



**Conclusion.** The single-trough method performed similarly to the more laborious P/T method. No patient would have received a dose adjustment based on the two different AUC estimation methods. The single-trough method may represent a resource and work-force conscious AUC estimation method for patients meeting population assumptions.

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### 1108. Evaluation of Vancomycin Dosing in Adolescents

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**Session:** P-62. PK/PD Studies

**Background.** Pediatric vancomycin dosing varies based on age and renal function. Recent literature suggests previously recommended doses of 45-60 mg/kg/day may be insufficient to achieve an AUC:MIC ratio of 400-600 mg-hr/L and higher doses of at least 60 mg/kg/day may be required. However, data to guide dosing in adolescents is limited.

**Methods.** A single-center, retrospective chart review of patients aged 12 to 18 years who received vancomycin and had therapeutic drug monitoring (TDM) performed between July 2017 to June 2020 were included. The primary endpoint was the median total daily dose (TDD) of vancomycin required to achieve therapeutic serum concentrations. Secondary endpoints were to characterize how factors such as age, weight, trough versus AUC monitoring, malignancy, and trauma may influence dosing. The safety endpoint was the development of acute kidney injury (AKI).

**Results.** 130 vancomycin courses in 86 patients were included. Baseline characteristics are presented in Table 1. Of the 130 vancomycin courses, 50 courses (38%) achieved therapeutic serum concentrations at a median TDD of 49.8 mg/kg/day (IQR 42 - 59.4). This was not statistically different from the sub- or supra-therapeutic groups (p=0.22). Based on age, the median TDD for 12-14 year olds was higher at 60 mg/kg/day (IQR 45-78.8; n=14) than for 15-16 and 17-18 year olds [45.3 mg/kg/day (IQR 41.1-51; n=15), 48 mg/kg/day (IQR 42-52; n=21), respectively]. Obese patients needed a median TDD of 43.5 mg/kg/day vs at least 51 mg/kg/day in healthy and overweight patients. Finally, AUC guided dosing resulted in a slightly lower overall median TDD vs trough guided dosing (45.8 mg/kg/day vs 50.5 mg/kg/day). Additional dose requirements based on age, weight, TDM and other characteristics are presented in Table 2. Of the 15 patients who developed AKI per pRIFILE criteria, 2 were classified as injury and 3 as failure.

Table 2. Total Daily Dose Course Analysis

Category	Total Daily Dose (mg/kg/day)			p-value
	Therapeutic	Sub-therapeutic	Supra-therapeutic	
Primary Outcome	49.8 (42 - 59.4) n=50	47.5 (45 - 60) n=42	57 (45 - 60) n=38	0.22
Age (n=130)				
Age 12 - 14 n=41	60 (45 - 78.8) n=14	56.8 (45 - 60) n=13	57.7 (45 - 60) n=14	0.32
Age 15 - 16 n=33	45.3 (41.1 - 51) n=15	46.6 (45 - 60) n=14	67.5 (56 - 75) n=4	0.05
Age 17 - 18 n=56	48 (42 - 52) n=21	47.6 (37.6 - 51) n=15	50.8 (44.8 - 61.2) n=20	0.26
Age 15 - 18 n=89	46.6 (41.8 - 51.7) n=36	47 (45 - 56) n=29	54.5 (45 - 63.1) n=24	0.088
Weight (n=129)				
Underweight n=7	n=0	47 (45 - 84) n=7	n=0	-
Healthy n=73	51 (45 - 60) n=29	50.7 (45 - 60) n=21	58.4 (48.2 - 62.4) n=23	0.46
Overweight n=19	51.2 (43.8 - 58.3) n=8	45.7 (43.2 - 51.8) n=8	75 (57 - 75) n=3	0.078
Obese n=30	43.5 (33.6 - 50.5) n=12	45 (27.8 - 60) n=6	45 (33.6 - 60) n=12	0.51
Trough based dosing (n=85)				
All patients	50.5 (43.2 - 56.7) n=30	47.2 (44.5 - 56.4) n=28	58.4 (45 - 60.1) n=27	0.17
Median Trough Level	12.9	8.0	20.2	-
Age 12 - 14 n=22	60 (45 - 79) n=7	56.8 (45 - 63.2) n=7	60 (57.6 - 60.1) n=8	0.84
Age 15 - 16 n=20	46.8 (38 - 51) n=7	45 (45 - 47) n=9	67.5 (56 - 75) n=4	0.03
Age 17 - 18 n=43	50.5 (42.6 - 53.2) n=16	48.5 (39.8 - 51.8) n=12	48.2 (44.6 - 60) n=15	0.72
AUC based dosing (n=45)				
All patients	45.8 (39.3 - 60) n=20	55.2 (45 - 60) n=14	57 (40.5 - 59.7) n=11	0.78
Median AUC Level	470.4	341.5	762	-
Age 12 - 14 n=19	60 (37.5 - 78.8) n=7	52.2 (27.8 - 60) n=6	48.3 (39.5 - 57) n=6	0.20
Age 15 - 16 n=13	45.2 (43 - 50.7) n=8	60 (60 - 84) n=5	n=0	0.057
Age 17 - 18 n=13	41.6 (37.2 - 46.3) n=5	46.2 (28.8 - 51) n=3	59.7 (57 - 62.4) n=5	0.09
Active Malignancy n=32	46.8 (43.3 - 59.4) n=15	60 (47.5 - 63.2) n=9	54.3 (48.3 - 58.5) n=8	0.18
Trauma n=25	50 (42 - 52) n=9	47.6 (42 - 51) n=11	59.7 (57 - 62.4) n=5	0.046

