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BONE CEMENT - BOON OR BANE (AN OVERVIEW)

Orthopaedics

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KEYWORDS

BONE CEMENT

Polymethyl methacrylate (PMMA), is commonly known as bone cement, and is widely used for implant fixation in various Orthopedic and trauma surgery. In reality, "cement" is a misnomer because, the word cement is used to describe a substance that bonds two things together. However, PMMA acts as a space-filler that creates a tight space which holds the implant against the bone and thus acts as a 'grout'.[1] Bone cements have no intrinsic adhesive properties, but they rely instead on close mechanical interlock between the irregular bone surface and the prosthesis. Other types of commercially available bone cement like calcium phosphate cements (CPCs) and Glass polyalkenoate (ionomer) cements (GPCs) are successfully used in a variety of orthopedic and dental applications. CPCs are bio resorbable and biocompatible, but are mainly used in cranial and maxillo-facial surgeries because of their low mechanical strength.[2] HistoryThe pioneering work on PMMA technology is widely credited to German chemist Dr. Otto Rohm. In 1933, he patented Plexiglas, a PMMA product used in submarine periscopes and airplane canopies. This led to a sharp increase in demand and interest before and during the war. Kulzer (1936) found that a dough made by mixing his pulverized PMMA powder and liquid monomer hardened when he added benzoyl peroxide and heated it to 100°C in a stone mold, making it malleable[4]. His first clinical use of this PMMA mixture was in 1938, for the purpose of plugging a skull defect in a monkey. Surgeons used the heat-stable polymer Paladon 65 to close a human skull defect. This material was assembled into sheets in the laboratory and then molded in the operating room[4]. His modern day PMMA bone cement dates back to a patent by Degussa and Kulzer (1943). The patent described how MMA polymerizes at room temperature upon the addition of co-initiators (eg tertiary aromatic amines). Dentists were the first to use this technology in dental fixatives and dental instruments. British surgeon Dr. David Martin is widely credited for the first use of bone cement in orthopedics. By John Charnley using "Dentacryl" for total hip arthroplasty in 19585. Initial clinical results were unsatisfactory due to mechanical and biological reasons for both the cement and the loading platform[4]. Dr. Charnley developed a new product called "bone cement" (Plexiglas) with more adaptive biological properties, which he actively marketed to the global orthopedic community. American orthopedic surgeon trained under Dr. Charnley learned groundbreaking techniques at Wrightington Hospital[7]. When these surgeons returned to the United States, they often brought back bags of bone cement, but this illegal trade began in the mid-1970s when the Food and Drug Administration approved the use of bone cement technology in the United States.Component PMMA is an acrylic polymer made by mixing two sterile ingredients (Table 1).A liquid MMA monomer and a powdered MMA-styrene copolymer.[8] When the two components are mixed, the liquid monomer polymerizes around the prepolymerized powder particles and hardens to form PMMA.An exothermic reaction produces heat.

Constituents of bone cement.

Powder	Liquid
I) Polymer: Polymethyl methacrylate/co-polymer (PMMA)	I) Monomer: Methyl methacrylate (MMA)
II) Initiator: Benzoyl peroxide (BPO)	II) Accelerator: N, N-Dimethyl para-toluidine (DMPT)/di(Methyl para-toluidine (DMpt)
II) Radio-opacifier: Barium sulphate (BaSO4)/Zirconia (ZrO2) III)	Stabilizer: Hydroquinone
V) Antibiotics (e.g. Gentamycin)	

PMMA, along with the presence of various additives, imparts many physical and chemical properties to the mixture.[9] Premature polymerization of liquid components may occur when exposed to light or high temperatures. Therefore, hydroquinone is added as a stabilizer or inhibitor to prevent premature polymerization. An initiator, dibenzoyl peroxide (BPO), is added to the powder, and an accelerator (usually N,N-dimethyl-p-toluidine (DmpT)) is added to the liquid to facilitate polymerization of the polymer and monomer at room temperature. (cold hardening cement).

A contrast agent is added to make the cement radiopaque. Commercial cements use zirconia (ZrO2) or barium sulfate (BaSO4). Zirconium dioxide is 100 times less soluble than barium sulfate and has little effect on the mechanical properties of cement.

The cement heats up during the exothermic radical polymerization. This heat of polymerization reaches a temperature of about 82-86 °C in the body. The reason for the low polymerization temperature in the body is the relatively thin layer of cement, which should not exceed 5 mm, and the large surface of the prosthesis and the heat dissipation due to the blood flow.[10]

Antibiotic Bone Cement

Bone cement has proven particularly useful because certain active ingredients, such as antibiotics, can be added to the powder component. This makes bone cement a state-of-the-art drug delivery system that delivers needed drugs directly to the surgical site. The local active substance levels of bone cements are significantly below the clinical routine dosages for systemic single injections. Research has shown that adding various types of antibiotics to bone cement, in quantities less than 2 g per standard packet of bone cement, does not adversely affect some of the cement's mechanical properties (compressive or diametrical tensile strengths), although quantities exceeding 2 g did weaken them.[11] Various antibiotics have been successfully mixed and used with bone cements like Gentamycin, Tobramycin, Erythromycin, Cefuroxime, Vancomycin, Colistin etc. The basic requirement, being that the mixable antibiotic should be heat resistant and should last for longer duration of time.

