Oral

[O26-2] O26-2: Immunosuppressive drugs: clinical practice

Chairs: Mikio Kakumoto, Japan / Olga Millan, Spain

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[O26-2-2] A comparison of dosage, blood, kidney and hepatic tissue Tacrolimus concentrations in transplant recipients and the influence of the concentrations and dosage on efficiency of treatment in immunosuppressive therapy

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Keywords: Tacrolimus, kidney and hepatic tissue, LC-MS/MS

Background

Close monitoring of Tacrolimus (TAC) concentrations is required to avoid the risk of acute rejection or side effects. The latest results in some studies indicate that inter-tissue TAC concentration can be better prognostic parameter in regards to acute rejection episode than TAC concentration in whole blood. Therefore, the aim of the study was to assess correlation between dosage, blood, hepatic and kidney tissue concentration of Tacrolimus measured by a validated LC-MS/MS and clinical outcomes in a larger cohort of 100 liver and renal transplant recipients.

Methods

The biopsy samples were collected for histological study and the remaining tissue was stored at - 80˚C. Dried biopsies were weighed, mechanically homogenized and then TAC was extracted using methyl-tert-butyl ether. The organic layer was evaporated to dryness and dissolved in the mobile phase. An QTrap 4000 tandem mass spectrometer coupled to a Agilent LC-1260 liquid chromatograph operating in the electrospray-positive ionization mode was used to detect TAC and TAC^{13}C-d$_2$ (I.S.) in human tissue. Multiple reaction monitoring of TAC was performed (TAC: *m/z* 821.5®764.4; I.S. *m/z* 824.6 ®771.5). Blood concentrations of TAC corresponding to the time of biopsy collection were determined also using LC-MS/MS method.

Results

There was no significant difference between TAC concentrations in liver and kidney tissues There was also no correlation between dosage, blood (C_0) and tissue TAC concentrations. TAC concentrations determined in liver and kidney biopsies ranged from 8.5 pg/mg up to 160.0 pg/mg and from 7.1 pg/mg up to 215.7 pg/mg respectively. It displayed mean ±SD values of TAC concentration in liver and kidney tissue 45.9 ±31.1 pg/mg and 54.5 ±47.8 pg/mg respectively.

Conclusions

Intra-tissue concentrations of TAC were significantly lower in transplant recipients experiencing rejection versus those who did not. Therefore, it suggests that both hepatic and kidney tissue concentration level <19 - 21 pg/mg may serve a reliable predictor of acute cellular rejection. Further studies are needed to

demonstrate practical utility of measuring intra-tissue concentration of TAC and to define a cut-off value of concentration as prognostic parameter of acute rejection episode in liver and renal transplant patients.