2022 TOA Annual Conference Abstract Submission

PRESENTATION TITLE:
Intrawound Vancomycin Achieves Sustained High Interstitial Concentrations in Injured Human Extremities

AUTHOR:
Taylor Bates

DEGREE:
MD

INSTITUTION:
San Antonio Military Medical Center

CO-AUTHORS:
Gerardo R. Garcia
Matthew Burgess
Sarah Pierrie

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No

LIST ANY DEVICES NOT CURRENTLY APPROVED FOR USE BY THE FDA:
n/a

STRUCTURED ABSTRACT (PURPOSE, METHODS, RESULTS, AND CONCLUSIONS) IN LESS THAN 400 WORDS:

PURPOSE:
To evaluate the concentration of vancomycin powder administered upon closure of open wounds associated with adult long bone fractures.

METHODS:
Patients with open fractures were enrolled in a non-randomized observational study evaluating the pharmacokinetics of circulating antibiotics in traumatized tissue. Subjects whose surgeon placed vancomycin powder within the traumatic wound were included. Following debridement, a microdialysis catheter was placed into the wound bed. A second catheter was placed in an uninjured (control) limb. Whole blood and dialysate samples were collected over 24 hours. Free vancomycin was analyzed by ultra-high performance liquid chromatography. Pharmacokinetic parameters were estimated by noncompartmental analysis from time concentration curves of free (f, non-protein bound) antibiotic measured in plasma and interstitial fluid (ISF) using dedicated pharmacokinetic software assuming first order elimination. Systemic and peripheral tissue antibiotic exposure were expressed as area under the time-concentration curve (f AUC0→24hrs, hr·µg/mL) and peak concentration (f Cmax, µg/mL) with matched tissue ISF concentrations for the injured limb and uninjured (control) limb at each sampling point.

RESULTS:
Five adult patients (1 female, 4 male; 1 fibula, 4 tibias) with an average age of 40 years were included in this analysis. The soft tissue injuries, classified using the Gustilo-Anderson system, consisted of 3 grade II injuries and 2 grade IIIA injuries. The total local vancomycin dose ranged from 1 to 2 grams per patient. The average maximum concentration of free vancomycin (f Cmax) in injured limbs was 193.16 µg/mL. This decreased to 63.42 µg/mL ± 39.87 at the end of the sampling period, representing a 67.2% decrease in vancomycin concentration after 24 hours. Free vancomycin exposure over 24 hours (f AUC0→24hrs,

2463.46 hr·µg/mL) in injured limbs was significantly greater than that of uninjured limbs (15.00 µg/mL) and of plasma (2.10 µg/mL). When f AUC0→24hrs is compared to minimum inhibitory concentration (MIC) data for methicillin-resistant Staphylococcus aureus (MRSA) (using organism frequency data based on the EUCAST MIC table January 2022), the free vancomycin level in the injured limb exceeds MIC 8 µg/mL over 24 hours.

CONCLUSION:

When a common vancomycin dose is placed in the wound, the free vancomycin level remains above the breakpoint MIC for MRSA (1 µg/mL) through this period. The concentration of vancomycin in the uninjured extremity and in plasma was negligible during the same period and remained below systemic toxicity levels (< 20-25 µg/mL). Vancomycin powder is likely to remain effective and safe beyond 24 hours if a therapeutic concentration is delivered.