EV0080

ePoster Viewing

Antimicrobials: antimicrobial PK/PD, pharmacogenomics, pharmacoeconomics and general pharmacology, drug interaction studies

Creatinine-clearance as predictor for meropenem clearance

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Objectives:

In critically ill patients individualisation of antibiotic drug therapy is strongly recommended. Serum creatinine and bodyweight are directly available from the patient records, but the correlation between drug clearance and creatinin clearance for dose adaptions has been questioned. The purpose of this study was to investigate whether there is a reasonable correlation between calculated creatinine-clearance by Cockcroft and Gault (CrCl) and meropenem clearance in critically ill patients.

Methods:

Meropenem concentrations were determined by HPLC during continuous infusions in steady state in 238 patients on 557 occasions in the setting of routine therapeutic drug monitoring in our clinic. Doses were adjusted if judged as necessary. Meropenem clearance was determined from concentration and actual dose. CrCl was calculated using Cockroft and Gault formula in overweight patient corrected to ideal body weight. Relationships between meropenem clearance and CrCl and demographic variables (weight, length, BMI, sex, IBW) and CrCl were explored using Graphpad Prism 5.0 and SAS 9.2.

Results:

In stepwise regression, CrCl was the most important predictor for meropenem clearance. However, a clear discrepancy in correlation between CrCl and meropenem clearance below and above a calculated CrCl of 7 L/h was observed. Below that value there was a linear relationship described as meropenem clearance = CrCl* 1.484 -1.436 ($p<0.0001$; $r2=0.47$). In contrast, there was no correlation at all between CrCl and meropenem clearance above that value ($n=78$, $P=0.54$).

Conclusion:

Using a fixed Meropenem dose cannot be recommended. Although CrCl is often used as an indicator for clearance of antibiotics and to adjust dosing regimens, the present study shows that adjustment of meropenem dosing on body weight or creatinine concentration offers hardly any advantage. Although it is reasonable for patients with a calculated CrCl of 7 l/h and less to adapt meropenem doses according to CrCl, for patients with a higher estimated CrCl this study shows that therapeutic drug monitoring is mandatory to avoid antibiotic underdosing with the risk of treatment failure or overdosing resulting in potential side effects.