High intrapatient variability in tacrolimus exposure is not associated with immune-mediated graft injury after liver transplantation

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Aims

A high intrapatient variability in tacrolimus exposure is associated with impaired long-term clinical outcome after kidney transplantation [1,2]. It remains to be determined if a high tacrolimus intrapatient variability is equally detrimental for liver transplant recipients [3]. The objective of the study was to investigate the association between a high intrapatient variability in tacrolimus exposure and immune-mediated graft failure after a liver transplantation.

Methods

For 326 liver transplant recipients, transplanted between 2000 and 2015, the tacrolimus intrapatient variability was calculated from at least 5 tacrolimus trough samples between month 6 and 18 after the liver transplantation and was expressed as the coefficient of variation. Patients were divided into a low and high tacrolimus variability group based on the coefficient of variation. For the primary outcome, a composite endpoint was used, consisting of graft failure due to immunological causes (including chronic rejection, biopsy proven late acute rejection and suspected late acute rejection) after month 6 post-liver transplantation. Secondary outcomes were the influence of tacrolimus intrapatient variability on (1) the loss of renal function per year of follow- up and (2) cytomegalovirus viremia after month 6 post-liver transplantation.

Results

Of the 326 included liver transplant recipients, 70 patients reached the primary composite endpoint. There was no significant difference in reaching the primary composite endpoint between the low and high tacrolimus variability group (p=0.068). Tacrolimus variability modeled as a continuous variable remained non-significantly associated in the multivariate analysis (p=0.324). MELD-score pre-transplantation and number of acute rejections were identified as predictors for immune-mediated graft failure (p=0.049, p=0.016). A higher tacrolimus variability with an impaired kidney function at baseline (eGFR < 40 ml/min) was associated with more loss of renal function per year of follow-up (p=0.007). Tacrolimus variability was not associated with cytomegalovirus viremia after month 6 post-liver transplantation.

Conclusion

A high intrapatient variability in tacrolimus exposure beyond month 6 post-liver transplantation was not found to be associated with immune-mediated graft failure.

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