)(56).

the graft material possesses the osteoconduction properties on account of porous structure of the graft, the cross-linked collagen matrix and the available surface for osteoprogenitor and endosteal cell attachment (Bauer and Muschler, 2000; Fleming et al. 2000 Ladd, 1999)(56).

The efficacy of the osteoinduction and osteoconduction potential of the allogenous bone grafts completely relies on the graft stable fixation and the close contact between the graft and the recipient bed (Sinibaldi, 1989)(57).

One of the most important disadvantages of the graft materials is high risk of infectious disease transmission from the donor to the recipient (Betz, 2002; Fleming et al. 2000; Kerwin et al. 1996; McLaughlin and Roush, 1998; Muschler, 1996; Vaccaro, 2002).

Graft contamination, presence of toxins and the most important disadvantages, the potential for immunological rejection are the other allograft weakness (Dueland et al. 1989; Fleming et al. 2000).

The technique of processing the allograft does affect the mechanical properties and its effectiveness as a graft material. Freez dried and irradiated bone grafts are weaker than frozen grafts (Ladd, 1999).

Cancellous Bone Allografts

This type of graft material is not used as common compared to cortical allografts. There use in veterinary surgery is also limited (Dueland et al. 1989; Kerwin et al. 1996; Rose et al. 1986). Since this graft material is highly cellular, it has the higher potential to stimulate and initiate the immune response and would result to the immune rejection by the host (Kerwin et al. 1996).

, it should undergo a procedure to remove the cellular component. While this procedure is taking place the osteogenesis potential would be limited but it would keep its osteoinduction and osteoconduction characteristics (Kerwin et al. 1996).

At 12^{th} week post implantation, osteoblastic and osteoclastic activity would be significantly increased and the graft becomes incorporated (Wilson et al. 1985). This study also showed that the incorporation process of cancellous allograft is much slower than cancellous autograft (Wilson et al. 1985).

Cortical Bone Allograft

This graft material is to be used when the mechanical support is required at the grafting site. Their common use in veterinary and human surgery is in cases of multi-fragmantary fractures and in bone losses because of tumors or cysts (Kerwin et al. 1996). As their osteogenic potential is very low, they are considered to be depended very little on grafted cell survival for their success (Alexander, 1987; Kerwin et al. 1996).

Bone formation and revascularization are significantly slower and less extensive in this graft material (Bauer and Muschler, 2000; Burchardt and Enneking, 1978).

Bonfiglio and Jeter, (1972) showed that a lymphocytic, eosinophilic and macrophages exudates develop between the graft and the surrounding soft tissue of the host, while cortical allograft implanted. The inflammatory reaction is more severe at the earlier stages.

The smaller the allograft the more rapidly replaced by host, while larger pieces take longer time for replacement or they may never been resorbed and replaced (Sinibaldi, 1989).

Allograft even might not be incorporated or get separated after eight years. Wilson and Hoefle (1990) showed that in a dog the femoral allograft was enveloped by a layer of host new bone but there was no evidence of graft resorption.

Burchardt and Enneking (1978) stated there are two different ways for allografts repair procedure. The first method, involved in rapid and utter resorption of the allograft materials.

The process bridging callus is obvious but mostly leads to delay union, fatigue fracture less new bone growth in comparison with cortical autograft and reduction in graft zie (Burchardt and Enneking, 1978).

The phase of incorporation process relies more on host cells and this is the phenomena happening in cortical allograft implantation (Sinibaldi, 1989; Zamprogno, 2004).

IV. Conclusion

Current avenues of research in molecular biology, progenitor cell use and biomimetics scaffolds holds promise for the future of bone replacements by defining and employing the complex of stimuli and process that can result in bone formation. Postnatal progenitor cells have demonstrated the capacity to differentiate into a multitude of cell types.

Mesenchymal stem cells can be harvested from bone marrow and demonstrate extensive proliferative ability and the capacity to be guided into bone-forming cell types. Their availability is a limiting factor because their fraction in marrow has been estimated to be as low as 1 in 27,000 cells.

Adipose tissues-derived progenitor cells also have been investigated. They possess the advantages of availability and accessibility and have demonstrated capabilities similar to bone marrow-derived cells. In vitro and in vivo studies have demonstrated their ability to form bone.

The molecular processes of the multitude of factors in platelet rich plasma, pro-osteogenic cytokines (BMP) and angiogenic factors leading to osteoblastic bone formation are being elucidated. The delivery or support of these biochemicals or cellular elements, depends on a carrier or scaffolding system.

Collagen, hyaluronic acid, calcium phosphate, chitosan and hydroxyapatite have been studied in the past. Polymer chemistry has yielded polyglycolic acid-polylactic acid. Although these polymers are biocompatible, their breakdown products are potentially tissue damaging.

The goal is to configure these materials as competent carriers of the biomolecular pro-osteogenics or as supportive scaffolds for cellular proliferation and bone formation. One technique that is showing more promise is three-dimensional printing technology. Three-dimensional complex shapes or structures can be computer generated, constructed in a three dimensional printer and then used as protein or cellular carriers for custom implantable bone graft substitutes.

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