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 there is no other alternative, VCZ pharmacokinetic monitoring is recommended to ensure the effectiveness of antifungal treatment.

REFERENCES AND/OR ACKNOWLEDGEMENTS

http://www.hanstenandhorn.com/news.htm

No conflict of interest.

4CPS-059 EFFECTIVENESS OF MEROPENEM TREATMENT IN CRITICAL PATIENTS: PHARMACOKINETIC STUDY

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Background Pharmacokinetic/pharmacodynamic efficacy index (PK/PD) for carbapenems, in critical patients, is the maintenance of a free concentration drug, 4–5 times above the minimum inhibitory concentration (MIC) in the isolated germ during 100% of the dosage range. Ensuring this goal is important and requires the use of pharmacokinetic monitoring (TDM).

Purpose Analyse the efficacy of pharmacokinetic optimised 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.

Material and methods Naturalistic retrospective, observational cohort study, carried out in critically ill patients treated with meropenem from May 2011 to December 2017. Patients were divided into two cohorts: cohort A if they had pharmacokinetic intervention or cohort B if not. In pharmacokinetic analysis two serum samples per patient were extracted (peak and elimination point) to quantify total and free concentration of meropenem. Individual pharmacokinetic parameters were estimated by the Sawchuk–Zaske method to find out what percentage of time, free concentration exceeded four times MIC of isolated germ and dosage regimen was adjusted when necessary. When CMI was not available, the epidemiological limit of $EUCAST_{(ECOFF)}$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: 0.82 to 3.23, p=0.167), 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

https://www.ijaaonline.com/article/S0924–8579(16)30268–0/fulltext

No conflict of interest.

4CPS-060 PREVALENCE OF VANCOMYCIN-RELATED NEUTROPAENIA, THROMBOCYTOPAENIA AND ACUTE KIDNEY INJURY

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Background Vancomycin is a glucopeptide antibiotic widely used to treat Gram positive related infections. It is well known for its nefrotoxic and ototoxic profile, but neutropaenia and thrombocytopaenia are not so well described.

Purpose The aim of this study was to describe the prevalence of some relevant vancomycin-related adverse events (AE): neutropaenia, thrombocytopaenia and acute kidney injury (AKI).

Material and methods This retrospective observational study was conducted in all patients admitted to Donostia University Hospital that received vancomycin during 2016 and 2017 and were monitored by the pharmacy department (PD).

Exclusion criteria: patients with neutropaenia, thrombocytopaenia or AKI prior to vancomycin therapy.

Collected data: diagnosis, absolute neutrophil count (ANC), absolute platelet count (APT) and creatinine clearance (CrCl, calculated with Cockcroft–Gault formula) prior and during vancomycin therapy. Neutropaenia was defined as ANC<1000 cel/microL, thrombocytopaenia as APT <100.000 cel/microL and AKI as CrCl <60 ml/min or decrease in CrCl of 25%.

Results A total of 177 patients were reviewed, with a mean age of 63.4±16.4 and 32.8% were women. Almost half of the patients 48.6% (n=86) had an ostearticular infection: bacteriemia accounted for 36.2% (n=64). The rest of the infections were related to the central nervous system 3.4% (n=6), endovascular system 3.4% (n=6) and others 8.4% (n=15).

Patients excluded: eight due to neutropaenia (n=169), 15 due to thrombocytopaenia (n=162) and 14 due to AKI (n=163) prior to vancomycin therapy.

Neutropaenia was developed in seven patients (=1:24), thrombocytopaenia in 12 patients (=1:14) and AKI in 26 patients (=1:6). The prevalence of nephrotoxicity is described as common (1:100–1:10) in the summary product characteristics (SPC). However, neutropaenia and thrombocytopaenia are classified as rare undesirable effects (1:10.000–1:1.000).

Conclusion The prevalence of AE related to vancomycin therapy is higher than reported in SPC. In our study neutropaenia was reported in 7:169 patients, thrombocytopaenia in 12:162 and AKI in 26:163.

