EVALUATION OF INTRA-PATIENT VARIABILITY OF THE INFLUENCE OF THE ROUTE AND PHARMACEUTICAL PREPARATION IN INTRA-PATIENT VARIABILITY OF TACROLIMUS PLASMA LEVELS IN DIFFERENT PERIODS AFTER LIVER TRANSPLANT

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Background: Immunosuppressive therapy in liver transplant patients (LTP) is divided into several temporary periods after surgery. The priority is to avoid acute rejection in the earliest stages, and advancing in time, to preserve a longer graft survival and to minimise pharmacological adverse events.

Purpose: To assess the mean concentration, intra-patient variability (IPV) of FKs, and their evolution during the different periods after liver transplant to evaluate the therapeutic situation of LTP.

Material and methods: Observational retrospective study since January 2015, with a minimal post-transplant follow-up of 1 year. Clinical data was collected from the hospital’s medical records.

Variables of the study were calculated considering different periods of liver post-transplant according to our hospital medical protocol: 0–1 month (S1), 1–3 months (S2), 3–6 months (S3), 6–9 months (S4) and 9–12 months (S5). FKs mean, coefficient of variation (CV), proportion of patients with CV >30% (CV30), and estimated daily area under the curve (AUCd) and proportion of FKs values <5 ng/mL (P5) per patient were calculated. CV was used to characterise the IPV.

Results: Eighty-eight patients and 1206 measures of FKs were included. The values of variables analysed – mean FKs, P5, estimated AUCd and CV30 – were expressed in the temporal order of the follow-up period – S1, S2, S3, S4, S5 – as follows:

- Mean FKs: 7.5 ng/mL (95% CI: 7.0 to 8.0), 8.0 ng/mL (95% CI: 7.6 to 8.6), 7.0 ng/mL (95% CI: 6.5 to 7.4), 6.5 ng/mL (95% CI: 6.0 to 7.0) and 6.5 ng/mL (95% CI: 5.9 to 7.1).
- P5: 30.0% (95% CI: 25.0 to 35.0), 18.4% (95% CI: 12.7 to 24.2), 21.4% (95% CI: 14.2 to 28.6), 23.3% (95% CI: 15.1 to 31.4) and 29.5% (95% CI: 19.2 to 39.8).
- AUCd: 7.1 ng/mL.day (95% CI: 6.5 to 7.7), 7.8 ng/mL.day (95% CI: 7.1 to 8.5), 6.1 ng/mL.day (95% CI: 5.5 to 6.7), 7.9 ng/mL.day (95% CI: 6.5 to 9.3) and 9.1 ng/mL.day (95% CI: 7.4 to 10.9).

Conclusion: FKplasm and IPV during induction are higher than in EM and LM. However, patients with CV >30% remain in the maintenance periods between 29.9% and 31.8%, and with values <5 ng/mL between 9.3% and 13.1% which would justify a greater need for pharmacokinetic monitoring and therapeutic control, in order to preserve a longer graft survival and to minimise the events of pharmacological adverse reactions.

REFERENCES AND/OR ACKNOWLEDGEMENTS
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No conflict of interest.

4CPS-151 INFLUENCE OF THE ROUTE AND PHARMACEUTICAL PREPARATION IN INTRA-PATIENT VARIABILITY OF TACROLIMUS SERUM LEVELS IN THE LIVER TRANSPLANT PATIENT

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Background: In the earliest stages, immunosuppressive therapy in liver transplant patients (LTP) is targeted to avoid acute rejection and/or greater pharmacological toxicity. The use of different administration routes or immediate-prolonged release preparations could influence tacrolimus serum levels (FKs) and variability.

Purpose: To assess the mean concentration and the intra-patient variability (IPV) of FKs after their administration through immediate-prolonged release preparations and/or different administration routes in LTP.


Clinical data was collected from the hospital’s medical records, including: type of transplant, date of surgery, tacrolimus pharmaceutical form (TacPP), administration route and FKs values within 1 month after liver transplant.

FKs mean levels, coefficient of variation (CV), proportion of patients with CV >30% (CV30) and proportion of FKs values lower than 5 ng/mL (P5) per patient were calculated.
The influence of the TacPP administered (immediate/prolonged/extended release) and the administration route (oral/nasogastric tube), in case of immediate-release tacrolimus form was also analysed.

Therapeutic control was considered inadequate if CV30 occurred, or P5 was higher than 20%.

Statistical analysis was done using SPSS. Variance analysis and the Kruskal–Wallis test was used to compare quantitative variables.

Results Eighty-four patients were included. The values of the variables analysed – mean FKs, P5 and CV30 observed – were 8.0 ng/mL (SD, 4.2), 19.3% (SD, 39.6) and 66.0% (DE, 46.9). Technically, 68.3% patients had poor FKs control levels.

According to TacPP, values for mean FKs, P5 and CV30 observed were:

- Immediate-release tacrolimus: 8.5 ng/mL (95% CI: 6.2 to 10.9), 28.6% (95% CI: 12.8 to 44.3) and 58.1% (95% CI: 39.7 to 76.5).
- Prolonged-release tacrolimus: 7.9 ng/mL (95% CI: 6.2 to 10.9), 10.5% (95% CI: 1.0 to 25.6) and 66.7% (95% CI: 55.0 to 78.3).
- Extended-release tacrolimus: 9.6 ng/mL (95% CI: 8.0 to 11.3), 8.3% (95% CI: 0.0 to 27.0) and 83.3% (95% CI: 58.6 to 100.0).

According to the administration route (immediate-release tacrolimus form), values for mean FKs, P5 and CV30 observed were:

- Oral: 8.5 ng/mL (95% CI: 6.2 to 10.9), 28.6% (95% CI: 6.7 to 24.9) and 58.1% (95% CI: 40.0 to 76.5).
- Nasogastric tube: 6.8 ng/mL (95% CI: 5.5 to 8.0), 32.3% (95% CI: 14.8 to 49.7) and 76.0% (95% CI: 58.0 to 94.0).
- Mean FKs, P5 and CV30 observed varied widely among the TacPP and administration route: statistical differences were only achieved for P5 within TacPP (p=0.044).

Conclusion Taking into account the limitations of this study, our findings suggest that high IPV of FKs exist, at least within the first month after the transplant date. Moreover, the IPV of FKs after their administration through immediate-prolonged release preparations and/or a different administration route shows a wide range of variability that in concrete cases (P5) raises statistical significance.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

4CPS-153 COMPARATIVE ANALYSIS BETWEEN ORIGINATOR AND BIOSIMILAR INFLIXIMAB ACCORDING TO TROUGH LEVELS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background The introduction of biosimilar infliximab (IFX-B) has led to a decrease in the costs of patients with inflammatory bowel disease (IBD). The molecular complexity in the manufacture of biological drugs makes it difficult to verify the similarity between the different drugs. Infliximab (IFX) therapeutic drug monitoring allows for objective decision-making in patients with IBD.

Purpose To compare the percentage of patients in therapeutic IFX concentrations, between originator infliximab (IFX-O)