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A Review on Bone Grafting in Veterinary Patients

Khatiwada, S (2012)
Institute of Agriculture and Animal Science, Tribhuwan University, Rampur, Chitwan, Nepal
(Review work)
Correspondence to: Khatiwada, S, meksushil@gmail.com; +9779803246234

ABSTRACT

Diseases such as arthritis, tumors, and trauma can lead to defects in the animal skeleton requiring an operation to replace the lost bone where enhancement of the bone healing and restoration of the skeletal integrity are still a huge challenge. Hence, bone grafting have been used to hasten orthopedic repairs in human and veterinary surgery for several decades and still widely being researched looking for new interventions to promote bone healing following incidences of bone complications. Bone grafts are bone transplants necessary to provide support, fill voids and enhance biologic repair of skeletal defects for which bone harvested from donor site is the gold standard. They are classified into autogenous and allogenic grafts as well as synthetic bone graft which are bone graft substitutes. Exploring new sites and tools for graft harvests are the major concerns of researchers to minimise the morbidities of donor site in autografts while the agents escalating the inductivity are looked after in the allografts Drawbacks of autograft and allograft have prompted for the development in the field of bone graft substitutes which are available in large quantities and variants but themselves have demerits like low incorporation rate and low biodegradability. Recent advances in gene therapy and tissue engineering are also modeling the prospectful field of bone grafting. This review would consider all grafting methods and materials that would open new windows to the bone grafting techniques in veterinary orthopedics.

Keywords: Bone graft, veterinary orthopedics, graft substitutes

INTRODUCTION

Delayed union or non-union of the fracture are mainly due to combination of deficiencies in vascularity and angiogenesis, robustness of the chondro-osseous response and stability or physical continuity which greatly complicates the approach of treatment and management. For a bone grafts to enhance fracture healing, it must provide that which is deficient. Bone grafting is possible because bone tissue, unlike most other tissues, has the ability to regenerate completely if provided the space into which to grow. As native bone grows, it will replace the graft material completely, resulting in a fully integrated region of new bone. These grafts have varying capacities to provide active bone formation, to induce bone formation by cells of the surrounding soft tissue, and to serve as a substrate for bone formation. However, the graft cannot exert its biologic activity in isolation, dependent as it is on the surrounding environment for cells to respond to its signals and, in some cases, for blood supply. Successful graft incorporation requires that an appropriate match must be made between the biologic activity of a bone graft, the condition of the perigraft environment, and the mechanical environment. The task of the veterinary surgeon that performs a bone grafting procedure for the enhancement of fracture healing is to choose the right graft or combination of grafts for the biologic and mechanical environment into which the graft will be placed. Autogenous fresh cancellous and cortical bone most frequently are used in veterinary orthopedics, but other common grafts include allogeneic frozen, freeze dried, or processed allogeneic cortical, corticocancellous and cancellous grafts, and demineralised bone matrix. The emergence of various sophisticated techniques and instruments have further ramified the use bone grafting in veterinary orthopaedic patients.

LITERATURE REVIEW

Bone grafting is a surgical procedure that replaces missing bone in order to repair bone fractures that are extremely complex, pose a significant health risk to the patient, or fail to heal properly. Kaveh (2010) states that 'these bone transplants from a site to another have been commonly indicated in the veterinary orthopedic surgery that include gaps at fracture sites, comminuted fractures delayed unions and non-unions, arthrodeses, corrective osteotomies, fresh fractures and spinal fusion'.

History of Bone grafting

Tissue grafting began with Hunter (1728-1793) who assessed the joint disorders and insisted that bone diseases require mechanical supports. Bone grafting was then pioneered by Louis Xavier Eduard Leopold Ollier (1830-1900). He suggested that bone growth may be inhibited to correct certain deformities by resecting the epiphyseal plate and had faith that it might be possible to treat patients by stimulating their cartilaginous ossification. Sir William Macewen (1848-1924) then contributed bone grafting afterward by completing many osteotomies and developed a one-piece osteotome. He had keen interest on the bone growth and performed pioneering bone grafts. Sir Robert Jones (1855-1933) who was one of the greatest orthopaedic surgeons advocated tendon transplantation, bone grafting and restorative procedures. Willis Campbell (1880-1941) then appeared as key figure in bone grafting by performing inlay full thickness grafts for non-union fixed with screws of beef bone (Kaveh, 2010).

Bone grafts and their classification

Bone grafts have been used to augment orthopaedic repairs in veterinary as well as human surgery for several decades and still being researched to look for new approaches to improve bone healing (Fox, 1984; Griffon, 2002). Bone grafts are bone transplant and are classified as autograft, allograft, xenograft, synthetic graft and combination graft (Bauer and Muschler, 2000).

