Bone cement and the implications for anaesthesia

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Key points

Bone cement is a radio-opaque compound composed of poly(methyl methacrylate) (90%) and a small quantity of radio-opaque crystals.

Antibiotic-loaded bone cement combined with systemic antibiotics provides the best prophylaxis against postoperative infection.

Bone cement implantation syndrome (BCIS) is poorly understood, and clinical features include hypoxia, hypotension, cardiac arrhythmias, and cardiac arrest.

The effects of BCIS can be moderated by the recognition of high-risk patients and modifications of surgical technique to reduce cardiopulmonary compromise.

Management of BCIS is mainly focused towards treating pulmonary arterial hypertension and right ventricular failure.

Poly(methyl methacrylate) (PMMA) was developed in 1928 and was first marketed under the name of ‘Plexiglas’. Since then, PMMA has been used in a huge number of applications, including transparent glass substitutes in windows, semiconductor research, and for the bodies of electric guitars. PMMA has a good degree of biocompatibility, which has made it an important component of replacement intraocular lenses, dentures, and dental filling composite materials. In orthopaedic surgery, PMMA bone cement is used to affix implants and to remodel lost bone.

The medical orthopaedic use of PMMA is universally credited to Sir John Charnley, who was inspired by his dentist to use dental acrylic for prosthetic fixation in total hip replacement (THR) procedures in 1957. In 1965, he began to use bone cement (CMW Bone Cement™) that was developed specifically for THRs rather than dental acrylic. Bone cement is now routinely used in a variety of orthopaedic procedures.

The microscopic structure of bone cement comprises two substances glued together. The so-called ‘pearls’ in bone cement consist of small particles of pre-polymerized PMMA, which are present as white powder. The second substance is a liquid monomer of methyl methacrylate (MMA). Both substances are mixed together in theatre after the addition of a catalyst that initiates the polymerization of the monomer fluid. When the bone cement hardens, the individual pearls are entrapped and glued within the net of the polymerized monomer, but no chemical binding occurs between the pearls and the polymerized monomer.

Antibiotics can be incorporated within the polymerized matrix in the form of a soluble powder that is subsequently released into the joint cavity.

Bone cement is used to fill all small openings in the spongy skeleton and to fill all of the hollows on uneven surfaces. This means that bone cement can be strongly adherent to the surface of the THR prosthesis (Table 1).

The role of antibiotics in bone cement

Data from the Scandinavian Joint Registries showed that antibiotic-loaded bone cement was used in 95% of revision hip or knee arthroplasties. In Norway, 48% of surgeons, compared with 85% of those in Sweden, used antibiotic-loaded bone cement for primary joint replacements. In the National Hip Replacement Outcome Project in Great Britain, 69% of the surgeons who responded stated that they used antibiotic-loaded bone cement in their primary THR procedures.

Antibiotic-loaded bone cement is a well-accepted adjunct for the treatment of an established infection. However, its role in the prevention of infection remains controversial. Many different antibiotics, including gentamicin, cefuroxime, vancomycin, and tobramycin, have been loaded into bone cement. In contrast to the treatment of infection, prophylaxis requires low doses of antibiotics in the bone cement. The use of low doses also avoids the adverse mechanical effects of the antibiotics on the cement. In general, low-dose antibiotic-loaded bone cement is defined as ≤1 g of powdered antibiotic per 40 g of bone cement.

Antibiotic-loaded bone cements have also been implicated as a cause of postoperative renal failure. This is a rare cause of postoperative renal failure as serum antibiotic levels after the placement of antibiotic laden bone cement remain below toxic levels; however, there have been recent case reports describing patients who developed acute renal failure after placement of aminoglycoside laden bone cement. The development of renal failure in these case reports was associated with pre-existing co-morbidities (which placed them at...
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Table 1 Composition of bone cement

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
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<tbody>
<tr>
<td>Poly(methyl methacrylate) (PMMA) (90%)</td>
<td>Powder polymer: pre-polymerized PMMA</td>
</tr>
<tr>
<td>Liquid monomer (MMA)</td>
<td>Initiator: dibenzoylperoxide</td>
</tr>
<tr>
<td>Activator: N,N-dimethyl-p-toluidine</td>
<td>Gentamicin, tobramycin, clindamycin</td>
</tr>
<tr>
<td>Radiographic contrast material (10%)</td>
<td>Zirconium dioxide or barium sulphate</td>
</tr>
</tbody>
</table>

Table 2 Potential disadvantages of antibiotic-loaded bone cement

<table>
<thead>
<tr>
<th>Area</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alteration in the mechanical and structural properties of the bone cement</td>
<td>Antibiotic resistance</td>
</tr>
<tr>
<td>Allergic reactions</td>
<td></td>
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<tr>
<td>Systemic toxicity</td>
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<tr>
<td>Cost implications</td>
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Thus, the use of antibiotic-loaded bone cement should follow national guidelines with careful monitoring of patients at high risk of developing renal failure (Table 2).

