A Tale Of Two Transplants: Be Cautious When Combining Cobicistat And Tacrolimus

Duncan A[1], Inserra V [1], Mackie K [1], Brown C[1], Hoy J[2,3], Walker R[,3,4]

[1] Pharmacy Department, Alfred Health, [2]Department of Infectious Diseases, Alfred Health, [3] Central Clinical School, Monash University, [4]Department of Renal Medicine, Alfred Health

Background

Solid organ transplantation in people living with HIV (PLHIV) is becoming more common. Medications for immunosuppression including tacrolimus, cyclosporin and corticosteroids may interact with some antiretroviral therapies (ART), resulting in drug toxicity or sub-optimal immunosuppression. Cobicistat inhibits cytochrome P450-3A4 and p-glycoprotein, resulting in increased exposure to both tacrolimus and corticosteroids used after renal transplantation. Modifying ART can mitigate these issues, however is not always possible.

Aim

To describe management of two complex PLHIV taking cobicistat and requiring renal transplantation.

Case Descriptions - Background

Two virologically suppressed patients were scheduled for renal transplantation at The Alfred Hospital, Melbourne. Due to past resistance and co-morbidities, both were taking darunavir-cobicistat plus dolutegravir; so switching ART at the time of transplant was not possible.

Patient 1

- Managed in HIV-General Practice
- Comorbidities: renovascular disease, hypertension, hyperlipidaemia, anxiety, reflux, gout
- A deceased donor renal transplant occurred on a weekend in late 2017, with no prior Infectious Diseases (ID) or Pharmacy input

Patient 2

- Receiving hospital-based outpatient care for HIV, renal disease and haemophilia
- Comorbidities: glomerulosclerosis, ischemic heart disease, Barrett's oseophagus, Hepatitis B, Hepatitis C (cured), hypertension, hyperlipidaemia, gout
- The transplant was planned with input from the Haemophilia and ID teams including specialist pharmacists

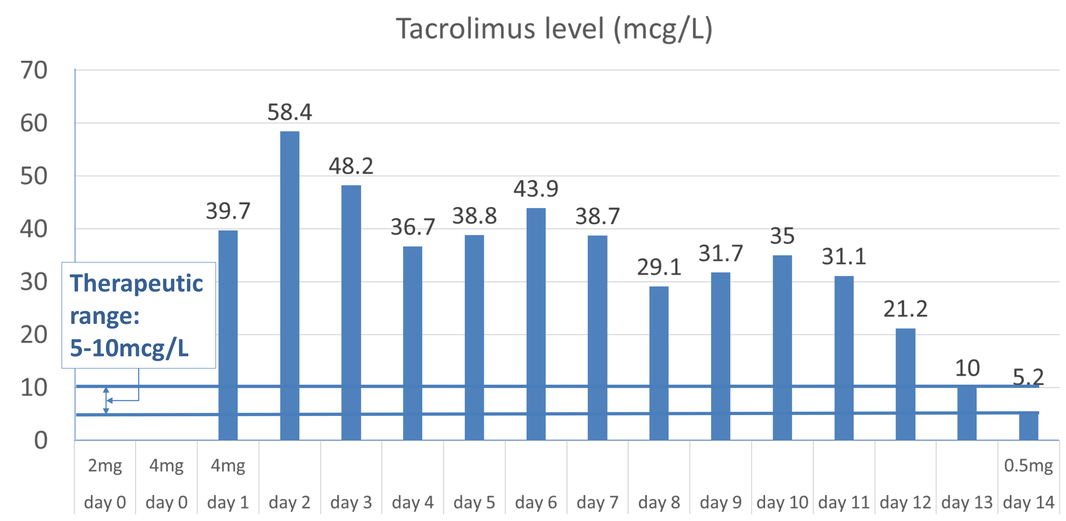
Case Descriptions - Management

Patient 1

- Tacrolimus was prescribed at standard transplant doses, with 6mg received on the day of transplant and tacrolimus charted at 4mg twice daily thereafter
- Concern was raised by the weekend pharmacist on Day 1 regarding a potential interaction with cobicistat, and tacrolimus was withheld pending levels
- A level taken on Day 2 was supra-therapeutic at 39.7mcg/L (aim 5-10mcg/L) (Figure 1)
- No further tacrolimus doses were given
- Tacrolimus level peaked at 58.4mcg/L on Day 3, and took a further 11 days to fall below 10mcg/L (Day 14)
- Levels varied due to entero-hepatic recycling of tacrolimus

Case Descriptions - Management

Figure 1: Tacrolimus levels post renal transplantation: Patient 1

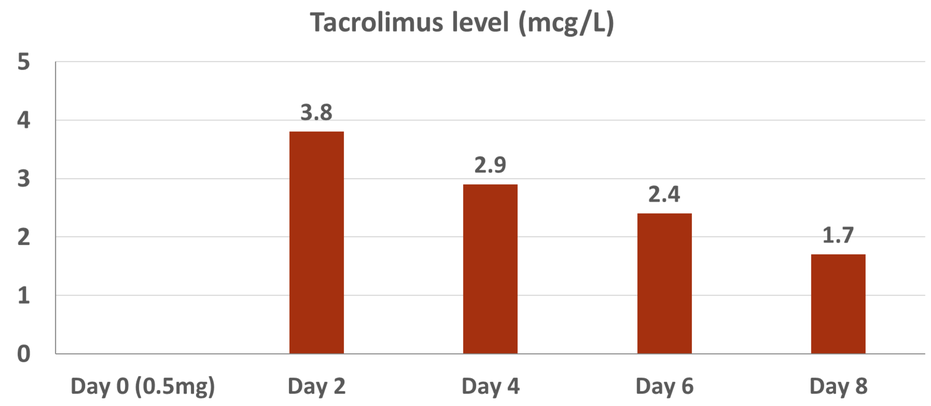


- Tacrolimus was reintroduced and stabilised at 0.5mg given once weekly; later this was decreased to 0.5mg every 10 days to achieve a lower level (aim 4-8mcg/L)
- The reduced tacrolimus dose and frequency is similar to comparable cases described in the literature [1]

Patient 2

- Pre-transplant, a multidisciplinary meeting was held to discuss the transplant plan, including medication management. In attendance were Renal, Haemophilia and ID physicians and Renal and ID pharmacists
- Tacrolimus was trialed pre-transplant to monitor levels and determine clearance time, with a single dose of tacrolimus 0.5mg administered
- The drug took more than 8 days to clear
- Dosing for the transplant was planned, with 1mg to be administered pre-transplant and subsequent close monitoring with daily tacrolimus levels

Figure 2: Tacrolimus levels following trial with single-dose: Patient 2



- This patient will receive a paired kidney exchange transplant in September 2018

Conclusion

For PLHIV undergoing solid organ transplantation, consideration of drug interactions is paramount. Advanced identification of patients on transplant waiting lists provides opportunity and time to carefully plan medication management.

A multidisciplinary team-based approach can help prevent drug interactions when ART cannot be changed, ensuring safe and optimal outcome for complex patients.

References

1. Mertz et al *Am J Kidney Diseases* 2009; 54 (1)