Current and future perspectives of polymethylmethacrylate bone cement in veterinary orthopaedics: A review

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Abstract
Fracture of long bones have been a long term concern in the field of veterinary orthopaedics. Many implants have been used in stabilization of fractures and such implants are subjected to a variety of implant failures like implant loosening, migration resulting in malunion, non-union and delayed union. In this view various biomaterials have been identified and used in fracture treatment to enhance and accelerate bone healing via callus formation and to improve the implant stability by acting as an agent to hold the implant against the bone. Polymethylmethacrylate or PMMA bone cement is one such biomaterial used in the veterinary orthopaedics for numerous applications. The introduction of pmma bone cement in veterinary field, its preparation and delivery, presentation, application, advantages and side effects and its future perspectives are discussed here.

Keywords: Veterinary, fractures, long bones, polymethylmethacrylate

1. Introduction
Fractures are one of the most common orthopaedic affections in small animals particularly canines. Fractures usually occur after a traumatic event like accident, slipping, falling from height, human violence and fighting. Fractures causes considerable degree of pain, damage to the surrounding soft tissue and loss of function of the affected limb. Thus there is an immediate requirement of surgical intervention to reduce the fracture fragments to anatomical position and to stabilize the fracture fragments thereby to promote accelerated fracture healing and early functional use of the affected limb. Among the fractures in canines, fractures of weight bearing long bones like femur, tibia and fibula, humerus and radius-ulna are common followed by fractures of the pelvis and that of vertebrae.

Traditionally metallic implants have been used for fracture fixation which include external skeletal fixators, intramedullary Steinmann pins, Kirshner wire, cerclage wire, rush pins, bone plates and screws and intramedullary nails. The use of biomaterials in fracture stabilisation and bone regeneration is an age old technique in human orthopaedics but its application in veterinary orthopaedics is still in the advancement stage. A biomaterial is defined as an inert material that is used inside a biological system to stimulate, enhance, regenerate, augment or replace the function of a tissue or an organ as such. Large variety of biomaterials with various applications are available in the market and the use of such biomaterials improves the quality of life. All biomaterials used are host compatible which means that their use inside a living tissue do not evoke a host immune response.

A large number of biomaterials to enhance fracture healing are available in the market for use in orthopaedics. Different augmentation techniques and materials available include autograft, allograft, Tricalcium phosphate, hydroxyapatite, demineralized bone matrix and polymethylmethacrylate bone cement which are used at various anatomical locations for therapeutic and prophylactic purposes. To date only acrylic bone cements and acrylic based composites offer the required strength for high load bearing applications and among the acrylic bone cements, polymethylmethacrylate (PMMA) is most commonly used in orthopaedics (Klein, 2015) [7].
1.1 History
Polymethylmethacrylate (PMMA) commonly known as bone cement was introduced in the 1960s in human orthopaedics for the purpose of hip arthroplasty, joint replacements and as a material in osteoporotic bone and in cases of pathological fractures in age old. Since its advent it has been largely used in human and veterinary orthopaedics for a wide variety of fixation systems.

1.2 Composition
Polymethylmethacrylate is supplied as a two component system consisting of a powder and liquid part. They are available in the market in packings of 40gm and 20gm powder along with 20ml and 10ml liquid component respectively. The powder and liquid are mixed in ratio of 2:1 to initiate an exothermic polymerization reaction that results in the formation of the final product in the form of a paste which is then used for orthopaedic purposes.

Powder component consist of methyl methacrylate (Styrene copolymer), benzoyl peroxide (1.7%), polymethylmethacrylate and barium sulphate. Benzoyl peroxide acts as an initiator to initiate the polymerization reaction. Barium sulphate act as a contrast agent for radiographic purpose. Their detection on radiograph depends on the amount and quantity of the bone cement applied to the bone and fine quantities are found to be undetectable on radiographic examination.

The liquid component consist of a monomer-methyl methacrylate, an accelerator – N, N-Dimethyl paratoluoluidine, and a stabilizer to prevent premature polymerization from exposure to light or high temperature during storage (Ranjan et al., 2017)[9].

1.3 Preparation and delivery
Preparation of pmma cement involves the mixing of the powder and liquid component in a container or a vessel. The liquid part should be added to the powder and then mixed thoroughly using a inert device until the powder is completely saturated in the liquid.

The preparation of bone cement involves four different phases: mixing, waiting, working and setting. Mixing phase is the initial phase that involves mixing of powder and liquid component until a saturated paste is formed. Waiting phase is the phase during which the cement attains the required viscosity for application. Working phase is the actual working time during which the cement is applied to the bone or used for prosthesis preparation and setting phase is the hardening phase, beyond which the cement cannot be manipulated. All these phases are influenced by environmental conditions like temperature and humidity.

The prepared bone cement can be applied to the site of interest in a number of ways. Sterile syringe applicator can be used for application to bone defects and fracture gaps when the cement is in its low viscosity state. Once the cement turns into a doughy mass it can be applied manually to the required site. For preparation of prosthesis, the cement is poured into the suitable mould while in its liquid state and allowed to set. Viscosity of the bone cement affect the handling characteristics, handling time and its penetration into the cancellous bone and therefore the quality and longevity of the fixation achieved. Optimal viscosity helps the cement to penetrate the bone for good attachment (Ranjan et al., 2017)[9].

