

IMPACT OF DONOR *CYP3A5* GENOTYPE ON PHARMACOKINETICS OF TACROLIMUS IN SOUTH AFRICAN PAEDIATRIC LIVER TRANSPLANT PATIENTS

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Abstract

Tacrolimus is characterised by a narrow therapeutic target range and wide interpatient variability. Pharmacogenetic research attributes *CYP3A5* single nucleotide polymorphisms to the variable inter-patient tacrolimus concentration dose ratios (CDR). In this study, we compared the mean tacrolimus CDR in paediatric liver transplant recipients and their living liver donors' *CYP3A5* rs776746 T>C genotypes (**1/*1*, **1/*3* and **3/*3*), accounting for donor and recipient characteristics. The graft-to-recipient weight ratio and the *CYP3A5* donor genotypes were found to be independent factors significantly impacting the mean tacrolimus CDR. Donor *CYP3A5* expressors (**1/*1* and **1/*3*) were shown to have significantly lower recipient tacrolimus CDRs, therefore, higher dosages would be required in comparison to *CYP3A5* non-expressors to reach the same therapeutic target range. The potential implementation of a stratified medicine dosage algorithm, combining living liver donor *CYP3A5* genotyping with the calculation of the graft-to-recipient weight ratio, may predict the optimal tacrolimus dosage schedules for liver transplant recipients.