Gentamycin, when used in combination with tobramycin, shows a synergistic effect, with a 68% greater elution of tobramycin (P = 0.024), and 103% greater elution of vancomycin from the bone cement (P = 0.007), compared to controls containing only one antibiotic.[12]

van Staden in his study reported that Bacteriocins may be a possible alternative to antibiotics incorporated into bone cement. The in vitro results of the study showed that bacteriocins incorporated into brushite cement did not significantly alter the characteristics of the matrix and that the peptides were released in an active form. Finally, brushite cement supplemented with nisin F was shown to control S. aureus infection in mice [13].

Silver-containing nanoparticles have also been shown to be effective antimicrobial agents that can be added to bone cement[14]. Vitamin E supplementation (10%) showed beneficial effects on free radical oxidative and thermogenic activity, although the reduction was modest (<5%).). Tensile strength .[15]

Compared to intramuscular administration, systemic concentrations of gentamicin in bone cement are low, typically peaking at <1 µg/mL (<10%). Systemic levels are no longer detectable 7 days after administration. After administration of bone cement, urinary

gentamicin concentrations range from 10 µg/mL initially to 1–2 µg/mL after 7 days.

Different bone cements have different chemical formulations, resulting in different antibiotic bone cements with different handling characteristics suitable for a wide range of clinical needs and surgical techniques.

3.3. Curing process

The curing process is divided into four phases.
a) mixing, b) bonding/holding, c) machining, and d) curing.

Mixing can be done manually or using centrifugation or vacuum techniques.

Bone cement is heat sensitive. Temperature increases or decreases (either ambient temperature and/or cement components and mixing equipment) above the recommended temperature of 23°C (73°F) will affect cement handling properties and curing time. Manual work and body temperature will reduce the final cure time. Humidity fluctuations affect the handling properties and curing time of cement. It is recommended to store unopened cement components at 23°C (73°F) for at least 24 hours prior to use. Vacuum mixing the cement can also reduce the hardening time of the cement.

High viscosity cements may be pre-chilled for use in mixing systems to facilitate mixing and extend working time. Also, the setup time will be longer. Relative humidity can also affect handling characteristics. For this reason, cement processing and hardening times may differ between winter and summer.In contrast to the polymerization reaction of PMMA, calcium phosphate cements harden by a process of dissolution and precipitation, where the precipitated crystals intertwine to harden[16].

Stages of bone cement:

Mixing Stage – The mixing stage describes the time it takes for the powder and liquid to mix thoroughly. Benzoyl peroxide is released into the mixture as the monomer begins to dissolve the polymer powder.

Waiting Phase/Dough Time – During this phase, which usually lasts a few minutes, the cement reaches a manageable viscosity (ie it can be handled with gloves without being sticky). At most of this stage, cement is a sticky dough. Dough time is the time from the start of mixing until the cement stops sticking to surgical gloves. Under typical conditions (23°C to 25°C, 65% relative humidity), the dough time for most bone cements is 2-3 minutes after mixing begins. Prior to this point, after the ingredients are well mixed, the bone cement can be filled into a syringe, cartridge, or injection gun to aid application.

Working Phase/Working Time - The working phase is the period during which the cement can be manipulated to place the prosthesis. During the working phase, the viscosity increases and the cement heats up. The implant must be implanted before the working phase is finished. Processing time is the time between dough and curing time, typically 5-8 minutes. Using a mechanical insertion aid such as a syringe or cartridge will extend this time by 1-1.5 minutes.

Hardening Stage – At this stage the cement is fully hardened (cured) and the temperature reaches its peak. As the cement cools to body temperature, volumetric shrinkage and heat shrinkage follow. Curing is affected by cement temperature, operating room temperature, and patient body temperature. Setting time is the time from the start of mixing until an exothermic reaction heats the cement to a temperature midway between ambient and maximum (i.e. 50% of maximum), typically about 8-10 hours. minute. The temperature rise is due to the conversion of chemical energy to thermal energy during polymerization. [17]

METHODS OF APPLICATION

There are several methods of placing cement on bone or articular surfaces[18].

