IN VITRO ELUTION CHARACTERISTICS OF ANTIBIOTIC LADEN HYDROXYAPATITE BONESOURCE™ BONE CEMENT

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INTRODUCTION: The infusion of antibiotics in bone cement can prevent and treat postoperative infections commonly associated with orthopaedic surgery [1,2]. Using bone cement as a drug-delivery vehicle may be more beneficial than systemic delivery because vascular supply to the affected area can be compromised as a result of the infection of traumatized tissue. Resorbable, osteoconductive bone cement does not require a removal surgery, which may be more convenient than commonly used PMMA. In this study, BoneSource™, a calcium phosphate – hydroxyapatite (HA) bone cement, was loaded with antibiotic and evaluated in vitro to determine its elution capabilities with regard to varying concentrations of tobramycin and vancomycin.

METHODS: Nine groups of antibiotic loaded cement cylinders were prepared and placed in saline for 24 hours. Elution rates of tobramycin and vancomycin from BoneSource™ (Stryker-Howmedica-Osteonics, Rutherford, NJ) were evaluated at high, medium, and low doses of antibiotic as outlined below:

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobramycin (g)</td>
<td>.36</td>
<td>.18</td>
<td>.09</td>
<td>.36</td>
<td>.18</td>
<td>.09</td>
<td>.01</td>
<td>.05</td>
<td>.025</td>
</tr>
<tr>
<td>Vancomycin (g)</td>
<td>.01</td>
<td>.05</td>
<td>.025</td>
<td>.01</td>
<td>.05</td>
<td>.025</td>
<td></td>
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</table>

The mean elution rates for tobramycin and vancomycin in all groups and time points were compared using a two-way ANOVA test. Statistical significance was defined as a P < 0.05.

RESULTS: Elution rates of tobramycin in groups 1, 2, and 3, are shown in Figure 1. The rates of the three concentrations did not vary significantly from one and other. There was no significant difference between the elution rates of tobramycin from BoneSource™ and when BoneSource™ was loaded with both vancomycin and tobramycin (Fig. 2). The concentration of tobramycin eluant decreased steadily overtime at comparable rates for all concentrations. In all the tobramycin samples, tobramycin did not drop below the Minimum Inhibitory Concentration (MIC ≤ 4 µg/ml) for the duration of the study.

Elution rates for vancomycin in groups 4, 5 and 6, are shown in Figure 3. The elution rates at the three concentrations did not differ significantly (P ≤ 0.05) after 36 hours (Fig. 3). The elution rates of the medium and low doses of vancomycin (groups 8 and 9) were higher when tobramycin was present than when it was not (groups 5 and 6) (Fig. 4). The vancomycin eluant concentration of group 4 (high dose) differed significantly (P ≤ 0.05) from the concentration in group 6 (low dose) for all time points up to 336 hours. Additionally, group 4’s eluant concentration remained above the MIC (MIC ≤ 4 µg/ml) for the duration of the study.

DISCUSSION: Our results suggest that a combination of BoneSource™ with tobramycin and vancomycin may have clinical applications beyond its current use. The elution rates are comparable to those from PMMA [3]. Antibiotic eluted from the cement can maintain the MIC level of ≤ 4 µg/ml for up to 28 days, indicating possible utility for longer term treatment than is currently noted with PMMA [3]. Vancomycin and tobramycin combined in the cement allows for an increase of the antimicrobial range [4]. Our data additionally supports this combination of antibiotics by showing more effective elution rates, for medium to low doses of vancomycin when tobramycin is added to the cement. Also, at the high dose of tobramycin there was an observed change in the consistency of the cement which may explain the behavior of vancomycin at the high dose mixture. The use of medium to low doses of tobramycin reduces the chance of changing the consistency of the cement. The elution characteristics of tobramycin and vancomycin from the cement support BoneSource™ as a convenient and effective vehicle for antibiotic delivery. Further studies are being conducted to confirm the in-vivo elution characteristics of vancomycin and tobramycin from BoneSource™ and the system’s ability to treat local infection.


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