Interinstitutional Comparison of Vancomycin Area Under the Concentration–Time Curve Estimation in Korea: Need for Standardized Operational Protocols for Therapeutic Drug Monitoring Consultation

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Supplemental Data. Patient and therapeutic drug monitoring (TDM) data for the case challenge.

Case 1

1. Sex/age (birth date)/ethnicity: **M/50 yrs (1973-03-01)/Korean**
2. Height/body weight: **170 cm/65 kg**
3. Diagnosis: methicillin-resistant *Staphylococcus aureus* (**MRSA) pneumonia**
4. Vancomycin dosing history: [23-06-01 09:00 (#1) – 23-06-03 09:00 (#5)]* **900 mg q12hr IV (1-hr infusion)**

* Infusion start time

5. Serum albumin concentration: [23-06-03 06:00] **3.1 g/dL**
6. Serum creatinine concentration: [23-06-03 06:00] **0.86 mg/dL** (76.0 μmol/L)
7. Serum vancomycin concentrations: [23-06-02 23:30] **19.8 mg/L (peak)**, [23-06-03 08:45] **11.4 mg/L (trough)**

The time indicated in items 5 to 7 is the time of blood collection.

Case 2

1. Sex/age (birth date)/ethnicity: **F/80 yrs (1943-03-01)/Korean**
2. Height/body weight: **155 cm/70 kg**
3. Diagnosis: **MRSA pneumonia**
4. Vancomycin dosing history: [23-06-01 09:00 (#1) – 23-06-03 09:00 (#5)]* **1,000 mg q12hr IV (1-hr infusion)**

* Infusion start time

5. Serum albumin concentration: [23-06-03 06:00] **3.1 g/dL**
6. Serum creatinine concentration: [23-06-03 06:00] **0.45 mg/dL** (39.8 μmol/L)
7. Serum vancomycin concentration: [23-06-03 08:45] **14.5 mg/L**

The time indicated in items 5 to 7 is the time of blood collection.

Case 3

1. Sex/age (birth date)/ethnicity: **M/50 yrs (1973-03-01)/Korean**

2. Height/body weight: **170 cm/65 kg**

3. Diagnosis: **MRSA pneumonia**

4. Vancomycin dosing history:

[23-06-01 09:00 (#1) – 23-06-03 09:00 (#5)]* **800 mg q12hr IV (1-hr infusion)**

[23-06-03 21:00 (#6) – 23-06-06 09:00 (#11)]* **1,000 mg q12hr IV (1-hr infusion)**

[23-06-06 21:00 (#12) – 23-06-12 09:00 (#23)]* **800 mg q12hr IV (1-hr infusion)**

* Infusion start time

5. Serum albumin concentration: [23-06-03 06:00] **3.1 g/dL**

6. Serum creatinine concentrations:

① [23-06-01 06:00] **1.01 mg/dL** (89.3 μmol/L)

② [23-06-03 06:00] **0.95 mg/dL** (84.0 μmol/L)

③ [23-06-06 06:00] **1.02 mg/dL** (90.2 μmol/L)

④ [23-06-08 06:00] **1.22 mg/dL** (107.8 μmol/L)

⑤ [23-06-09 06:00] **1.06 mg/dL** (93.7 μmol/L)

⑥ [23-06-10 06:00] **0.91 mg/dL** (80.4 μmol/L)

⑦ [23-06-12 06:00] **0.89 mg/dL** (78.7 μmol/L)

7. Serum vancomycin concentrations:

① [23-06-03 08:45] **8.7 mg/L**

② [23-06-06 08:45] **19.1 mg/L**

③ [23-06-08 08:45] **14.8 mg/L**

④ [23-06-10 08:45] **13.9 mg/L**

⑤ [23-06-12 08:45] **14.5 mg/L**

The time indicated in items 5 to 7 is the time of blood collection.

Supplemental Data Table S1. Differences in AUC24 values according to the renal function equation used, using the same built-in population model of the MwPharm++ program for questions Q1-C and Q2

Question	eGFR equation	eGFR* (mL/min/1.73m^2)	AUC24 value calculated by authors† (mg·hr/L)	AUC24 values reported by respondents‡ (mg·hr/L)
Q1-C	Cockcroft–Gault	93	479	477, 479, 479, 481
	CKD-EPI (2009)	101	477	(386), (431), 476, 477
	MDRD (IDMS-traceable)	94	479	478, 479
	Jelliffe	85	481	481, 481
Q2	Cockcroft–Gault	77	653	614, 652, 653, 653
	CKD-EPI (2009)	95	646	620, 646, 646, 663
	MDRD (IDMS-traceable)	134	635	635, 635
	Jelliffe	77	653	(148), 653

*Ideal body weight calculated according to the Chennavasin equation was used for the Cockcroft–Gault and Jelliffe equations. Creatinine clearance values were normalized to a body surface area of 1.73 m^2. The 1972 version of the Jelliffe equation was used (Jelliffe II in MwPharm++; Jelliffe RW and Jelliffe SM. A computer program for estimation of creatinine clearance from unstable serum creatinine levels, age, sex, and weight. Math Biosci 1972;14:17-24).

†Bayesian individual PK parameter estimation and time–concentration curve simulation were conducted with MwPharm++ (version 2.4.0.363; Mediware a.s., Prague, Czech Republic), using the built-in two-compartment model named "#vancomycin_adult_k_C2." The population PK parameters (mean ± SD) were V1 = 0.21 ± 0.04 L/kg, k_{elr} = 0.00327 ± 0.00109 hr^{-1}/(mL/min/1.73m^2), k_{12} = 1.12 ± 0.28 hr^{-1}, and k_{21} = 0.48 ±

0.12 hr^{-1}, where V1 is the volume of distribution of the central compartment; k_{elr} is the renal elimination rate constant for the central compartment; k_{12} is rate constant from the 1st (central) to the 2nd (peripheral) compartment; and k_{21} is rate constant from the 2nd to the 1st compartment. The metabolic elimination rate constant for the central compartment (k_{elm}) was fixed: $k_{elm} = 0.0143\ hr^{-1}$. The relationship between the total elimination rate constant (k_{el}) and creatinine clearance (CL_{cr}) was k_{el} (hr^{-1}) = k_{elm} (hr^{-1}) + k_{elr} (hr^{-1}/[mL/min/1.73m^2]) × CL_{cr} (mL/min/1.73m^2), where calculated creatinine clearance or eGFR was used for CL_{cr}. All option settings, such as assay error (SD = 0.15 × C_{obs}), were set to default.

‡Even when the same population model and renal function equation were used in the same program, MwPharm++ provides various options, such as assay error, body weight type, fitting algorithm, and weighting method, which may lead to different AUC values depending on the settings used or owing to clerical error.

The values in parentheses are outliers excluded from the mean, SD, and CV calculations in Table 2.

Abbreviations: eGFR, estimated glomerular filtration rate; AUC24, 24 hr-normalized area under the concentration–time curve; MDRD, modification of diet in renal disease; IDMS, isotope dilution mass spectrometry.