Poster
#1599

AUC24 vancomycin Bayesian-based dosing: Increasing therapeutic target attainment with decreased TDM cost

Paul E. Sabourenkov, Mbioinf(Adv), Robert C McLeay, PhD – DoseMe, Brisbane, Australia

Corresponding author:

Paul Sabourenkov, Mbioinf(Adv)
Computational Biologist
DoseMe / Tabula Rasa HealthCare
psabourenkov@dosemehealth.com

Background

- Vancomycin efficacy is optimally predicted by the area under the concentration-time profile (AUC24), yet for clinical ease, surrogate Cmin (trough) targets have traditionally been used.
- The variable relationship between trough and AUC24 has been demonstrated to lead to overexposure in approximately 40% of patients, who will achieve a therapeutic AUC24 with a trough lower than the traditional 10-20 mg/L target, with unnecessary increased nephrotoxicity risk *(Chavada R, et al. Antimicrob. Agents and Chemo. 2017;61:e02535.)*
- Traditional AUC24-based dose calculation methods involve analytic pharmacokinetic calculations that require both peak and trough drug levels, increasing cost and time compared to trough-based dosing.
- Recent literature (Rybak *et al. ASHP draft vancomycin guidelines 2019)* suggest that Bayesian dosing tools alleviate the cost and difficulty of implementing AUC24-based dosing in order to improve patient outcomes.

Objectives

- Compare therapeutic range attainment amongst 5 hospitals across the US, Europe, and Australia using trough-based dosing versus 5 hospitals using either Bayesian-supported AUC24 dosing or Bayesian-supported trough-based dosing with AUC24 prominently displayed at time of decision-making.

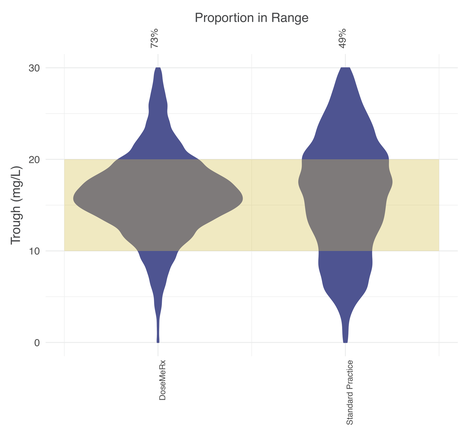
Methods

- De-identified data from retrospective chart reviews for patients receiving vancomycin were available from five hospitals across the US, EU, and Australia that used a trough-based dosing method.
- De-identified data from five matched-size hospitals that implemented Bayesian-based AUC24 dosing (n=2) or trough-based dosing with AUC24 prominently presented (n=3) using commercially available software (DoseMeRx) were collected.
- The proportion of doses in the therapeutic target range was determined for each hospital, and the number and cost of therapeutic drug monitoring (TDM) levels required were compared.

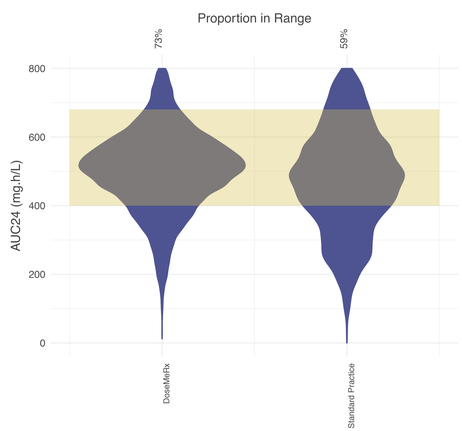
Results

- Five hospitals using clinician-led trough-based dosing without Bayesian or model-informed precision dosing had data for 409 adult patients, 13,775 doses, and 5,660 drug levels collected.
- Five hospitals using model-informed precision dosing (DoseMeRx) had data for 1,499 patients, 21,107 doses, and 7,310 drug levels collected.

