Influence of the Route and Pharmaceutical Preparation in Intra-Patient Variability of Tacrolimus Serum Levels in the Liver Transplant Patient

S. García García 1, C. Dopazo Taboada 2, M.B Aller Hernández 1, I. Bilbao Aguirre 2, E. Pericas Bosch 3, J.B. Montoro Ronsano 1
1 Pharmacy Service, 2 Hepatobiliary Surgery Service, 3 Artificial Intelligence Information Service, Vall d’Hebron University Hospital, Barcelona, Spain.

Purpose

Immunosuppressive therapy in liver transplant patients is targeted to avoid rejection to preserve graft survival and to minimize the risk of adverse reactions.

To assess the mean concentration and the intra-patient variability of tacrolimus serum levels after their administration through:
- Immediate-prolonged release preparations
- Different administration routes in liver transplant patients.

Material and Methods

Observational retrospective study: January 2015- December 2017
Liver transplanted patients > 18 years old

Analized variables

- Mean of tacrolimus serum levels
- Coefficient of variation
- Proportion of tacrolimus serum values lower than 5 ng/ml (P5)
- Proportion of patients with coefficient of variation superior to 30%
- The influence of the pharmaceutical form of Tacrolimus
- The administration route

Oral Nasogastric tube

Global analysis: The values of the variables analyzed—mean FKs, P5 and CV30 observed—are 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.

Results

84 patients

Pharmaceutical form | Mean of tacrolimus serum levels | P5 | Proportion of patients with coefficient of variation superior to 30%
---|---|---|---
Immediate-release tacrolimus | 8.5 ng/mL (IC95%,6.2-10.9), | 28.6 % (IC95%,12.8-44.3) | 58.1% (IC95%,39.7-76.5)
Prolonged-release tacrolimus | 7.9 ng/mL (IC95%,6.2-10.9), | 10.5 % (IC95%,1.0-25.6) | 66.7% (IC95%,55.0-78.3)
Extended-release tacrolimus | 9.6 ng/mL (IC95%,8.0-11.3), | 8.3 % (IC95%,0.0-27.0) | 83.3% (IC95%,58.6-100.0)

Administration route | Mean of tacrolimus serum levels | P5 | Proportion of patients with coefficient of variation superior to 30%
---|---|---|---
Oral | 8.5 ng/mL (IC95%,6.2-10.9), | 28.6 % (IC95%,6.7-24.9) | 58.1% (IC95%,40.0-76.5)
Nasogastric tube | 6.8 ng/mL (IC95%,5.5-8.0), | 32.3 % (IC95%,14.8-49.7) | 76.9% (IC95%,58.0-94.0)

Conclusion

Our findings suggest that high intra-patient variability of tacrolimus serum levels exist, at least within the first month after the transplant date. Moreover, the intra-patient variability of tacrolimus serum levels 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.