The difference between SPC and our clinical practice is considerable. However, it should be noticed that only patients monitored by PD were reviewed, and therefore the number of patients included is low. It is of high importance to continue reporting any AE related to vancomycin therapy to the appropriate pharmacovigilance institution in order to better understand the toxic profile of the drug.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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4CPS-061 EXTENDED INFUSION OF MEROPENEM IN A NEONATE WITH COMPLICATED KLEBSIELLA PNEUMONIAE MENINGITIS

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Background Extended infusion of beta-lactam antibiotics is aimed at achieving microbiological eradication and clinical resolution of complicated bacterial infections. For meropenem, the best predictor of bacterial killing is the time over which free-drug concentration exceeds 4–6xMIC of the microorganism (desirable 40% fT >MIC).

Purpose To describe the course and monitoring of prolonged treatment with meropenem by extended infusion of 4 hours in a neonate with ventriculitis due to ESBL-producing *Klebsiella pneumoniae*.

Material and methods We present the case of a 25 weeks' preterm newborn, who presented with a septic episode with clinical, laboratory and ultrasonographic signs of ventriculitis at 93 days of age, in February 2018.Treatment was started with meropenem 40 mg/kg/8 hour, in an extended infusion of 4 hours. Concentrations of meropenem were determined in plasma and CSF samples before the administration of a dose (Cmin), once steady-state equilibrium was reached. For the quantification of the levels, high-performance liquid chromatography validated techniques were used.

Results ESBL-producing *Klebsiella pneumoniae* sensitive to carbapenems (MIC Meropenem <1 mg/L) was isolated from CSF cultures. From the beginning of meropenem treatment, CSF showed progressive improvement in inflammatory parameters, and the microorganism was not isolated after 2 days of treatment. Meropenem levels in plasma and CSF were determined at 4 weeks of treatment, which were 7.6 mg/L (pre-dose) in plasma and 4.7 mg/L in CSF. These levels showed an excellent penetration of the antibiotic in CSF (CSF/plasma concentration ratio of 0.62), ensuring a time above MIC>100% in both plasma and CSF. Likewise, no potentially toxic levels were observed despite a prolonged and extended infusion strategy. The patient continued treatment until completing 8 weeks. The ventricular drain was replaced by a ventriculoperitoneal shunt after 62 days. Clinically, the patient showed progressive improvement in neurological status. However, in view of the risk of neurodevelopmental impairment, the infant is currently under outpatient follow-up.

Conclusion With the dosing strategy used, optimal concentrations of meropenem were achieved, which allowed reaching the PK/PD index of time >4 times the MIC during 100% of the dose interval, both in plasma and in CSF.

The extended infusion of meropenem in 4 hours in our patient showed criteria of efficacy and the safety of prolonged treatment.

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No conflict of interest.

4CPS-062 IMPACT OF ANTIMICROBIAL STEWARDSHIP PROGRAMME ON CARBAPENEMS RESISTANCE AND CONSUMPTION IN A TERTIARY HOSPITAL: A BEFORE-AND-AFTER INTERVENTIONAL STUDY

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Background The treatment of infections caused by multiresistant gram-negative bacteria is a growing challenge in many hospitals. To combat this problem, the development of antimicrobial stewardship programmes (ASP), consisting of specialists in antimicrobial use from different units coordinated by infectious diseases specialists, is recommended.

Purpose The aim was to assess the impact of ASP on carbapenems resistance and consumption in a tertiary university hospital.

Material and methods A quasi-experimental study was designed before (March 2013–February 2014) and during the intervention (March 2014–February 2016). Patients prescribed carbepenems (meropenem, imipenem) were identified daily through the prescription drugs computer system (Farmatools). We recorded the impact of the programme on carbapenems consumption, in terms of defined daily dose (DDD)/1000 hospital stays, and the impact on the development of strains of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, other *Enterobacteria* and *Acinetobacter baumannii* resistant to carbapenems using the percentage of resistance (number of resistant isolates/