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Xenograft – A Review

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Abstract

Periodontal regeneration is one of the procedure which strives for the development of normal periodontium including the periodontal ligament and bone. Surgeons have used various materials for periodontal tissue engineering which has helped to improve the clinical outcome. Many synthetic and biological extract grafts have been used in treating several different bone defects. Xenograft is one of such novel material which is used from the past as a regenerative material owing to its properties similar to that of human bone. It acts as a scaffold which by its osteoconductive property induce bone formation. Thus apart from using as periodontal regenerative material, it is also used in ridge augmentation, sinus lift procedures and in osseointergration around implants

Keywords: Bone graft, xenograft, advantages, disadvantages

Introduction

Periodontitis is the second most prevalent disease among the world population. Treatment of periodontitis had faced challenges in the past to treat and restore the health of periodontium. In modern days, this has been achieved by using various techniques and materials to regain soft and hard tissue harmony. Bone grafts are used for replacement and formation of bone and periodontal regeneration. Open flap debridement, which is conventionally used improved periodontal form and architecture but they do not help in recontouring or restoring the periodontal tissues. Bone grafting materials function act as structural scaffolds and matrices for proliferation and attachment of anchorage-dependent osteoblasts. Job van Mee'kren in 1600[1] the first to document xenograft.

Anorganic bovine bone (ABB) is associated with partial non resorbability with no evidence of graft particle substitution [2]

Characteristics of ideal bone graft

Paradigm for an ideal bone graft material BOYNE 1973[3]

i. Availability and no second site surgery.
ii. Deliver prompt osteogenesis
iii. Exhibit No immune response-biocompatibility
iv. Bone growth should not be impeded
v. Provide support and continuity where mobility exist
vi. Enhance revascularization
vii. Provide osteoconductivity
viii. Provide a medium for formation of new attachment apparatus.
ix. Bone grafts help in osteogenesis , cementogenesis resulting in the formation of functional new attachment of periodontal

ligament.(Rose and Rosenberg 1998[4]; Nasr et al. 1999[5]).

Bone graft material is commonly classified as

1. Autogenous bone
2. Allograft
3. Xenograft
4. Non bone graft materials
5. Alloplast

New research and development in material science have broken the boundaries in various bone replacement grafts[6] (Reynolds et al. 2010).

Xenografts are graft tissues obtained from non human species and are osteoconductive with limited potential.

Non-human source materials are

i) Bovine hydroxyapatite (anorganic bovine derived bone graft)

ii) Calf bone

iii) Keil bone

iv) Porcine bone

v) Equine bone

vi)Coralline calcium carbonate

Advantages

1. No donor site required from patient and therefore no additional surgical intervention.
2. Unlimited supply of material available
3. Material is easily handle.
4. When noble surgical principles are carried on the results are good. .
5. Biocompatible since all proteins are removed [7].
6. Xenograft have no adverse reaction.
7. Composition is similar to that of human bone, thus resorption occurs in the same phase[8].
8. Xenograft also activates cartilage-related pathways[9] (Annalisa et al. 2008).
9. No fibrous tissue capsule formation unlike hydroxyapatite crystals.

Disadvantages of xenograft

1. Sinus and maxillary bone pathology,
2. Easy dislodgement of the graft materials
3. Involvement of Oro-antral communication
4. Implant failure,
5. foreign body response,
6. encapsulation,
7. chronic inflammation,
8. soft-tissue fenestrations, and cysts
9. slow rate of resorption[25].

The bovine bone xenograft is not biodegradable. Mordenfeld et al. provided evidence of deproteinized bovine bone particles not biodegraded after 10 years[26]. Ayna et al. showed the presence of residual bovine bone particles in humans after 14 years[27] .

Bovine bone encephalopathy (BSE) prion inactivation by anorganic bovine bone manufacturing processes has yet to be proven. BSE is a type of transmissible spongiform encephalopathies caused by prion proteins. Prions are well known for their resistance to conventional chemical and physical decontamination methods, and the heat treatment used for anorganic bovine bone material preparation (300°C for Bio-Oss®, 1100°C for PepGen P-15®) has not proven to inactivate BSE prion.

Chronic inflammation of the soft tissue associated with the bovine bone was evidenced and the inflammatory processes resolved after the removal of the bovine bone materials. The plausibility of bovine-derived bone substitutes in producing immune reactions is present.

