4CPS-124 ADHERENCE TO SELECTIVE IMMUNOSUPPRESSIVE DRUG TREATMENTS IN PATIENTS WITH INFLAMMATORY IMMUNE MEDIATED DISEASES

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Background and importance The paradigm of patients with immune mediated autoimmune diseases has changed with the introduction of biological medicines. The correct use of these drugs is necessary to guarantee their effectiveness.

Aim and objectives To analyse adherence in immune mediated diseases patients treated with selective immunosuppressive drugs (adalimumab or etanercept) and to establish a link with patient characteristics and treatment duration.

Material and methods A retrospective study in a third level hospital was conducted in patients receiving treatment with adalimumab or etanercept from January to December 2018. Adherence was measured via the medication possession ratio (MPR) over 1 year. Variables recorded were sex, age, pathology, previously taken biological drug treatments, treatment duration in days and number of auto-injectors. Statistical analysis of the data was made with SPSS.

Results The sample population was 146 patients, 55.5% (81) men, mean age 53.58 ± 12.47 years, and 55.5% were treated with adalimumab, 39.7% with etanercept and 3.9% with the biosimilar etanercept. Medium treatment duration was 5.07 ± 3.09 years. The main pathologies and frequency were: rheumatoid arthritis in 32.2% (47) of patients, spondyloarthropathy in 18.5% (27), psoriatic arthritis in 17.8% (26), psoriasis in 13.7% (20), Crohn's disease in 11% (16), ulcerative colitis in 4.8% (7) and other pathologies in 2.1% (3). Regarding adherence, the overall rate was 89.3%. For each patient group, adherence was 86.24% in patients with rheumatoid arthritis, 89.36% in patients with spondyloarthropathy, 94.5% in patients with psoriatic arthritis, 84.11% in patients with psoriasis, 94.63% in patients with Crohn's disease, 93.01% in patients with ulcerative colitis, 84.38% in patients with Verneuil's disease and 84.11% in patients with systemic lupus erythematosus. In total, 78.1% (114) of all patients were adherent (MPR $\geq 80\%$). We did not observe statistically relevant associations between any of variables except for lower adherence to treatment and longer treatment duration ($p=0.038$).

Conclusion and relevance Patients had good adherence to selective immunosuppressant treatments according to the MPR method. Sex, pathology or drug type were not related to absence of adherence. However, lack of adherence was observed the longer treatment lasted, which implies that it would be useful to have closer pharmacotherapeutic monitoring of this kind to reinforce adherence in patients.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

4CPS-125 ACCEPTANCE OF PHARMACOKINETIC RECOMMENDATIONS FOR EVEROLIMUS IN RENAL TRANSPLANT PATIENTS

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Background and importance Pharmacokinetic monitoring of the transplanted patient is essential to keep blood concentrations of immunosuppressive drugs in range, and to reduce the risk of organ rejection and the adverse effects associated with these drugs.

Aim and objectives To assess the degree of acceptance by the nephrology service of recommendations made by the clinical pharmacokinetics unit after monitoring everolimus blood concentrations at a third level general university hospital.

Material and methods This was a retrospective observational study in renal transplant patients with at least two everolimus determinations between January 2016 and September 2019. Patients were identified from the Gestlab programme and data collected were: age, sex, date of testing, concomitant immunosuppressive treatment, blood concentrations and pharmacokinetic recommendations. The number of blood determinations per patient, percentage of pharmacokinetic recommendations accepted by the physician and the proportion of values lower and higher than the established therapeutic range were evaluated; the target therapeutic interval for monotherapy is 6–10 ng/mL and in combination with calcineurin inhibitors is 3–8 ng/mL.

Results Pharmacokinetic monitoring was performed in 49 patients, 59% men, with an average age of 60 ± 12 years and an average of 9 ± 5.3 everolimus determinations. In 65.3% of patients, treatment was with everolimus and tacrolimus simultaneously. A total of 443 samples were analysed, with a dose adjustment required in 34.7%. The average everolimus percentages lower and higher than the target range were 23% and 11.3%, respectively. The dosing recommendations of these patients were accepted in 69% of cases. After this adjustment, 66.1% of patients tested showed drug concentrations in range. Of the total recommendations not accepted, 31% of medical actions differed from the recommendation in the prescribed final dosing regimen.

Conclusion and relevance During the study period, posology individualisation was necessary in almost 35% of the analyses performed by the clinical pharmacokinetics service, with the pharmacokinetic recommendations accepted by the prescriber in more than 60% of cases.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

4CPS-126 A POPULATION PHARMACOKINETIC MODEL OF ADALIMUMAB IN A COHORT OF PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PRELIMINARY ANALYSIS

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Background and importance Therapeutic drug monitoring is useful to optimise adalimumab therapy in patients with inflammatory bowel disease (IBD).

Aim and objectives The objective of this study was to perform a preliminary pharmacokinetic (PK) model of adalimumab to evaluate covariates potentially responsible for the PK variability in paediatric patients with IBD.

