Abstract

SUBGROUP ANALYSIS OF BAYESIAN-DERIVED VANCOMYCIN AUC AND AUC/MIC FOR MRSA-ASSOCIATED INFECTIONS AND SPECIAL POPULATIONS

Rationale for Study/Background:

In 2020, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists released an updated vancomycin guideline that recommends a Bayesian-derived AUC/MIC ratio of 400 to 600, assuming MIC is 1 mg/L, as the preferred optimal pharmacokinetics and pharmacodynamics target over trough concentrations. While data is limited, multiple studies have shown that an AUC range of 700 to 1300 mg*h/L has been associated with an increased risk of nephrotoxicity. Despite this, there are limited studies on the subgroup analysis of the AUC threshold for vancomycin nephrotoxicity for different types of MRSA-associated infections and vancomycin special populations. Similarly, there are limited studies on the generalizability of vancomycin's efficacy target of an AUC/MIC ratio ≥400 for different types of MRSA-associated infections and vancomycin special populations. An AUC/MIC ratio ≥400 was initially extrapolated from the clinical success of using this target to treat Staphylococcus aureus pneumonia. It was then largely derived from numerous retrospective, single-center observational studies of patients with MRSA bacteremia. Limited studies on the proposed target's generalizability warrants further investigation on vancomycin's optimal AUC/MIC ratio for efficacy and maximum AUC to minimize nephrotoxicity in different MRSA-associated infections and vancomycin special populations.

Objectives: To retrospectively investigate the optimal Bayesian-derived AUC and AUC/MIC targets for MRSA-associated infections such as pneumonia, bacteremia, sepsis, endocarditis, septic joints, SSTIs, infected hardware, and osteomyelitis and also vancomycin special populations such as amputees, methamphetamine users, intravenous drug users, HIV patients, ICU patients, and patients on concomitant immunosuppressants or nephrotoxins.

Primary Outcomes: Clinical improvement defined as resolution, disappearance, or marked improvement of acute infection; clinical failure defined as persistence of acute infection despite vancomycin or vancomycin-susceptible infection requiring change in therapy; nephrotoxicity defined as increase in serum creatinine by ≥0.3 mg/dL within 48 hours or 50% increase from baseline within 7 days

Secondary Outcomes: Time-to-achieve symptomatic improvement, time-to-achieve normal WBC, time-to-achieve afebrile

Methodology: Medical records were reviewed at San Joaquin General Hospital to identify hospitalized patients treated with vancomycin between June 2019 to June 2020. Patients aged ≥18 years who require vancomycin for treatment of an infection, on vancomycin for ≥48 hours, and have ≥1 vancomycin concentration collected were eligible for inclusion. Patients were excluded if they were pregnant, on any form of renal replacement therapy, on vancomycin for surgical prophylaxis, on vancomycin continuous infusion, or have a MRSA infection with vancomycin MIC ≥2 mg/L. Collected patient demographic and treatment characteristic data included comorbidities, ICU admission, methamphetamine use, intravenous drug abuse, concomitant immunosuppressants or nephrotoxic drugs, isolated bacterial species, and infection indicated for vancomycin. Clinical outcomes assessed included clinical improvement, time-to-achieve symptomatic improvement, normal WBC, and afebrile, clinical failure, and nephrotoxicity. Using a Bayesian dose-optimizing software, PrecisePK, the average cumulative AUC over 24 hours (AUC24h), average steady-state AUC24h, and their respective AUC24h/MIC were estimated. These values will be

stratified and a subgroup analysis of MRSA-associated infections and vancomycin special populations will be conducted to assess the clinical outcomes. Statistical analysis will be done using the SPSS Statistics 26 software. Categorical variables will be summarized using frequencies and percentages and continuous variables will be summarized using means and standard deviations. For comparisons, Fisher's exact test will be used for categorical data and student's t test will be used for continuous data. Classification and regression tree (CART) analyses will be performed to determine the significant AUC24h/MIC and AUC24h thresholds for vancomycin efficacy and nephrotoxicity, respectively.

Results: Preliminary results will be presented.

Conclusion: This research is in progress.