[FP63] BIOFILM PREVENTION OF CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE) AND VANCOMYCIN RESISTANT ENTEROCOCCI (VRE) BY ANTIBIOTIC-LOADED CALCIUM SULFATE BEADS (ABLCB) IN VITRO.

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Aim: Carbapenem-resistant Enterobacteriaceae (CRE) and vancomycin resistant Enterococci (VRE) have emerged as multi-drug resistant Gram-negative pathogens associated with Periprosthetic Joint Infections (PJI). In this study, we evaluated the efficacy of antibiotic-loaded calcium sulfate beads (ABLCB) to inhibit bacterial growth, biofilm formation and eradicate preformed biofilms of ***K. pneumoniae*** and ***E. faecalis***.

Method: Three strains of ***K. pneumoniae*** (carbapenem resistant BAA1705, New Delhi metallo-beta-lactamase producing BAA2146 [NDM-1], a carbapenemase producing BAA2524) and a vancomycin resistant strain of ***E. faecalis*** (ATCC51299) were used. 4.8mm diameter ABLCBs (Stimulan Rapid Cure, Biocomposites) were loaded with vancomycin (VAN) & gentamicin (GEN) at 500 and 240 mg/10cc pack or VAN & rifampicin (RIF) at 1000 and 600 mg/10cc pack respectively and placed onto tryptic soy agar (TSA) plates spread with each of the four strains independently and incubated for 24 hours at 37°C. The beads were transferred daily onto fresh TSA medium spread with the test cultures. The zone of inhibition was recorded until no inhibition was observed. Biofilm prevention efficacy was investigated in 6 well plates. Bacterial cells ($5x10^5$ CFU/mL in tryptic soy broth) were treated with ABLCBs. Media was removed and challenged with bacteria daily for 7 days. CFU counts were taken after 1, 2, 3 and 7 days. For biofilm killing, ABLCB were added to 3 day formed biofilms in 6 well plates. CFU counts were estimated at 1, 3 and 7 days with daily media exchange.

Results: ABLCB demonstrated effective initial eluting concentrations depending on the strains. The NDM-1 strain of ***K. pneumoniae*** had lower sensitivity than other strains towards VAN & RIF and resistant towards VAN & GEN. ***E. faecalis*** was sensitive to both combinations. For repeat challenges, ABLCBs prevented colonisation and reduced biofilm formation, except for the NDM-1 strain which grew in the presence of VAN & GEN. Preformed biofilms were more difficult to reduce with antibiotics than in the prevention assay. Biofilm growth was observed at 1 week of contact with ABLCBs, despite negative cultures at earlier time points for ***K. pneumoniae*** and ***E. faecalis***. However, there was a significant killing (2-3 logs, $P<0.05$) of biofilm bacteria with all antibiotic combinations compared to unloaded beads.

Conclusions: This study provides evidence that local release of antibiotics from ABLCBs may be useful in the treatment of multidrug resistant strains of ***K. pneumoniae*** and ***E. faecalis*** (CRE and VRE) associated with PJIs. ***In-vitro*** results do not necessarily correlate to clinical results.