Post-Debridement Local Antimicrobial Delivery from PNDJ Gel is Effective for Orthopaedic Infections: A Rabbit Study

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ABSTRACT INTRODUCTION:
Previously, we showed that debridement followed by antimicrobial delivery from PNDJ Gel is effective for Staphylococcus aureus (UAMS-1, ATCC 49230) osteomyelitis with an implant, but no systemic antimicrobial was used in the ‘debridement alone’ group. Now, we study four treatment groups: debridement + local delivery from 1) Gel (PNDJ gel); 2) ALBC (low-dose); 3) SCT (systemic subcutaneous tobramycin), or 4) Gel against infection caused by MRSA (USA-300 strain, ATCC BAA-1556). Is local tobramycin delivery from PNDJ gel following debridement effective for orthopaedic infections?

METHODS:
A 1cm defect was made in the left radius of 26 New Zealand white rabbits, a 1 cm Kirshner wire (K-wire) was inserted, and the site was inoculated with 7.5x10⁶ CFUs of either S. aureus (MSSA, ATCC 49230) or S. aureus (MRSA, ATCC BAA-1556) before closing the wound. Infection established for three weeks before debridement was completed. The subsequent treatment groups were block randomized. The treatment groups include Gel, ALBC, and SCT. Gel (n=6 MSSA, 6 MRSA) was 1 mL of 3.14 wt% tobramycin (release profile similar to high-dose ALBC); ALBC (n=7) was 1 low-dose, standardized 6 x 12mm cylinder (ASTM 451-08) of 1 gm tobramycin per batch Simplex-P bone cement; SCT (n=7) was systemic tobramycin, 10 mg subcutaneous after closure then daily for 4 weeks.

Systemic tobramycin levels were taken at 6 hrs, 1, 3, 7, 14, 21, and 28 days. Treatment success was determined by culture. Necropsies were performed at 28 days for soft tissue, bone and implant culture. Necropy culture data (+ve or –ve) were analyzed by treatment group using Fisher’s Exact Test, alpha=0.05.

RESULTS SECTION:
Infection was resolved (culture –ve with no clinical sign of infection) at 28 days in 1) Gel- 6/6 MSSA and 6/6 MRSA, 2) ALBC- 5/7 MSSA and 3) SCT- 3/7 MSSA. Despite 100% treatment success in the Gel groups, statistical significance was not observed compared for MSSA treatment with Gel vs. SCT (p=0.0699) or Gel vs ALBC (p=0.4615).

DISCUSSION:
PNDJ Gel is an absorbable, thermostensitive hydrogel controlled-release carrier for antimicrobials. All Gel-treated rabbits were culture negative and the other treatment groups had failures. Four rabbits were removed from the study for causes unrelated to treatment (culture-negative at debridement, uncontrolled spread to the foot and joint space, or Pasteurella infection not communicating with the surgical site). One additional success in the Gel/MSSA group would be needed to reach significance versus SCT. When bone cement is not used, PNDJ Gel could be an effective local antimicrobial delivery vehicle; situations such as single stage treatment for PJI.

SIGNIFICANCE:
PNDJ Gel (3.14 wt% tobramycin) provides effective local antimicrobial delivery for MSSA or MRSA in a rabbit infection model.

ACKNOWLEDGEMENTS:
The authors would like to thank Drs. B. Vernon, PhD and M. Caplan, PhD for use of their facilities and ASU DACT for their help in this project.