The Journal of Arthroplasty 30 (2015) 858–863

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

The Effects of Different Mixing Speeds on the Elution and Strength of High-Dose Antibiotic-Loaded Bone Cement Created With the Hand-Mixed Technique

Kongkit Pithankuakul, MD, Wallob Samranvedhya, MD, Boonyarak Visutipol, MD, Sombat Rojviroj, MD

Bangkok Orthopedic Center, Bangkok Hospital Group, Bangkok, Thailand

ARTICLE INFO

Article history:
Received 27 June 2014
Accepted 2 December 2014

Keywords:
elution
compression strength
porosity
high-dose antibiotic-loaded bone cement
periprosthetic joint infection

ABSTRACT

We evaluated the effects of the mixing speed of hand-mixed bone cement and the different phases of antibiotic mixing on the elution, mechanical properties, and porosity of antibiotic-loaded bone cement. Vancomycin-loaded Palacos LV bone cement was prepared at two hand-mixing speeds, normal and high-speed, and with antibiotic addition during three phases (directly mixing with the PMMA powder, in the liquid phase, and in the dough phase). The cumulative antibiotic elution over 15 days in the high-speed group was increased by 24% compared with the normal-speed group ($P < 0.001$). The delayed antibiotic addition produced higher vancomycin elution ($P < 0.05$), but no difference was observed between the liquid and dough phases ($P > 0.05$). Our study demonstrated that bone cement prepared with high-speed hand mixing and delayed antibiotic addition can exhibit increased vancomycin release.

Deep peri-prosthetic joint infection (PJI) following total joint arthroplasty is a major complication and problem for orthopedic surgeons [1]. One of the most efficient current standard treatments for late chronic infection is two-stage revision arthroplasty including removal of the prosthesis and cement through debridement, placement of an antibiotic-loaded bone cement (ALBC) spacer, a course of intravenous antibiotics, and a delayed component reimplantation [1]. Insall et al first described a two-stage procedure for chronic indolent periprosthetic infections in 1983 [2].

Acrylic bone cement based on polymethyl methacrylate (PMMA) has been used in joint reconstruction since the 1950s [3]. In 1970, Buchholz and Engelbrecht were the first to incorporate antibiotics into PMMA bone cements for total joint arthroplasty [4]. The advantages of using ALBC as a spacer are the maintenance of alignment, the prevention of soft tissue contracture, and the production of high local drug concentrations with less risk of systemic complications [1]. The use of ALBC spacers is now considered to be standard care for patients with chronic infection at the site of a total joint arthroplasty [1,5].

The effectiveness of the use of ALBC as a spacer to deliver local antibiotic is dependent on the increased antibiotic release over a longer period of time [1,3]. The elution characteristics of ALBC can be affected by certain factors that include the porosity of ALBC, the type of bone cement, the preparation method, the type of antibiotic, and the dose of antibiotic [3,5,6]. Many studies have reported that increasing the porosity of ALBC can increase antibiotic elution [7,8]. Therefore, dextran [9], hydrogen peroxide (H_2O_2) [10], calcium sulfate ($CaSO_4$) [11], sucrose [12], xylitol [12], and glycine [13] have been used as porogens or space fillers to obtain more porous ALBC. Additionally, the porosity of PMMA can be increased up to 10% via the use of high-speed of hand mixing [14,15]. Currently, there are no studies that have evaluated the effects of the use of different hand-mixing speeds in the production of ALBC on the elution of antibiotics.

Because high-dose preparations of ALBC are not commercially available, surgeons have to mix antibiotics in bone cement during their operations. Different techniques for the addition of antibiotic to bone cement have been used [16,17]. Some surgeons have attempted to homogeneously mix the antimicrobial powder into the PMMA powder components via hand-stirring with a simple bowl and spatula before polymerization. Some studies have revealed that the delay of antibiotic addition until the dough phase of polymerization can help to increase the elution of ALBC [16,17]. However, the optimal timing of antibiotic addition is unknown.

In this study, we evaluated the effects of two major factors of mixing techniques on the elution, mechanical properties, and porosity of antibiotic-loaded bone cement. The first factor was the speed of hand-mixing the bone cement and antibiotic. The second factor was the timing of the addition of the antibiotic to the PMMA; i.e., during different phases of polymerization. The results of this study will help to identify a suitable technique for high-dose ALBC preparation.

Materials and Methods

Study Design

Experimental study.

No author associated with this paper has disclosed any potential or pertinent conflicts which may be perceived to have impending conflict with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2014.12.003.

Reprint requests: Kongkit Pithankuakul, MD, Bangkok Orthopedic Center, Bangkok Hospital Medical Center, 2 Soi Soonvijai 7, New Petchburi Rd., Bangkok 10310, Thailand.

http://dx.doi.org/10.1016/j.arth.2014.12.003
0883-5403/

ALBC Preparation

Palacos LV (Heraeus Kulzer GmbH & Co., Germany) was prepared for the ALBC used this study. A standard plastic bowl and spatula were used for the hand-mixing of the PMMA powder and the liquid monomer. Four grams of vancomycin hydrochloride powder (Lek Pharmaceuticals, Slovenia) was added to each 40-g batch of cement. The ALBC was divided into two groups according to the different speeds at which the bone cement was hand-mixing (Fig. 1). In the normal-speed mixing group, the mixtures were stirred at one revolution per second for 60 seconds to produce a homogenous dough. In the high-speed mixing group, the components were stirred at 3 cycles per second for 60 seconds to produce a homogenous dough. Each group was further separated into three subgroups in which the bone cement and vancomycin were mixed during different phases (Fig. 1). These acrylic bone cements were mixed in controlled temperature and humidity conditions of 22 ± 1 °C and 40–60%, respectively [18].

