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Influence of the method of blending an antibiotic powder with an acrylic bone cement powder on physical, mechanical, and thermal properties of the cured cement

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Abstract

Two variants of antibiotic powder-loaded acrylic bone cements (APLBCs) are widely used in primary total joint replacements. In the United States, the antibiotic is manually blended with the powder of the cement at the start of the procedure, while, in Europe, pre-packaged commercially-available APLBCs (in which the blending is carried out using an industrial mixer) are used. Our objective was to investigate the influence of the method of blending gentamicin sulphate with the powder of the Cemex® XL formulation on a wide collection of properties of the cured cement. The blending methods used were manual mixing (the MANUAL Set), use of a small-scale, easy-to-use, commercially-available mechanical powder mixer, OmoMix®1 (the MECHANICAL Set), and use of a large-scale industrial mixer (Cemex®Genta) [the INDUSTRIAL Set]. In the MECHANICAL and MANUAL Sets, the blending time was 3 min. In preparing the test specimens for each set, the blended powder used contained 4.22 wt% of the gentamicin powder. The properties determined were the strength, modulus, and work-to-fracture (all obtained under four-point bending), plane-strain fracture toughness, Weibull mean fatigue life (fatigue conditions: ± 15 MPa; 2 Hz), activation energy and frequency factor for the cement polymerization process (both determined using differential scanning calorimetry, at heating rates of 5, 10, 15, and 20 K min^{-1}), the diffusion coefficient for the absorption of phosphate buffered saline, PBS, at 37 °C, and the rate of elution of the gentamicin into PBS, at 37 °C (E). Also determined were the particle size, particle size distribution, and morphology of the blended powders and of the gentamicin. For each of the cured cement properties (except for E), there is no statistically significant difference between the means for the 3 cements, a finding that parallels the observation that there are no significant differences in either the mean particle size or the morphology of the blended cement powders. Notwithstanding these results, it is suggested that when the powder mixture is blended in the operating room, using the OmoMix®1 is more likely to produce a more consistent and reproducible mixture than when manual mixing is used.

Keywords: Acrylic bone cement; Gentamicin sulphate; Physical properties; Mechanical properties; Thermal properties

1. Introduction

Although the incidence of infections in the periprosthetic membrane and in the synovial fluid, during and after implant fixation in primary arthroplasties is low—of the order of between 0.3% [1] and 2% [2] at 10 years—the problem is difficult to control to the point of intractability. Hence, the cost of control of such infections is very high, amounting to about $250 million per annum in the United States [3]. Such control invariably involves the use of one or more broad-spectrum antibiotics, the most popular ones being gentamicin sulphate, vancomycin chloride, tobramaycin, and clindamycin hydrochloride powders. The antibiotic(s) are delivered to the infected site either therapeutically (that is, administered systemically) or

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prophylactically (an antibiotic powder-loaded acrylic bone cement, APLBC, is used to anchor the prosthesis to the contiguous bone [4]). Although there are few well-designed comparisons of these two methods in a given population of infected cases [5,6], the prophylactic method is more popular than the therapeutic one. For example, it has been reported that over 90% of orthopaedic surgeons in the United States use an APLBC for primary arthroplasties [7], and Espehaug et al. [8] reported that, in Norway, the use of APLBCs for the fixation of total hip joint replacements increased from 40% in 1989 to 94% in 1999.

To date, only very limited attention has been given to the issue of how the method used to blend the antibiotic powder with the powder of a cement influences the various properties of the cured cement [9,10]. In each of these studies, only one property was determined, these being ultimate tensile load [9] and gentamicin release rate [10]. Furthermore, in the Conrad et al. study [9], no antibiotic was included in the powder for the control cement. It is desirable to enhance this aspect of the knowledge base because, in current clinical practice when an APLBC is used in cemented primary hip and knee replacements, one of two approaches are taken. The first is to use a commercially-available pre-packaged APLBC (in which the antibiotic and the cement powder are blended using an industrial process). Alternatively, the antibiotic powder is blended with the powder of a plain cement at the start of the operation. (The former method is widely used in, for example, Europe, while the latter is widely used in, for example, the United States.)

Our objective in the present work was to investigate the influence of the method used to blend gentamicin sulphate powder with the powder of one commercially-available plain acrylic bone cement brand on a wide collection of mechanical, thermal, and physical properties of the cured cement. The blending methods used were a manual technique, use of a small-scale commercially-available mechanical powder mixer, and an industrial process. In all cases, the blended cement powder was mixed with the liquid monomer in a bowl that was open to the ambient atmosphere. The properties of the cured cement determined were strength, modulus, and work-to-fracture (all under four-point bending), plane-strain fracture toughness, fatigue life, activation energy (Q) and the frequency factor ($\ln Z$) for the polymerization reaction, the diffusivity (D) for the absorption of phosphate buffered saline, PBS, at 37 °C, by the cement, and the rate of elution of the gentamicin into PBS, at 37 °C, after 7 days. Q and $\ln Z$ were computed from measurements made using differential scanning calorimetry, which has been shown to be a reliable and powerful method for measuring the amount of heat released upon polymerization of acrylic bone cement [11,12]. D was computed using measurements made of the temporal change in mass gain of a cement specimen due to its absorption of the PBS until equilibrium is achieved, an approach that has been shown to be valid for acrylic bone cement [13,14]. Also obtained were the particle sizes, particle size distributions, and morphologies of the blended cement powders and of the gentamicin. The results for these blended cement powder characteristics were used to comment on their influence on the properties of the cured cement.

2. Materials and methods

2.1. Materials, preparation of blended cement powder, and mixing of cements

Three sets of cement powders were used. In the first set (the MANUAL Set), we used a pestle to blend gentamicin sulphate powder (>99% pure; Sigma-Aldrich, Inc., St. Louis, MO, USA) with the powder of Cemex®XL (Tecres S.p.A., Verona, Italy) in a bowl that was open to the ambient atmosphere. In the second set (the MECHANICAL Set), we blended the gentamicin with the cement powder using a small-scale, easy-to-use commercially-available powder mixer that was designed specifically for this application (OmoMix®1; Tecres). In the third set (the INDUSTRIAL Set), the powder was that of Cemex®Genta LV (Tecres), which is a commercially-available variant of Cemex®XL in which the gentamicin was blended with the cement powder using an industrial process. In all sets, the amount of gentamicin in the blended cement powder, expressed as a mass percentage of the total mass of the blended powder (4.22%) was the same, and that value, in turn, was the same as is the case for Cemex®Genta LV. Also, in the MANUAL and MECHANICAL Sets, the blending time was the same, this being 3 min, which is the typical duration for manual blending an antibiotic with a cement powder in preparation for implantation of a hip or knee replacement [15].

In preparing the test specimens for all sets, the cement dough was obtained by using a polymeric spatula to manually mix, at about 1 Hz, the blended powder and the liquid monomer together in a polymeric bowl that was open to the ambient atmosphere.

2.2. Characterization of blended powders and gentamicin

The particle sizes, particle size distributions, and morphologies of the blended cement powders as well as of the gentamicin were determined using a laser diffraction system (Sympatec Particle Size Analyzer, Model HDD200; Sympatec GmbH, Golar, Germany), and an environmental scanning electron microscope (Model XL30; Philips, Achtsewed, The Netherlands) operated at an accelerating voltage of 15 kV, respectively.