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Atazanavir–bilirubin interaction: a pharmacokinetic–pharmacodynamic model [Corrigendum]

Lozano R, Domeque N, Apesteguia AF. *Clinical Pharmacology: Advances and Applications*. 2013;5(1):153–159.

On page 155, "Deriving Michaelis–Menten's equation,²⁶

$$V = \frac{K_{cat}E_{o}C}{K_{m}+C},$$

for bilirubin and ATZ, we have

$$\frac{\mathrm{dV}_{\mathrm{ATZ}}}{\mathrm{dC}_{\mathrm{ATZ}}} = \mathrm{K}_{\mathrm{cat}}^{\mathrm{ATZ}} \mathrm{E}_{\mathrm{o}} \mathrm{K}_{\mathrm{m}}^{\mathrm{ATZ}}$$

and

 $\frac{dV_{BIL}}{dC_{BII}} = K_{cat}^{BIL} E_o K_m^{BIL}$

at SS, when

$$dV_{ATZ} = dV_{BIL}$$

then we have

$$\Delta[\text{ATZ}]_{\text{SS}} = \frac{K_{\text{cat}}^{\text{BIL}} K_{\text{m}}^{\text{BIL}}}{K_{\text{cat}}^{\text{ATZ}} K_{\text{m}}^{\text{ATZ}}} \Delta[\text{BIL}]_{\text{SS}}$$

and

$$\frac{\Delta[\text{ATZ}]_{\text{SS1}}}{\Delta[\text{ATZ}]_{\text{SS2}}} = \frac{\Delta[\text{BIL}]_{\text{SS1}}}{\Delta[\text{BIL}]_{\text{SS2}}},$$
[1]

where V = glucuronidation reaction rate for bilirubin and ATZ, respectively; $E_o = UGT1A1$ enzyme concentration; $K_m = Michaelis$ -Menten constant for bilirubin and ATZ,

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respectively; and K_{cat} = turnover number for bilirubin and ATZ, respectively." should have been written as, "Deriving Michaelis–Menten's equation,²⁶

$$V = \frac{K_{cat}E_{o}C}{K_{m}+C},$$

for bilirubin and ATZ, we have

$$\frac{\mathrm{dV}_{\mathrm{ATZ}}}{\mathrm{dC}_{\mathrm{ATZ}}} = \frac{\mathrm{K}_{\mathrm{cat}}^{\mathrm{ATZ}} \mathrm{E}_{\mathrm{o}} \mathrm{K}_{\mathrm{m}}^{\mathrm{ATZ}}}{\left(\mathrm{K}_{\mathrm{m}}^{\mathrm{ATZ}} + \mathrm{C}_{\mathrm{ATZ}}\right)^{2}}$$

and

$$\frac{\mathrm{dV}_{\mathrm{BIL}}}{\mathrm{dC}_{\mathrm{BIL}}} = \frac{\mathrm{K}_{\mathrm{cat}}^{\mathrm{BIL}} \mathrm{E}_{\mathrm{o}} \mathrm{K}_{\mathrm{m}}^{\mathrm{BIL}}}{\left(\mathrm{K}_{\mathrm{m}}^{\mathrm{BIL}} + \mathrm{C}_{\mathrm{BIL}}\right)^{2}}$$

 $\Delta V_{ATZ} = \Delta V_{BIL}$,

at SS, when

then we have

 $\Delta[\text{ATZ}]_{\text{SS}} = \frac{K_{\text{cat}}^{\text{BIL}} K_{\text{m}}^{\text{BIL}}}{K_{\text{cat}}^{\text{ATZ}} K_{\text{m}}^{\text{ATZ}}} \Delta[\text{BIL}]_{\text{SS}}$

and

$$\frac{\Delta[\text{ATZ}]_{\text{SS1}}}{\Delta[\text{ATZ}]_{\text{SS2}}} = \frac{\Delta[\text{BIL}]_{\text{SS1}}}{\Delta[\text{BIL}]_{\text{SS2}}},$$
[1]

where V = glucuronidation reaction rate for bilirubin and ATZ, respectively; $E_o = UGT1A1$ enzyme concentration; $K_m =$ Michaelis–Menten's constant for bilirubin and ATZ, respectively; and $K_{cat} =$ turnover number for bilirubin and ATZ, respectively."

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