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INTERINDIVIDUAL AND INTRAINDIVIDUAL PHARMACOKINETIC VARIABILITY OF TACROLIMUS WITHIN THE FIRST YEAR AFTER RENAL TRANSPLANTATION: EFFECT OF CYP3A5 GENE POLYMORPHISM

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The aim of this study was to evaluate potential influence of cytochrome P450 3A5 (CYP3A5) 6986A>G gene polymorphisms on inter- and intravariability (IPV) in tacrolimus (Tac) exposure within the first year after renal transplantation. Secondary, we aimed to analyze the change in distribution of patients regarding IPV between early (<6 months) and late posttransplant period (>6 months). The study enrolled 91 renal transplant recipients, who were on Tac-based immunosuppressive protocol. Dose–adjusted concentration (C0/D) of Tac was used as a measure of Tac exposure, while coefficient of variation (CV%) and mean absolute deviation (MAD%) of C0/D as IPV parameters. Individuals carrying CYP3A5*1/*3 genotype had lower C0/D than CYP3A5*3/*3 carriers within the entire observation period ($p < 0.01$). The study reported higher IPV in a period of 1-6 months compared to a period of 7-12 months post-transplant, for CV% and MAD% ($p < 0.05$). The results showed that there was no difference in IPV regarding CYP3A5 genotype. Considering CV%, 32% and 24% of the patients had high IPV (above 30%) in the first and second half of the first post-transplant year, respectively. Analyzing the MAD%, 13% and 7% of the patients had high variability of Tac exposure in the first and second half of the first year, respectively. This study confirms that the CYP3A5 gene polymorphism contributes to the interindividual, but not in intraindividual, variability in Tac exposure within the first post-transplant year.

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