Preparation of xenograft

Xenograft are indicated in 2- wall defect, circumferential peri implant defects, 2 and 3 wall extraction sockets, ridge split / expansion, GBR, Sinus augmentation, horizontal ridge augmentation:

The cancellous bones of the tibias of young Charolais cattle are collected and then the soft tissue, cartilage and bone marrow were removed. The cancellous bones were made into cuboid-shaped sticks with dimensions of 0.5 cm × 0.5 cm × 3 cm which were then defatted in a Soxhlet extractor by petroleum ether extraction method. Deproteinization of the bone sticks was carried out by immersing 8 hours in 30% hydrogen peroxide and later washed repeatedly in double distilled water (ddH_2O) and dried. In Pepsin deproteinization procedure , bones

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were digested by 0.3 mg/mL pepsin dissolved in pH 2 phosphate buffer (1.97 g NaH2PO4, 1.20 mL H3PO4 in 100 mL ddH2O) at 25°C for 8 hours. This reaction is terminated by adjusting pH to 9 with NaOH to deactivate the pepsin. 15 min later, similar to hydrogen peroxide deproteinization sticks of bone were washed repeatedly with Dd H_2O for 30 min and dried.

Anorganic bovine derived bone xenograft(BDX)

Anorganic bone is ox bone of which the organic material has been removed by means of ethylenediamine, and sterilized by autoclave. This is a deproteinized, sterilized bovine bone with 75-80% porosity and available as cortical granules in the size of 10μ[13]. 1999. The physical and chemical properties are identical to human bone[14].

Invitro studies

BDX possess excellent osteoconductive properties[15]. Angiogenesis and migration of osteoblast are facilitated due to large interconnecting pore system[16]. In haversian canals, small capillaries, mesenchymal cells and osteoblast were present. No voids are present at boundary between particles and newly formed bone[17]. Mature compact bone which surrounds BDX particles are connected by bridges of such vital newly formed bone [18] (Figure 1).

Commercially Available Bovine Derived Bone Xenografts

1. Bio –oss
2. Bio-0ss collagen
3. Osteograf/N
4. PepGen -15
5. Gen-ox
6. Laddec

Bio-oss (Geistlisch biomaterials, Switzerland)

It is a porous bone mineral matrix, obtained naturally and has no antigenic property. Bio-oss is obtained by elimination of all organic content from bovine bone. It is manufactured by chemical extraction process at low heat 300°C . By this process all organic components are eliminated, without disturbing the natural architecture of bone[19]. The resulting product is calcium carbonate containing apatite with scarce hydroxyl group and possess a crystalline structural design. Calcium carbonate ratio is similar to natural bone mineral in humans[7] .The presence of pores in granules increase the surface area and favours osteoconduction and enables bone growth in the pores. The material will be least degraded because the fast absorption of biomaterial jeopardise adequate repair(Figure 2).

Bio-oss collagen

Bio-oss collagen is made up of Spongiosa granules of 0.25–1 mm by addition of 10% highly purified porcine collagen. The internal surface area of the Bio-oss collagen is large and porous and thus it acts as scaffold for ingrowth of bone. The easy adaptability of the material is due to the collagen component thus it makes the application simple . Resorption takes place within 4-6 weeks and the particles remain cohesive even in absence of membrane. This material is used in periodontal regeneration in cases of intrabony defects [20]. Healing with bio-oss collagen occurs by the formation of new cementum, periodontal ligament and new bone. Due to the osteoconductive property of the graft material, it is surrounded by bone and leads to the formation of new periodontal attachment apparatus [21] .

Osteograf/N

Osteograf is made up of hydroxyapatite in its pure and natural form which is also main content of enamel and bone.

OsteoGraf/N is biocompatible and remodeling occurs at the rate same as that of the host . Of all the xenograft , OsteoGraf/N fulfils all ASTM [American Society for Testing and Materials] standards for “Composition of Anorganic Bone for Surgical Implants (F1581-95).” The physical property of this material is hydrophilic– cohesive during hydration. The particles are rounded and radiopaque and is available in 2 sizes:

1. OsteoGraf/N - 300 (250 –420 mm)
2. OsteoGraf/N-700 (420–1,000 mm)

PEP GEN P -15

PepGen P-15R , a unique regenerative product . this product is made up of bovine bone which is calcined hydroxyapatite (1,100°C) and treated with penta - decapeptide.P-15 represents a part of collagen sequence. The granules are of size of 0.25–0.42 mm . PepGen P-15 validates an greater expression of growth factors and provides an suitable environment

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for bone formation. Comparatively there is greater reduction in probing depth and gain in clinical attachment level compared to Bio-oss (Figure 3).

