Δ Characterization of Silver Carboxylate's Biocompatibility and Efficacy as an Antimicrobial Agent

***Dioscaris R. Garcia, PhD**; Colin D. Whitaker; Benjamin Stone; Liam Connolly; Sai Siddharth Allu; Drew James Clippert; Valentin Antoci, MD, PhD; Christopher T. Born, MD, FIOTA*

Purpose: Surgical site infections (SSIs) are a major orthopaedic concern, and contribute to increased costs and high morbidity rates. This problem is compounded in the face of increasingly prevalent multidrug-resistant pathogens, and necessitates the investigation into alternative antimicrobials such as silver for the perioperative setting. Previous silver formulations have limited clinical applications due to their unpredictable pharmacology and known eukaryotic cytotoxicity. Silver carboxylate (AgCar) has emerged as a biocompatible antimicrobial that has the potential to address these concerns. This study aims to quantify both silver carboxylate's safety across primary human cell lines, and efficacy against bacterial strains often implicated in SSIs.

Methods: The safety of AgCar was compared with that of 4 gold-standard antibiotics (linezolid, polymyxin E, tobramycin, and vancomycin), silver nanoparticles, and colloidal silver. Four primary cell lines (endothelial, keratinocytes, osteoblasts, and musculoskeletal) were incubated with the conditions, and cell viability and % cytotoxicity were measured via MTT and LDH (lactate dehydrogenase), respectively. The efficacy of these conditions were compared against Acinetobacter baumannii, Pseudomonas aeruginosa, and methicillin-resistant Staphylococcus aureus (MRSA) via dose-response antimicrobial curves and Kirby Bauer assays.

Results: MTT assays showed that a 1X (minimum inhibitory concentration (MIC) of AgCar resulted in similar or higher cell viability for musculoskeletal (88.6%), endothelial (104.3%), and osteoblast (68.2%) cells when compared to cell viability rates for gold standard antibiotics and other silver forms. 1X AgCar demonstrated 38.7% viability for keratinocytes, a value that was similar to or lower than other conditions. LDH assays were inconclusive across 4 cell lines. Kirby Bauer assays demonstrated that 1X AgCar was as good or better than tobramycin and polymyxin E at inhibiting both A. baumannii and P. aeruginosa over 72 hours. Dose response data suggest that AgCar was significantly effective compared to tobramycin against A. baumannii, and at least 1.5 times more effective against P. aeruginosa. The assay also showed AgCar to be more effective against P. aeruginosa than polymyxin E. AgCar resulted in a low reduction in bacterial load and a lower inhibitory effect than vancomycin against MRSA.

Conclusion: Silver carboxylate shows safety promise across primary cell lines and demonstrates effectiveness at neutralizing gram-negative bacteria, with some effectiveness against gram-positive bacteria. AgCar should be considered for future in vivo models, perhaps investigating AgCar as a synergistic adjuvant with antibiotics for SSIs.

Δ OTA Grant