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Bone cement

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Abstract
Polymethyl methacrylate (PMMA) bone–cement was introduced in the 1960s for fixation of total hip arthroplasty replacement components. The use of PMMA bone cement has been a key factor in the advent of joint replacement as a surgical option. Long-term results of cement fixation for hip and knee arthroplasty have been extremely good. Although the use of PMMA bone–cement has enabled long-term survival of joint arthroplasty implants, there has been concern about aseptic loosening.Despite revolutionary changes in joint replacement technology for the treatment of hip and knee arthritis, the use of PMMA bone cement in its intraoperative application has not significantly changed. Bone cement implantation syndrome (BCIS), It is an important cause of intraoperative mortality and morbidity in patients undergoing cemented hip arthroplasty and may also be seen in the postoperative period in a milder form causing hypoxia and confusion. It is possible to identify high risk groups of patients in which avoidable morbidity and mortality may be minimized by surgical selection for uncemented arthroplasty. Invasive anaesthetic monitoring should be considered during cemented arthroplasty in high risk patients.

Keywords: Bone cement, Joint replacement, Arthroplasty, Antibiotic, Viscosity, Bone cement implantation syndrome

Introduction
Polymethylmethacrylate (PMMA) bone cement is an essential component in many total joint arthroplasty procedures. In a cemented arthroplasty, the main functions of the cement are to immobilize the implant, transfer body weight and service loads from the prosthesis to the bone, and increase the load-carrying capacity of the prosthesis-bone cement-bone system. The term “cement,” however, is misleading since bone cement acts more like a grout, filling in space in order to create a tight space to hold the implant against bone. Good quality cement is essential for long-term implant survival. Accurate bone cement mixing and precise application techniques are critical to ensuring the stability and longevity of the prosthesis. Since bone cement is prepared and used in the operating room environment, it is important that all perioperative personnel recognize the unique safety considerations that are related to its preparation and its use.

Components of Bone Cement
PMMA bone cements are usually supplied as two-component systems made up of a powder and a liquid. These two components are mixed at an approximate ratio of 2:1 to start a chemical reaction called polymerization, which forms the polymethylmethacrylate (PMMA) cement.

Powder components
- Copolymers beads based on the substance polymethylmethacrylate (PMMA)
- Initiator, such as benzoyl peroxide (BPO), which encourages the polymer and monomer to Polymerize at room temperature
- Contrast agents such as zirconium dioxide (ZrO2) or barium sulphate (BaSO4) to make the bone cements radiopaque and
- Antibiotics (eg, gentamicin, tobramycin).

Liquid components

- A monomer, methylmethacrylate (MMA)
- Accelerator (N,N-Dimethyl para-toluidine) (DMPT)
- Stabilizers (or inhibitors) to prevent premature polymerization from exposure to light or high temperature during storage

Chlorophyll or artificial pigment sometimes added to cements for easier visualization in case of revision.

There is a difference between PMMA bone cement and PMMA; however, many healthcare personnel use the terms interchangeably and PMMA has become shorthand for "bone cement". However, PMMA is the substance from which copolymers are derived for the powder component. When the copolymer powder is mixed with the MMA monomer liquid, polymerization occurs and PMMA bone cement is created.

Types of Bone Cement

There are several types of bone cement in regards to its viscosity. Viscosity affects the bone cement's handling characteristics, handling time, and its penetration into the cancellous bone and therefore, the quality and longevity of the fixation achieved. Optimum viscosity helps cement penetrate the bone for good attachment, i.e., the cement must be liquid enough to be delivered and then to penetrate the interstices of cancellous bone. There are two requirements for bone cement viscosity during the working phase: first, viscosity must be sufficiently low to facilitate the delivery of the cement dough from the syringe to the bone site; secondly, it must penetrate into the interstices of the trabecular bone. On the other hand, the viscosity of the bone cement should be sufficiently high to withstand the back bleeding pressure, thereby avoiding the risk of the inclusion of blood into the cement. Different type of bone cement according to viscosity describe below.

Low viscosity cements: These cements remain in a runny state for a much longer period of time as compared to medium or high viscosity cements. Typically they have a long waiting phase. The true working time in which the cement can be picked up with a gloved hand usually is short, and the setting time can vary.

Medium viscosity cements: These types of cements can offer versatility for various types of procedures. Medium viscosity cements are both low and high in viscosity, depending on the time at which the cement is delivered. Medium viscosity cements are considered to be dual phase cements. They begin in a low viscosity state while being mixed, which allows for the easy and homogenous mixing of the powder and the liquid.

