Symposium

[S-3] S-3: Biomarkers and TDM of immunosuppressive drugs

Chairs: Uwe Christians, USA / Satohiro Masuda, Japan
2017年9月25日(月) 15:00 ～ 17:00 Main Hall (1F)

(2017年9月25日(月) 15:00 ～ 17:00 Main Hall)

[S-3-5] High intrapatient variability of tacrolimus exposure is associated with poorer outcomes after liver transplantation

Camille Tron[1], Michel Rayar[2], Caroline Jezequel[3], Antoine Petitcollin[4], Pauline Houssel-Debry[5], Christophe Camus[6], Marie-Clemence Verdier[7], Laurent Sulpice[8], Eric Bellissant[9], Karim Boudjema[10], Florian Lemaitre[11]
(1.Rennes University Hospital, 2.Rennes University Hospital, 3.Rennes University Hospital, 4.Rennes University Hospital, 5.Rennes University Hospital, 6.Rennes University Hospital, 7.Rennes University Hospital, 8.Rennes University Hospital, 9.Rennes University Hospital, 10.Rennes University Hospital, 11.Rennes University Hospital)
キーワード：Tacrolimus, Intra-patient variability, Liver transplantation, Patient outcomes, Therapeutic drug monitoring

Background

Tacrolimus (TAC) is the cornerstone of immunosuppressive regimen in organ transplantation particularly in liver transplantation. Its pharmacokinetics is characterized by a high inter- and intra-patient variability leading to unpredictable dose-response relationship. Recent works in kidney transplantation have identified the intra-patient variability (IPV) of TAC as a key factor of its efficacy and tolerance. To date, no data are available in liver transplantation.
The aim of our study was to evaluate the impact of IPV in TAC trough whole blood concentrations in the early period after liver transplantation on graft and patient’ s outcomes.

Methods

The study population consisted of 812 liver transplant recipients treated with TAC. IPV of TAC concentrations was estimated by calculating the coefficient of variation (CV) of whole blood trough concentrations measured for each patient between post-operative days 8 to 30. Patients were categorized in two groups: low IPV (CV<40%) and high IPV (CV>40%). Clinical and biological parameters were retrospectively analyzed to determine risk factors of high IPV and its influence on outcomes.

Results

There were significantly more neurologic complications (31.2% vs. 16.6%, p<0.001), cardiovascular complications (19.7% vs. 9.7%, p<0.001) and acute renal failure requiring dialysis (8.5% vs. 2.2%, p<0.001) in the high-CV group than in the low-CV group while acute rejection rate was similar (19.7% in high−CV group vs. 17% in low-CV group, p=0.417). Moreover, long-term graft survival was significantly poorer in high-CV group than in low-CV group (p=0.003) as well as patient’ s survival (p=0.001). A pre-transplantation elevated MELD score (p<0.001) and Child-Pugh grade (p<0.001) were identified as being a risk factor of presenting a high-CV.

Conclusions

To our knowledge, this is the first study aiming at evaluating the role of early CV of TAC concentrations in liver transplant recipient’ s outcomes. A high IPV in TAC concentrations was found to be predictive of TAC related toxicity and poorer survival. Patients who are at higher risk of presenting high-CV should be proposed to a more intensive therapeutic drug monitoring.