1. Autogenous bone graft

It is defined as the bone harvested from one site and transplanted in other site in the same individual which include cancellous, cortical, corticocancellous and vascularised bone grafts (Fox, 1984; Bauer and Muschler, 2000; Zamprogno, 2004). It can be classified by anatomy (cortical, cancellous and corticocancellous), methods of processing (fresh, frozen, freeze-dried and demineralised) method of sterilization (sterile, irradiated, ethylene oxide) and handling process (powder, gel, particulate, chips, strips, blocks and massive). Allograft in the genetically related individuals is termed isogenous graft (Zamprogno, 2004).

2. Xenogenous bone graft

It is described as the bone harvested from an individual and implanted into another from different species.

3. Synthetic bone grafts

It includes various synthetic materials that are supposed to promote bone healing such as ceramics, coral derives ceramics, ceramic combined with collagen, bio active glass 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).

Bone graft incorporation

It depends on contact between the recipient bed and the donor tissue along with initiation of several independent processes such as osteogenesis, osteoinduction, osteoconduction and osteopromotion (Zamprogno, 2004).

1. Osteogenesis

It is defined as bone formation by living transplanted cell within the graft or on the other hand, a graft that supplies and supports bone forming cells is termed osteogenic (Attawia et al., 2003). The successful osteogenesis depends on the survival of the osteobasts and osteocytes of the graft materials (Alexander, 1987; Ladd, 1999). These cells are preserved by diffusion from the surrounding host tissues until revascularization founding (Alexander, 1987).

2. Osteoinduction

It is process by which bone formation is being induced by active employment of bone forming cells or growth factors from within the transplanted tissue. Materials that have the capacity to induce bone formation, when placed into a site where no bone formation will occur are termed osteoinductive (Attawia et al., 2003). These materials do not work alone but recruit bone forming cells or their progeny to infiltrate the material (chemo-attraction and migration) then induce the multipotential cells to multiply and become cells that comprise the regenerating bony callus (proliferation and differentiation).

3. Osteoconduction

It is process in which the graft materials working as a suitable scaffold facilitating the bone positioning to its surface, improving attachments, migration and distribution of the cells involved in vascularization and bone healing (Ladd, 1999; Attawia et al., 2003). It varies greatly in different grafting materials and relies on graft's three dimensional structures, porosity, surface chemical properties and the rate and mechanism of degradation.

4. Osteopromotion

It is promotion of bone healing and regeneration by encouraging the biologic and mechanical environment. Thus materials or physical impetus that results in enhancement of regenerating bone is termed osteopromotive (Attawia et al., 2003). It can function at various stages during bone healing and provide different stimulatory signals to bone regenerating tissues. It differs from osteogenesis or osteoconduction as bone formation is enhanced without cells or a scaffold however, osteopromotive stimuli alone cannot induce bone formation. Eventually, successful bone graft incorporation requires a combination of osteogenesis, osteoinduction and osteoconduction but factors like physiology of the graft, bearance of the mechanical load on surface texture, age and level of health also play vital role (Zamprogno, 2004).

Table 1: Comparative properties of bone grafts (Mclaughlin and Roush, 1988; Parikh, 2002; Kaveh, 2010)

S.N	Bone graft	Strength	Osteogenesis	Osteoinduction	Osteoconduction
1.	Cancellous autograft	No	+++	+++	++
2.	Cortical autograft	Yes	++	++	++
3.	Corticocancellous autograft	No	+++	+++	+++
4.	Frozen cancellous allograft	No	No	+	++
5.	Freeze-dried cancellous allograft	No	No	+	++
6.	Frozen cortical allograft	Yes	No	No	+
7.	Freeze-dried cortical allograft	Yes	No	No	+

Bone graft physiology

The incorporation of a bone graft is the process of envelopment and interdigitation of the donor bone tissue with new bone deposited by the recipient. This process pursues a typical multistep cascade the bone graft produces a response leading to the accumulation of inflammatory cells followed by the chemotaxis of host mesenchymal cells to the graft site. Thereafter, the host cells differentiate into chondroblasts and osteoblasts under the influence of various osteoinductive factors. The additional process of bone graft revascularization and necrotic graft resorption occur concurrently. Finally, bone production from the osteoblasts onto the graft's three-dimensional framework occurs, followed by bone remodelling in response to mechanical stress (Goldberg and Stevenson, 1993).

