Rapid attainment of pharmacodynamic parameter goals in patients receiving vancomycin or aminoglycosides for serious infections

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Objectives: Compare the AUC_{24}/MIC ratio for initial vancomycin doses and the Cmax/MIC ratio for initial gentamicin/tobramycin doses selected by treating clinicians using estimated population parameters and actual computed parameters to those attained after individualized adjusted doses were prescribed.

Methods: 298 patients (152 vancomycin/146 aminoglycoside) were included using the following criterion: treating clinicians self-identified vancomycin treatment goal of AUC_{24}/MIC>400 or aminoglycoside treatment goal of Cmax/MIC≥10, culture-documented MRSA or gram-negative infection, MIC measured using the Etest method, vancomycin or aminoglycoside plus serum creatinine concentrations during therapy. Estimated population AUC_{24} for vancomycin was determined using the following equation: $AUC_{24} = D/\{[(CrCl_{est} \bullet 0.79) + 15.4] \bullet 0.06\}$, where D is vancomycin dose in mg for a 24 hour period and $CrCl_{est}$ is estimated creatinine clearance in mL/min [Cockcroft-Gault for nonobese patients (within 30% IBW)

(Methods, cont): and Salazar-Corcoran for obese patients (> 30% over IBW)]. Estimated population Cmax for gentamicin/tobramycin was determined using the following equation: $Cmax = [(D/t')(1-e^{-kt'})]/[kV(1-e^{-kt})]$, where D is aminoglycoside dose, t' is the infusion time, t is the dosage interval, k is the elimination rate constant ($k = 0.00293(CrCl_{est})+0.014$ and $CrCl_{est}$ is estimated creatinine clearance in mL/min), V is the volume of distribution (0.26 L/kg for nonobese, or ABW for obese [ABW=IBW+[0.4(TBW-IBW)], TBW=total body weight). Estimated population MIC for each bacteria was the average institutional value for the organism during the past 6 months. Actual and adjusted AUC_{24} vancomycin or Cmax aminoglycoside values were computed using a Bayesian computer program (using a measured trough vancomycin concentration 2-5 doses after initial dosing or a dosing adjustment began, or a measured aminoglycoside concentration 2-6h post-dose, 2-3 doses after initial dosing or a dosing adjustment began). Initial antibiotic doses were determined by the treating clinicians, and adjusted antibiotic doses were prescribed to attain treatment goals.

Results: While treating clinicians expected all doses initially prescribed to patients to attain the treatment goal, only 51% of the vancomycin dosage regimens were expected to achieve goal using population estimates for AUC_{24} and MIC, and only 76% of the aminoglycoside dosage regimens were expected to achieve goal using population estimates for Cmax and MIC. For initial dosing of vancomycin, only 35% of patients actually achieved the goal of AUC_{24}/MIC>400. For initial dosing of aminoglycosides, only 64% of patients actually achieved the goal of Cmax/MIC≥10. Subsequently, the adjusted dosage achieved the treatment goal in all cases (100%; p<0.01).

Conclusions: Antibiotic doses can be rapidly individualized using Bayesian techniques to attain widely-used pharmacokinetic/pharmacodynamic goals. Clinician-prescribed initial doses or doses computed using population estimates will not achieve this goal for all patients, but at the outset a higher percentage of aminoglycoside patients will reach goal pharmacodynamic values compared to vancomycin patients (p<0.05).

	Vanco AUC24 /MIC	Vamco AUC24 /MIC	AGS Cmax /MIC	AGS Cmax /MIC
	≤ 400	> 400	< 10	≥ 10
Clinician expected, initial dose	0 %	100%	0 %	100%
Est. Pop. PK/PD, initial dose	49%	51%	24%	76%
Actual PK/PD, initial dose	65%	35%	36%	64%
Actual PK/PD, adjusted dose	0%	100%	0%	100%