Local Antibiotic Delivery With Hydrogels: Pre-Clinical Results

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Infection is a challenging complication in trauma surgery, with detrimental consequences for the patient and generate significant healthcare costs. Systemic antibiotics are often unable to treat infection because of the dose limitations imposed by systemic toxicity and vascular impairment in infected tissues. Hydrogels are ideal local delivery systems in complex surgical sites as they can cover surfaces of every shape and reach small spaces. In this study we evaluated a gentamicin sulphate (GS) loaded thermoresponsive hyaluronan hydrogel (THH) which is a fluid at room temperature and a gel at body temperature in the treatment of a chronic intramedullary (IM) nail-related infection in a large animal model.

THH was synthesized grafting poly N-isopropylacrylamide to hyaluronan via amidation and reconstituted at 13% w/w with 1% GS under sterile conditions. Twelve Swiss alpine sheep received an IM tibia nail and their IM cavity was inoculated with Staphylococcus aureus. A chronic infection was let to develop for 8 weeks. At revision surgery the IM canal was debrided and filled with 25ml of THH containing GS for half of the animals (treatment group) and left empty for the control. All sheep were given systemic amoxicillin and clavulanic acid.

Eight weeks after bacterial inoculation all sheep displayed radiographic signs of infection and the biopsies taken were culture positive with S. aureus. At euthanasia, bacteria were detected in the THH/GS group in 0/6 IM nails, 1/6 bone marrow, and 1/30 tissue samples. For the control group treated with only systemic antibiotics, bacteria were detected in 5/5 IM nails, 5/5 bone marrows, and 8/25 tissue samples (one animal excluded prior to completion of the study).

In conclusion, a human-sized model of device-related infection was successfully established. Local GS delivery by a THH in combination with systemic antibiotics significantly reduced the infection rates whereas systemic therapy alone did not eradicate the infection.