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Meropenem dosing requirements against Gram negative bacteremia in an intensive care unit

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Objective:

The aim of this study is to evaluate the influence of the susceptibility patterns of gram negative bacteria isolated in patients with nosocomial bacteremia on meropenem dosing requirements in critically ill patients with different degrees of renal function by estimation of the probability of pharmacokinetic/pharmacodynamics target attainment.

Material and methods:

90 Gram negative bacteria isolated during a two year period were included. Six meropenem doses were evaluated: 0.5 g, 1 g and 2 g every 8 h given as 0.5h or 3h infusions.

Pharmacokinetic data in critical patients were obtained from the literature (Vd:77.7±15.8 mL/min; Cl:17.1±2.1 L/h).

Time above minimum inhibitory concentration (MIC) was obtained according to the following equation:

$$fT>MIC=[(t2-tinf)-t1]x(100/\tau)$$

t1= ime at which the free serum concentration reached the MIC

t2= post-infusion time at which the free serum concentration equalled the MIC in the elimination phase, and τ is the dosing interval.

MIC: obtained by broth microdilution method.

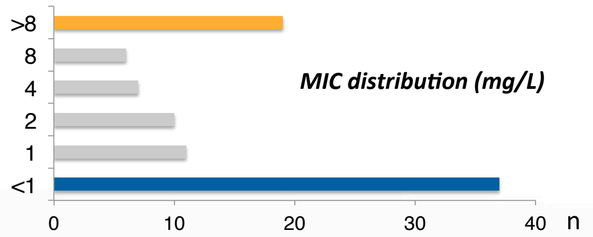
A 1000 subject Monte Carlo simulation was performed using Microsoft Excel® per dosing regimen and degree of renal function. The dosing regimen was considered successful if the probability of target attainment (PTA) value fT>40%MIC was higher than to 90%.

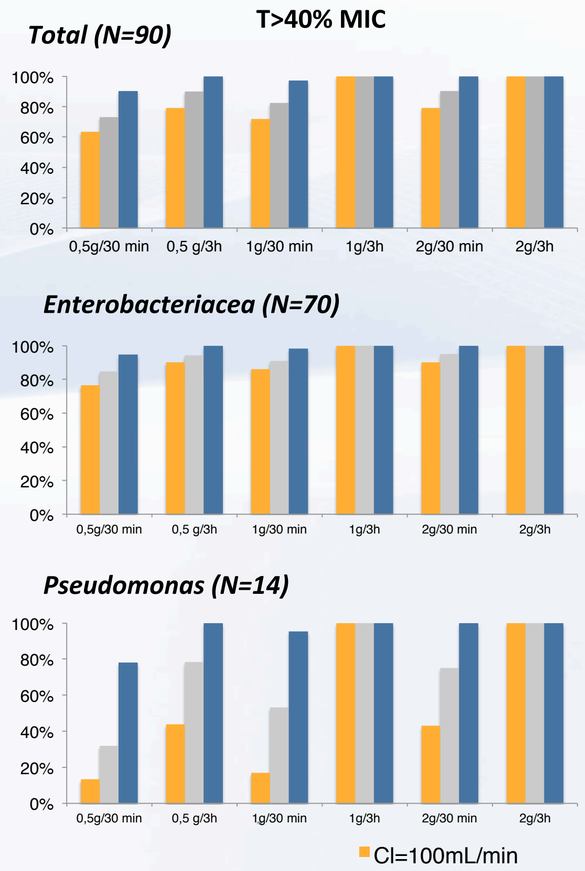
Results:

The PTA increased when increasing the dose and decreasing the creatinine clearance (ClCr). For any degree of renal function, meropenem 1g in 3h infusion had a PTA ≥90 %.

The same dose in 30 min provided a PTA=78,1% and 87,2% in patients with creatinine clearance of 70 and 100 mL/min. In patients with ClCr≤35 mL/min, meropenem 0,5/8h in 3h reached a PTA>90%.

For Enterobacteriacea spp, 1g in 30 min was enough for patients with ClCr<=70 mL/min. For Pseudomonas aeruginosa, 1g or 2g dose in 3h was necessary to achieve a successful regimen in patients with ClCr of 70 and 100 mL/min.





Conclusion:

Based on our results, meropenem 1 g dose administered as extended infusion is the best option to empirical treatment. In patients with suspected Pseudomonas infection 1 or 2 g dose in 3h infusion should be administered.