Ideal graft would possess the following potentials: an osteoconductive matrix that provide a nonviable three-dimensional framework, osteoinductive factors that recruit the recipient's mesenchymal cells through chemotaxis and then induce bone formation, osteogenic cells with the potential to differentiate into osteoblasts providing mechanical support in order to lay down the new bone (Gazdag *et al*., 1995).

Many bone grafts types available today possess some of the aforementioned properties but the best graft is one which carries all properties simultaneously. Veterinary surgeon's choice of graft material depends greatly on which of the four elements are most crucial to the particular surgical application. Between graft material the autogenous graft are pioneered in carrying the four properties and that is the reason it is the gold standard graft material and most common graft in use worldwide.

Autogenous bone graft (bone autograft)

Fresh autogenous bone graft is deemed as the gold standard graft material since it provides the highest number of viable osteoprogenitor cells and contains noncollagenous matrix protein and growth factors with the osteoinduction property. It also carries bone mineral and collagen which provide a scaffold for osteoconduction (Ladd, 1999). It has got significant limitations like donor site morbidity, inadequate amount, and inappropriate form.

I. Cancellous bone autograft

Characteristics: On proper handling and transplantation it offers the considerable amounts of viable cells that boost the osteogenesis, matrix protein that promoting osteoinduction and bone matrix. Hence, attributed to these factors it is the most common graft material used in practice and is considered an ideal graft material (Alexander, 1987; Fox, 1984; Griffon, 2002; Ladd, 1999). Indication includes conditions with scare osteoblast cell population such as long bone defects, pre-traumatized tissues, infection affected sites and highly vascular damaged bones (Fleming *et al*., 2000). The most common harvesting site for this bone graft is the iliac crest, tibial crest, humeral greater tubercle and greater trochanter of femur (Alexander, 1987; Damien and Parsons, 1991; Fox, 1984; Griffon, 2002).

Incorporation procedure**:** This procedure relies on status of surrounding host tissue, the host graft cell survival percentage, size and location of the recipient bed, condition of vascularity and the age of the patient (Bauer and Muschler, 2000). Incorporation process is primarily achieved by a process termed creeping substitution. Once the graft implanted, the donor cells of the graft are replace by the host mesenchymal cells which would be differentiated into osteoblasts. The osteoblasts are responsible for new bone production and formation. The creeping substitution continues to the point that all of the graft cells are removed and replaced by new host bone (Alexander, 1987).

II. Cortical bone autograft

Characteristics: It supply structural support at the transplanted site and is sufficiently competent to fill large defects with the proficiency to fill the defects up to 12 cm. The sites of graft material harvesting are fibula,

ribs, distal ulna and iliac wing. More invasive harvesting procedure and higher donor morbidity than cancellous graft limits its clinical use (Bauer and Muschler, 2000; Fleming *et al*., 2000).

Incorporation process: The early stage of graft incorporation behaves similar to that of cancellous autograft. However, in later phases the graft is almost enveloped by new bone trabeculae that originated from the graft bed. Bone production is highly depended on environmental conditions such as nutrition and chemical stimulation.

III.Corticocancellous bone autograft

Overall characteristics: This class of graft material does not offer structural support, but boost the new bone formation by osteogenesis, osteoinduction and osteoconduction potentials (McLaughlin and Roush, 1998). The most common site for harvesting corticocancellous bone autograft is ribs and the craniodorsal iliac wing.

Incorporation process: The incorporation of cancellous bone graft is comparable to corticocancellous bone graft (Millis and Martinez, 1993). It is initially revascularized and then replaced by host bone but the revascularization is quicker than cortical autograft as it is less dense.

The osteogenic potential of this type does not require long time for resorption and degradation like what is being seen in cortical bone graft. The bone graft incorporation and bone induction cascade has often been separated into three prominent phases.

Phase I: It is the initial phase that involves mesenchymal cell chemotaxis and proliferation. This is a growth factor stimulated accumulation of primary mesenchymal cells and is critical to the ensuing phases of bone induction.

Phase II: This phase includes the differentiation of the stem cells into chondroblasts and chondrocytes with the subsequent production of cartilaginous matrix and concludes when blood vessels invade the newly formed cartilage carrying primitive mesenchymal cells along to populate the cartilage with osteogenic precursors.

Phase III: It is the final phase that involves mesenchymal cell differentiation into osteoblasts and osteocytes followed by bone and bone marrow production (Gregory *et al*., 2009).

