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Cyclosporine absorption in kidney transplant recipients

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Dear Editor,

Rostami *et al.* (1), had described the lack of accurate and reliable methods of cyclosporine (CYA) assays in their editorial. Although CYA level at 2 hours post-dose (C2) is the best way to predict area under the curve in kidney recipients and it correlates with acute allograft rejections and nephrotoxicity better than trough level (C0), we should keep in mind that optimized drug level early after transplantation is still a problem for most organ transplant patients (2). We agree with Rostami *et al.* (1) that we need a reliable way of monitoring CYA therapy since the adequate blood level of CYA is required to avoidance of the acute rejection and nephrotoxicity, but C2 blood level is not also an ideal marker for CYA assay, so we would like to discuss about CYA absorption which should be concerned.

Although it has been observed that CYA absorption is highly heterogeneous early after renal transplantation, it enhances immediately post-transplant period allowing a decrease in CYA dose to achieve constant exposure (3). Nonetheless, a wide variation in CYA absorption was observed among kidney transplant patients due to variable pharmacokinetics of the drug; impact of other medications and foods are also important (4). It is obvious that higher initial CYA doses early after kidney transplantation is required to achieve the therapeutic levels of the drug and prevent acute allograft rejection (2). Higher initial dose of CYA is required because of low initial absorption of the drug and low relative bioavailability early after transplantation. A significant increased time-dependency in steady state of CYA exposure, also observed during the first post-transplant month (5). It has been reported that a high intra-individual variability of C0 levels is associated with a high prevalence of acute and chronic rejections (6). Using sufficient dose of CYA is necessary for maximum absorption phase of the drug which is vital for inhibition of T-cells (4). The extent of T-cells inhibition is correlated to the CYA blood levels (4). In addition, the relative CYA bioavailability increase over time (3). This increased trend probabely attributed to a progressive augment in CYA absorption from GI tract and a progressive increase in CYA metabolism. The absorption window of drug in the small intestine, and differences in content and activity of CYP3A4 and P-glycoprotein may still considerably affect the absorption of CYA (7).

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