LETTER TO THE EDITOR

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An equation for tacrolimus daily dose calculation in renal transplant patients – simple and cost saving?

Formula za izračunavanje dnevne doze takrolimusa kod bolesnika sa transplantiranim bubregom – jednostavna ušteda novca?

Dear Editor,

One of the most important services given by clinical pharmacologists in the Serbian health care system is therapeutic drug monitoring (TDM) [1]. In the Military Medical Academy, tertiary health care hospital in Belgrade, TDM for tacrolimus, one of the most important immunosuppressant used for prevention of allograft rejection in kidney transplantation, is used in routine clinical settings [2]. This is due to the fact that inappropriate tacrolimus blood concentrations are often met as a result of considerable between-and within-subject pharmacokinetics variability. Numerous factors identified as contributors are gender, body mass index, hematocrit, albumin concentration, liver dysfunction, corticosteroids and other comedication, food, gene polymorphism, etc. [2–7]. Since tacrolimus through concentrations (TTC) are routinely monitored and the dose is adjusted, based mainly on measurements, the influence of aforementioned multiple factors are not supervised in the consistent manner by various transplantation centers. In an attempt to obtain a novel, better approach, tacrolimus concentration/dose (C/D) ratio, a relatively simply obtained TDM tool, has been suggested to better define tacrolimus exposure profile [3, 8]. Gender, comedication of renal transplant recipients with proton pump inhibitors, diuretics, calcium channel blockers, various doses of corticosteroids as well as genetic polymorphisms of CYP3A4 and CYP3A5 enzymes and P-glycoprotein drug transporter, were shown as the most important factors affecting both TTC and tacrolimus C/D ratio [5, 6, 8]. However, even more practical approach was needed until validation of a target C/D ratio is performed, i.e., a correlation with clinical endpoints in the real clinical settings. Therefore, relatively simple equation for tacrolimus dosing was constructed depending on variables analyzed. It was obtained by a multiple regression analysis and related total daily dose of tacrolimus per body weight, corticosteroid dose, gender as well as proton pump inhibitors dose, since they were shown as the most prominent factors in our analysis [8]. Former equations concerning improved tacrolimus dosing are based on population pharmacokinetics principles [9, 10], while ours result from parameters used in everyday practice related to TTC. Equation 1 goes as following:

Tacrolimus daily dose per body weight (mg/kg) = 0.032628 + 0.00312*TTC + 0.005220*gender – 0.013887*proton pump inhibitors + 0.012488*corticosteroid

where TTC is desired value previously set, gender value is 1 for females and 0 for males; proton pump inhibitors has value 1 if they are used, while 0 is correct if they are not used; corticosteroid value should be 1 for its doses < 0.15 mg/kg, 2 for 0.15–0.25 mg/kg dose and 3 if it exceeds values of 0.25 mg/kg. According to this equation table 1 presents recommendations for tacrolimus dosing.

This relatively simply constructed calculations based on the gender of the transplant recipients, proton pump inhibitors use, corticosteroid dose applied and preset value of tacrolimus through concentrations may help in optimization of tacrolimus daily dosing in patients subjected to numerous control examinations in our transplantation center after surgery [2]. We do hope that its introduction and validation would also make cost savings possible both for patients and our health care system as a whole.

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