• ACCELERATED FRACTURE HEALING BY PERCUTANEOUS INJECTION OF rhBMP-2 AND alpha-BSM

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Introduction: Recombinant human bone morphogenetic protein type-2 (rhBMP-2), a signaling molecule in the transforming growth factor beta (TGF-β) family, initiates transcription through serine-threonine kinase receptors and stimulates new bone formation through chemotaxis, mitosis, and differentiation of mesenchymal cells to chondroblasts and osteoblasts, resulting in initiation of endochondral bone formation (1). Clinical application of BMP is dependent on a suitable delivery system or carrier that can provide localized retention of BMP and ensure controllable bone formation. Percutaneous delivery of BMP/carrer may be superior to direct surgical application in some clinical situations. Several carriers of rhBMP-2 have been utilized in previous work. This study utilized a rapidly resorbable novel synthetic apatitic calcium phosphate bone substitute (α-BSM™, Exet Corporation, Cambridge, MA) that can be injected into the fracture line percutaneously (2). The objective of the study was to determine the effect of BMP on fracture healing and return the bone to intact biomechanical values more rapidly than α-BSM alone.

Methods: All procedures were approved by the institutional animal care and use committee. Sixteen mature female purpose-bred dogs were used for this project. Maturity was confirmed by the radiographic closure of the distal femoral physis. A 1-mm fracture gap was created bilaterally by performing a fluoroscopically guided percutaneous injection of rhBMP-2/α-BSM (0.9 mg)/α-BSM (0.9 mg) in the canine tibia stabilized with an external fixator. We hypothesized that percutaneous injection of rhBMP-2/α-BSM would accelerate fracture healing and return the bone to intact biomechanical values more rapidly than α-BSM alone.

Results: All dogs recovered uneventfully from surgery and were walking within 5 days of surgery. There was no difference between control groups (C vs. CN) for all indices evaluated, therefore these data were combined (C) for subsequent analysis. Bone mineral density (BMD) was higher for BMP than C at 4 weeks in R1, R2, R4, and R5 and at 8 weeks in R1, and BMD for BMP was higher than BSM at all time points and in all ROIs (Fig. 1). For all other times and ROIs there was no difference. When BMD was evaluated over time, the BMD for the BMP group was significantly different compared to intact canine tibia at 8 weeks after surgery (3). Controlled osteotomies were performed in this study to remove variability in fracture configuration. Delayed fluoroscopically guided injection during a second surgery was utilized in an attempt to mimic closed repair of fractures in clinical surgery. This study demonstrates that rhBMP-2/α-BSM injection may be indicated as an adjuvant in the closed repair of fractures prone to delayed or nonunion even in areas of reduced soft tissue coverage where the number of undifferentiated cells may be reduced.

Discussion: This study demonstrates rhBMP-2’s ability to stimulate localized bone formation following percutaneous injection with a rapidly resorbable apatitic calcium phosphate cement. BMP stimulated rapid callus formation as indicated from radiographs and DXA. Callus area, BMD and porosity indicates that callus maturation was more advanced in the BMP group than BSM and C groups. Mechanical testing demonstrated that BMP was not different compared to intact canine tibia at 8 weeks after surgery (3). Controlled osteotomies were performed in this study to remove variability in fracture configuration. Delayed fluoroscopically guided injection during a second surgery was utilized in an attempt to mimic closed repair of fractures in clinical surgery. This study demonstrates that rhBMP-2/α-BSM injection may be indicated as an adjuvant in the closed repair of fractures prone to delayed or nonunion even in areas of reduced soft tissue coverage where the number of undifferentiated cells may be reduced.

For all figures; bars represent means ± SEM; different letters indicate significant difference within each grouping, (p<0.05)

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