#2018 - Experimental Study / Free Papers

Radioimmunotherapy Combating Methicillin-Resistant Staphylococcus Aureus And Its Biofilm In Vitro: A Promising Approach

Orthopaedics / Musculoskeletal Infections / Miscellaneous

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Background
Prosthetic Joint Infection (PJI) is a devastating complication of arthroplasties, causing a critical burden in healthcare. Biofilm formation is the main challenge, as it concurrently shields bacteria from host immune responses and confers resistance to antibiotics. The emergence of Methicillin-resistant *Staphylococcus aureus* (MRSA) further complicates PJI management. This study investigates the potential of radioimmunotherapy as a targeted approach to address the challenges posed by MRSA and its biofilm.

Objectives
This study aims to develop a specific monoclonal antibody (mAb) for MRSA labeled with lutetium-177 (^{177}Lu), initiating with in vitro quality control tests as a first step in the production of a new radiopharmaceutical. Furthermore, we intend to assess the specificity and bactericidal efficacy of these radiolabeled antibodies on both planktonic MRSA and biofilm in vitro.

Study Design & Methods
The mAb 4497-IgG1, which targets wall teichoic acids that are cell and biofilm specific, was labeled with ^{177}Lu using DOTA as chelator. Radiochemical purity was determined using thin layer chromatography. Immunoreactivity assay was assessed on planktonic MRSA and antibacterial efficacy of the radionuclide-antibody complex was evaluated on planktonic cells and biofilms of MRSA after 96 hours by CFU counting and XTT reduction assay.

Results
The radiochemical purity of the ^{177}Lu-mAbs complex was determined to be 96±0.4%. Immunoreactivity of the complex was measured at 83±0.6%. ^{177}Lu-mAbs exhibited significant and dose-dependent antimicrobial effects on both planktonic MRSA and biofilm. Treatment of planktonic bacteria with 7.4MBq and 14.8MBq of ^{177}Lu-mAbs resulted in a 2.5-logarithm and 6-logarithm reduction in CFU count, respectively. Biofilm treatment with the same radioactivity levels caused a 2-logarithm and 3.5-logarithm reduction in CFU count, respectively.

Conclusions
Our in vitro study show the proof-of-concept of the specificity and bactericidal efficacy of ^{177}Lu-labeled antibodies. This indicates that radioimmunotherapy could be a potential targeted therapeutic strategy against MRSA and its biofilm. Further research in preclinical and clinical settings is warranted to validate and refine these findings on biofilm-associated implant infections.