Increasing the Elution of Vancomycin from High Dose Antibiotic Loaded Bone Cement: A Novel Preparation Technique

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INTRODUCTION

Although numerous antibiotics have been successfully incorporated within bone cement, the quantity and formulation of added antibiotic has an important effect on cement’s mechanical properties. Surgeons must determine the appropriate amount of antibiotic to place in bone cement while weighing the impact on biomechanical strength. Studies have demonstrated that approximately 6 g of vancomycin cement may be added while maintaining the industry standard of 70 MPa for compressive strength. Mixing environment during preparation of the cement has also demonstrated effects on ultimate cement strength.

This study specifically evaluates the effects of two variations in mixing technique on the elution and mechanical properties of the antibiotic laden cement. The first variation is an increase in the ratio of liquid monomer to powdered polymer. The second variation is a delay in the addition of antibiotic until after initiation of the polymerization process (delayed antibiotic technique).

METHODS

Two types of bone cement were used in this study: Simplex P (Stryker/Howmedica, Limerick, Ireland) and SmartSet MV (DePuy, Blackpool, England). Five grams of vancomycin hydrochloride powder ( Hospira Inc., Lake Forest, IL) was added to each batch of cement. The cement and vancomycin mixtures were prepared using three different techniques described below. In each case, the vancomycin was ground with the cement powder (5g) by hand for 30 seconds. Next, 20 ml of liquid monomer (the manufacturers recommended amount for normal cement preparation) was added and mixed for 30 seconds in a 30 kPa vacuum environment. This technique represents the method commonly used in operating rooms.

The second preparation technique (referred to as the “double liquid monomer technique”) again involved mixing the cement powder (40g) with vancomycin powder (5g) by hand for 30 seconds. Next, 40 ml of liquid monomer (double the manufacturer’s recommended dose of 20 ml) was added and mixed for 60 seconds at 30 kPa vacuum.

The third preparation (referred to as the “delayed antibiotic technique”) consisted of first blending the cement powder (40g) with 20 ml of liquid monomer under a 30 kPa vacuum for 30 seconds. The vacuum was removed and 5g of vancomycin was then added, followed by an additional 30 seconds of vacuum mixing at 30 kPa.

The previously mentioned cement preparations were injected with a 60 cc syringe into an array of holes measuring 6.0 mm in diameter and 12.7 mm deep. Immediately after cement injection, molds and samples were stored for one hour in an incubator at 23°C. The pellets were tapped out of their molds and inspected for major defects or cracks. Exclusion of pellets was based upon ASTM standards [28]. The pellets found to be suitable for testing were ground to 12mm length to meet the ASTM standard. Fifteen total pellets from each preparation were selected for compression testing. Five of these pellets were compression tested at 24 hours. Of the remaining 10 pellets, half were placed in a solution of phosphate buffered saline (wet environment) and half were placed within an empty test tube (dry environment). These 10 pellets were then incubated at 37°C for six weeks. Following incubation, compression testing was performed on the pellets. Compression testing was carried out on a materials testing machine at a crosshead speed of 22 mm/min (ASTM specifications). The effects of mixing techniques and elution on the ultimate compressive strength (UCS) were determined and compared to ISO standard of 70 MPa, ISO 5833-2).

RESULTS

Elution testing over the entire six weeks revealed significantly higher rates of vancomycin release from cement prepared using the delayed antibiotic addition technique than from cement prepared using the standard technique (p<0.0001). The addition of double liquid monomer reduced vancomycin elution over six weeks compared with the standard technique (p<0.0001). Total vancomycin elution over six weeks from Simplex P was 52 percent greater in the delayed antibiotic group than in the standard surgical group (Figure 1). Compared with the delayed antibiotic technique, the use of double liquid monomer led to a 56 percent decrease in vancomycin elution from Simplex P over six weeks (Fig 1). Compression testing proved that all three mixing techniques provided high dose antibiotic loaded cements within industrial standards, measuring above the recommended 70 MPa at 24 hours. Statistical analysis demonstrated no significant difference in strength between similarly prepared pellets at 24 hour testing and six week testing after dry environment exposure (p=0.95). However, comparison of compression strength of similarly prepared pellets at 24 hours to pellets after six weeks of elution demonstrated a statistically significant decrease in strength (p<0.001). We observed this decrease in strength within all three cement preparation techniques. All post elution compression testing resulted in average cement strength remaining above 70 MPa. Furthermore, strength after six weeks of elution was significantly lower in the SmartSet MV standard surgical preparation group than in either the delayed antibiotic group or the double liquid monomer group (p<0.01).

DISCUSSION

This study clearly demonstrates the superiority of the delayed antibiotic technique when preparing high dose antibiotic loaded bone cement. Adding antibiotic after initiating the polymerization process created higher elution profiles and mechanical strength that met industrial standards in both the Simplex P and SmartSet MV groups after six weeks of elution. Furthermore, doubling the amount of liquid monomer was proven to lead to a significantly lower elution profile than the other two preparations. Therefore, we propose preparation of high dose antibiotic bone cements using the delayed antibiotic addition technique. We do not recommend incorporating additional liquid monomer when preparing antibiotic cements.

SIGNIFICANCE

The preparation of the bone cement is shown to have significant and substantial effects on both the elution rates and strength.

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