Oral

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

Chairs: Mikio Kakumoto, Japan / Olga Millan, Spain

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[O26-2-1] Is the whole blood TDM of immunosuppressors the best way to manage treatment of pediatric patients undergoing liver transplantation?

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Background

Tacrolimus and everolimus are immunosuppressors used to treat pediatric patients undergoing liver transplantation. Hematic tacrolimus and everolimus TDM by liquid chromatography became standard practice. Moreover, it does not always reflect concentrations at their active site. Our aim was to try to have more evidences on the usefulness of their whole-blood TDM, understanding if there is a really correlation between the whole-blood concentration and the intracellular one, quantifying these two drugs into their real target site: Peripheral-Blood-Mononuclear-Cells (PBMCs).

Methods

PBMCs were collected using Cell-Preparation-Tubes; cells number and MCV were evaluated by an automatic cell counter. Tacrolimus and everolimus were quantified using an already published and validated UHPLC-MS/MS (ESI+) method, coupled with an automated on-line SPE platform. Chromatographic run was performed on an Acquity UPLC® BEH C18 1,7 m (2,1 x 50 mm) column, heated at 45°C, for 6 minutes at 0.5 mL/min. The chromatographic gradient was of water and methanol, both with 2mM ammonium acetate and 1mL/L formic acid). XBridge® C8 10m (1x10mm) SPE cartridges were used. The internal standard was ascomycin.

Results

Calibration curves were linear (r2=0.998) and intra- and inter-day imprecision and inaccuracy were <15%. Drug amounts in 139 “real” PBMCs samples from 61 pediatric patients in treatment (or co-treatment) with TAC and EVE resulted within the calibration range (0.039-5ng). Concentrations from each patient were standardized using their evaluated MCV: intra-PBMCs concentration was meanly 25.6 and 237.4 times higher than the hematic one for TAC and EVE, respectively. To date, our TAC results underline a good correlation between intracellular and hematic data, despite of some outliers (R=0.476, p0.001, n=117). This is not valid for the data obtained for EVE, a poor correlation was underlined: R=0.182, p=0.328, n=37, both in EVE co- and mono-therapy.

Conclusions

Although our study is still on going and the number of patients and samples is increasing, the obtained intracellular data seem give real information on TAC and EVE therapy.