Bone cement implantation syndrome

Bone cement implantation syndrome (BCIS) is a poorly understood phenomenon and currently has no agreed definition. It is an important cause of intraoperative mortality and morbidity and is most commonly, but not restricted to, being associated with cemented hip arthroplasty. The clinical features of BCIS typically occur at the time of cementation, prosthesis insertion, reduction in the joint, or deflation of a limb tourniquet. A classification system for BCIS has been proposed according to its severity† as follows:

- **Grade 1**: moderate hypoxia ($pO_2 < 94\%$) or a decrease in systolic arterial pressure (SAP) > 20%.
- **Grade 2**: severe hypoxia ($pO_2 < 88\%$) or hypotension (decrease in SAP > 40\%) or unexpected loss of consciousness.
- **Grade 3**: cardiovascular collapse requiring cardiopulmonary resuscitation.

BCIS has a wide spectrum of clinical features that range from transient desaturation and hypoxia to cardiac arrhythmias and cardiac arrest at the time of cement deployment. Clinical reports and studies all demonstrate the presence of right ventricular failure secondary to increased pulmonary artery pressure (PAP) as the underlying cause of systemic hypotension and sudden cardiac arrest. The cause of the acute increase in pulmonary vascular resistance (PVR) remains uncertain. It may be due to deposition of cement or fat emboli or may be a result of systemic absorption of the volatile monomer. Regardless of the cause, the thin-walled and compliant right ventricle rapidly dilates and shifts of the interventricular septum to the left thereby reducing the volume of the left ventricular cavity. This occurs because the total volume of the heart cannot expand within such a rapid time frame, as it is constrained by the pericardium.

These changes cause an immediate decrease in left ventricular compliance, reduced ventricular filling, and cardiac output (CO). Studies in humans have demonstrated the presence of emboli in the cerebral circulation in patients undergoing cemented hip arthroplasty using transcranial Doppler imaging. This may occur as a result of the transpulmonary passage of the emboli or emboli passing through a patent foramen ovale, but none of the patients in these studies developed any neurological deficit. However, these emboli may be a contributory factor for postoperative delirium that commonly occurs in elderly patients (Table 3).

Aetiology and pathophysiology of BCIS

While the aetiology and pathophysiology of BCIS is poorly understood, several models have been proposed. First, the monomer-mediated model arose after it was demonstrated that circulating MMA monomers cause vasodilatation in vitro. However, this hypothesis is not supported in vivo, where the plasma MMA concentration after cemented hip arthroplasty is considerably lower than the concentration required to cause adverse pulmonary or cardiovascular effects.

The embolus-mediated model proposes two possible aetiologies: mechanical and mediator effects. According to the former, debris, including marrow, fat, cement particles, air, bone particles, and aggregates of platelets and fibrin, embolize to the right atrium, right ventricle, and pulmonary artery intraoperatively. High intramedullary pressure is the main causative factor for the release of these deposits into the circulation, and this has been confirmed in both in vitro and in vivo studies.

Furthermore, one study compared the incidence of embolic events using conventional vs modified cementing techniques in 120 patients undergoing THR procedures. The modification consisted of a suction catheter placed in the proximal femur to reduce the increase in intramedullary pressure during the insertion of the prosthesis. Embolic events were imaged during the insertion of the prosthetic stem in 93.4% of the patients with the use of the conventional cementing technique and 13.4% of the patients with the modified technique. It should be noted that the degree of cardiovascular compromise is not necessarily proportional to the degree of the embolic load.

In terms of the mediator effects, vasoactive or pro-inflammatory substances are released as a result of systemic embolization of the bone cement. These can directly increase PVR by raising the blood levels of thrombin and tissue thromboplastin. Other
mechanisms that cause mediator release include mechanical stimulation or endothelial damage by the cement emboli, which induce reflex vasoconstriction through the release of endothelial mediators.

These mechanisms result in increased PVR, which is responsible for V/Q mismatch resulting in hypoxaemia. C3a and C5a are potent mediators of vasoconstriction and bronchoconstriction. An increase in C3a and C5a levels has been demonstrated in cemented hemiarthroplasty in some studies; this may play a role in pulmonary vasoconstriction and the desaturation seen during cement implantation. Raised levels of histamine have also been found in patients who were hypotensive after cemented hip arthroplasties, which could be either the result of a hypersensitivity reaction or a direct effect of the cement.

In vitro studies found that the quantity of emboli and the severity of cardiorespiratory changes observed during total hip arthroplasty with the use of bone cement were greater than those seen when cement was not used. A study that involved the use of transoesophageal echocardiography in humans showed that the insertion of the femoral component with cement caused more severe and more prolonged embolic cascades than the insertion of the component without cement. Intraoperative pulmonary shunt values increased significantly when the femoral component was inserted with cement, but the shunt values did not change when the component was inserted without cement. These findings suggest that patients who require a total hip arthroplasty, especially those who have underlying cardiorespiratory disease, may have less morbidity if the femoral component is inserted without cement than if it is inserted with cement.

