A skeletal drug delivery system: gentamicin- and vancomycin-incorporated calcium phosphate cement

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ABSTRACT INTRODUCTION

Callos® Impact Bone Void Filler is a calcium phosphate (CaP) based cement designed to be moldable and digitally impactable. Antibiotics delivered systemically often do not result in adequate local concentrations. Local delivery of antibiotics by CaP cement carriers may be pharmacologically more effective and safer for prophylactic measures and treating infections. The main challenges that researchers often faced with antibiotic addition in CaP cements are: (a) maintaining the mechanical strength of the cements; and (b) delivery rate and antimicrobial activity of the antibiotics. The purposes of the present study were to:

1) investigate the effects of added antibiotics on the mechanical properties and chemical composition of the cement; and
2) determine the in vitro release kinetics and activity of gentamicin and vancomycin following incorporation into the calcium phosphate cement.

MATERIALS AND METHODS

- A calcium phosphate cement (Callos® Impact Bone Void Filler) were used as directed and supplied by the manufacturer (Skeletal Kinetics, Cupertino, CA).
- Commonly used antibiotics such as gentamicin (powder form, Hospira Inc., Lake Forest, IL) and vancomycin (liquid form, Hospira Inc., Lake Forest, IL) were used to incorporate into the cement.
- The phases of the initial powder component of cement and all cement samples were analyzed through X-ray diffraction (XRD). The surface morphology of initial powder component and all cement samples (with and without antibiotics) were analyzed using field emission scanning electron microscope (FESEM).
- The functional properties of the cement with added antibiotics were evaluated using modified ASTM methods. Setting and tensile strengths of antibiotic-loaded cements were examined and compared with control Callos® cement without antibiotics.
- Cement loaded with antibiotics was soaked in phosphate buffered saline (PBS, pH=7.4) and maintained at 37°C. The elution kinetics of gentamicin and vancomycin from cement were examined over 42 days at 11 time points.
- Activity of gentamicin and vancomycin was determined by the ability of clute (PBS containing antibiotics) to inhibit colony formation of Staphylococcus epidermidis, Staphylococcus aureus, Enterococcus faecalis and Escherichia coli.

RESULTS SECTION

- Antibiotic addition showed a minimal effect on the behavior and handling of the cement. The kinetics of transformation into poorly crystalline apatite was unaffected by the addition of antibiotics.
- The micrograph of cement without antibiotic (Fig. 2a) shows submicron sized inter-mingling inter-locking needles of apatite. Fig. 2b shows the microstructure of antibiotic-loaded cement and no change was observed.

DISCUSSION

Calcium phosphate cement maintained structural integrity and compositional attributes after it was mixed with two types of common antibiotics. This study demonstrates the feasibility of one-step surgical debridement of open fractures or osteomyelitis lesions, thereby eliminating conventional two-step procedures used with antibiotic-loaded PMMA beads or cements. However, currently Callos® Impact Bone Void Filler is not approved by FDA for use with antibiotics.