Poster

[P26-5] P26-5: Immunosuppressive drugs (4): Individualized dosage adjustment

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[P26-5-1] Overweight kidney transplant recipients are at risk of being overdosed following standard bodyweight-based tacrolimus dosing

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Background

Bodyweight-based dosing of tacrolimus is considered standard care, even though the available evidence is thin. An increasing proportion of transplant recipients is overweight, prompting the question if the starting dose should always be based on bodyweight. The aim of this study was to investigate whether a tacrolimus starting dose based on bodyweight leads to the achievement of tacrolimus target whole-blood predose concentrations (C_0) in overweight patients on day 3 after transplantation. This was defined as the first steady state concentration attained after five unaltered tacrolimus doses.

Methods

This is a *post-hoc* analysis of a randomized-controlled trial investigating whether adaptation of the tacrolimus starting dose according to *CYP3A5* genotype increases the proportion of kidney transplant recipients reaching the target tacrolimus predose concentration. In this trial, patients were randomized to receive tacrolimus in either the standard, bodyweight-based dose of 0.20 mg/kg/day according to the package insert, or to a dose based on their *CYP3A5* genotype. For the analysis, the data were divided into three groups: the standard-dose group, the genotype-based group, and all patients scaled to the standard bodyweight dose. The correlation between tacrolimus C_0 and bodyweight (or BMI) was investigated by calculating the goodness of fit. Dosing guidelines were calculated using linear regression lines.

Results

Data was available for 203 kidney transplant recipients with a median BMI of 25.6 (range 17.2-42.2) and bodyweight of 78.9 kg (range 37.6-123.1). More than 50% of the overweight or obese patients had a tacrolimus predose concentration above the target range of 10-15 ng/mL. The CYP3A5 non-expressers tended to be above target when they weighed more than 67.5 kg or had a BMI of 24.5 or higher. If the BMI is 25-30, only 85% of the standard dose (0.2 mg/kg/day) should be prescribed to reach the target concentration, and if the BMI is 30-35 we propose 75% of the standard dose. The dosing guideline for patients with an unknown genotype was validated using the FDCC dataset.

Conclusions

This study demonstrates that dosing tacrolimus solely on bodyweight results in overexposure in more than half of overweight or obese patients.

References:
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