P-1240

Optimal Vancomycin Model Selection for Obese Patients Receiving Outpatient Parenteral Antimicrobial Therapy (OPAT)

Kimberly A. Couch, PharmD, MA, FIDSA, FASHP[1];
Quyen Luu, MD[2]; Richard C. Prokesch, MD, FACP, FIDSA[3];
John S. Adams, MD, FIDSA, FSHEA[4];
Joseph F. John, Jr., MD, FACP, FIDSA[5];
Lucinda J. Van Anglen, BS, PharmD, FIDSA[1]

[1]Healix Infusion Therapy, Sugar Land, TX; [2]Central Georgia Infectious Disease, LLC, Macon GA; [3]Infectious Disease Associates, PC, Riverdale, GA; [4]Knoxville Infectious Disease Consultants, Knoxville, TN; [5]Low Country Infectious Disease, Charleston, SC

Key Findings

- **Model selection is most important at initiation of therapy**
- **Obesity models provided good a *priori* performance and are recommended for initiation of therapy in the obese population**
- **Crass and Hughes models provided the best results a *priori* for obese patients**
- **For *a posteriori* predictions, non-obese models were non-inferior to obese models in our OPAT population**

IDWeek2024
October 16-19, 2024
Los Angeles, CA

HEALIX

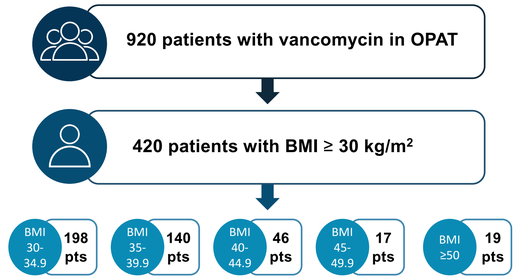
Background

- The incidence of obesity in the U.S. was 41.9% in 2017-2020.
- Optimal OPAT dosing of vancomycin (VAN) is challenging in obese patients.
- Multiple Bayesian pharmacokinetics (PK) models to aid in AUC estimation exist, including several obesity-specific models.
- PK population models in the absence of drug serum levels (*a priori*) are useful to initiate therapy, but once drug serum levels are obtained, model performance is based upon individual patient PK (*a posteriori*).
- This study is the first evaluation of the optimal PK model for obese patients receiving OPAT.

Methods

- The patient population included the following:
  - All OPAT pts who received vancomycin in 2022-2023
  - Patients who had at least 1 vancomycin level
  - Patients with a body mass index (BMI) ≥ 30 kg/m^2
- Data collection included:
  - Demographics and Anthropometrics
  - Treatment information
  - Laboratory values
- Ten models were used to predict vancomycin serum concentrations and calculate AUC24 utilizing a Bayesian dosing software program
  - 6 models were not specifically designed for the obese population
  - 4 models were developed for obese population
  - Goti model was modified by removing a rule that rounded serum creatinine to 1 mg/dL in pts > 65 years
  - Thomson model was modified by capping the creatinine clearance at 150 mL/min
- Model performance was assessed by using a *priori* root mean square error (RMSE) and a *posteriori* RMSE
- The average RMSE was calculated for patients with a BMI 30-39.9 kg/m^2 and for patients with a BMI ≥ 40 kg/m^2
- The best model performance was identified for each BMI category as the model which had the lowest RMSE

Patient Population



Patient Characteristics

Table 1. Patient Population Characteristics

Characteristic	Results (N=420)
Age, median (IQR) years	61 (52-68)
Male, n (%)	248 (59)
Weight, kg, median (IQR)	
Measured	106.8 (IQR 95.2-120.9)
Ideal	66.2 (IQR 57.0-75.3)
Adjusted	84.2 (IQR 74.6-92.8)
Height, cm, median (IQR)	172.7 (IQR 165.1-182.0)
BMI, n (%)	
BMI 30-34.9	198 (47)
BMI 35-39.9	140 (33)
BMI 40-44.9	46 (11)
BMI 45-49.9	17 (4)
BMI ≥ 50	19 (5)
BMI Average Groups, n (%)	
BMI 30-39.9	338 (80)
BMI ≥ 40	82 (20)

Results

Table 2. Comparison of Models

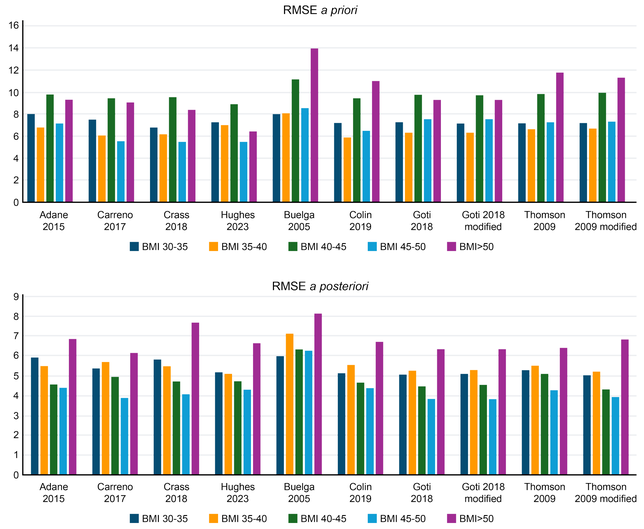
Model (Author Year)	Age Range (years)	Weight Range (kg)	BMI Range (kg/m^2)	Model Population Features
Adane 2015	38.5-53	142.8-178.3	44.3-54.8	Obesity model
Carreno 2017	23-74	110-250	NR	Obesity model
Crass 2018	19-88	69.6-293.6	30.1-85.7	Obesity model
Hughes 2023	24.2-89.3	79.8-218	40-70.3	Obesity model
Buelga 2005	35.6-76.4	53.1-76	NR	Hematologic malignancy population
Colin 2019	0.0027 – 101	0.42-160	NR	Included all ages
Goti 2018	17-101	33-255	NR	Included HD, CRRT and ICU patients
Goti 2018 modified	17-101	33-255	NR	-
Thomson 2009	16-97	40-159	NR	-
Thomson 2009 modified	16-97	40-159	NR	-

