An In-vivo Evaluation of the Effect of a Hydroxyapatite Coating With and Without the Use of BMP-7 on Extracortical Bone Bridging Using a Canine Segmental Defect Model

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INTRODUCTION

Aseptic loosening remains a primary mode of failure of total joint replacements. One technique used to theoretically reduce aseptic loosening rates is extracortical bone bridging. Extracortical bone bridging and ingrowth have been shown to reduce stresses on the stem and cement mantle of tumor endoprostheses. Complex bone grafting techniques have been devised in canine models to enhance extracortical bone bridging. Despite encouraging results in canines, microscopic ingrowth of the bridge by bone has not been observed when using porous coated implants. Bone morphogenetic proteins are growth factors and cytokines that induce bone formation. The purpose of this study was to assess the effect of bone morphogenetic protein 7 (BMP-7) delivered by Peri-Apatite (PA, Stryker Orthopaedics) hydroxypatite coating on porous segmental replacement prostheses with respect to bone ingrowth and extracortical bone bridging in a canine segmental defect model.

METHODS

Appropriate approval from our institutional review board and animal care committee was obtained prior to starting this study. Eighteen skeletally mature mongrel canines weighing between 32 to 44 kg were implanted with unilateral segmental replacement prostheses. The prosthesis is made of a cobalt-chromium (Co-Cr) alloy and is coated with two layers of sintered Co-Cr alloy beads (diameter 600 to 800μm). There were three test groups of six canines each. The control group consisted of a plain porous coated segmental prosthesis without any PA coating. Group two consisted of a PA-coated segmental prosthesis coated with buffer solution. Group three consisted of a PA-coated segmental prosthesis loaded with rBMP-7 (Stryker Biotech) in a buffer solution carrier.

A unilateral femoral diaphyseal segmental extraarticular resection measuring 6.2cm was performed followed by implantation of the segmental replacement prosthesis. Group 2 had the buffer solution evenly applied to the porous coat 30 minutes prior to implantation and group 3 had 2.9 mg of BMP-7 in liquid buffer solution evenly applied to the prosthesis 30 minutes prior to implantation. After closure and recovery from the anesthetics, the canines were allowed to fully bear weight without restrictions. The femurs were retrieved at twelve weeks for radiographic and histologic analysis.

Orthogonal radiographs were assessed for a bridging callous, the area of bone formation over the porous segment, and the percentage of bone apposition. Longitudinal thin sectioning of the implants was performed for microscopic analysis of the height of the callous at the shoulder of the implant, percentage depth of bone ingrowth into the porous region of the implant, and bone apposition along the porous coated region.

Statistical analysis between groups was conducted using the one-way ANOVA test with the Tukey-Kramer Multiple Comparison Test for post-hoc comparisons. A p-value of less than 0.05 was considered a significant difference.

RESULTS

Gross and radiographic [Table 1] data of the retrieved specimens showed that all six PA-coated implants augmented with BMP-7 had complete bone bridging; whereas, only one of the PA-coated implants and only two of the plain porous implants were completely bridged. The statistical analysis of the radiographic data showed there was a significantly greater percentage of bone apposition for the BMP-7 augmented PA-coated group compared to both the plain (p=0.0026) and the PA-coated (p=0.0001) groups. There was no significant difference in bone formation or bone apposition between the plain and PA-coated groups.

Bone ingrowth was measured on thin section histology [Fig 1]. Microscopic analysis [Table 2] revealed significantly greater depth of bone ingrowth in the BMP-7 augmented PA-coated group as compared to the plain (p<0.0001) and the PA-coated (p=0.0001) groups. Furthermore, there was also significantly greater bone apposition in the BMP-7 augmented PA coated groups as compared to the plain (p=0.0014) and PA-coated (p=0.0067) groups. There was no significant difference in depth of bone ingrowth or bone apposition between the plain and PA-coated groups.

<table>
<thead>
<tr>
<th>Test Group</th>
<th>Bridging Callous (µm)</th>
<th>Bone Formation (mm²)</th>
<th>% Bone Apposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain</td>
<td>2</td>
<td>186</td>
<td>27</td>
</tr>
<tr>
<td>PA</td>
<td>1</td>
<td>230</td>
<td>16</td>
</tr>
<tr>
<td>BMP-7</td>
<td>6</td>
<td>852</td>
<td>72</td>
</tr>
<tr>
<td>p-value</td>
<td>0.085</td>
<td>0.046</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Fig. 1. Representative thin cut histology of a PA-coated specimen (A) revealing no bone formation or ingrowth as compared to a BMP-7 augmented PA-coated specimen (B) showing significant bone formation and ingrowth.

DISCUSSION

The radiographic and microscopic analysis of our data clearly showed superior extracortical bone bridging, bone ingrowth and bone apposition in PA-coated implants augmented with BMP-7. The effects of BMP-7 on augmenting bone ingrowth and extracortical bone bridging has been reported. Fukuroku et al reported on the effects of BMP-7 when used with allograft in comparison to autograft alone and showed that the BMP-7 augmented allograft combination was far superior to that of autograft alone. Although similar there is a difference between our study and this study. We purposely used no bone graft in our model to remove that factor from the equation. The results of our study when compared to these findings suggest that it is possibly the BMP-7 and not necessarily the autograft or allograft that is enabling the improved ingrowth and bridging suggesting the need for exogenous growth factors to enhance extracortical bone bridging and ingrowth.

There are some limitations to this study. First off, the BMP-7 was applied in a liquid form. Because of this we do not know how the elution or local concentration of BMP-7 varied with time. Nonetheless, our results clearly show that the BMP-7 augmented group had significantly better ingrowth, bridging and apposition. A second major limitation is the short term assessment of the effects of the BMP-7 on the PA-coated implants. It is difficult to speculate on how the extracortical bone bridging and ingrowth would hold up in the long term.

In conclusion, we have demonstrated that BMP-7 when used to augment PA-coated prostheses in a canine segmental defect model can significantly improve extracortical bone bridging and bone ingrowth. In addition, PA-coated implants may be considered to deliver the exogenous biological growth factors.

REFERENCES