Porcine derived bone xenograft

The xenograft derived from porcine bone is a replica of autogenous bone since OsteoBiolR Gen-Os consists of same matrix form and pores as that of autologous bone. The osteoconductive property is high. Similar to any other xenograft this is biocompatible. Resorption occurs in a gradual manner thus preserving the original shape and volume of the newly formed bone. Due to its hydrophilic nature porcine graft can be used as carrier for certain medications. The particle sizes are 250–1,000 micro and porosity is 33%[22]. To activate the collagen matrix the graft material must be mixed with few drops of saline which also increases the adhesion properties . Started to resorb at 8 weeks [23]. Indicated for maxillary sinus and alveolar crest augmentation, [21]as a filler in post extractive alveolus [22] and for implant treatment [23].Histological studies showed new bone formation sandwiched between graft particles and preexisting bone (Figure4).

Coralline calcium carbonate

Coralline calcium carbonate are derivative of exoskeleton of marine madreporic corals. Porites consists of 97–99% calcium carbonate, signifying the coral exoskeleton. The physical and mechanical properties bear a resemblance to cancellous bone. The numerous oligoelements comprising 0.5–1% magnesium ,0.05% to 0.2%sodium , 0.4–0.5% amino acids are present. The oligoelements takes part in the bone mineralization and in the initiation of enzymatic responses with osteoid cells. The preparation of the graft takes place at high temperature under pressure in the presence of aqueous phosphate solutions. Thus conversion of coral to calcium hydroxyapatite takes place, keeping intact the extremely organized, pervious and interconnecting pore structure [24] .

Physical properties

The average diameter of pore is 200 µm similar to cancellous bone. Porosity/void spaces are 60% which permits for superior resorption and new bone infiltration. High osteoconductive potential. Advantages of the graft are greater defect filling in periodontal regeneration applications and no fibrous encapsulation. Presence of Fluorine amounts to 1.25–2.5 times more in coral as that in bone. This aids in bone formation by osteoblast proliferation. The organic content is restricted to 1–1.5%. Biocoral(Figure 5) is a commercially available graft. Calcium carbonate is resorbable and so there is no potential for fibrous encapsulation[16] (Piattelli et al. 1997).In human maximum particles were present even after a 6 -month period[16] .

Mechanism of bone formation around xenograft

ABB shows formation of bone through osteoconductivity in which the graft act as scaffold and helps in the ingrowth of new vasculature and penetration of osteogenic precursor cells[10] .

When there is a surgical trauma large quantities of cytokines such as BMP-2 , PDGF, TGF-β and VEGF are released. The woven bone is formed from the walls of traumatised bone ,which causes bone matrix to expose in turn stimulating osteoblastic precursors. This creates a biochemical environment which is hypoxic [O_2 tension of 3-10 mmHg] acidic [$_pH4$-6]and rich in lactate.

Degranulation of platelets takes place in an hour thus releasing PGDF which depends on oxygen gradient. This activates mitogenesis of osteogenic cells and angiogenesis of capillaries.

Budding capillaries are present on outer surface of graft by third day and by 10-14 day a vascular network penetrates the graft. Mesenchymal stimulators of TGF -β family and macrophage – derived growth factor [MDGF] replace PDGF.

Chemical and cellular activity takes place during the first 3-4 weeks in Phase I bone regeneration. Here osteoconductive phase is initiated by forming the scaffold framework which leads to formation of disorganized woven bone .

Phase -II bone, less cellular, more mineralized and structurally organized bone is formed by resorption and remodelling which is carried out by osteoclast formed from new vasculature[11].

In coral-derived xenograft, dense fibrous tissue and bony trabeculae enter the HA particles at 4 weeks , the outer surface of granules and lining of pores are covered by thin layer of woven bone[12].

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At 12 weeks the pores become more dense where the parallel fiber and lamellar bone reinforce the newly formed woven bone. At 24 weeks this bone is replaced by lamellar bone which is limited to bone compartment and does not extend into neighbouring coralline material, thus shows partial non resorbability.

Conclusion

In modern days autologous bone grafts are not the only choice as there are other bone grafts derived such as xenograft which had chemical and physical properties almost alike of human . Thus properties of such grafts must be studied in detail for the full fledged usage in clinical conditions for the best results and outcome to be established.