Table 3. Model Performance Assessment

RMSE performance by model (mg/dL)										
RMSE a *priori* predictions (mg/dL)										
Body Mass Index	**Obesity Models**				**Other Models**					
BMI (kg/m^2)	**Adane 2015**	**Carreno 2017**	**Crass 2018**	**Hughes 2023**	**Buelga 2005**	**Colin 2019**	**Goti 2018**	**Goti 2018 modified**	**Thomson 2009**	**Thomson 2009 modified**
BMI 30-34.9	8.00	7.48	**6.79**	7.26	8.00	7.21	7.24	7.15	7.15	7.19
BMI 35-39.9	6.75	6.05	6.14	7.00	8.06	**5.88**	6.30	6.31	6.63	6.70
BMI 30-39.9[a]	7.38	6.77	**6.46**	7.13	8.03	6.55	6.77	6.73	6.89	6.95
BMI 40-44.9	9.75	9.44	9.54	**8.89**	11.13	9.43	9.77	9.71	9.80	9.91
BMI 45-49.9	7.13	5.56	5.49	**5.08**	8.52	6.50	7.52	7.54	7.23	7.29
BMI≥50	9.30	9.04	8.39	**6.43**	13.92	11.01	9.29	9.30	11.74	11.28
BMI≥40[a]	8.73	8.02	7.81	**6.80**	11.19	8.98	8.86	8.85	9.59	9.49
RMSE a *posteriori* predictions (mg/dL)										
BMI 30-34.9	6.01	5.36	5.84	5.20	5.93	5.17	5.10	5.12	5.29	**5.05**
BMI 35-39.9	5.52	5.73	5.50	**5.12**	7.13	5.57	5.27	5.32	5.52	5.22
BMI 30-39.9[a]	5.77	5.55	5.67	5.16	6.53	5.37	5.19	5.22	5.41	**5.13**
BMI 40-44.9	4.58	4.96	4.76	4.74	6.35	4.69	4.50	4.55	5.11	**4.33**
BMI 45-49.9	4.42	3.92	4.08	4.33	6.26	4.42	**3.85**	3.86	4.32	3.95
BMI≥50	6.85	**6.16**	7.70	6.66	8.13	6.73	6.34	6.34	6.44	6.82
BMI≥40[a]	5.28	5.01	5.51	5.24	6.91	5.28	**4.90**	4.92	5.29	5.03

[a]average value calculated for the combined group
RMSE = Root Mean Squared Error

Figure 1. Model Performance Assessment



DISCUSSION

- Obese models for vancomycin dosing are relatively new, with few available.
- Four models specifically designed for the obese patients were evaluated along with six non-obese models with this OPAT population.
- Crass and Hughes obese models performed best *a priori* in this obese OPAT pt population.
- Thomson modified and Goti non-obese models performed best *a posteriori.*
- Limitations
  - There were few patients with BMI ≥ 40 kg/m^2 who had data and could be included in this evaluation of PK models.
  - Additional patients with BMI ≥ 40 kg/m^2 and especially with BMI ≥ 45 kg/m^2 are needed for enhanced evaluation of this patient population with Class III Obesity.
  - RMSE does not allow determination of whether the model overestimates or underestimates vancomycin dosing and ensuring early adequate therapy is important for efficacy.

References

1. Adane ED, Herald M, Koura F. Pharmacotherapy. 2015 Feb;35(2):127-39.
2. Carreno JJ, Lomaestro B, Tietjan J, et al. Antimicrob Agents Chemother. 2017 Apr 24;61(5):e02478-16.
3. Crass RL, Dunn R, Hong J, et al. J Antimicrob Chemother. 2018 Nov 1;73(11):3081-3086.
4. Hughes MA, Hughes JH, Endicott J, et al. Ther Drug Monit. 2024 May 10.
5. Buelga DS, del Mar Fernandez de Gatta M, Herrera EV, et al. Antimicrob Agents Chemother. 2005 Dec;49(12):4934-41.
6. Colin PJ, Allegaert K, Thomson AH, et al. Clin Pharmacokinet. 2019 Jun;58(6):767-780.
7. Goti V, Chaturvedula A, Fossler MJ, et al. Ther Drug Monit. 2018 Apr;40(2):212-221. Erratum in: Ther Drug Monit. 2019 Aug;41(4):549.
8. Thomson AH, Staatz CE, Tobin CM, et al. J Antimicrob Chemother. 2009 May;63(5):1050-7.
9. Vance-Bryan K, Guay DR, Gilliland SS, et al. Antimicrob Agents Chemother. 1993 Mar;37(3):436-40.
10. Chen A, Gupta A, Do DH, et al. Pharmacol Res Perspect. 2022 Dec;10(6):e01026.
11. Broeker A, Nardecchia M, Klinker KP, et al. Clin Microbiol Infect. 2019 Oct;25(10):1286.e1-1286.e7.
12. https://www.cdc.gov/obesity/php/data-research/adult-obesity-facts.html accessed 2024 Aug 08.

Acknowledgments

We acknowledge the support from Tiffany Lee, PharmD and Jonathan Faldasz, PharmD with Insight RX and Joyce Gee, PharmD with Healix Infusion Therapy, LLC.

Scan for Digital Poster