HIGH VARIABILITY IN TACROLIMUS BLOOD LEVELS IN PATIENTS WITH KIDNEY, LIVER OR HEART TRANSPLANT.

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The introduction of tacrolimus treatment into clinical practice improved patient survival after organ transplant due to a significant reduction of organ rejection. However, this drug is characterized by a narrow therapeutic index, a high inter and intra individual pharmacokinetic variability, and severe adverse effects. A number of studies found a close correlation between the pharmacokinetic parameters of tacrolimus and the clinical outcome. Nevertheless, despite the long-time use of the drug in clinical practice, the best way to use tacrolimus is still a matter of intense debate. Due to the narrow therapeutic range of the drug, therapeutic drug monitoring (TDM), is strongly suggested, but a wide proportion of patients results out of range. The aim of this study is to analyze tacrolimus levels in patients with kidney, liver or heart transplant and to investigate the presence of genetic polymorphisms in patients out of range. A total of 100 patients (60 adults and 40 children; 35 females and 65 males) with kidney (80), liver (13) or heart (7) graft, referring to the Therapeutic Drug Monitoring Unit of the A.O.U. “G. Martino” of Messina, were used for the analysis. Tacrolimus plasma levels were analyzed using the Siemens Viva-E. Average values of tacrolimus were 7.8 ng/ml ± 2.67; the 23% (95%CI 14.7-31.2) of samples resulted below the therapeutic range and the 7% (95%CI 2.0-12.0) above the therapeutic range. Specifically, the 25% (95%CI 14.0-35.9) of adults and 20% (95%CI 7.0-32.0) of pediatric patients were below than therapeutic range, while 6.7% (95%CI 3.5-12.9) of adults and 7.5% (95%CI 0.6-15.6) of pediatric patients were above the therapeutic range. No gender differences were observed within patients below the therapeutic range, while 10.8% of males and none of the females were above the therapeutic range. The 46.2% of liver transplanted patients were below the therapeutic range, compared to the 19.5% of the other transplants (p=0.033). No patients with liver graft were above the therapeutic range. Patients with tacrolimus levels out of the therapeutic range will be genotyped for CYP3A5*1 (G6986A) ABCB1(C3435T)(C1236T)(G2677A), CYP3A4*1B (A392G), to investigate whether the high variability of tacrolimus levels might be related to a genetic variant. Our results suggest the presence of a high variability of tacrolimus levels in transplanted patients that might be due, at least in part, to genetic polymorphisms.