For the testing of subgroup 1, four grams of vancomycin powder was poured directly into 40-g of cement powder and mixed in a plastic bowl to form a homogeneous powder. Then, 20 ml of liquid monomer was added and stirred with a spatula for 60 seconds at normal speed. For the high-speed hand-mixing group, another batch of bone cement and four grams of vancomycin were used with the same procedures with the exception that the speed used during mixing was different.

For the testing of subgroup 2, cement powder and liquid monomer were completely mixed in a plastic bowl before the antibiotic was added. After 1 minute of mixing, four grams of vancomycin powder was added to the PMMA, which was still in the liquid phase, and followed by 30 seconds of mixing. Two speeds of hand-mixing of the PMMA were also tested for this subgroup.

For the testing of subgroup 3, a mixture of cement powder (40 g) with 20 ml of liquid monomer was prepared for each group at different speeds. Five minutes was allowed before four grams of vancomycin powder was added to the PMMA, which was in the late dough state.

All tests were performed in strict adherence to the American Society for Testing and Materials (ASTM) F451-99a standards [19]. After mixing, each ALBC preparation was packed into a steel mold that contained 25 cylindrical holes of 6 mm in diameter and 12 mm in depth. The cylindrically shaped specimens were then tapped out of the mold and inspected for major defects or cracks. Each specimen was measured with precision calipers. The cylinders that were suitable for testing were grounded to 12 mm in length and 6 mm in diameter to meet the ASTM standard. Specimens that deviated from the ASTM standard were excluded from analysis [19].

Elution Testing

Four cylindrical cement specimens from each preparation were fully immersed in 5 ml of phosphate buffered saline (PBS) in individual covered test tubes in a 37 °C chamber. At the designated sampling intervals, each specimen was removed from the test tube, rinsed with 10 ml of normal saline and placed in a 5-ml fresh PBS bath in a fresh test tube. Test tube of eluant from each of the cement specimen at each of the time intervals of 1, 3, 5, 7 and 15 days was stored at −20 °C until analysis, which occurred within 10 days. The collected samples were analyzed for vancomycin concentrations via high-performance liquid chromatography (HPLC) on a Waters module (Milford, MA, USA) with the Atlantis dC18 column, ultraviolet detection at 210 nm, and a mobile phase consisting of 0.05 M phosphate buffer solution: acetonitrile (91:9) at a flow rate of 1 ml/min. The concentration of vancomycin in each PBS sample was determined from a calibration curve [20].

Mechanical Property Testing

Eight cylinders from each subgroup were used for mechanical strength testing at two time points. Four cylinders from each subgroup were tested before elution, and the other four cylinders were tested 15 days after elution. The compression testing of each cylinder was

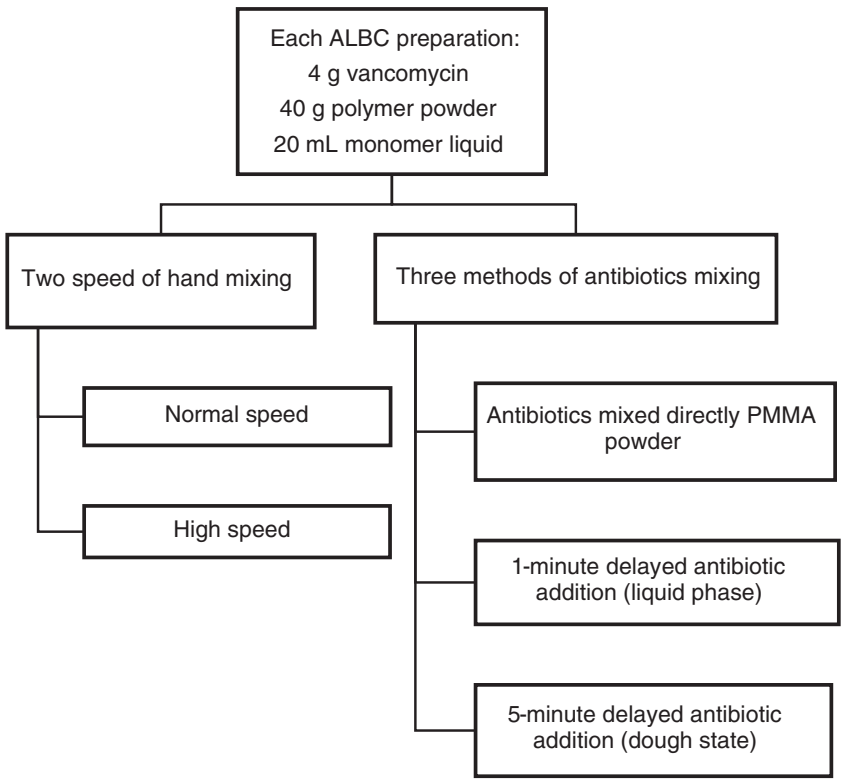

Fig. 1. The diagram shows the experimental design for mixing methods of high-dose ALBC preparation.