Concurrent Release of BMP-2 and Gentamicin in an Infected Open Fracture Model

[1]Rena L. Stewart, [1]Joseph T. Cox, [1]Lisa Keenan, [1]David Volgas, [1]James Stannard,
[2] Lynn Duffy, [2]Ken B. Waites, [3]Tien-Min G. Chu

[1] Division of Orthopaedics, University of Alabama at Birmingham, Birmingham, AL. USA
[2] Department of Pathology, University of Alabama at Birmingham, Birmingham, AL. USA
[3] Department of Restorative Dentistry, Indiana University School of Dentistry, Indianapolis, IN. USA

Introduction: Treatments for open fractures have suboptimal success in preventing and treating infection. One strategy for treating fractures with bone loss is the use of biodegradable, load-bearing scaffolds as a vehicle for osteoinductive molecules. The purpose of this study was to determine whether a scaffold loaded with BMP and antibiotics, implanted in an infected open fracture, decreased the occurrence of osteomyelitis.

Methods: An open femur fracture with 5mm defect and soft tissue injury was created in 32 rats and inoculated with Staphylococcus aureus and Escherichia coli. A scaffold composed of polypropylene fumarate (PPF)/tricalcium phosphate (TCP) was loaded with 10 μg of bone morphogenic protein-2 (BMP-2), and fixed in the defect. Gentamicin was loaded on the scaffold at either control dose (n=10), low dose (n=12), or high dose (n=10) (0mg, 10mg, and 20mg respectively). Serial radiographs were analyzed for evidence of osteomyelitis and callus formation. At 12 weeks, biomechanical testing, microbiological or histological analysis was performed.

Results/Discussion: Radiographically, the highest rate of infection (100%) and lowest rate of callus formation (11%) were seen in the control animals. The low dose antibiotic group showed the lowest infection rate of 50% and the high dose group had an infection rate of 60%. Callus formation was greater in the low dose and high dose groups at 50% and 40%, respectively, compared to controls at the end of the study at 12 weeks.

	Wk 3	Wk 6	Wk 12
Control (BMP)	11%	20%	11%
Low Dose (BMP+10mg Gen)	25%	58%	50%
High Dose (BMP+20mg Gen)	30%	40%	40%

Table 1: Rates of bridging callus formation among the control, low dose, and high dose Gentamicin groups as determined by radiographic analysis.

Complete bridging callus was seen in only 4 specimens. Fibrous non-union was observed in the majority. Positive cultures were found in all control specimens, while both the low dose and high dose groups showed substantially lower occurrences of positive bone cultures.

Conclusions: Decrease in infection rate and increase in bone callus formation rate suggest that gentamicin applied to a biodegradable PPF/TCP scaffold is effective at improving outcomes of open fractures in a rat model.

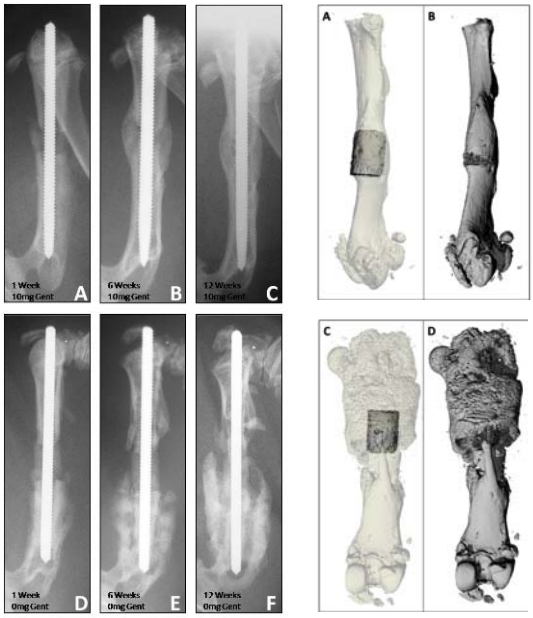

Fig. 1 (Left) X-ray of low dose group (A-C) and control group (D-F) at 3, 6, and 12 weeks. (Right) Micro Ct of high dose group (A, B) and control group (C, D) at 12 weeks.

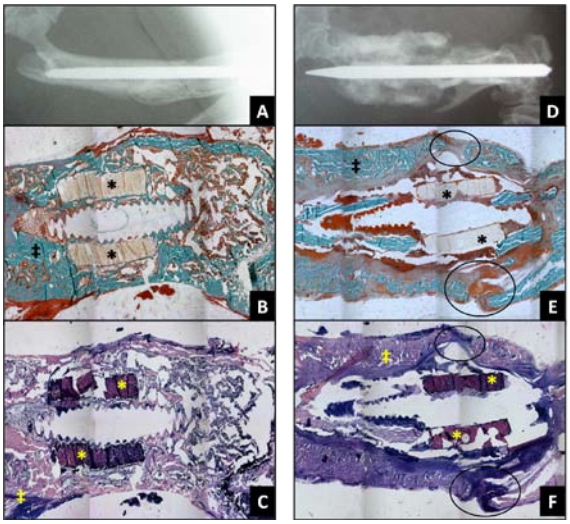

Fig. 2. The x-ray (A), trichrome stain (B) and paragon stain (C) of high dose group at 12 weeks showing callus bridging the fracture gap. The x-ray (D), trichrome stain (E) and paragon stain (F) of control group at 12 weeks showing fibrous tissue in the fracture gap.