Allogenous bone graft

Its use is becoming more common in human as well as veterinary medicine as it is superior to bone autograft and also could be provided in an unlimited quantity either alone or as the extender to the autogenous bone graft (Fleming *et al*., 2000; Griffon *et al*., 1996). It has osteoinduction potential owing to the presence of growth factor in the graft material. Veterinary allogenous bone graft materials are commercially available in different forms including gel, powder, pastes, blocks and fibers. Its disadvantages include lack of osteogenesis potential, higher cost of collection and processing and high risk of infectious disease transmission from the donor to the recipient.

I. Cancellous bone allograft**:** Owing to the higher cellularity it has much higher potential to stimulate the immune response resulting in the immune rejection by the host so its use in veterinary surgery is limited (Kerwin *et al*., 1996). In order to avoid rejection cellular components should be removed. The incorporation process of cancellous allograft is much slower than cancellous autograft.

II. Cortical bone allograft: Their common use in veterinary and human surgery is in cases of multifragmentary fractures and in bone losses because of tumours or cysts to provide mechanical support at the grafting site (Kerwin *et al*., 1996).

Incorporation process: Cortical allograft incorporation procedure differs completely from that of cortical autograft as bone formation and revascularization are significantly slower and less extensive (Bauer and

Muschler, 2000). Incorporation process here is known by osteoclastic activity which increases the porosity and deteriorates the graft.

III. Corticocancellous bone allograft: This kind of graft material works almost similar to cortical allograft but its use is not such common in veterinary medicine.

Xenogenous bone graft

It has its origin from a species other than the graft recipient species, such as bovine. Xenografts are usually only distributed as a calcified matrix.

Synthetic bone grafts (Bone graft substitutes)

They include material used to fill the osseous defect in human and veterinary medicine. To be suitable for in vivo implantation, they should be biocompatible and permit fast incorporation. They must have mechanical properties to prevent graft deformation and must also permit regulated osteoclastic resorption. These materials should be easy to handle, inexpensive, easy to implant and fast manufactured (Zamprogno, 2004). These substitutes can be divided according to their properties.

Table 2: Classification of bone graft substitutes based on their properties (Parikh, 2002)

S.N	Property	Description	Classes
1.	Osteoconduction	Provide a passive porous scaffold to support or direct bone formation	Calcium sulphate Ceramics Calcium phosphate Cements Collagen Synthetic Polymers
2.	Osteoinduction	Induce differentiation of stem cells into osteogenic cells	Demineralised bone matrix (DBM) Bone morphogenetic proteins(BMP) Growth factors Gene therapy
3.	Osteogenesis	Provide stem cells with osteogenic potential, which directly lay down new bone	Bone marrow aspirate
4.	Combined	Provide more than one of the above mentioned properties	Composites

Table 3: Summary of bone graft substitutes (Moore et al., 2001)

Substance	Bioactive glass	Glass inomers	Aluminium oxide	Calcium sulphate
Form	Granules, blocks, rod	Powder	Granules, blocks,	Powder, pellets
Reabsorption	Non-resorbable to resorbable	Non-resorbable	Non-resorbable	Dissolves in 5-7 weeks
Incorporation of antibiotics	Not possible	Yes	Not possible	Yes
Mechanical properties	Stronger than HA implants	Compressive strength and elasticity comparable to the cortical bone	Stronger than HA implant, does not osteointegrate	No structural properties
Uses	Bone graft expander, vertebral body prosthesis, ossicular replacement, orbital implants	Dental maxillofacial ossicular replacement	Bone graft expander, wedge, osteotomy, ossicular replacement	Void filler, bone graft expander, osteomyelitis

DISCUSSION AND CONCLUSION

Bone grafting techniques are important part mostly of small animal orthopedic surgery for many years. Autogenous cancellous bone grafts have long been considered the most effective graft material for accelerating bone healing which are useful when cellular transfer and osteoinduction are needed, but mechanical strength of the graft is not essential. Harvesting autogenous cancellous bone requires a separate surgical approach during the primary procedure and is limited by the amount of bone graft material present at each donor site. Cortical allografts have been used in veterinary surgery to provide mechanical support and as a template for new host bone formation but they must be harvested prior to surgery and maintained in a bone bank. Xenograft bone implants may also hold a place for use in fracture management.

Wide shortcomings of the autograft and allograft have paved for the use of alternatives as the bone graft substitutes which are available in large quantities, shape and size but themselves suffer from lots of drawbacks including low incorporation rate, low biodegradability rate and potentials to transmit diseases. With the advent of recombinant bone-derived tissue growth factor technology, bone grafting may someday become a practiced technique of the past. For now, however, bone grafting still holds a strong place in veterinary orthopedic surgery.

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