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

¹L Domènech*, ²JM Guíu Segura, ¹JB Montoro Ronsano. ¹Vall d'Hebron University Hospital, Pharmacy Department, Barcelona, Spain; ²Consorci de Salut i Social de Catalunya, Pharmacy Department, Barcelona, Spain

10.1136/ejhp-pharm-2019-eahpconf.295

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

¹F Fuentes*, ¹S Abdel-Aziz, ²D Bullas. ¹Barnsley Hospital NHS Foundation Trust, Pharmacy, Barnsley, UK; ²Barnsley Hospital NHS Foundation Trust, Gastroenterology, Barnsley, UK

10.1136/ejhp-pharm-2019-eahpconf.296

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

to intolerance and three patients (with normal TPMT levels) due to recurrent hepatotoxicity. 30/44 patients tolerated combined therapy. 27/30 patients achieved an optimised TGN:MeMP ratio (<11). Specific ratios included 0 ($n=13$), 1 ($n=9$), 2 ($n=4$), 3 ($n=1$). 3/30 patients required Allopurinol 100 mg to obtain a ratio <11 .

Conclusion The majority of patients (90%) obtained an effective TGN:MeMP ratio with reduced Allopurinol dosing at 50 mg. Those that did not achieve this ratio (10%) responded to dose escalation to 100 mg. TPMT status did not appear to influence the effect of low-dose Allopurinol. Hepatotoxicity may still occur with combined Allopurinol and thiopurines therapy. Low-dose Allopurinol may be considered a viable therapeutic strategy providing that appropriate clinical and biochemical surveillance is maintained.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Thanks to gastroenterologists and the chief pharmacist.
No conflict of interest.

4CPS-148 ANALYSIS OF INTRA-PATIENT VARIABILITY OF PLASMATIC LEVELS OF TACROLIMUS IN EARLY MAINTENANCE OF RENAL POST-TRANSPLANT

¹S García García*, ²DS Oleas Vega, ³MB Aller Hernández, ⁴I Torres Rodríguez, ⁵BO Chamoun Huacón, ⁶E Pericas Bosch, ⁷JB Montoro Ronsano. ¹Vall d'Hebron Hospital, Pharmacy Service, Barcelona, Spain; ²Vall d'Hebron Hospital, Nephrology Service, Barcelona, Spain; ³Vall d'Hebron Hospital, Artificial Intelligence Information Service, Barcelona, Spain

10.1136/ejhp-2019-eahpconf.297

Background Tacrolimus is a calcineurinic inhibitor characterised by a narrow therapeutic window and high variability of plasmatic levels.

Purpose To assess the intra-patient variability (IPV) of tacrolimus plasmatic levels (FKplasm) in kidney-transplanted patients (KTP) during the early maintenance period (EMP), 3 to 6 months after surgery. In EMP begins a progressive reduction of immunisation to establish the future immunosuppressant dosage.

Material and methods Observational retrospective study in KTP within 2015–2017, monitored along the EMP and at least one determination of FKplasm.

The clinical data was collected from the hospital's medical records, including kind of transplant, FKplasm and analysis date.

The FKplasm were analysed for each patient along the EMP. The mean and standard deviation of plasma concentrations, the number of blood determinations, the coefficient of variation (CV), the proportion of values lower than 5 and 7 ng/ml (P5 and P7) and the area under the concentration-estimated time (AUC-Min) were evaluated in EMP. To describe the IPV the CV was used.

The range of therapeutic FKplasm values was established between 5–20 ng/ml. The therapeutic control was considered inadequate if IPV was superior to 30% or the P7 or P5 was superior to 20%.

To evaluate the IPV and to compare the intra-patient values obtained, the analysis of variance and the Fisher–Snedecor F distribution were used (statistical analysis with SPSS).

Results Two-hundred and eleven patients and 996 tacrolimus determinations were included. The mean of FKplasm was 8.57 ng/ml (95% CI: 8.26 to 8.88) and the mean number of determinations was 4.72 (95% CI: 4.17 to 5.26) during the follow-up period.

The mean CV of FKplasm was 25.41% (95% CI: 23.09 to 27.74). A total of 31.75% (95% CI: 25.42 to 38.09) of the

patients had a CV greater than 30%. The AUC-Min was 7.61 ng/ml/day (95% CI: 7.2 to 8.0).

Finally, the mean percentages of FKplasm lower than 7 ng/ml and 5 ng/ml were 27.20% (95% CI: 23.16 to 31.24) and 9.28% (95% CI: 6.49 to 12.06), respectively. The proportion of patients with values higher than 20% was 52.3% (95% CI: 45.6 to 58.8) P7 and 17.2% (95% CI: 12.3 to 21.8) P5.

The IPV of FKplasm during the EMP was higher than recommended in 31.75% of cases, similarly, 27.2% of the determinations were <7 ng/ml.

Conclusion Taking into account the limitations of this study, the early detection of patients with high IPV, or analytical values <7 ng/ml in the EMP is essential, since these are associated in the long term with a worse prognosis, leading to chronic rejection of the graft and/or greater pharmacological toxicity.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Thanks to all authors for their involvement.
No conflict of interest.

4CPS-149 EVALUATION OF INTRA-PATIENT VARIABILITY OF THE TACROLIMUS PLASMATIC LEVELS IN THE DIFFERENT PERIODS OF THE KIDNEY POST-TRANSPLANT

¹S García García*, ²DS Oleas Vega, ³MB Aller Hernández, ⁴I Torres Rodríguez, ⁵BO Chamoun Huacón, ⁶E Pericas Bosch, ⁷JB Montoro Ronsano. ¹Vall d'Hebron Hospital, Pharmacy Service, Barcelona, Spain; ²Vall d'Hebron Hospital, Nephrology Service, Barcelona, Spain; ³Vall d'Hebron Hospital, Artificial Intelligence Information Service, Barcelona, Spain

10.1136/ejhp-2019-eahpconf.298

Background The management of immunosuppression in kidney transplant (KT) is divided into: induction from 0 to 3 months, early maintenance (EM) from 3 to 6 months and late maintenance (LM) from 6 months. During the induction, more intense immunosuppression is required to prevent acute rejection of the graft.

Purpose To assess the mean concentration, the intra-patient variability (IPV) of tacrolimus plasmatic levels (FKplasm) and their evolution during the different periods of KT.

Material and methods Observational retrospective study included kidney transplanted patients since January 2015, with a minimum post-transplant follow-up of 2 years.

The clinical data was collected from the hospital's medical records, including: kind of transplant, surgery date and FKplasm from the transplantation date to 2 full years of follow-up.

The variables of the study were calculated considering the different stages of KT: induction, EM and LM: 6–12 months (LM1), 1–2 years (LM2) and 2–3 years (LM3). The mean of FKplasm, the number of analytical determinations performed and the percentage of patients with concentrations lower than 5 ng/mL were calculated. The therapeutic range of FKplasm value was 5–20 ng/mL.

To describe the IPV of FKplasm, the coefficient of variation (CV) was calculated. The IPV was considered inadequate when the CV values were higher than 30%.

The statistical analysis was carried out using SPSS, and to compare population means the variance analysis and Fisher–Snedecor's F distribution were used.

Results Two-hundred and twelve patients and 4180 measures of FKplasm were included. The values of the variables analysed were expressed in the temporal order of induction, EM, LM1, LM2 and LM3:

Mean FKplasm: 9.63 ng/ml (95% CI: 9.33 to 9.92), 8.57 ng/ml (95% CI: 8.26 to 8.88), 8.01 ng/ml (95% CI: 7.71