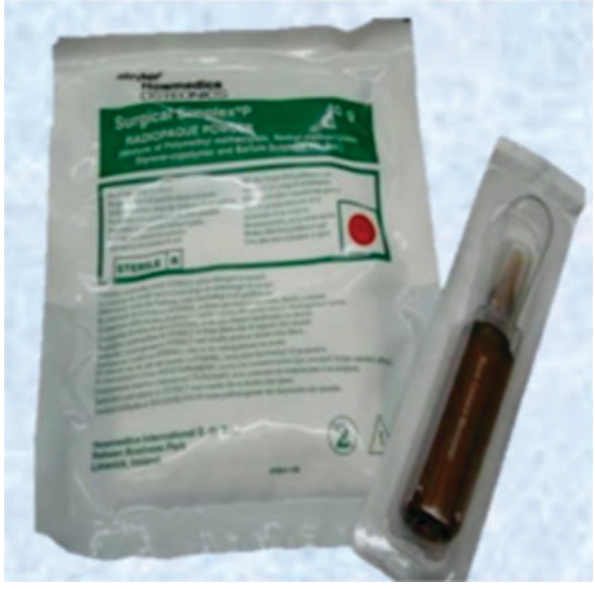
Digital

All antibiotic bone cements can be applied digitally. Cement is carefully and thoroughly mixed to minimize air inclusions. Once the dough has formed, the surgeon should wait until the cement stops sticking to the glove and the surface is dull rather than shiny. Then take the cement with your gloved hands and knead it thoroughly. Premature introduction of cement can lead to hypotension in the patient and must be avoided at all costs. Importantly, this stage occurs at different times for different types of cement.

The timing of cement application and prosthesis placement is at the discretion of the surgeon and depends on the surgical technique used. In general, implant placement should be delayed until the cement has developed sufficient viscosity to withstand excessive displacement through the implant. However, implant placement should not be delayed so much that the hardening of the cement risks preventing the surgery from being completed. Once the implant is placed, it must be held firmly in place so that it does not move, and pressure must be maintained until the cement has fully hardened. Excess bone cement must be removed before the cement is fully cured.

2. Syringe application

Antibiotic gentamicin bone cement can be applied using a suitable cement gun and syringe. The surgeon must make an empirical judgment when the cement has reached the correct viscosity for extrusion. This only happens after the cement has formed a dough. A small amount of cement should be extruded from the syringe and visually assessed to ensure that the surface of the cement appears dull and has stopped excessive flow due to gravity. Prior to extrusion, it is recommended to insert a cement restrictor into the prepared bone cavity to the desired depth[19]. Placement of bone cement into the prepared bone cavity should be done retrograde. Once the cavity is filled, it is recommended to apply sufficient pressure and maintain it until it hardens.



3. Vacuum Mixing & Delivery

Adopted from the dental field, vacuum mixing was developed for bone cement in the early 1980s. Vacuum mixing reduces the porosity of the bone cement, reducing monomer evaporation and exposure in the operating room.

Mixing and collecting cement under vacuum results in a homogeneous mixture without affecting cement viscosity and other properties. [20]

4. Pressure

The pressure on the cement must be greater than the blood pressure so that the cement is not forced out of the bone. Pressure must be applied until the viscosity of the bone cement is high enough to withstand the blood pressure. Many studies have stated that pressurization promotes bone penetration, improves the bone-cement interface, and increases cement fatigue strength. When the cement in the femur is pressurized, it extrudes a mark on the greater trochanter (the so-called "sweating trochanteric sign") as a positive sign of pressurization.[21]

5. Viscosity

The polymerization process is initiated by mixing powder and liquid components. During the reaction, the viscosity of the cement increases slowly at first, but then increases more rapidly. Studies have shown that high-viscosity cements provide better prosthesis fixation than low-viscosity cements[22].

Bone cements can be classified into his three types:
Low viscosity, medium viscosity and high viscosity.
Low viscosity: These cements have a long liquid or mixed phase, which reduces working time. Therefore, when using low-viscosity cement, the processing time must be strictly adhered.

High viscosity: These cements have a short mixing stage and quickly lose their stickiness. This lengthens the working phase and gives the surgeon more time to apply. The ideal viscosity is high enough to prevent the cement from mixing with blood or fat/bone material from the implant area, but low enough to allow sufficient penetration into the bone.

6. Cement restrictor

The use of intramedullary plugs in cement-retained total joint arthroplasty is now considered routine by most surgeons. Small bone fragments or cement restrictors can be used to occlude the stem to achieve good filling and compression within the hip joint. The limiter should be placed within 2 cm of the tip of the shaft. The main purpose of occluding the intramedullary canal during total hip arthroplasty is to enhance cement penetration into the cancellous bone proximal to the intramedullary occlusion. This improves penetration and increases stability of the prosthesis.

