Session: P-59. PK/PD studies

Background. New vancomycin (VAN) guidelines have been published, with recommendations that dosing in patients (pts) with methicillin-resistant S. aureus (MRSA) infections be guided by VAN area under the concentration-time curve from 0 to 24 h to MIC ratio (AUC/MIC). The guidelines emphasize daily AUC values should be between 400-600 mg*h/L to maximize efficacy and minimize likelihood of acute kidney injury (AKI). Our physicians and clinical pharmacists currently use trough levels to manage outpatient VAN dosing with a general target of 15-20 mg/L. The current pharmacokinetic (PK) model provides an option for dosing using trough or calculated AUC.

Methods. We identified pts receiving VAN for S. aureus infections (default MIC of 1 mg/mL) from 2018-2020. We conducted a PK evaluation of pts with ≥1 trough level and compared it to model predicted AUC<sub>T</sub>. Data collected included pt characteristics, VAN regimen, trough concentrations, PK evaluation, and AKI, defined as a 50% decrease in CrCl from baseline. A Bayesian PK model was used to calculate predicted dosing based upon trough concentrations (DoseMeRx, Moorstown, NJ).

Results. 100 pts (mean age: 61±15 yrs, 62% male) from 6 ICUs were included, with 82% treated for MRSA and 18% for methicillin-sensitive S. aureus infection. Mean initial dose of VAN in the ICU was 2.6±1 g/d in divided doses, most frequently every 12 hrs (68%). Median duration of outpatient therapy was 28 days [IQR, 16-36], 69% received VAN in the hospital prior to the OIC. 100 pts had 239 trough levels with a corresponding PK analysis. Mean trough levels were 17.1±6.4 mg/L. Mean corresponding AUC<sub>T</sub> was 498±98 mg*h/L. The relationship between trough and AUC<sub>T</sub> is shown in Fig 1. 25 evaluations indicated an AUC<sub>T</sub> > 400, with 8 (32%) resulting in a dose increase. 13 evaluations indicated AUC<sub>T</sub> > 600, with 6 (46%) resulting in a subsequent dose decrease. 4 pts developed reversible AKI, all with AUC<sub>T</sub> > 540. Use of AUC<sub>T</sub> for dose management provided opportunities to adjust dosing in 38/239 evaluations (16%).

Conclusion: This PK evaluation showed a correlation between trough levels and AUC<sub>T</sub>, with opportunities for VAN dose adjustment using AUC<sub>T</sub>, and to identify pts at risk for developing AKI. Dosing with AUC<sub>T</sub> is particularly useful in the outpatient setting in which true trough evaluations can be difficult to obtain.

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1328. Vancomycin exposure and utilization following implementation of an AUC-guided monitoring guideline in children

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Background. The 2009 guideline for vancomycin (VAN) monitoring recommended trough (TR) of 15-20 mg/L to target AUC/MIC ≥ 400. Studies have suggested attainment of target AUC/MIC ratio with TR 7-11 mg/L in most children. Prior to 2018, TR 15-20 mg/L was the primary target for VAN therapeutic monitoring at CHOC Children’s. Beginning in 2018, a clinical guideline was implemented which recommend targeting AUC/MIC of 400-600 or TR of 7-15 mg/L. Our objectives are to evaluate differences in VAN utilization, exposure, nephrotoxicity and cost savings between pre (Pre-guideline, pG) and post implementation (Post-guideline, PG) of a VAN monitoring guideline at CHOC Children’s.

Methods. Retrospective chart review of patients prescribed VAN between Jan 2016 – Jun 2017 (pG) and Jan 2018 – Jun 2019 (PG). Primary objectives evaluated differences in pharmacokinetic (PK), AUC and rate of nephrotoxicity in patients 3 months to < 18 years who received VAN ≥ 24 hour with ≥ 1 TR. Secondary objectives assessed differences in overall VAN utilization following guideline implementation.

Results. Seventy patients were included in the PK analysis, 35 in pG and 35 in the PG group. Median age, weight, gender, baseline creatinine, concurrent nephrotoxic agents were similar. There were no differences in duration of therapy or starting doses (mg/kg/day) between the two groups. The highest daily dose (mg/kg) and AUC (mg*h/L) attained was significantly higher in pG compared to PG group (7.49 vs. 5.99, p = 0.002 and 647 vs. 469, p < 0.0001, respectively). Changes in AUC from the initial regimen to the highest adjusted regimen was also higher in pG group (532 vs. 647, p = 0.0008) while there was no difference in PG group (459 vs. 469, p = 0.647). More patients experienced nephrotoxicity in pG compared to PG (11.4% (4/35) vs. 0 (0/35), p = 0.039). Logistic regression analysis identified AUC 800-900 as a significant risk for nephrotoxicity. Compared to pG, PG resulted in a net reduction in VAN utilization of 19.7 DDD per 1000 patient days, savings of $140,150 and 738 fewer levels drawn.

Conclusion. In line with the 2020 consensus guideline recommendation for AUC-based VAN monitoring, our study found AUC-guided VAN monitoring in children resulted in less exposure, utilization, and nephrotoxicity.

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