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APPENDICES

APPENDIX

A. Equations

B. Example of measurement absolute and relative performance

APPENDIX A

A. Equations used for calculation of the creatinine clearance

Equation 1 :

$$IBW\ (male) = 50 + (height\ in\ inches - 60) \times (2.3) \quad kg$$

Equation 2 :

$$IBW\ (female) = 45.5 + (height\ in\ inches - 60) \times (2.3) \quad kg$$

Equation 3 :

$$CrCl\ (male) = \frac{(140 - age) \times TBW\ (kg)}{72 \times Scr\ (mg/dl)} \quad ml/min$$

Equation 4 :

$$CrCl\ (female) = \frac{[(140 - age) \times TBW(kg))] \times (0.85)}{72 \times Scr\ (mg/dl)} \quad ml/min$$

B. Equations used for calculation of the elimination rate constant and volume of distribution

Equation 5 :

$$Kel\ (Scr)_F = 0.015 + 0.00238 \times (CrCl) \quad hour^{-1}$$

$$Vd\ (mean) = 0.26 \quad L/kg$$

Equation 6 :

$$Kel\ (Scr)_T = 0.042 + 0.00247 \times (CrCl) \quad hour^{-1}$$

$$Vd\ (mean) = 0.26 \quad L/kg$$

Equation 7 :

$$Kel\ (blood) = \frac{\ln (Cmax/Cmin)}{\tau - t_1} \quad hour^{-1}$$

$$Vd(mean) = 0.26 \quad L/kg$$

Equation 8 :

$$Kel\ (blood) = \frac{\ln (Cpost/Cmin)}{\tau - t'} \quad hour^{-1}$$

$$Vd(mean) = 0.26 \quad L/kg$$

Equation 9 :

$$Kel\ (blood) = \frac{\ln(Cmax/Cmin)}{\tau - t_1} \quad hour^{-1}$$

$$Vd\ (blood) = \frac{MD\ (1-e^{-kelt'})}{kelt'\ (Cmax-Cmin\ e^{-kelt'})} \quad L$$

C. <u>Equations used for calculation of serum gentamicin concentrarion and dosage regimen</u>

Equation 10 :

$$\tau = t' \frac{-1}{kel} \ln \frac{Cpmin}{Cpmax} \quad hour$$

Equation 11 :

$$Cpmax = \frac{MD(1-e^{-kelt'})}{Kel\ Vd\ t'(1-e^{-kel\tau})} \quad \mu g/ml$$

Equation 12 :

$$Cpmin = Cpmax\ e^{-kel(\tau-t')} \quad \mu g/ml$$

Equation 13 :

$$MD = \frac{t' \; kel \; Vd \; Cpmax \; (1-e^{-kel\tau})}{(1-e^{-kelt'})} \quad mg$$

Equaiton 14 :

$$MD = \frac{t' \; kel \; Vd \; Cpmin \; (e^{kel\tau}-1)}{(e^{kelt'}-1)} \quad mg$$

IBW = Ideal body weight (kg)

TBW = Total body weight (kg)

CrCl = Creatinine Clearance (ml/min)

Scr = Serum Creatinine (mg/dl)

Vd(mean) = Volume of Distribution estimated using mean population value(L/kg)

Vd(Blood) = Volume of Distribution estimated using serum concentration (L)

$Kel(Scr)_F$ = Elimination Rate Constant estimated from foreign population parameter ($hour^{-1}$)

$Kel\ (Scr)_T$ = Elimination Rate Constant estimated from Thai population parameter ($hour^{-1}$)

Kel(blood) = Elimination Rate Constant estimated using serum concentration ($hour^{-1}$)

MD = Maintenance dose (mg)

Cmax = Measured peak concentration (µg/ml)

Cmin = Measured trough concentration (µg/ml)

Cpmax = Predicted peak concentration (µg/ml)

C_Pmin = Predicted trough concentration (µg/ml)

Cpost = Measured concentration at 60 minutes after dosing

τ = Time of dosing interval (hour)

t' = Duration of infusion time (hour)

t_1 = Time of first blood sample drawn

APPENDIX B

Example of measurement absolute and relative performance from Table 9

Measured Trough (True value)	Predicted Trough (Prediction)	Error (pe)	$Error^2$ (pe^2)	Predicted Trough (Prediction)	Error (pe)	$Error^2$ (pe^2)
1.03	2.53	1.50	2.25	1.80	0.77	0.59
0.45	1.70	1.25	1.56	1.23	0.78	0.61
0.60	0.97	0.37	0.13	0.70	0.10	0.01
0.45	0.93	0.48	0.23	0.68	0.23	0.05
2.21	4.39	2.18	4.76	3.05	0.84	0.70
2.23	0.69	-1.54	2.37	0.50	-1.73	2.98
0.67	0.37	-0.30	0.09	0.27	-0.40	0.16
0.55	0.80	0.25	0.06	0.58	0.03	0.00
1.74	4.30	2.56	6.54	2.96	1.22	1.50
0.55	0.81	0.26	0.07	0.59	0.04	0.00
0.84	3.57	1.73	3.99	1.84	1.00	1.00
0.49	0.64	0.15	0.02	0.46	-0.03	0.00
1.53	0.44	-1.09	1.20	0.31	-1.22	1.48
1.79	1.15	-0.64	0.42	0.83	-0.96	0.93
1.94	2.08	0.14	0.02	1.51	-0.43	0.19
0.60	0.64	0.04	0.00	0.47	-0.13	0.02
0.67	1.23	0.56	0.31	0.89	0.22	0.05
1.39	0.66	-0.73	0.54	0.48	-0.91	0.83
0.73	1.46	0.73	0.53	1.06	0.33	0.11
1.09	0.20	-0.89	0.79	0.14	-0.95	0.90