CEMENTING TECHNIQUE EVOLUTION

Overall, cementation advances can be classified into 'first generation' to 'third generation' techniques, depending on changes in bone bed preparation, cement preparation, and cement delivery. [23,34]

1. First generation cementing technology

Cement was manually mixed in the intestine. The femoral canal was minimally prepared and the cancellous bone was left in place. The canals were irrigated and aspirated prior to applying digital cement. The prosthesis was then inserted into the femoral canal. In the 1980s, these techniques were refined. Measures have been taken to reduce the porosity of cement and thereby extend the fatigue life. Cement compression was introduced to improve cement osseointegration, and the importance of a good cement mantle around the prosthesis was more clearly understood.

2. Second generation cementing technology

All cancellous bone was removed as close as possible to the endosteal surface and a distal cement limiting device was also used. A pulsatile irrigation, compaction, and drying of the femoral canal is performed, followed by retrograde placement of cement using a cement gun. The prosthesis is again manually positioned[25]. Further refinements have led to the development of the 3rd generation cementation technology.

3. Third generation cementing technology

Cement is now manufactured using vacuum centrifugation to further reduce porosity. Flush the femoral canal with pulsatile lavage and fill with adrenaline-saturated swabs. After placing the cement retrograde, the cement is pressurized. Finally, insert the prosthesis with distal and proximal centerers to ensure a uniform cement mantle (4th generation).

Precautions and side effects

Hypotensive episodes and cardiac arrest have been reported during cement placement[25].

Bone compression and extensive irrigation from bone marrow removal has been associated with the development of pulmonary embolism, and this risk was found to be increased in patients with severe osteoporosis and those diagnosed with femoral neck fractures. I'm here. Reaming of the medullary canal can have a similar effect on mean arterial pressure as bone cement placement. When digitally placing cement, the medullary canal must be aerated. Premature placement of bone cement can cause a drop in blood pressure, which is unproven but related to the availability of methyl methacrylate on the device surface. This hypotension, in addition to accidental or intentional hypotension, can cause arrhythmias or ischemic myocardium. However, one report limits the potential mortality risk associated with the use of cement-retained implants to the early postoperative and perioperative period[27].

The antihypertensive effect of methyl methacrylate is enhanced when patients suffer from hypovolemia.

The most commonly reported side effects of acrylic bone cement are:

- Temporary reduction in blood pressure.
- Elevated serum gamma-glutamyl transpeptidase (GGTP) up to 10 days after surgery.
- Thrombophlebitis.
- Looseness or misalignment of the prosthesis.
- Superficial or deep wound infections.
- Trochanteric bursitis.
- Short-term cardiac conduction abnormalities.
- Heterotopic new bone formation.
- Trochanteric separation.

BCIS (bone cement implantation syndrome)[28,29] is characterized by a constellation of clinical features including hypoxia, hypotension, arrhythmia, increased pulmonary vascular resistance (PVR) and cardiac arrest. It is most commonly associated with, but not limited to, total hip replacement surgery[28]. Usually he in surgery occurs in one of five stages. Reaming the femur, cementing the acetabulum or femur, inserting a prosthesis, or reducing the joint. It is an important cause of intraoperative mortality and morbidity in patients undergoing cement-retained total hip arthroplasty and can also present in the postoperative period in milder forms causing hypoxia and confusion.

- Bronchospasm
- Adverse tissue reactions.
- Hematuria.
- Dysuria.
- Bladder fistula
- Hypoxemia.
- Arrhythmia
- Focal neuropathy
- Local vascular erosion and occlusion
- The pain is temporarily exacerbated by the heat released during polymerization.
- Delayed entrapment of the sciatic nerve by pushing the bone cement beyond its intended coverage.
- Intestinal obstruction due to ileal adhesions or strictures due to heat released during cement polymerization.

Pathophysiology of BCIS [30]

Increased intramedullary pressure with prosthesis insertion and cementation

⬇

Push bone marrow contents into the circulation and cause a pulmonary embolism

⬇

This causes hypoxia and pulmonary vasoconstriction.

⬇

Increased right ventricular (RV) afterload

⬇

Ultimately there is right ventricular failure with systemic hypotension.

Donaldson et al. (2009) [31] defined a severity classification of BCIS (Grade 1, 2, and 3)

- Grade 1: moderate hypoxia (SpO_2<94%) or hypotension [fall in systolic blood pressure (SBP) >20%].
- Grade 2: severe hypoxia (SpO_2<88%) or hypotension (fall in SBP >40%) or unexpected loss of consciousness.
- Grade 3: cardiovascular collapse requiring CPR.
- Various patient related risk factors that are associated with bone cement implantation syndrome are old age, male sex, osteoporosis, use of diuretics, poor preexisting physical reserve, impaired cardiopulmonary function, pre-existing pulmonary hypertension , high ASA score, congestive heart failure , chronic obstructive pulmonary disease

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