2. Veterinary application of bone cement
Polymethylmethacrylate bone cement was introduced in veterinary orthopaedics for hip arthroplasty and joint fixation. It is the most common commercially available material to fix cemented prosthesis to the host bone (Juszczzyk et al., 2008)[5]. Good stability of fracture site enhances early weight bearing, functional limb usage and accelerated callus formation thereby helping in earlier return to normal activity. Thus pmma bone cement can be used as a filling material in bone gaps or fracture gaps to enhance the fracture stability thereby promoting earlier weight bearing and functional use of limb. It can also be used as bone replacement material in cases of pathogenic bone loss and in cases where osteogenesis is delayed as in old age. The metallic implants used for fracture fixation like intramedullary pins, plates and screws suffer from serious failures like pin migration, pin loosening, screw and implant failure. Polymethylmethacrylate bone cement can be thus be used as stabilizing agent and when used in combination with metallic implants can be used to attach the implant to the host bone thereby preventing the failure of implants.

PMMA bone cement can be moulded into different shapes and sizes and hence the potential of polymethylmethacrylate for various applications are enormous. PMMA confers to the shape of the surroundings, allows even distribution of implant loads and forms a strong mechanical bond with the implants (Kim et al., 2004)[6]. The formed bone cement is hard and at the same time light weight in nature and thus are used for artificial prosthesis preparation like femur head and bone, acetabulum and implant systems. The other reported applications of bone cement includes use in arthroplasty, rimplacment of osteoporotic bones, hip endoprosesis, hip replacement and Cranioplasty (Arora et al., 2011)[11]. It has also been used to prepare plates which along with screws are used for mandibular fracture repair in dogs. Beaver et al. (1996)[2] used pmma bone cement in combination with bone screws for repair of fracture luxations of 7th lumbar vertebrae and reported that it provided an effective and practical means of stabilisation Bioactive bone cements are being prepared nowadays to have sufficient penetration of the cement into cancellous bone for adequate anchorage of implant. For bioactivation, certain agents like calcium phosphate, hydroxyapatite and bioactive glass ceramics have been used. This improves the implant holding capacity of the cement as well as accelerates bone healing process.

3. Advantages and side effects of bone cement
Cement augmentation is reported to enable faster rehabilitation as the strength of the cement makes it possible to allow full weight bearing earlier than conventional metal implants alone (Larsson, 2006)[8]. PMMA can be used to increase the implant stability imparted by the fixation construct (Scolaro and Lackman, 2014)[10]. In addition antibiotics can be incorporated in the bone cement during its preparation thereby providing an aseptic media for internal application. Gentamicin and tobramycin antibiotics are the most commonly and commercially used antibiotics along with pmma cement (Sharifi et al., 2002)[11]. PMMA thus can act as a scaffold to deliver antibiotic preparations in infective areas. Main disadvantage in the use of pmma bone cement is attributed to its exothermic reaction during curing, the inability of the cement to be remodelled, the risk of inhibiting fracture healing and difficulty in removing pmma if revision surgery is required (Larsson, 2006)[8]. The most frequent adverse reactions reported with acrylic bone cements reported in humans include transitory fall in blood pressure, elevated serum gamma-glutamyl transpeptidase, thrombophlebitis,
superficial or deep wound infections, short term cardiac conduction irregularities and heterotrophic new bone formation (Ranjan et al., 2015) [9].

4. Future perspectives
Since Charnley introduced PMMA bone cement for prosthesis fixation, it has been used widely in orthopaedic surgery as it achieves good stabilisation of implants by mechanical interlocking (Fujita et al., 1998) [4]. Preparation of bioactive bone cements have been a recent area of interest by combining the strength of polymethylmethacrylate along with the osteoinductive and osteoconductive potentials of natural bone powder like hydroxyapatite, calcium phosphate, bio glass and chitosan. Presentation of pmma bone cement in a much easier mixing and applicable forms and in smaller quantities required for veterinary use have to developed. More research is needed in the field of nanoparticle additives to bone cement, enhanced bone cement interface and other developments in quest for improving the quality and eliminating or reducing the undesired side effects of bone cement (Ranjan et al., 2017) [9]. Many efforts have been made to improve the long term result of bone cement by either enhancement of the mechanical properties of pmma by fibre reinforcement or vacuum mixing and improvement of bone-cement interface through development of bioactive bone cement (Fottner et al., 2015) [3].

5. Conclusion
Accurate bone cement mixing and precise application techniques are critical to ensure the stability and longevity of the prosthesis (Ranjan et al., 2017) [9]. PMMA bone cement has numerous potentials but suffers serious disadvantages due to its adverse effects. Yet pmma bone cement have been found efficient to stabilise fractures, to hold implants against the bone, treatment of vertebral fractures, application in hip arthroplasty and osteoporotic bones and in preparation of various prosthesis for internal applications. Research is still required in this field to identify novel applicability of bone cement and in development of bone cements with less adverse effects and toxicity.

6. References