High viscosity cements: These types of cements primarily are comprised of PMMA with no methylmethacrylate-styrene-copolymer content; they have no runny state at all. Immediately after mixing, the cement is doughy and ready to apply by hand to the implant surface. The working time for high viscosity cements needs to be closely monitored; it is not always easy to determine the end of the working time before it is too stiff to interdigitate with the bone.

Antibiotic Cements

Not all antibiotics are suitable for use in bone cements. The following bacteriologic and physical and chemical factors should be considered in the choice of an antibiotic

- Preparation must be thermally stable and able to withstand the exothermic temperature of polymerization.
- Must have broad antimicrobial coverage.
- Must be available as a powder.
- Must have a low incidence of allergy.
- Must not significantly compromise mechanical integrity.
- Must elute from the cement over an appropriate period of time.

Gentamicin and tobramycin are the only antibiotics available in U.S. commercial antibiotic bone cement products; tobramycin is the most often used and studied antibiotic added to cement worldwide, but gentamicin is more common in the United States. Other antibiotics (singly or in combination with other antibiotics) that have been studied include vancomycin, cephalothin, clindamycin, meropenem, teicoplanin, ceftazidime, imipenem, piperacillin, and ciprofloxacin.

Polymerization

Polymerization is a chemical reaction in which two or more small molecules combine to form larger molecules that contain repeating structural units of the original molecules. In the case of bone cement, the polymerization process starts when the copolymer powder and monomer liquid meet, reacting together to produce an initiation reaction creating free radicals that cause the polymerization of the monomer molecules. The original polymer beads of the powder are bonded into a dough-like mass, which eventually hardens into hard cement.

The polymerization process is an exothermic reaction, which means it produces heat. With a maximum *in vivo* temperature of 40 °C to 47 °C, this thermal energy is dissipated into the circulating blood, the prosthesis, and the surrounding tissue. Once polymerization ends, the temperature decreases and the cement starts to shrink.

Phases And Times

The polymerization process can be divided into four different phases:

Mixing, waiting, working, and setting Time. Dough Time and Setting Time are measured from the beginning of mixing; Working Time is the interval between Dough Time and Setting Time.

Mixing Phase

The mixing phase represents the time taken to fully integrate the powder and liquid. As the monomer starts to dissolve the polymer powder, the benzoyl peroxide is released into the mixture. This release of the initiator benzoyl peroxide and the accelerator DMPT is actually what causes the cement to begin the polymerization process. It is important for the cement to be mixed homogeneously, thus minimizing the number of pores.

Waiting Phase/Dough Time

During this phase, typically lasting several minutes, the cement achieves a suitable viscosity for handling (I.e, can be handled without sticking to gloves). The cement is a sticky dough for most of this phase.

Dough time is the time point measured from the beginning of mixing to the point when the cement no longer sticks to surgical gloves. Under typical conditions (23°C-25°C, 65% relative humidity), dough time is 2-3 minutes after beginning of mixing for most bone cements. Before this time point, after the components are well mixed, the bone cement may be loaded into a syringe, cartridge, or injection gun for assisted application.

Working Phase/Working Time

The working phase is the period during which the cement can be manipulated and the prosthesis can be inserted. The working phase results in an increase in viscosity and the generation of heat from the cement. The implant must be implanted before the end of the working phase. Working time is the interval between the dough and setting times, typically 5-8 minutes. The use of mechanical introduction tools, such as syringes and cartridges, extends this time by 1 to 1.5 min.

Setting Phase/Setting Time

During this phase, the cement hardens (cures) and sets completely, and the temperature reaches its peak. The cement continues to undergo both volumetric and thermal shrinkage as it cools to body temperature. Hardening is influenced by the cement temperature, the operative room temperature, and the body temperature of the patient. Setting time is the time point measured from the beginning of mixing until the time at which the exothermic reaction heats the cement to a temperature that is exactly halfway between the ambient and maximum temperature (ie, 50% of its maximum value), usually about 8-10 minutes. The temperature increase is due to conversion of chemical to thermal energy as polymerization takes place.

Factors that affect dough, working, and setting times include the following

- **Mixing Process:** Mixing that is too rapid can accelerate dough time and is not desirable since it may produce a weaker, more porous bone cement.
- **Ambient Temperature:** Increased temperature reduces both dough and setting times approximately 5% per degree Centigrade, whereas decreased temperature increases them at essentially the same rate.
- **Humidity:** High humidity accelerates setting time whereas low humidity retards it.

