# Effectiveness of meropenem treatment in critically ill patients: Utility of therapeutic drug monitoring

Idoate Grijalba AI, Aquerreta González I, Aldaz Pastor A.

Pharmacy department. University Clinc of Navarra Pamplona

Pharmacokinetic/ pharmacodynamic effectiveness index (PK/PD) proposed for carbapenems in critical patients is to maintain serum free concentration drug 4-5 times above the minimum inhibitory concentration (MIC) in the isolated microorganism during 100 % of the dosing interval. Ensuring this goal is a priority and requires the use of pharmacokinetic monitoring (TDM).

## Objectives

Analyze the effectiveness of pharmacokinetic optimized meropenem´s regimen based on PK/PD criteria and compare it with empirical carbapenem´s regimen adjusted by renal function in patients admitted to the intensive care unit

## Patients, material and methods

- Naturalistic retrospective, observational cohort study, carried out in critically ill patients treated with meropenem from May-2011 to December-2017.
- Subjects were divided in two cohorts: cohort-A (CA) if they had pharmacokinetic intervention and cohort-B (CB) if not.
- For pharmacokinetic analysis, two serum samples per patient were drawned (peak and elimination point) to quantify total and free concentrations of meropenem. Individual pharmacokinetic parameters were estimated by Sawchuk-Zaske method and then were used to calculate the PKPD. Dose adjustment was made if necessary.
- When MIC was not available, the epidemiological median stablished at our hospital of 1 mcg/mL was used.
- Clinical cure (normalization of clinical markers as procalcitonin, C-reactive protein (CRP), leucocytosis or fever resolution and improvement of radiological images) and bacteriological cure (bacterial culture negativization) were the main goals.
- The outcome variables were compared between both cohorts by: Student´s T method in normal quantitative variables, Mann Whitney in not normal quantitative variables or Chi-squared method in qualitative variables. Both cohorts were balanced by the propensity score (PS) without replacement to avoid selection and confusion bias of an observational design.

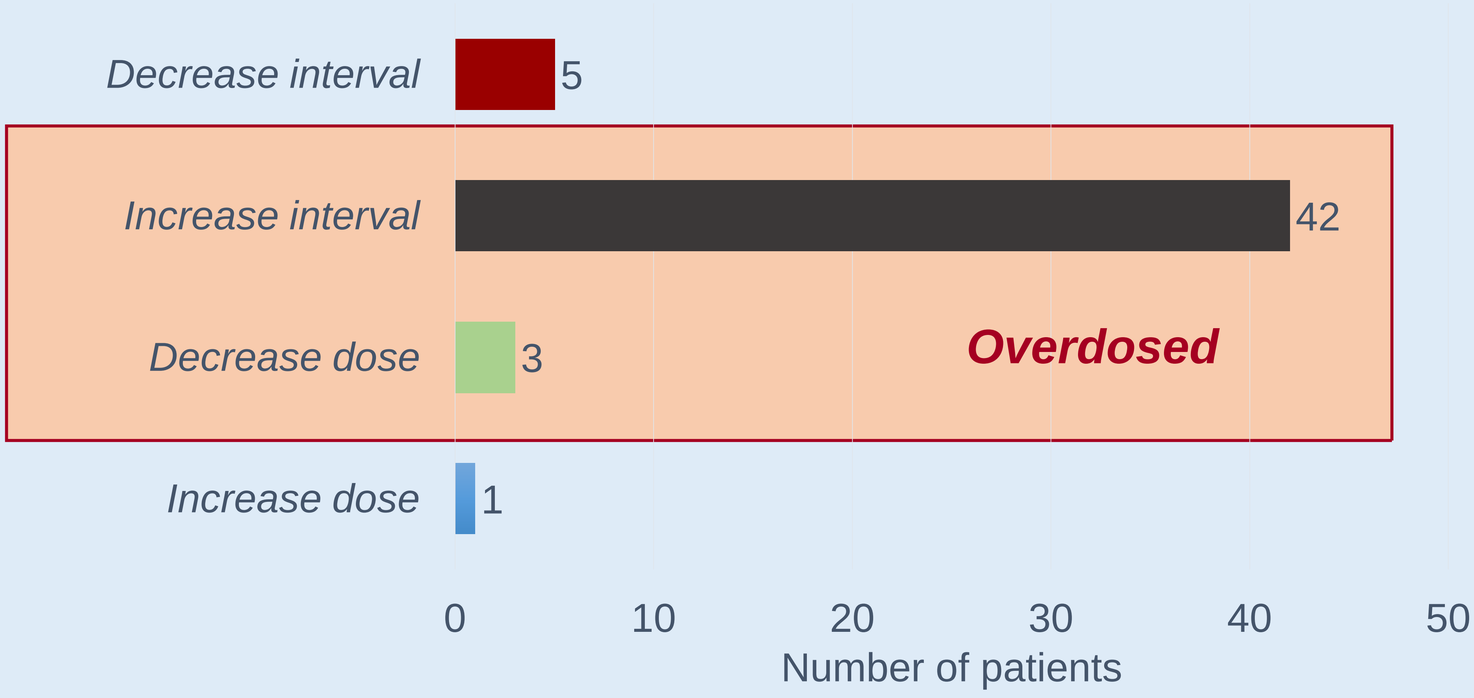
| Variables | CA | CB |
|---|---|---|
| n | 78 (62.8% men) | 78 (62.8% men) |
| Age (years) Mean (SD) | 64.16 (14.1) | 68.42 (13.9) |
| Infectious diagnostic | 65 (83.3%) | 58 (74.4%) |
| Sepsis | 59 (75.6%) | 53 (67.9%) |

## Results

✓ Dose adjustment was performed in 65.4%(n=51) of patients to reach the objective PK/PD.

✓Cohort A obtained better results than cohort B in clinical cure (Risk Ratio =1.159; p=0.165), bacteriological cure (RR=1.081; p=0.290) and normalization of clinical markers as leukocytosis (RR=1.016; p=0.848), CRP (RR=1.113, p=0.127), procalcitonin (RR=1.015, p=0.591) and fever resolution (RR=1.191; p=0.037).

✓There are no statistically significant differences in aspects related to safety between both cohorts.




Only 15% of analyzed microorganisms had a MIC higher than 1 mcg/mL.

80% of analyzed microorganisms had a mean MIC of 0.185 mcg/mL (range [0.016-0.5]).

Free Cmin/MIC at the end of dosing interval was much higher than PK/PD target, with a median of 50 (range [1.7-303.12]).

## Conclusion

✓Both clinical (74.36%, n=58) and bacteriological (85.89%, n=67) response was better in Cohort A and it was reached in most of the patients (67.95% ,n=53) in our study.

✓Dose adjustment was performed in 65.4% (n=51) of patients to attain the objective PK/PD. Therefore meropenem dosage regimens recommended in literature were not adequate in our population.

✓In 57.69% (n = 45) of critically ill patients was necessary to increase the interval or decrease the dose according to PK/PD criteria and it can be concluded that recommended dosing in the literature overdose our population.

✓ TDM is an important tool to fight against antimicrobial resistance, guarantees safety and allows to reduce healthcare cost.