Antibiotic Eluting Calcium Sulphate Beads Lower Bacterial Burden and Prevent Infection in Mouse Model of Prosthetic Joint Infection

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INTRODUCTION: Delayed inoculation of orthopaedic implants in the early postoperative period (i.e. persistent wound drainage, bacterial seeding of a post-operative hematoma, or incisional breakdown) can result in periprosthetic joint infection (PJI). Local antibiotic powder and antibiotic-releasing calcium sulphate beads are two prophylactic strategies used despite limited *in vivo* data comparing efficacy. Our purpose was to (1) Establish a novel in vivo mouse model of PJI via delayed inoculation. (2) Compare the efficacy of systemic vancomycin, local antibiotic powder, and vancomycin-loaded calcium sulphate beads in lowering bacterial burden and preventing infection using the model.

METHODS: A novel mouse model of knee PJI secondary to delayed inoculation was used. A titanium pin was implanted into the distal femur, with 1 mm protruding into the knee joint. Mice were randomized into experimental groups, with treatments given on POD 0: sterile control (SC, n=4); infected control (IC, n=7); 120 mg/kg of perioperative systemic vancomycin (SV, n=9); 2 mg of vancomycin powder (VP, n=18); and vancomycin bead containing 2 mg of vancomycin (VB, n=16). On POD 7, an arthrotomy was performed and the knee was inoculated with $1x10^5$ CFUs of a bioluminescent strain of *S. aureus*. Bacterial burden was monitored *in vivo* (Figure 1). On POD 21, all animals were sacrificed. Implants and soft tissue were harvested and sonicated for CFU analysis. Ex vivo bacteria from each experimental group was collected following CFU analysis on POD21 and was tested for bacterial resistance.

RESULTS: In vivo bioluminescence in the VB group was lower at all time points compared to the other experimental groups. There was an 88% decrease in average soft tissue CFUs in the VB group compared to IC (4.2×10^3 vs. 4.0×10^4, respectively, p=0.027). There was a 98% decrease in average implant CFUs in the VB group compared to IC ($1.6x10^0$ vs. $8.2x10^1$, respectively, p=0.04). There was no difference between any of the other groups. Combined soft tissue and implant infection was prevented in 8/16 (50%) of animals in the VB groups, as opposed to 5/18 (28%) in the VP group, and 0% in the SV and IC groups. There was no change in vancomycin susceptibility in the bacteria cultured from any of the experimental groups.

DISCUSSION AND CONCLUSION: Compared to vancomycin powder, vancomycin loaded calcium sulphate beads reduced bacterial burden and prevented implant and periarticular tissue infections. We present the first *in vivo* data showing efficacy of antibiotic-loaded calcium sulphate beads in lowering bacterial burden and preventing infection following delayed bacterial inoculation in a model of PJI. Antibiotic resistance did not develop in any of the groups treated with vancomycin.

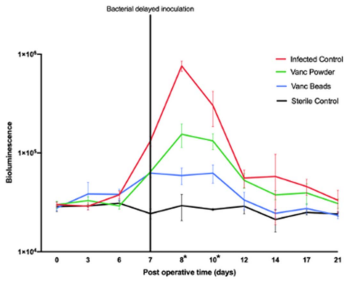

Figure 1. In vivo bioluminescence. *VB with significantly lower bioluminescence compared to all other experimental groups, p<0.05

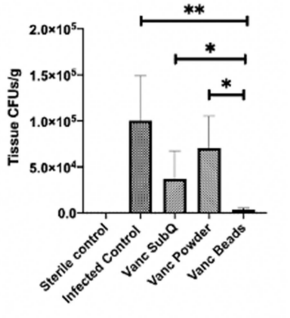

Figure 2. Mean *ex vivo* Tissue CFUs. *Statistical significance, p<0.05

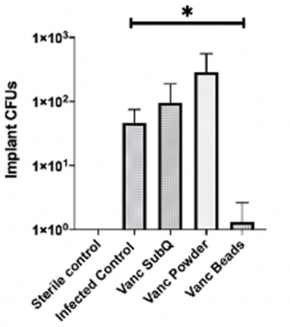

Figure 3. Mean *ex vivo* Implant CFUs. *Statistical significance, p<0.05