Material and methods A 3 year retrospective multicentre study was performed including children and adolescent (≤ 18 years) diagnosed with IBD and treated with adalimumab. Demographic and clinical data were collected, including serum albumin, C reactive protein and faecal calprotectin. Pre-dose serum samples were carried out before administration. Adalimumab concentrations and anti-adalimumab antibodies (AAA) were determined by ELISA. The model was developed in NONMEM V.7.4 by approximating the non-linear mixed effects models. The first order conditional estimation method with interaction (FOCEI) was used for model building. Concentrations below the lower limit of quantification (LLOQ) were set to LLOQ/2. Body weight (WGT) was included in the PK parameters following an allometric relationship.

Results Twenty-three paediatric patients (10 women) were included, 3 were diagnosed with ulcerative colitis and 20 with Crohn disease. Median age (range) was 14.0 (5–18) years and weight 55.9 (20.4–80) kg. A total of 75 concentrations ($2 < \text{LLOQ}$) were determined, with a medium concentration of 10.72 (0.1–24.7) $\mu\text{g/mL}$. Median (range) serum albumin level was 4.0 (2.8–5.0) g/dL. Only one patient developed AAA. Population PK model (PopPK): a one compartment with first order absorption and elimination described adequately the serum adalimumab concentration–time data. The absorption rate constant was fixed ($K_a=0.008/\text{hour}$) according to Sharma *et al.* Among the clinical variables analysed, only albumin was significant on the apparent clearance (CL/F). The final PopPK model in the absence of AAA was as defined as: $V/F=11.30 \times (\text{WGT}/56 \text{ kg})$ and $\text{CL}/F (\text{L}/\text{day})=0.42 \times (\text{albumin}/4 \text{ g/dL})^{-2.32} \times (\text{WGT}/56 \text{ kg})^{0.75}$. Covariate analysis reduced the interindividual variability associated with CL (IIVCL) from 34.1% to 21.3%. Proportional residual error estimated was 28.4%.

Conclusion and relevance Adalimumab PK in paediatric patients with IBD was best described by a one compartment model with first order absorption and elimination. WGT was included in the PK parameters following an allometric relationship. Albumin showed statistically significant differences on adalimumab CL/F , explaining 62.5% of its variability.

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No conflict of interest.

4CPS-127 ECONOMIC IMPACT OF INTENSIFICATION REGIMENS IN INFLAMMATORY BOWEL DISEASE

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Background and importance Biological treatments have improved the therapeutic options for inflammatory bowel disease (IBD) and have shown high clinical efficacy. Nevertheless, some patients do not respond to initial treatment or present

loss of response over time. To prevent the loss of efficacy, treatment intensification has been employed, usually applied empirically based on the clinical condition of the patient and biochemical parameters. The introduction of tumour necrosis factor antagonist (anti-TNF) monitoring in clinical practice allows a more accurate selection of strategies.

Aim and objectives To analyse the number of patients receiving treatment with a biological agent for IBD and requiring an intensification regimen, including increasing dosage or shortening the administration interval, and to evaluate the economic impact of this intensification strategy.

Material and methods This was a retrospective observational study in patients diagnosed with IBD and under an intensified regimen of a biological agent. The cost per patient was estimated based on the extrapolation of the price of each medication for 1 year of treatment. In addition, the difference in costs per patient and year for each treatment and the total economic impact were calculated.

Results A total of 549 patients with IBD were receiving a biological treatment and 239 required an intensification regimen (table 1).

Conclusion and relevance Intensification regimens, including

Abstract 4CPS-127 Table 1

Drug	Intensification regimen	No patients (%) intensifications per drug)	Patient annual cost (€)	Difference with respect to standard regimen (€)	Incremental annual total cost (€)
Adalimumab	40 mg q1 week	34 (18)	4860	2430	82620
Golimumab	100 mg q4 weeks	13 (52)	11082	725	9425
Ustekinumab	q8 weeks	52 (68)	16063	5362	278 824
	q6 weeks	9 (12)	21425	10725	96525
	q5 weeks	1 (1)	25700	15000	15000
	q4 weeks	13 (17)	32125	21425	278 525
Vedolizumab	q6 weeks	14 (19)	13791	3452	48328
	q4 weeks	16 (22)	20678	10339	165 424
Infliximab	10 mg/kg q8 weeks	77 (43)	6341	3170	244090
	5 mg/kg q6 weeks	9 (5)	4229	1058	9522
	5 mg/kg q4 weeks	1 (1)	6341	3170	3170
	5 mg/kg q4 weeks				
Total		239			1 231 453

increasing dosage or shortening the administration intervals, were frequent in our hospital, both for anti-TNF and for other biological agents used for the treatment of IBD. These strategies involve an important economic impact, as well as a high risk of infection for patients. Intensification should be guided by pharmacokinetic monitoring. More studies are needed to validate therapeutic algorithms that allow optimisation of resources for all biological agents used.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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