with LIN and after at least 3 days of combined therapy were analysed by liquid chromatography (HPLC). Oral VCZ clearance (CL/F in L/h) was estimated before (CL/Fb) and during treatment with LIN (CL/Fd LIN). It was assumed as VCZ therapeutic range 1.5–4.5 mcg/mL in Candida spp. infections and 2–4.5 mcg/mL in Aspergillus spp. Demographic variables (age, sex), treatment (dosing schedule, date and time of each administration), clinics (diagnosis, microbiological information, etc.) and kinetics (date and time of each sample extraction) were collected.

Results Five patients were analysed with a median age of 67 years (range: 57–73), all of them males. Mean daily dose ±SD administered were 454.5±157.2 mg (VCZ) and 1,200 mg (LIN). Serum baseline concentration of VCZ before LIN was 2.7±0.8 mcg/mL. CL/Fb and CL/Fd of VCZ were, respectively, 6.3±1.7 L/h and 22.09±11.74 L/h, which represents a large increase of 250%. VCZ and LIN interaction generated infra-therapeutic VCZ concentrations in 80% of patients (n=4). Three patients had to change anti-infective treatment and two patients required increased VCZ dose up to 75% to reach at least the lower limit of the therapeutic range.

Conclusion Adding LIN to VCZ treatment increases VCZ clearance between 250%–700% and serum antifungal concentrations decrease clinically. This translates into a loss of effectiveness in antifungal treatment in 80% of cases. Therefore, the use of this combination is contraindicated and if clinically necessary. When CMI was not available, the epidemiological limit of EUCAST ECOPFF 2 mcg/mL was used.

Clinical and bacteriological responses were the main goals. Data was analysed using STATA12.0. Propensity score (PS) of each patient was calculated and patients in cohort A were compared and paired one by one with those of cohort B with similar PS.

Results One-hundred and fifty-six patients were included, 78 in each cohort after matching by PS. Main antimicrobial treatments were targeted (71.8% in cohort A and 73% in cohort B). Median duration of meropenem was 11 days (range: 2–31 days). In cohort A, dose adjustment was performed in 65% (n=51) of patients and in up to 88% (n=45) of them it was recommended to reduce dose or extend dosage range. Cohort A was associated with clinical improvement (OR: 1.624, 95% CI: 1.02 to 2.52, p=0.040), bacteriological (OR: 0.636, 95% CI: 0.27 to 1.48, p=0.292), fever resolution (OR: 2.415; 95% CI: 1.04 to 5.61, p=0.040), decreased inflammatory parameters (statistically significant PCR (p=0.0065) and procalcitonin (p=0.0099), lower hospital mortality (OR: 1.184; 95% CI: 0.52–2.68, p=0.685) and early mortality during first 14 days after hospital discharge (OR: 0.7505, 95% CI: 0.1184 to 4.76, p=0.761) against cohort B.

Conclusion Meropenem daily dose was decreased in 56% of critical patients monitored. TDM is important in fighting against antimicrobial resistance, it is a guarantee of safety and it allows a reduction in healthcare cost.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.