Poster

[P25-1] P25-1: Anti-infective drugs (1): Aminoglycosides and beta-lactams

Chair: Andrew McLachlan, Australia

Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall)

[P25-1-2] The effect of gentamicin peak concentration based dosing on gentamicin target attainment in critically ill patients

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Keywords: gentamicin, population pharmacokinetics, critical illness, therapeutic drug monitoring, peak concentration

Background

Adequate gentamicin peak concentrations (C_{max}) are important for optimal clinical efficacy. Substantial variability in C_{max} can occur within a critically ill patient over time, hampering the efficacy of therapeutic drug monitoring (TDM). The aim of this study was to evaluate the effect of gentamicin dosing based on C_{max} after the first administration on gentamicin target attainment in critically ill patients.

Methods

From critically ill patients receiving gentamicin, dosing information, clinical parameters and serum concentrations (both from routine TDM and randomly from waste material) were collected prospectively. A population pharmacokinetic model was developed using nonlinear mixed-effects modeling to estimate C_{max} after each administration. To evaluate the efficacy of routine TDM, percentages of C_{max} within the therapeutic range ($\%C_{ther}$, 15-20 mg/L), below ($\%C_{subther}$, <15 mg/L) and above the therapeutic range ($\%C_{suprather}$, >20 mg/L) after the first vs second administration were compared. Additionally, Monte Carlo simulations were performed to evaluate the impact of TDM.

Results

416 measurements from 59 patients receiving 130 gentamicin doses were included. TDM increased $\%C_{ther}$ in the 30 patients with >1 administration from 40% after a first median dose of 5.0 mg/kg to 50% after the second administration, decreased $\%C_{subther}$ from 47% to 30% and increased $\%C_{suprather}$ from 13% to 20%. Simulations using a 5 mg/kg starting dose showed that after the second administration $\%C_{ther}$ increased from 28% to 37% by application of TDM as compared to no TDM, $\%C_{subther}$ decreased from 57% to 29% and $\%C_{suprather}$ increased from 15% to 34%. In addition, with a simulated starting dose of 5 mg/kg, $\%C_{ther,}$ $\%C_{subther}$ and $\%C_{suprather}$ after the first administration were 28%, 58% and 14% respectively; corresponding percentages for 6 mg/kg were 33%, 36% and 31%. TDM after a starting dose of 6 mg/kg had no substantial effect with $\%C_{ther}$, $\%C_{subther}$ and $\%C_{suprather}$ after the second administration of 37%, 29% and 34% respectively.

Conclusions

Gentamicin dosing based on C_{max} after the first administration increased $\%C_{ther}$ and decreased $\%C_{subther}$, but did not result in therapeutic C_{max} in half of the patients. Based on our simulation a higher starting dose may decrease $\%C_{subther}$ and reduce the beneficial effect of TDM.