MECHANICAL STRENGTH AND IN VITRO RELEASE PROFILE OF VANCOMYCIN-LOADED CALCIUM PHOSPHATE CEMENT

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Postoperative infections are an important cause for the failure of orthopaedic treatments, in particular, of operations related to the substitution of joint prostheses. The addition of antibiotics to bone cement give rise to a great clinical interest for the opportunity of preventing or treating infections. The disadvantage of using PMMA cement include that the reaction of polymerization is exothermic to inactivate antibiotics and require removal operation of the cement. The purpose of this study is to examine the mechanical strength and in vitro release of vancomycin loaded calcium phosphate cement as a good defect filler and a carrier of antibiotics.

**Materials and Methods**

Calcium phosphate cement was supplied from Mitsubishi Material Inc., Saitama, Japan. The composition of the powder component is: alpha-tricalcium phosphate (75%), dicalcium phosphate dibasic (5%), hydroxyapatite (2%) and tetracalcium phospho monoxide (18%). The liquid component is composed of distilled water containing sodium succinate (12%) and sodium chondroitine sulphate (5%). Vancomycin hydrochloride was supplied from Eli Lilly and Shionogi Inc., Osaka, Japan.

Thirty columns of 7mm in diameter and 14mm in length were made for mechanical and elution study at each condition (consistency of 14mm and 24mm in diameter, containing 0% (w/w), 2.5% (w/w), 5% (w/w), 10% (w/w) vancomycin). An Instron universal Testing machine Type 4466 was used at a crosshead speed of 0.5mm/min to measure the compressive strength. The strength of columns were evaluated at days 0, 1, 3, 5, 7.

The elution study was conducted in PBS (pH7.4 at 37 degrees). Solutions were exchanged at days 0, 2, 1, 3, 5, 6, 7, 9, 10, 14, 17, 24, 29, 36 during the immersion period of 36 days. The concentration of vancomycin was measured by band culture method using Bacillus subtilis ATCC 6633.

**Results**

Compressive strength of vancomycin loaded calcium phosphate cement (consistency of 14mm in diameter) is shown in Figure 1. For the first 5 days the values indicated a slow rise in vancomycin loaded cement. Cement with 2.5% (w/w) vancomycin showed useful strength of 45.7 MPa at the 5th day when the strength of control was 74.5 MPa. The value of 5% (w/w) and 10% (w/w) loaded cement were lower of 16.7 and 10.9 MPa. Cumulative release of vancomycin from calcium phosphate cement (consistency of 24mm in diameter) is shown in Figure 2. The release rate and the amount released of calcium phosphate cement were load-dependent, but there were differences of release profile of the three. Cement with 10% (w/w) vancomycin showed rapid release at the first day. A sustained vancomycin release of 2.5% (w/w) loaded cement was observed during 36 days of immersion though sustained release of 5% (w/w) and 10% (w/w) cement was up to 24 days. Calcium phosphate cement (consistency of 14mm in diameter) with 2.5% (w/w), 5% (w/w) and 10% (w/w) vancomycin showed continuous release up to 36 days and cummulative release rate of 30%.

**Discussion**

Calcium phosphate cement (consistency of 14mm in diameter) with 5% wt and 10% wt vancomycin showed low compression strength but cement with 2.5% (w/w) vancomycin indicated useful compression strength and continuous release at the 36th day. There remained vancomycin of 70% with cement containing 2.5% (w/w) vancomycin at the 36th day of elusion test. Calcium phosphate cement has good biocompatibility with bone tissue, bonds directly to it and resorbs in vivo. The elution of the remaining vancomycin was expected for longer time as cement resorbs.

In conclusion, this study demonstrated that calcium phosphate cement with 5% (w/w) and 10% (w/w) vancomycin is effective for treating infection and that calcium phosphate cement with 2.5% (w/w) vancomycin is useful to prevent the infection and act as good bone defect filler in such reivision arthroplasty.