<u>Equations use calculation as follows:</u>

1. Absolute Bias

$$me = \frac{1}{N} \sum_{i=1}^{N} pe_i$$

$$pe = \text{Prediction-True value}$$

2. Absolute Precision

$$mse = \frac{1}{N} \sum_{i=1}^{N} pe_i^2$$

3. Percentage of confidence interval for mean value (me,mse)

$$\bar{X} - t_{(N-1)} se_{\bar{x}} < X_i < \bar{X} + t_{(N-1)} se_{\bar{x}}$$

$$se_{\bar{x}} = \sqrt{\frac{\sum_{i=1}^{N} (X_i - X)^2}{N(N-1)}}$$

4. Relative Bias

$$\Delta me = me_1 - me_2$$

$$se_{\Delta me} = \sqrt{\frac{\sum_{i=1}^{N} [(pe_{1i} - pe_{2i}) - \Delta me]^2}{N(N-1)}}$$

5. Relative Precision

$$\Delta\, mse = mse_1 - mse_2$$

$$se_{\Delta mse} = \sqrt{\frac{\sum_{i=1}^{N} [(pe_{1i}^2 - pe_{2i}^2) - \Delta\, mse]^2}{N(N-1)}}$$

Example of calculation

1. Absolute Bias

$$me = \frac{1}{N} \sum_{i=1}^{N} pe_i$$

$$me_1 = \frac{(1.50+1.25+\_\_\_+(-0.89))}{20}$$

$$= 0.35$$

$$me_2 = \frac{(0.77+0.78+\_\_\_+(-0.95))}{20}$$

$$= -0.06$$

$$se_{\bar{x}} = \sqrt{\frac{\sum_{i=1}^{N} (X_i - X)^2}{N(N-1)}}$$

$$se_{me1} = \sqrt{\frac{(1.50-0.35)^2+(1.25+0.35)^2+\_\_\_+(-0.89-0.35)^2}{20 \times 19}}$$

$$= 0.24$$

$$se_{me2} = \sqrt{\frac{(0.77+0.06)^2+(0.78+0.06)^2+\_\_\_+(-0.95+0.06)^2}{20 \times 19}}$$

$$= 0.18$$

2. Absolute Precision

$$mse = \frac{1}{N} \sum_{i=1}^{N} pe_i^2$$

$$mse_1 = \frac{(2.25+1.56+\_\_\_+0.79)}{20}$$

$$= 1.24$$

$$mse_2 = \frac{(0.59+0.61+\_\_\_+0.90)}{20}$$

$$= 0.61$$

$$se_{\bar{x}} = \sqrt{\frac{\sum_{i=1}^{N} (X_i - X)^2}{N(N-1)}}$$

$$se_{mse1} = \sqrt{\frac{(2.25-1.24)^2+(1.56+1.24)^2+\_\_\_+(0.79-1.24)^2}{20 \times 19}}$$

$$= 0.40$$

$$se_{mse2} = \sqrt{\frac{(0.59-0.61)^2+(0.61-0.61)^2+\_\_\_+(0.90-0.61)^2}{20 \times 19}}$$

$$= 0.17$$

3. Relative Bias

$$\Delta\, me = me_1 - me_2$$

$$= 0.35-(-0.06)$$

$$= 0.41$$

$$se_{\Delta me} = \sqrt{\frac{\sum_{i=1}^{N} [(pe_{1i}-pe_{2i})-\Delta\, me\,]^2}{N(N-1)}}$$

$$= \sqrt{\frac{[(1.50-0.77)-0.41]^2+[(1.25-0.78)-0.41]^2+\_\_\_+[(-0.89+0.95)-0.41]^2}{20 \times 19}}$$

$$= \quad 0.08$$

95% Confidence interval

$$\bar{X}-t_{0.05(N-1)}se_x \; < \; X_1 \; < \; \bar{X}+t_{0.05(n-1)}se_x$$

$$0.41-2.093 \times 0.08 < X_1 < 0.41+2.093 \times 0.08$$

$$0.24 < X_1 < 0.58$$

4. Relative Precision

$$\Delta\, mse = mse_1-mse_2$$

$$= 1.24-0.61$$

$$= 0.64$$

$$se_{\Delta mse} = \sqrt{\frac{\sum_{i=1}^{N} [(pe_{1i}^2 - pe_{2i}^2) - \Delta\, me]^2}{N(N-1)}}$$

$$= \sqrt{\frac{[(2.25-0.59)-0.64]^2+[(1.56-0.61)-0.64]^2+\_\_\_+[(0.79-0.90)-0.64]^2}{20 \times 19}}$$

$= 0.34$

95% Confidence interval

$$\bar{X}-t_{0.05(N-1)}se_{\bar{x}} < X_i < \bar{X}+t_{0.05(n-1)}se_{\bar{x}}$$

$$0.64-2.093 \times 0.34 < X_i < 0.64+2.093 \times 0.34$$

$$-0.07 < X_i < 1.35$$

pe = prediction error

me = mean prediction error

Δ me = difference in two mean prediction error

mse = mean squared prediction error

Δ mse = difference in two mean squared prediction error

$se_{\bar{x}}$ = standard error of mean value

$se_{\Delta me}$ = standard error of Δ me

$se_{\Delta mse}$ = standard error of Δ mse

VITAE

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