Doses achieving C_{min} 10-20 mg/L



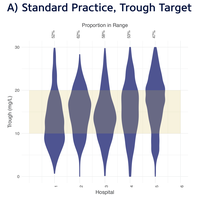
Doses achieving AUC_{24} 400-680 mg.h/L



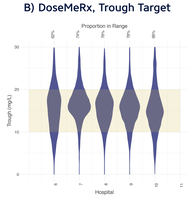
- Mean dose was significantly lower in the model-based dosing cohort (1118 mg vs 1413 mg; p < 1x10-15).
- Bayesian-dosing hospitals had a significantly higher proportion of doses achieving the therapeutic target for both AUC24 (73% vs 59%; Chavada et al. therapeutic target) and trough (73% vs 49%. p < 1 x 10-15; KS test).
- Variability was significantly higher in standard practice hospitals than those using DoseMeRx for trough-based target attainment with SD=6.9 mg/L vs 5.6 mg/L; AUC24 SD=154 mg.h/L vs. 137 mg.h/L.

	Standard Practice	DoseMeRx
# Patients	409	1499
# Male	268 (65.5%)	834 (55.6%)
Age (years)	60.0 (18.8-96.7)	66.7 (18.4-100.5)
Weight (kg)	80.1 (44-200)	79.9 (30-220)
Height (cm)	171.0 (150-198)	169.1 (122-202)
Doses Per Course	11.7 (11.3)	13.0 (15.3)
Conc. Per Course	4.4 (4.8)	3.5 (3.1)
Dose (mg)	1413 (740)	1118 (385)
Concentration (mg/L)	19.6 (7.5)	17.8 (6.4)

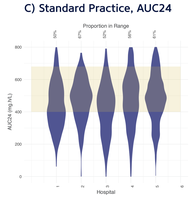
A) Standard Practice, Trough Target



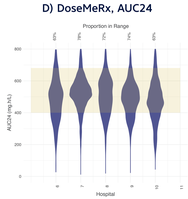
B) DoseMeRx, Trough Target



C) Standard Practice, AUC24



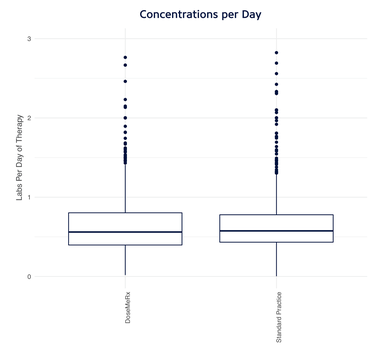
D) DoseMeRx, AUC24



Results

Cost data

- The median number of concentrations taken per day of vancomycin therapy were significantly lower at 0.56 for the DoseMeRx and and 0.58 for the standard-practice cohorts respectively (p<0.002; KS test).



- More variance was present in the number of concentrations taken per-day between hospitals within group than between standard-practice hospitals (1-5) and Bayesian-dosing hospitals (6-10).
- The Bayesian-dosing hospital with the fewest concentrations per day of therapy (Hospital 7; figure D) not only took fewer levels (0.36/day vs mean 0.58/day; 36.0% fewer concentrations; p<0.05), but also performed significantly better than the mean (78% vs 73% doses in AUC range), suggesting that Bayesian dosing may permit safe reduction in the number of vancomycin levels taken.

Conclusions

- Mean vancomycin dose was significantly lower in the Bayesian-based dosing cohort compared to the standard-practice cohort, suggesting a lower likelihood of acute kidney injury risk.
- The Bayesian-dosing cohort achieved a significantly higher proportion of doses within both the target trough and target AUC24 therapeutic ranges.
- Using model-informed precision dosing to target AUC24 avoided increased laboratory cost, with median number of assays per day of therapy slightly lower than for standard-practice trough-based dosing. Vancomycin dosing protocols could potentially be adjusted to reduce the number of concentrations taken by approximately one-third while maintaining efficacy and safety.

Disclosure: The authors of this paper disclose that they are employees of DoseMe, a commercial provider of model-informed precision dosing software.