

patients, such as increased volume of distribution and increased clearance. For instance, subtherapeutic plasma concentrations are a concern.

Aim and objectives The objective of this work was to determine if the current dosage of meropenem and piperacillin strategies in clinical practice are enough to achieve pharmacokinetic/pharmacodynamic targets (minimum 100% fT once above MIC, optimal 4–6 times above MIC).

Material and methods A prospective study was conducted from February to June 2019 of serum levels of meropenem and piperacillin in an intensive care unit in the south of Spain. In all patients, the initial dose was chosen by the prescribing intensivist (extended infusions, high doses and adjustments for renal impairment were also included). A predose sample (100% fT >MIC) of the target antibiotics within the first 48 hours was included. As the majority of treatments were empirical, the CMI target was defined by EUCAST PK/PD break points (MIC >16 µg/mL for suspected *Pseudomonas aeruginosa* in the case of piperacillin and >2 µg/mL in the case of meropenem)

Results Twenty-eight patients were included. Median age was 64 years (IQR 48–78 years), median APACHE II score was 15 (IQR 14–24) and 18/28 patients were men. Of the 28 patients treated, 10 did not reach 100% fT >MIC, mostly in the piperacillin group (6/9) and 4/9 in the meropenem group; 100% fT > 4–6×MIC was not achieved in 8/9 patients in the piperacillin group and in 12/19 in the meropenem group.

Conclusion and relevance Over 5 months, thanks to the active surveillance of patients who were candidates for beta-lactam therapeutic drug monitoring and the request for determination of plasma levels by the hospital pharmacist, more than 30% of meropenem and piperacillin prescriptions were found to be subtherapeutic and 70% were optimisable.

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No conflict of interest.

4CPS-049

UNDERDOSING WITH HIGH DOSE PIPERACILLIN/TAZOBACTAM ADMINISTERED VIA CONTINUOUS INFUSION IN OUTPATIENT PARENTERAL ANTIMICROBIAL THERAPY: A STABILITY OR VISCOSITY PROBLEM?

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Background and importance Continuous infusion of high dose piperacillin/tazobactam (16/2 g in 264 mL NaCl 0.9%) has been included in the UZ Leuven outpatient parenteral antimicrobial therapy (OPAT) protocol. Elastomeric pumps (Infusor LV10, Baxter) were selected as the drug delivery device, as the patient's mobility and comfort are maintained. Unfortunately, incomplete infusions after 24 hours were observed, related to a reduced flow rate. A mean daily residual volume of 50 mL, corresponding to a dose of 3/0.38 g piperacillin/tazobactam, was detected, resulting in substantial underdosing with the risk of treatment failure.

Aim and objectives To analyse two hypotheses: a reduced flow rate could be the result of particulate formation of piperacillin dimers due to the absence of stabilising excipients (hypothesis 1) or a result of high viscosity (hypothesis 2).

Material and methods Hypothesis 1: particulate formation was detected by comparing the flow rate of tazocillin (with stabilising excipients) versus generic piperacillin/tazobactam (without this excipients), by measuring light absorbance (600 nm) by spectrophotometry and by measuring total piperacillin content at different concentrations after storage for 24 hours at 33°C.

Hypothesis 2: the effect of concentration on the density and viscosity at 33°C was measured. Additionally, the relation between viscosity and flow rate was evaluated.

Results Hypothesis 1: no difference was observed in the flow rate between Tazocillin and generic piperacillin/tazobactam. No difference was observed in absorbance between Tazocillin and generic piperacillin/tazobactam, and no difference was observed in absorbance between piperacillin/tazobactam and a blank. Generic piperacillin/tazobactam seemed to be stable for 24 hours at 33°C.

Hypothesis 2: a linear relationship was observed between concentration and viscosity. An inverted linear relationship was observed between viscosity and flow rate of piperacillin/tazobactam solutions.

Conclusion and relevance The in vitro experiments suggest that the reduced flow rate is a result of high viscosity, related to the concentration of piperacillin/tazobactam. As it is impossible to lower the concentration, the final volume of the solution should be adjusted. Before being used in clinical practice for OPAT, this mode of administration will first be validated in five patients during hospitalisation. In general, healthcare teams need to be aware of factors which may lead to longer flow durations with these infusion devices.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

4CPS-050

CONFORMITY OF ANTIBIOTIC THERAPY DURATION IN PATIENTS WITH FEBRILE NEUTROPENIA, HOSPITALISED IN THE HAEMATOLOGY DEPARTMENT OF A UNIVERSITY HOSPITAL

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Background and importance The emergence of bacterial resistance and the proper use of antibiotics are major public health issues.

In 2011, the European Conference on Infections in Leukaemia (ECIL) published recommendations for the management of febrile neutropenia. In this context, a university hospital wanted to evaluate follow-up of these recommendations.

Aim and objectives To evaluate conformity for duration of antibiotic therapy in patients with febrile neutropenia, hospitalised in the haematology department.

Material and methods The study was monocentric, retrospective, observational and conducted over a 6 month period in the haematology department. Data collection was carried out via a collection form. Two algorithms, created with the ECIL guidelines, were used to evaluate febrile neutropenia episodes. Duration of the prescription was considered to conform if it

satisfied the following criteria: for undocumented infection, discontinuation of probabilistic antibiotic therapy at 72 hours of apyrexia; for documented infection, continuation of documented antibiotic therapy, according to the recommendations of the local antibiotic guidelines.

