therapeutic concentration target, reaching a maximum of 7.5 ng/mL in 8 days, and then decreasing to 3.7 ng/mL in 4 days.

After investigation, noncompliance and sampling problems were excluded.

Concerning drug interactions, the literature reported an increase in tacrolimus C_{res} when ertapenem (antibiotic from the same class as meropenem) was co-administered: consequently meropenem was excluded from the hypotheses. With caspofungin, a decrease in tacrolimus C_{res} was described during a 10 day co-administration. However, this hypothesis seemed insufficient to explain the very important decrease in C_{res}.

Concerning pharmacogenetics, the research found a need for higher doses of tacrolimus in patients carrying the CYP3A5*3 allele (from 0.15–0.25 mg/kg/day depending on genotype). This patient was found to be a heterozygous carrier of the g.6986A>G mutation, characteristic of the non-functional allele CYP3A5*3.

Due to the persistence of C_{res} low values, tacrolimus was finally replaced by cyclosporine.

Conclusion Pharmacogenetics may explain some resistance-to-treatment occurrence, so it is important to raise awareness in the healthcare teams. Characterisation of the cytochrome 3A5 genotype can be a predictive means of tacrolimus dose optimisation, permitting the achievement of effective C_{res} while avoiding toxic effects.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

4CPS-146 SUBLINGUAL AND ENTERIC TACROLIMUS WHOLE BLOOD LEVELS IN AN INTENSIVE CARE UNIT

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Background Tacrolimus is an immunosuppressive agent with a narrow therapeutic range (5–15 ng/ml for solid organ transplants). Achieving and maintaining appropriate tacrolimus exposure are critical for preventing rejection and minimising toxicity.

Although tacrolimus can be delivered either orally or intravenously, oral tacrolimus is associated with fewer adverse effects. It has been suggested that the sublingual route may be used as an alternative to oral in critical care patients when the enteric route is not available.

Purpose The aim of this study was to compare tacrolimus drug exposure after sublingual or enteric administration in solid organ transplanted critical care patients.

Material and methods A retrospective observational study was carried out of the adults in an intensive care unit of a tertiary hospital from June to December 2017.

All oral immediate release tacrolimus prescriptions were reviewed during this period. Patient records were reviewed and the following data was collected: patient number, administered drug, total daily dose, route, start day and last day of the administration.

Prescription data was linked to tacrolimus levels laboratory results for each patient and of treatment. Tacrolimus levels corresponding to each route were analysed, and mean and standard deviation was performed. Tacrolimus blood concentration levels considered toxic (>20 ng/ml) were identified.

Results Seventy-eight patients were treated with oral immediate release tacrolimus during the period of study: 1201 tacrolimus drug concentration level analysis were performed (mean of all drug blood concentrations: 11.12 ng/ml, standard deviation (SD): ±5.59 ng/ml).

Oral (by mouth) administration drug concentrations levels (n=209) mean was 9.68 ng/ml (SD=±4.39 ng/ml). Two drug results (0.96%) were reported to be >20 ng/ml.

Nasogastric tube administration drug concentration levels (n=572) mean was 11.11 ng/ml. (SD) ±6.29 ng/ml. 45 (7.87%) drug results were reported to be >20 ng/ml.

Sublingual administration drug concentration levels (n=420) mean was 11.85 ng/ml (SD=4.93 ng/ml). 30 (7.1%) drug results were reported to be >20 ng/ml.

Conclusion Tacrolimus drug exposure after sublingual administration is similar to enteric administration in this study. Sublingual administration of tacrolimus is as effective and safe as nasogastric tube administration when oral administration is not feasible, although the lack of an appropriate drug formulation.

REFERENCE AND/OR ACKNOWLEDGEMENTS

Aliment Pharmacol Ther 2017;45:1225–31.

No conflict of interest.

4CPS-147 CLINICAL EXPERIENCE OF OPTIMISING CO-ADMINISTRATION THERAPY OF LOW-DOSE ALLOPURINOL WITH LOW-DOSE THIOPURINES IN INFLAMMATORY BOWEL DISEASE PATIENTS ATTENDING A VIRTUAL PHARMACIST CLINIC

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Background Thiopurines play an important role in maintaining remission in inflammatory bowel disease (IBD). Optimising therapeutic strategies is of paramount importance in preventing treatment failure. Co-administration of Allopurinol, a Xanthine Oxidase inhibitor, with thiopurines has become established practice in achieving target thioguanine concentrations. The recommended dose of Allopurinol is 100 mg combined with modified thiopurine dosing (<25% of standard dose).

Purpose The aim of the study was to explore whether Allopurinol 50 mg could achieve the correct thioguanine nucleotide to methylmercaptopurine (TGN:MeMP) ratio while observing the side effects and safety profile of combined therapy.

Material and methods Combined Allopurinol and thiopurines therapy were started in a virtual pharmacist clinic in a cohort of patients who had failed thiopurines monotherapy. Patients were contacted by telephone, text or e-mail according to patients' preference. Thioguanine results were requested from our laboratory and obtained from Guy's NHS Hospital, which recommended the addition of Allopurinol if the ratio TGN:MeMP >11.

The total number of patients recruited was 44, of which 20 were female, 17 had Crohn's disease, 27 had ulcerative colitis. The average weight was 86 kg. Two patients were TPMT carriers ((10–25) pmol/h/mgHb), the rest were normal (26–51). The Azathioprine dosing range was (0.12–0.64) mg/kg (23 patients): the 6-Mercaptopurine dosing range was (0.11–0.54) mg/kg (21 patients).

Results Of the 44 patients entered into the study, 14 patients discontinued treatment during the first week, 11 patients due