Centrifugation of Antibiotic Impregnated Bone Cement

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ABSTRACT: Centrifugation is used to increase the strength of bone cement in total joint arthroplasty. Antibiotics have been incorporated into cement for the treatment and prophylaxis of infection. To determine the effect of centrifugation on antibiotic containing cement, tobramycin and cefamandole impregnated Surgical Simplex P polymethylmethacrylate was centrifuged using manufacturers' techniques. The concentration of antibiotics was measured throughout the cement column by a zone of inhibition bioassay. No difference in the distribution of the antibiotics could be demonstrated as compared to hand mixed controls. Centrifugation decreased the number of large air inclusions overall, however, a significant number were noted to remain at the top of the centrifugation gradient. It was concluded that centrifugation of an antibiotic impregnated bone cement, utilizing this technique, may be used without disturbing the antibiotic distribution. Discarding the top 1 cm of liquid centrifuged column to remove residual air inclusions is recommended.

Introduction

The use of antibiotic impregnated polymethylmethacrylate (PMMA) bone cement has gained popularity in the prophylaxis and treatment of deep bone and joint infections, especially in the field of total joint arthroplasty. While its clinical efficacy has yet to be proven, early reports show that antibiotic impregnated PMMA may be effective in preventing deep postoperative infections in cemented total hip arthroplasty.\textsuperscript{1-7} Certainly, in vivo studies have shown that the concentrations of antibiotics in cortical bone achieved by depot administration in PMMA are superior to those attained by systemic antibiotic.\textsuperscript{8} These local concentrations are sustained over a long period of time with no reported side-effects to date.\textsuperscript{9-13} Used in small concentrations (0.5 gm to 1 gm dry antibiotic/40 gm cement), these antibiotics only minimally affect the compressive, tensile, and shear strengths of the bone cement.\textsuperscript{14-16} Recent biomechanical studies have demonstrated that the tensile and fatigue properties of plain PMMA can be markedly improved by the use of centrifugation, which eliminates porosity caused by large air inclusions generated in mixing.\textsuperscript{17} Commercial centrifugation systems have currently become available for widespread use in bone cement preparation, however, the effect of this centrifugation on antibiotic impregnated PMMA, to date, has not been reported.

The purpose of this study was to investigate the effect centrifugation, as used clinically, has on the distribution of two antibiotics, specifically tobramycin and cefamandole (Eli Lilly and Company), in...
Surgical Simplex P (Howmedica, Inc) PMMA bone cement.

Materials and Methods

The Surgical Simplex P PMMA bone cement monomer and polymer were cooled to 4°C to slow polymerization. It was mixed with the antibiotics in the following concentration: tobramycin base 600 mg equivalent activity in 40 gm package PMMA and cefamandole 1000 mg equivalent activity in 40 gm package PMMA.

Sixteen cement columns were prepared by hand mixing, eight with tobramycin and eight with cefamandole. The powdered antibiotic and 4°C PMMA polymer were hand mixed for 3 min at room temperature. The 4°C monomer was added and hand mixed until the low viscosity state was obtained. The cement was poured into the Harris Femoral Cement Centrifugation tubes (Johnson and Johnson, Inc) and allowed to harden at 37°C.

Seventeen cement columns were prepared by centrifugation, eight with tobramycin, eight with cefamandole, and one blank control. The powdered antibiotic and 4°C PMMA polymer were hand mixed for 3 min at room temperature. The 4°C monomer was added and hand mixed until the low viscosity state was obtained. The cement was poured into the centrifugation tubes and centrifuged at 1060 rpm for 1 min. The columns were then allowed to harden at 37°C. All cement columns were sliced on a dry milling machine into eight uniformly spaced slices. The cement disks were placed between glass slides and stored at -70°C until bioassay was performed.

Bioassay was performed using a disk diffusion method. The disks of sliced PMMA were placed on Mueller-Hinton broth agar plates containing 2% Bacillus subtilis (strain ATCC 6633; American Type Culture Collection, Rockville, Maryland). The plates were incubated at 37°C for 24 hours. Zones of growth inhibition were measured, comparing those disks with antibiotics to the blank control disks.

Results

There was no layering of antibiotic activity noted in the centrifuged columns (Table). No zone of inhibition was produced by the blank control disks. There was random variation noted in all of the antibiotic impregnated samples with a maximum range of inhibition zone diameter of 5 mm. The coefficient of variation, as determined by the column range, divided by the mean for that column, and multiplied by 100%, was used to compare variations. Standard concentration disks of PMMA are not available to quantitate the zones of inhibition. However, in bioassays of this type using Bauer-Kirby standard disks, >25% and >16% in the coefficient of variation for tobramycin and cephalosporins, respectively, are necessary to detect a significant difference in antibiotic concentration. The small variations noted are within this standard error.

In slicing the cement columns, large air inclusions were noted throughout the column of the hand mixed samples. While centrifugation decreased the number of air inclusions within the column, significant large air inclusions were still present in the top layers of the centrifugation gradient (Figure).

Discussion

The combination of centrifugation and antibiotic impregnated cement clinically results in a bone cement which is mechanically stronger (than without centrifugation) and possibly prophylactic against deep infection in total joint arthroplasty. These results demonstrate no significant effect on the distribution of tobramycin or cefamandole in Surgical Simplex P PMMA bone cement with centrifugation. The Johnson and Johnson Cement Centrifuge was chosen for its simplicity and availability. Other commercial centrifuges are available which generate greater centrifugal gradients. The results show that clinical use of this technique of centrifugation with tobramycin or cefamandole impregnated PMMA, therefore, may be used without concern of an uneven distribution of antibiotics which might weaken the cement in areas of high concentration or result in areas around the prosthesis unprotected or toxic with antibiotics.

Even with this technique of centrifugation, significant large air inclusions persist in the top layers of the
centrifugation gradient. Discarding the top portion (1 cm) of the liquid column will achieve a cement mantle with even less porosity. Newer devices are becoming available which allow mixing within a vacuum to avoid these air inclusions. Further studies will be needed to determine the effect of these methods on antibiotic distribution.

It is concluded, therefore, that centrifugation of antibiotic impregnated PMMA, utilizing this technique, may be used to decrease its porosity without disturbing the antibiotic distribution and we recommend discarding the top 1 cm of the liquid centrifuged column to remove residual air inclusions.

References

Figure: Large air inclusions occur throughout the hand mixed samples. The centrifuged samples have fewer inclusions, but some still remain at the top of the centrifugation column.