Results Ninety infectious episodes were studied. The study population comprised 49 men (54%) and 41 women (46%). Average age was 56 years.

Cefepime or piperacillin/tazobactam were systematically introduced as probabilistic therapy. If the infection was undocumented (n=61/90), the duration of probabilistic antibiotic therapy conformed in 41% of cases (n=25/61). For clinical documentation (n=6/90), the conformity rate was 67% (n=4/6). For microbiological documentation (n=23/90), compliance rate was 74% (n=17/23).

Conclusion and relevance For most undocumented infections, probabilistic antibiotic therapy was prescribed for too long. This may be explained by the fragility of haematology patients and the fear of being confronted with recurrence of infection. For documented infections, conformity was very satisfying, as haematologists have extensive knowledge of infectiology. In order to harmonise prescription duration and continue to prevent the emergence of bacterial resistance, a guide for correct use of antibiotics and a second prospective study should be considered.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

4CPS-051 ANTIBIOTICS IN THE EMERGENCY DEPARTMENT: IS IT POSSIBLE TO IMPROVE PRESCRIPTIONS FOR INFECTIOUS RESPIRATORY DISEASES IN AMBULATORY PATIENTS?

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Background and importance Due to the rising rate of antibiotic resistance over the past years, healthcare authorities have developed different strategies to solve this problem. In Spain, the Health Care Service of Madrid (SERMAS) published the 'Antibiotics use guide for ambulatory treatment in adults' in 2019, which is used as a reference document for all health professionals, not only for ambulatory but also for hospital assistance.

Aim and objectives The main objective of the project was to evaluate the adequacy of the SERMAS guide for antibiotic prescriptions to ambulatory patients in the emergency department (ED) in one of the largest hospitals in Madrid

Material and methods One hundred patients who went to the ED during a random period in January 2019 were selected. All were diagnosed with a respiratory infection. Only patients who had an antibiotic prescription for the infectious respiratory disease and took the treatment at home were selected.

To evaluate prescription adequacy, the SERMAS guide was used as the reference. The evaluation took place in consecutive steps: (i) indication (necessity for an antibiotic), (ii) election (antibiotic coverage was correct) and (iii) selection (the selected antibiotic was the best option from the available possibilities). Duration and dose adequacy were evaluated.

Results One hundred patients (50 women and 50 men, median age 53 years old) were selected: 53% of patients (53/100) were treated with an antibiotic, and in 73.6% (39/53) the treatment was properly indicated. Antibiotic coverage was adequate in 94.9% (37/39) of cases. In 27.7% (10/37) of patients, the selected antibiotic was the one recommended by the SERMAS guide. Quinolones and high spectrum antibiotics were the more overused groups. In terms of posology, 15.1% (8/53) of patients had a prescription with the proper dose and 7.5% (4/53) received treatment with the proper dose and duration.

Conclusion and relevance The study showed what experts already knew: antibiotic prescriptions in the ED for ambulatory patients are poorly adjusted to the SERMAS guide, mainly due to longer duration and overuse of certain antibiotic groups. Improvement in antibiotic prescriptions should be a main target to reduce increasing antibiotic resistance.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

4CPS-052 EVALUATION OF PIPERACILLIN/TAZOBACTAM DOSAGE IN SEPTIC PATIENTS ATTENDING THE EMERGENCY DEPARTMENT

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Background and importance Although there is consensus for beta-lactam administration for extended infusions in critical care units, the use of this strategy in emergency departments remains unclear.

Aim and objectives To evaluate the probability of achieving an adequate pharmacokinetic/pharmacodynamic ratio for different dosages of piperacillin/tazobactam in septic patients attending an emergency department.

Material and methods A simulation study was carried out based on gram negative bacterial strains causing bacteraemia in septic patients treated in an emergency department (July 2018–December 2019). Two doses were evaluated, 4/0.5 g every 6 hours or 8 hours given as 0.5 hour or 3 hour infusion, in three different renal clearance rates (<30, 70 and 120 mL/min). Pharmacokinetic parameters were obtained from the literature. Minimum inhibitory concentration (MIC) values to piperacillin/tazobactam were obtained from Spanish records (trial database, TEST). Time above MIC was obtained according to the following equation: $fT > MIC = [(t_2 - t_{inf}) - t_1] \times (100/\tau)$, where t_1 was the time at which the free serum concentration reached the MIC, t_2 the post-infusion time at which the free serum concentration equalled the MIC in the elimination phase and τ the dosing interval. A 1000 subject Monte Carlo simulation was performed using Microsoft Excel per dosing and rate of renal function.

Results Sixty patients with gram negative bacteraemia were included. The predominant species were *Escherichia coli* (34, 56.7%), *Klebsiella pneumoniae* (14, 23.3%) and *Pseudomonas aeruginosa* (6, 10%). The probability of target attainment (PTA) $fT > 100\%$ MIC for piperacillin 4 g/8 hour dose was 60.3% and 81.8% for the 0.5 hour and 3 hour infusions for a $ClCr > 120$ mL/min and 75.1% and 94.3% for a $ClCr = 70$ mL/min. For the 4 g/6 hour dose, the PTA $fT > 100\%$ MIC