Poster

[P26-6] P26-6: Immunosuppressive drugs (5): Clinical practice

Chair: Hege Christensen, Norway

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[P26-6-8] Tacrolimus whole blood and unbound plasma concentrations early after heart and lung transplantation

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Background

Tacrolimus is the vital mainstay of the immunosuppressive regimen in heart (HTx) and lung transplantation (LTx). Therapeutic drug monitoring is used for optimal dosing. Pharmacokinetics of tacrolimus in the clinically unstable patient may highly vary, which may increase toxicity. Whole blood concentrations are a mediocre reflection of toxicity. [1] The unbound concentrations may be more useful and can now be analyzed with a direct measurement. [2] We hypothesized that whole blood tacrolimus trough concentrations (C12h) fluctuate more extremely in clinically unstable patients compared to clinically stable patients. The unbound tacrolimus plasma concentrations were explored.

Methods

In 10 HTx and 20 LTx patients, tacrolimus whole blood and unbound plasma concentrations were measured in the first 6 days after transplantation. The unbound concentrations at 6 hours were analyzed as described by Stientra et.al. [2] C12h was analyzed with high-performance liquid chromatography tandem mass spectrometric detection (HPLC-MS/MS). Equality of C12h variance was tested with a Mood test. [3]

Results

Table 1. shows the characteristics of the patients. Median whole blood tacrolimus concentrations were within the therapeutic
range (10-15 ng/ml) from day 3 on, though varied from 0.5-35 ng/mL (See Table 2). The C12h variance was larger than in clinically stable patients for the first 5 days (p

Conclusions

C12h shows enormous fluctuations in comparison to clinically stable patients, therefore we conclude that it is extremely difficult to dose tacrolimus correctly early after HTx and LTx. For the first time, we analyzed the unbound tacrolimus plasma concentrations and they show large variability as well. Establishing the therapeutic range of the unbound plasma concentrations could be helpful in improving therapeutic drug monitoring of tacrolimus.

References:

1. Zahir et.al., TDM, 2004
2. Stienstra et.al., TDM, 2016

3. Kuypers et.al., Clin Pharmacokinet, 2004

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tacrolimus concentrations in stable clinical conditions

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