Antibiotic Cement and Spine Surgery

Subjects: Surgery

Contributor: George M. Anderson, Camilo Osorio, Ellis M. Berns, Umar Masood, Daniel Alsoof, Christopher L. McDonald, Andrew S. Zhang, John Andrew Younghein, Eren O. Kuris, Albert Telfeian, Alan H. Daniels

Antibiotic bone cement (ABC) is an effective tool for the prophylaxis and treatment of osteomyelitis due to the controlled, sustained release of local antibiotics. ABC has been proven to be effective in the orthopedic fields of arthroplasty and extremity trauma, but the adoption of ABC in spine surgery is limited. The characteristics of ABC make it an optimal solution for treating vertebral osteomyelitis (VO), a serious complication following spine surgery, typically caused by bacterial and sometimes fungal and parasitic pathogens.

Keywords: antibiotic cement ; surgical site infection ; vertebral osteomyelitis

1. Fundamentals of Antibiotic Cement

ABC is made up of one or multiple antibiotics combined with polymethyl methacrylate (PMMA) and a radiopacifier. PMMA is a hard, scratch- and shatter-resistant, amorphous acrylate polymer formed by mixing two components: a liquid monomethyl methacrylate (MMA) component and a powdered MMA component [1]. After these components are mixed, curing occurs. Curing time varies between different brands of ABC from five minutes to over 20 min, and it releases approximately 57 kJ per mol of energy, increasing the core temperature to approximately 77.3 degrees Celsius. Polymerization also increases viscosity and density. The viscosity of PMMA determines the working properties of the cement and increases from around 50 Pas to around 100 Pas. Theoretically, bone cement can shrink by approximately 6–7%; however, air inclusions in the cement dough limit shrinkage [2].

PMMA is available in several different formulations with their own unique qualities, many of which have commercially available versions containing antibiotics. These include Palacos R + G, Depuy CMW1, CMW2 and CMW3, Simplex P, Refobacin Bone Cement R, Cobalt HV, and Osteopal G. Osteopal G is geared specifically towards kyphoplasty and vertebroplasty, while the others are used mainly in arthroplasty (**Table 1**).

Table 1. Characteristics of widely used, commercially available brands of premixed antibiotic cement.

Brand	Radiopacifier	Color	Antibiotics Mixture	Setting Time and Temperature	Viscosity	Use
Palacos R + G bone cement	**zirconium dioxide**	**green**	**0.5 g of gentamicin per 40.6 g**	**8 min, 45 s at 19 °C**	**high**	**arthroplasty**
Depuy CMW1	**barium sulfate**	**none**	**Optional: 1 g gentamicin per 40 g**	**12 min, 30 s at 19 °C**	**high**	**arthroplasty**
Depuy CMW2	**barium sulfate**	**none**	**Optional: 1 g gentamicin per 40 g**	**6 min, 30 s at 19 °C**	**high**	**arthroplasty**
Depuy CMW3	**barium sulfate**	**none**	**Optional: 1 g gentamicin per 40 g**	**12 min, 30 s at 19 °C**	**medium**	**arthroplasty**
Simplex P	**barium sulfate**	**none**	**Option 1 g tobramycin per 40 g**	**10 min at 19 °C**	**medium**	**arthroplasty**
Refobacin Bone Cement R	**zirconium dioxide**	**green**	**0.5 g gentamicin per 40 g**	**11 min at 19 °C**	**high**	**arthroplasty**
Cobalt HV	**zirconium dioxide**	**blue**	**Optional: 0.5 g gentamicin per 40 g**	**5 min at 23 °C**	**high**	**arthroplasty**
Osteopal G	**zirconium dioxide**	**green**	**0.325 g gentamicin per 26.53 g**	**23 min, 30 s at 20 °C**	**low**	**kyphoplasty and vertebroplasty**

Antibiotics can also be added to PMMA by the surgeon. In this case, antibiotics are mixed into the MMA powder combination with the MMA liquid. This results in the incorporation of antibiotics between PMMA chains during the polymerization process [2]. After the antibiotics have been incorporated, they are released by reciprocal diffusion, which can be divided into two phases. The initial release is referred to as the “burst release” and occurs in minutes to hours. In this phase, high levels of antibiotic are released and diffuse into nearby tissue and fluids. The second phase, called “sustained release”, occurs after several days, resulting in a lower, but prolonged local antibiotic concentration [2].

