A TALE OF TWO TRANSPLANTS: BE CAUTIOUS WHEN COMBINING COBICISTAT AND TACROLIMUS

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Background:
Solid organ transplant in HIV+ patients has become more common. Immunosuppressant agents including tacrolimus, cyclosporin and corticosteroids can interact with some antiretroviral therapy (ART), resulting in sub-optimal immunosuppression or toxicity. Cobicistat inhibits cytochrome P450 3A4 and p-glycoprotein; and increases exposure to both tacrolimus and corticosteroids used post renal transplantation. Switching ART can avoid these issues but is not always possible.

Methods:
Two HIV+ men (since 1991 and 1985 respectively) required renal transplantation at a tertiary care hospital. Due to past resistance or co-morbidities, were taking darunavir/cobicistat plus dolutegravir at the time of transplant. Both were virologically suppressed.

Patient 1 was managed in HIV-General Practice; his (cadaveric) renal transplant occurred on a weekend in late 2017, with no prior Infectious Diseases or pharmacist input.

Patient 2 received hospital-based outpatient care for HIV. His live donor transplant has been carefully planned to occur in May 2018, in conjunction with the Haemophilia and Infectious Diseases teams and specialist pharmacists.

Results:
Patient 1 received 2mg (~0.025 mg/kg) tacrolimus pre-transplant, 4mg on the evening of the transplant and the following morning (per standard transplant dosing). The weekend Pharmacist raised concern regarding an interaction with cobicistat, and a pre-dose tacrolimus level taken the morning of Day 2 was supra-therapeutic at 39.7mcg/L (target 5-10mcg/L). The tacrolimus level peaked at 58.4mcg/L; falling below10mcg/L only on Day14 with no further dosing. The patient experienced few side effects. His tacrolimus dose stabilised at 0.5mg administered every 10 days.

Patient 2 received a single test dose of tacrolimus 0.5mg (~0.01 mg/kg) one month pre-transplant; levels were taken daily to estimate clearance. It took >7 days to clear the drug. Dosing for the transplant was planned accordingly.

Conclusion:
For HIV+ patients on a transplant waiting list, consideration of drug interactions is paramount. Multi-disciplinary approaches ensure the safest outcomes for patients.

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