L04 - Immunosuppressive agents

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

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## 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 .

Influence in tacrolimus serum levels and variability.

## 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 → **Immediate release**, **Prolonged release**, **Immediate release**
- The administration route → **Immediate release**: Oral, Nasogastric tube

* To describe the intra-patient variability was used the coefficient of variation

## Results

84 patients

Range of therapeutic tacrolimus plasmatic levels values is established between 5-20 ng/ml

Therapeutic control is considered inadequate if intra-patient variability is superior to 30 % or P5 was higher to 20 %.

**Global analysis:**
The values of the variables analyzed -mean FKs, P5 and CV30 observed- are 8.0ng/mL (SD,4.2), 19.3% (SD,39.6) and 66.0% (DE,46.9);technically, 68.3% patients had poor FKs control levels.

| 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) | 76.0% (IC95%,58.0-94.0) |

* Mean FKs, P5 and CV30 observed varied widely among TacPP and administration route, statistical differences were only achieved for P5 within TacPP(P=0.044).

## 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.