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Figure Legend

1. Figure 1 : Bovine-derived xenograft (BDX)[Courtesy : Chemicals in Surgical periodontal therapy- A.L.Dumitrescu]

2. Figure 2 : Bio-oss[Courtesy : Chemicals in Surgical periodontal therapy- A.L.Dumitrescu]

3. Figure 3 : PEP GEN P 15[Courtesy : Chemicals in Surgical periodontal therapy- A.L.Dumitrescu]

4. Figure 4 : Osteobiol[Courtesy : Chemicals in Surgical periodontal therapy- A.L.Dumitrescu]

5. Figure 5 : Biocoral[Courtesy : Chemicals in Surgical periodontal therapy- A.L.Dumitrescu]

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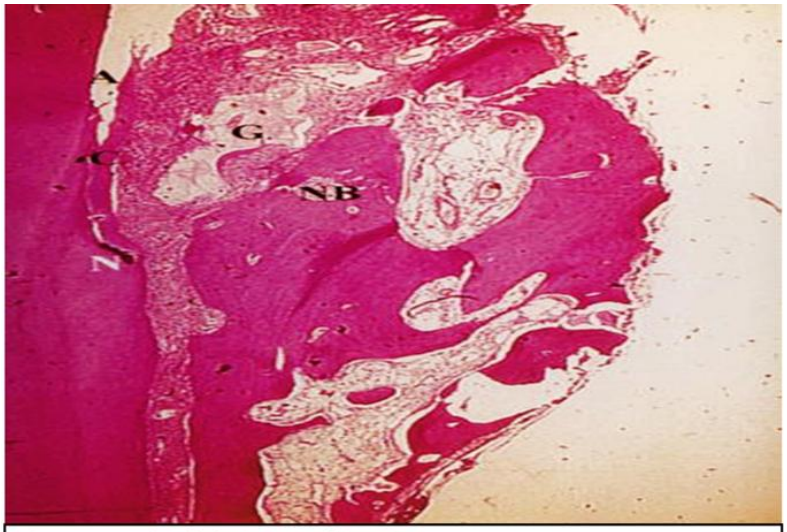

Figure 1: Bovine-derived xenograft (*BDX)*
New cementum with inserting collagen fibers (C) , New bone (NB), coronal to the notch (N) in the root surface. Bone surrounds the bovine-derived xenograft (*BDX)*.

Figure 2: Bio-oss

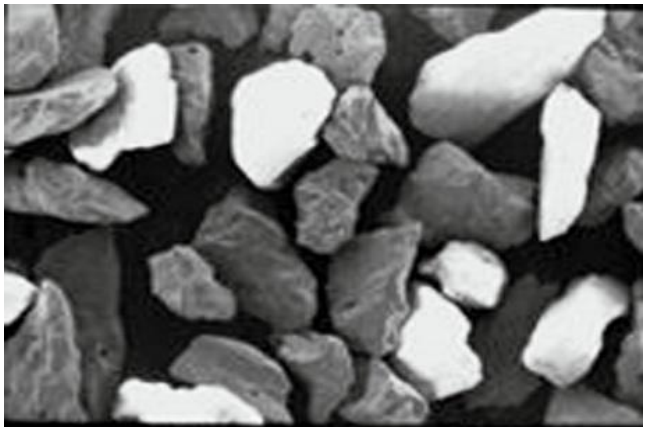

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Figure 3 : PEP GEN P 15

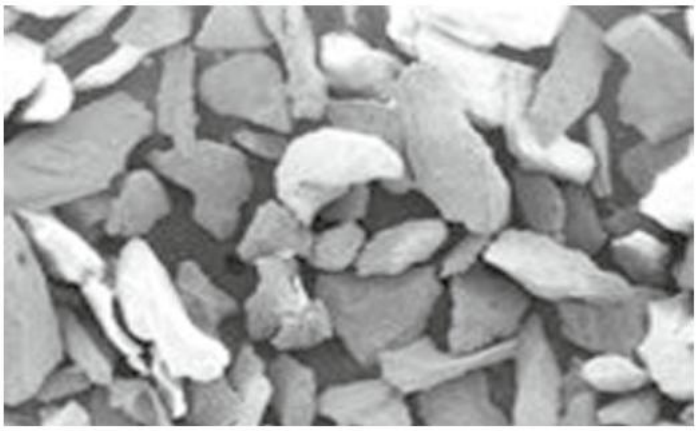

Figure 4 :Osteobiol

Resorption as well as remodelling was an ongoing process which was indicated by resorption lacunae and new osteons.

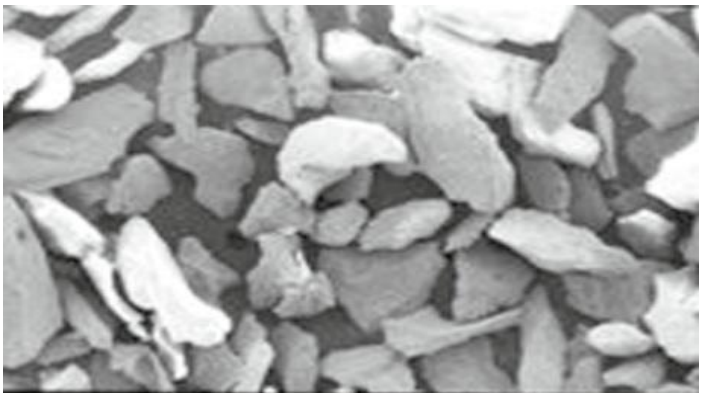

Figure 5 : Biocoral

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