The pharmacokinetic release profile of PMMA can be optimized. Each antibiotic has its own unique elution characteristics and combining multiple types of antibiotics can also increase elution. For example, Masri et al. showed that combining vancomycin and tobramycin in PMMA had a synergistic effect and caused vancomycin to release at higher concentrations for longer durations [3]. Adding polymeric fillers such as xylitol or glycine can also increase elution [2]. Furthermore, increasing the surface area increases elution as antibiotics release after contacting body fluids. Hand mixing PMMA, as opposed to vacuum mixing, results in a rougher and more porous surface, and therefore a higher surface area [2].

The intended use of ABC (for prophylaxis or treatment) and the susceptibility of the microorganisms identified or suspected determines the antibiotic choice. For prophylaxis, antibiotics should cover the most prevalent pathogens causing VO. Gentamicin, tobramycin, vancomycin, and clindamycin are the most widely used in ABC [4]. Aminoglycoside antibiotics such as gentamicin and tobramycin are effective against Gram-negative bacilli and tobramycin can also be used for some mycobacteria species. Many providers choose to use vancomycin, although there are some concerns with routine use for prophylaxis given the potential for antibiotic resistance [4][5]. Clindamycin is effective against anaerobic bacteria, Gram-positive cocci, and some atypical bacteria such as actinomyces [2].

Antibiotic combinations are also used in ABC, particularly when treating resistant infections. The efficacy of this strategy has been demonstrated both in vivo and in vitro. [6][7][8]. Combining tobramycin with vancomycin has been shown to be effective against a broad spectrum of bacteria, as well as against resistant species such as methicillin-resistant Staphylococcus aureus (MRSA). A combination of gentamycin and vancomycin has also been shown to be effective against MRSA. For cases of methicillin-resistant coagulase-negative Staphylococci, a combination of gentamycin, vancomycin, and clindamycin has been shown to be effective [9].

The ideal dose of antibiotic in ABC is a level high enough to inhibit bacterial growth for 3–4 weeks without inducing antibiotic resistance and a concentration low enough to avoid toxicity or structural compromise [10]. Depending on whether the goal is prophylaxis or treatment, different doses are required. For prophylaxis, ≤1 g antibiotic per 40 g of cement is recommended to avoid adverse structural effects, but this may be less important in spinal applications as compared to extremity joint applications [11]. For treatment of existing infections, higher doses are required for effective elution kinetics and for sustained therapeutic levels of local antibiotics [12]. In particular, 3.6 g of antibiotic per 40 g of cement has been suggested as an adequate dose for infection treatment as it is above the MIC for most microorganisms and limits structural compromise and potential toxicity [3].

2. Antibiotic Cement Use and Outcomes in Spine Surgery

Despite decades of proven use and study in orthopedic surgery, relatively little evidence exists regarding the efficacy of ABC in spine surgery.

Two studies demonstrated the use of ABC for infection prophylaxis in spine surgery. Opalko et al. showed no cases of VO during one-year follow-up in 50 patients who underwent kyphoplasty supplemented with prophylactic ABC [13]. Kim et al. reported no SSI during 6-month follow-up in 10 cases where loose pedicle screws were revised and augmented with ABC [14].

Six studies demonstrated the use of ABC for the treatment of spinal SSI. Chen et al. described the successful eradication of a bacterial infection at T11 with the use of ABC vertebroplasty combined with an intravenous antibiotic regimen [15]. Masuda et al. successfully treated 11 patients with spinal SSI refractory to other treatments using ABC [16]. Ogihara et al. successfully treated three cases of deep SSI after cervical spine deformity surgery using ABC placed over and around the instrumentation [17]. Laratta et al. published a case series showing complete resolution of deep surgical site infections in ten spine surgery patients treated with permanent implantation of ABC over exposed instrumentation [18]. Lee et al. reported a case of a 63-year-old man with a staphylococcal spinal epidural abscess treated successfully with intravenous antibiotics and ABC beads introduced locally [19]. Slavnic et al. treated 62 patients with pyogenic spondylodiscitis of the

thoracic spine with spinal reconstruction and fusion using antibiotic-impregnated PMMA. All patients achieved fusion and only one patient developed recurrent infection [20].

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