TOBRAMYCIN-CONTAINING BONE CEMENT AND SYSTEMIC CEFAZOLIN IN A ONE-STAGE REVISION MODEL

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Introduction:
A clinically important application of antibiotic-loaded bone cement is the use in revision operations for infected prostheses. Treatment of an infection can be complicated by the presence of a high bacteria load, necrotic bone and devascularization. A one-stage procedure for revision of an infected prosthesis has the advantage of less inconvenience for the patient, but lower success rates have been reported as compared to two-stage revisions. Earlier animal models showed that gentamicin- and/or vancomycin-loaded bone cement in a one-stage revision could not fully treat the infections. The purpose of the present study was to compare the efficacy of tobramycin-containing bone cement as compared to systemic cefazolin and controls for treatment of infection in a one-stage revision model.

Material and Methods:
The study was approved by the institutional review board. Thirty NZW rabbits (2.2 to 3.0 kg) were operated on. Under general anesthesia, a preformed implant (stainless steel pin with plain cement mantle, 20 mm long, 4 mm wide) was press-fit implanted in the proximal right tibia via the knee joint (Figure 1).

Prior to insertion the medullary canal was inoculated with 10^6 colony forming units (CFU) of Staphylococcus aureus in 0.1 ml saline. Infection was allowed to develop for 28 days. Figure 2 shows a radiograph of a right tibia with the implant still in situ just before the revision on day-28.

At 28 days, the implant was revised. After removal of the implant, the medullary canal was thoroughly debrided. Subsequently, approximately 1 gram of bone cement was injected into the canal. Three rabbits were lost prior to revision. Nine rabbits received tobramycin-containing bone cement, and eight rabbits received also plain bone cement and were treated with systemic cefazolin ("cefazolin"); 30 mg/kg subcutaneously, every 8 hours for 14 days total, starting 15 minutes preoperatively). During their follow-up, the rabbits were monitored for signs of infection (body weight, body temperature, ESR, WBC). Fourteen days after revision (day 42) the rabbits were killed and the femora were excised under aseptic conditions. The cortex adjacent to the cement plug was excised without damaging the cement. After homogenizing 1.0 g of bone in 10.0 ml PBS (pH 7.4), bacterial counts in the suspension were quantified by plating on blood agar (minimum 1000 CFU/g). Statistical analysis of the culture results were made using analysis of variance and Student’s two sample T-test (p<0.05).

Results:
No clear differences between the three treatment groups were seen in body temperature and loss of body weight, ESR and WBC. Results of culture of the cortex of the right femur (adjacent to the cement) showed a significant decrease for both antibiotic groups (tobramycin-cement and systemic-cefazolin) compared to the control group (p<0.05). Results of culture of the tobramycin-cement group were not significantly different from the systemic-cefazolin group. The results of cultures are depicted in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th># rabbits with positive culture</th>
<th>Culture (log CFU/g, mean ± SD)</th>
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<tbody>
<tr>
<td>Tobramycin</td>
<td>2/9</td>
<td>1.1 ± 2.2</td>
</tr>
<tr>
<td>Control</td>
<td>10/10</td>
<td>5.7 ± 1.4</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>0/8</td>
<td>0</td>
</tr>
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Table 1. Results of culture of the cortex of right tibia at day 42. Number of rabbits with positive cultures / total number of rabbits per group and the mean results of cultures.

Discussion:
In the current investigation we demonstrated that both tobramycin-containing bone cement and systemic cefazolin have a clear effect in treating an infection after a one-stage revision in rabbits. This model was set up to mimic a one-stage revision procedure for an infected joint arthroplasty, which provides for a challenging situation when testing for efficacy of an antibiotic treatment. In a previous animal model, tobramycin-containing bone cement could prevent all infections. In the present study, the same cement could not fully treat 2 out of 9 infected rabbits. This can be explained by the spread of infection at time of revision, not within the local area around the bone cement. For this matter, a combination of both antibiotic-containing bone cement and systemic antibiotic might be beneficial: Systemic antibiotics for the wound problems and bacteria outside the operative area, and antibiotic-containing bone cement for local, high release of antibiotic.

Conclusion: This model shows that both tobramycin-containing bone cement and systemic cefazolin used in a one-stage revision for an infected implant can reduce size and rate of infection.

References:

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