**Do pre-transplant therapeutic drug monitoring trials predict calcineurin inhibitor dose accurately in HIV-infected patients undergoing kidney transplantation?**

**Background**

Kidney transplantation in HIV-infected (HIV+) patients poses many unique challenges, one of which is potentially profound drug-drug interactions (DDIs) between anti-retroviral therapy (ART) and calcineurin inhibitors (CNIs). The protease inhibitor ritonavir (RTV) inhibits CYP3A4 leading to markedly reduced CNI dose requirements, while non-nucleoside reverse transcriptase inhibitors (NNRTIs) may increase the required CNI dose. Current UK guidelines recommend a therapeutic drug monitoring trial (TDM) of CNIs in patients with a predicted DDI.

**Aim**

To examine the accuracy with which pre-transplant TDM predicts CNI dose in the early post-transplant period in HIV+ kidney transplant recipients (KTRs), and its influence on the attainment of therapeutic drug levels.

**Methods**

Case notes and electronic records were reviewed for all HIV+ KTRs in a single UK centre since 2010, who underwent a pre-transplant TDM. The CNI dose predicted by TDM and prescribed at the time of transplant (T0) was compared with the prescribed dose at 12 weeks (T12) post-transplant. Serial CNI levels were analysed for each patient to ascertain the proportion falling above, within or below the therapeutic target at 1 week time point (T1), and between T0 and T12.

**Results**

8 HIV+ KTRs who underwent TDM were identified, of whom 6 were taking RTV and 2 were receiving NNRTIs. All received cyclosporin (CyA). The mean CyA dose prescribed at T0 was 70.8 ± 128.2 mg/day in RTV-ART patients, and 575 ± 175 mg/day in NNRTI-ART. The mean difference between prescribed CyA dose at T12 and T0 was 41.6 ± 98.4 mg/day (53 ± 47% discrepancy) and 175 ± 25mg/day (35 ± 15% discrepancy) in RTV-ART and NNRTI-ART patients respectively. All RTV-ART patients required lower CyA doses at T12 than T0. 6 of 9 patients had sub-therapeutic CyA levels at T1 (local target range 150-250 ng/ml) while 2 of 9, both of whom were on RTV-ART, had cyclosporin levels in excess of 490 at T1. For RTV-ART patients, 52 ± 28% of CyA levels between T0 and T12 fell within the target range, compared to 40 ± 0% in non-RTV ART patients.

**Conclusions**

Pre-transplant TDMs in HIV+ KTRs do not predict required cyclosporin dose with a high degree of accuracy, particularly in individuals receiving RTV. The high incidence of early CNI levels falling beneath the target range with TDM-predicted CyA doses may contribute to the increased incidence of rejection in HIV+ KTRs. This data supports pro-active revision of ART to regimes which minimise DDI prior to transplantation wherever possible.