All data presented as median (IQR)

Table 1. Patient Characteristics

Category	
Age (years), mean (SD)	15.7 (2.0)
Male, n (%)	63 (73)
Weight (kg), median (IQR)	68.5 (51.8 - 81)
Height (cm), median (IQR)	170.2 (160.7 - 175.3)
BMI, median (IQR)	23 (19 - 30)
Underweight, n (%)	6 (7)
Healthy, n (%)	44 (51)
Overweight, n (%)	12 (14)
Obese, n (%)	24 (28)
Active Malignancy, n (%)	20 (23)
Trauma, n (%)	16 (18.6)
Length of stay (days), median (IQR)	17 (8 - 35)
Baseline SCr (mg/dL), mean (SD)	0.63 (0.21)
Nephrotoxic Medication, n (%)	57 (66.3)
Nephrotoxic Medications per patient, mean (SD)	1.65 (1.7)

**Conclusion.** To achieve therapeutic levels, adolescents 12 to 14 years old need higher empiric doses of 60 mg/kg/day compared to 45 mg/kg/day in 15 to 18 year olds. Obese patients, however, may require lower TDD than underweight, healthy, and overweight patients. Patients that receive AUC versus trough monitoring may also require lower TDD to achieve therapeutic concentrations. More data is needed to further evaluate our findings.

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### 1109. Pharmacokinetics and Exposure of Cefepime in Critically Ill Patients Receiving Extracorporeal Membrane Oxygenation (ECMO)

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**Session:** P-62. PK/PD Studies

**Background.** ECMO is a life-saving tool utilized in critically ill patients that require respiratory and/or cardiac support. ECMO may also affect the pharmacokinetics (PK) of certain medications, including some antibiotics. Cefepime is a widely used antibiotic in this population due to its broad spectrum activity but limited data are available to guide dosing in patients requiring ECMO.

**Methods.** This was a prospective, single-center study of 6 critically ill adult patients receiving ECMO and receiving cefepime 2g q8h as a 3h infusion. After obtaining informed consent, 4-6 blood samples within the dosing interval were collected to determine cefepime concentrations. Population PK was conducted in Pmetrics using R. Final MAP Bayesian parameter estimates were used to simulate free time above MIC (%fT > MIC) for various cefepime dosing regimens. The target pharmacodynamic exposure was 70% fT > MIC.

**Results.** Patients were between 31-62 years old; 4/6 (66.7%) were on veno-venous (VV) ECMO and 2 veno-arterial (VA) ECMO. Two patients required continuous venovenous hemodiafiltration (CVVHDF) while the other 4 had a CrCl between 92-199 ml/min. A two compartment model fitted the data better than a one compartment model. Median (range) final population PK parameters were: clearance (CL), 9.8 L/h (7.6-33.1); volume of central compartment (V<sub>c</sub>), 6.9 L (4.7-49.8); and intercompartment transfer constants (k<sub>12</sub>), 2.04 h<sup>-1</sup> (1.48-2.29); and k<sub>21</sub>, 1.49 h<sup>-1</sup> (0.75-1.71). The 2g q8h (3h infusion) regimen resulted in target exposure in all patients up to an MIC of 8 mg/L (the susceptibility breakpoint for *Pseudomonas*), with 5/6 patients achieving this at 16 mg/L. A standard 2g q12h (0.5h infusion) regimen would have resulted in 5/6 patients achieving 70% fT > MIC at 8 mg/L and 1/6 at 16 mg/L.

**Conclusion.** These are the first data describing cefepime PK and exposure attainment in critically ill patients receiving ECMO. Cefepime 2g q8h (3h infusion) achieved target pharmacodynamic exposure up to the susceptibility breakpoint of 8 mg/L in all 6 patients, including 2 with concomitant CVVHDF. Additional studies are warranted to define cefepime PK in patients on ECMO across a robust range of CrCl to guide dosing.

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### 1110. In Vivo Pharmacodynamics of Vancomycin Against Staphylococci in Young Infants

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**Session:** P-62. PK/PD Studies

**Background.** Coagulase-negative staphylococci are the predominant pathogen causing late onset sepsis in young infants, however, the pharmacodynamic target for vancomycin therapy is unknown. This study aimed to determine the pharmacodynamic target of vancomycin in young infants with staphylococcal infections.