Pmma Bone Cement Mixing and Application

Manual Mixin

The liquid was injected into a powder bag and the two components were mixed by kneading. As mixing techniques evolved, an open bowl was used to mix the cement. The liquid and powder were poured into a plastic or stainless steel bowl and then mixed together with a spatula. Early in the use of open bowl mixing, exposure to the resulting noxious fumes created serious safety concerns. A certain amount of porosity in the final material remains unavoidable with conventional hand mixing techniques today, due to the air introduced by stirring during hand spatulation. In order to reduce both the harmful fumes as well as the introduction of air into the cement mixture, the closed bowl technique, using a paddle mixing system and wall suction to evacuate the fumes, was developed

Centrifugation

In this technique, cement was first mixed manually and then subjected to centrifugation to eliminate any air inclusions introduced during mixing and thus reduce porosity. The technique required chilling the liquid monomer prior to mixing in order to negate the shortening effect of centrifugation on setting time. The resulting low-viscosity mixture then was introduced into a cement syringe, which was centrifuged at high speed for a short period of time. The method succeeded in reducing porosity.

Vacuum Mixing

Mixing under vacuum was introduced to reduce exposure to fumes while also improving tensile strength and fatigue life of bone cement with a vacuum mixing system, the cement is mixed in a syringe, bowl, or cartridge. All of these systems consist of an enclosed chamber connected to a vacuum source (eg, wall suction or a dedicated vacuum pump). All ingredients are added and mixed while the system is closed.

The methods for application of bone cement include hand packing, injection, and gun Pressurization

Hand packing

The original method for hip arthroplasty was hand packing, where cement in the femoral canal was finger packed. The proximal end was packed with cement by pressing with the fingers or thumbs; this pressurization forced the cement into the bone interstices. Cementing in total knee arthroplasty is still commonly hand-packed because the surfaces are readily visualized, which makes the application with pressure by hand feasible.

Injection

Syringes are used to apply, or inject, the cement.

Gun pressurization

Injection of the cement with a gun offers a mechanical advantage that allows the surgeon to force more cement into the interstices of the bone via higher pressurization. The pressurization tips of these devices allow more cement to be forced tightly into the bone while also preventing overflow.

Caution and Adverse Effect

Hypotensive episodes and cardiac arrest have been reported during cement insertion.

The most frequent adverse reactions reported with acrylic bone cements are:

- Transitory fall in blood pressure.
- Elevated serum gamma-glutamyl-transpeptidase (GGTP) upto 10 days post-operation.
- Thrombophlebitis.
- Loosening or displacement of the prosthesis.
- Superficial or deep wound infection.
- Trochanteric bursitis.
- Short-term cardiac conduction irregularities.
- Heterotopic new bone formation.
- Trochanteric separation

Other known adverse effects

BCIS (Bone cement implantation syndrome) is characterized by a number of clinical features that may include hypoxia, hypotension, cardiac arrhythmias, increased pulmonary vascular resistance (PVR) and cardiac arrest.

Signs and symptoms of bone cement implantation syndrome may include one or more symptoms, including but not limited to:

- hypotension
- pulmonary hypertension
- increased central venous pressure
- pulmonary edema
- bronchoconstriction
- anoxia or hypoxemia
- decreased partial end tidal carbon dioxide
- cardiac dysrhythmia or arrhythmia
- cardiogenic shock

- transient decrease in arterial oxygen tension
- hypothermia
- thrombocytopenia
- cardiac arrest
- sudden death

Drawbacks of bone cement

One of the major drawbacks of bone cement in joint replacement is cement fragmentation and foreign body reaction to wear debris, resulting in prosthetic loosening and periprosthetic osteolysis. The production of wear particles from roughened metallic surfaces and from the PMMA cement promotes local inflammatory activity, resulting in chronic complications to hip replacements.

Bone cement generates heat as it cures and contracts and later expands due to water absorption. It is neither osteoinductive nor osteoconductive and does not remodel. The monomer is toxic and there is a potential for allergic reactions to cement constituents

Conclusion

The knowledge about the bone cement is of paramount importance to all Orthopaedic surgeons. Although the bone cement had been the gold standard in the field of joint replacement surgery, its use has somewhat decreased because of the advent of press-fit implants which encourage bone in growth. The shortcomings, side effects and toxicity of the bone cement are being addressed recently. More research is needed and continues in the field of nanoparticle additives, enhanced bone cement interface and other developments in quest for improving the quality and eliminating or reducing undesired side effects of bone cement.

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