Prevention of BCIS

The anaesthetist should be fully involved in the preoperative assessment of patients. This involves the identification of high-risk surgical patients before operation, the assessment and optimization of their cardiovascular reserve before surgery, and the appropriate use of this information to select the type of prosthesis, surgical procedure, and techniques in order to minimize the risk of cardiovascular complications.

Patient risk factors that have been implicated in genesis of BCIS after cemented THRs include grade III and IV ASA levels, old age, poor pre-existing physical reserve, impaired cardiopulmonary function, pre-existing pulmonary hypertension, osteoporosis, bony metastases, and concomitant hip fractures, particularly pathological or intertrochanteric fractures.

There is no clear evidence with regards to the effect of anaesthetic technique on the severity of BCIS. The general principles of management include the maintenance of normovolaemia to avoid the cardiovascular consequences of cementing and the maintenance of high inspired concentrations of oxygen. The use of high anaesthetic vapour concentrations should be avoided as it is associated with greater haemodynamic compromise with the same embolic load.

The use of intraoperative CO monitoring has been recommended in patients with one or more risk factors for BCIS. This can be in the form of semi-invasive transoesophageal Doppler monitor or invasive CO monitor (pulmonary artery flotation catheter). The use of intraoperative transoesophageal Doppler has been shown to aid the early detection of cardiovascular changes around the time of cementing, improve fluid management, and reduce postoperative cardiopulmonary complications in hip surgery. A transoesophageal Doppler study involving patients undergoing hip arthroplasty demonstrated the superiority in detecting cardiovascular changes during cementing compared with standard haemodynamic monitoring, recommending its use in high-risk patients. Pulmonary artery flotation catheter and transoesophageal echocardiography should also be considered in high-risk patients. But their use is limited by their availability and expertise required to use them.

Role of surgery in prevention of bone cement-associated complications

The use of a cementless hip prosthesis can reduce the morbidity associated with cement embolization and must be considered on an individual basis. Surgical measures that can reduce the incidence of complications associated with bone cement, especially BCIS, include thorough lavage of the intramedullary canal of the femoral shaft in order to remove debris, good haemostasis, the use of non-cemented prostheses, and drilling a vent hole in the distal femoral shaft. The latter technique reduces air trapping during the cementing process and acts as a pressure-relieving opening during the intramedullary reaming of the femoral canal. However, drilling a vent hole increases the risk of fracture and prosthetic instability.

The bone-vacuum cementing technique has been shown to reduce the embolic load during total hip arthroplasty. In this technique, a suction pressure of ~800 mbar (~80 kPa) is applied to a proximal drainage cannula placed along the linea aspera and a distal drainage cannula is placed in the diaphysis to produce a vacuum in the medullary cavity of the femur during the application of cement and the insertion of the stem. The reduction in embolic load using this technique was evident in intraoperative transoesophageal imaging.

The retrograde insertion of cement (from distal to proximal) by a cement gun causes the compartmentalization of the bone marrow contents. This can lead to a more uniform increase in intramedullary pressure and less physiological disturbance. Furthermore, mixing bone cement in a specific cement-mixing set, which is in a vacuum, reduces the load of volatile vasoactive compounds. This, and the use of low-viscosity cement, can reduce the incidence of BCIS.

Management of BCIS

Human and animal studies have shown that BCIS is a reversible, time-limited phenomenon. The PAPs can normalize within 24 h and non-diseased hearts can recover within minutes to hours. This means that aggressive resuscitation and supportive treatment is
essential to reduce the morbidity and mortality of this potentially life-threatening situation.

When BCIS is suspected, resuscitation should be based on general principles. The inspired oxygen concentration should be increased to 100%. The management of cardiovascular collapse should be in line with the treatment of right ventricular failure, including i.v. fluid therapy, the use of pulmonary vasodilators for reducing PAP, and the use of inotropes (dobutamine and milrinone) to maintain right ventricular contractility. If simple measures fail, intraoperative CO monitoring should be used, either in the form of non-invasive CO monitoring, such as transoesophageal Doppler imaging and PiCCO (arterial pulse contour analysis), or with invasive CO monitoring with the use of a pulmonary artery flotation catheter to guide vascular filling and the use of vasopressors and inotropes. Although central venous pressure monitoring does not accurately reflect the PAP, the insertion of a central venous catheter may be indicated for the administration of inotropic drugs. After operation, the patient should be managed in an intensive care unit setting.

Summary

BCIS is a poorly understood phenomena with a variety of clinical features. A number of theories have been proposed to explain the pathophysiology of this complex phenomenon, but it is postulated that the true aetiology may encompass a combination of mechanisms, partly modified by the patient’s own physiological response and pre-existing pathology. The identification of high-risk patients through thorough preoperative assessment and modification of surgical technique tailored to patients’ general condition may help in reducing the incidence of BCIS.

Declaration of interest

None declared.

References


Please see multiple choice questions 37–40.