INTRAPATIENT VARIABILITY IN PATIENTS SWITCHED FROM TWICE DAILY TO ONCE DAILY TACROLIMUS

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INTRODUCTION AND AIMS

Intrapatient variability (IPV) in tacrolimus exposure has been recently recognised as a risk factor of graft loss and is associated with higher incidence of tubular atrophy and interstitial fibrosis on protocol biopsies. Variable absorption related to interaction with food or other drugs is one of the proposed mechanisms leading to variable exposure from one day to the other. Noncompliance is another explanatory mechanism. Tacrolimus once daily can thus theoretically present an advantage over the twice daily formulation in terms of IPV. We aimed in this study to compare the IPV in stable kidney transplant recipients who have been switched from tacrolimus twice daily to tacrolimus once daily. We also aimed to evaluate self reported compliance with the two formulations.

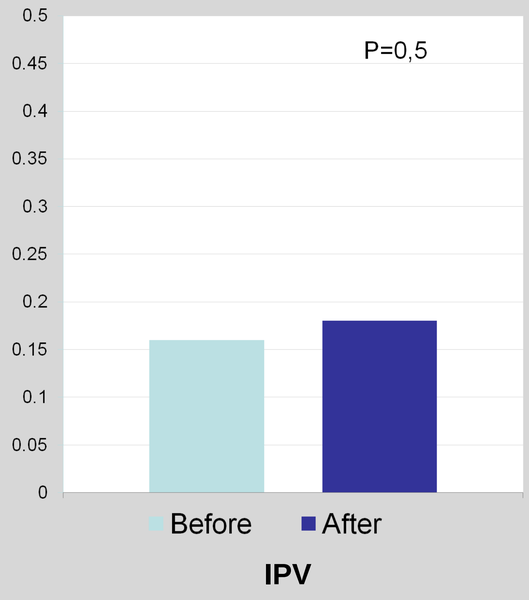
METHODS

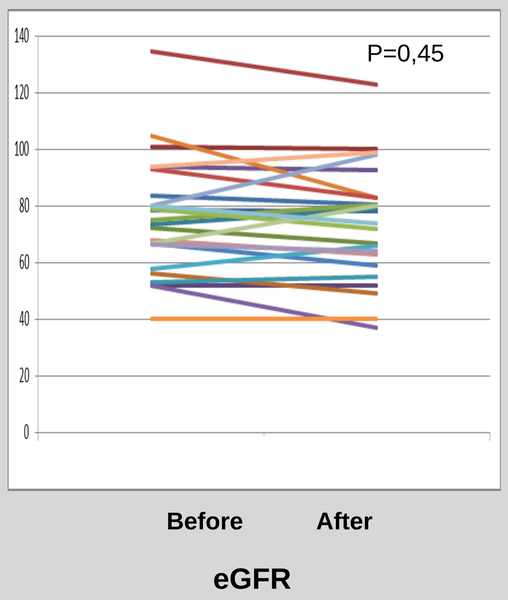
This is a retrospective analysis comparing IPV of tacrolimus trough levels of stable kidney transplant recipients switched from tacrolimus twice daily to tacrolimus once daily on a one to one mg basis.
Patients who needed dose adjustments to stay within the prespecified therapeutic range were excluded. We used the last 3 trough levels before and the first 3 trough levels after the switch to calculate IPV. We also compared eGFR (mean of 3 values) and mean dose of tacrolimus during the two periods. The self reported compliance was compared between the two formulations.

RESULTS

We included 34 patients, 21 males and 13 females, with a mean age of 44 years. The majority had their first living related transplant. The switch was done after a mean of 16 months after the transplantation. The mean trough level was 7.05 +/- 2.2 ng/ml before and 6.91 +/- 2.08 ng/ml after the switch. We found no significant difference in IPV using paired t test between the two periods (0.16 +/-0.12 v/s 0.18 +/- 0.13 p=0.5). Kidney function remained stable, mean CKD Epi 75.5 +/- 20.7 v/s 74,2 +/- 21.7 ml/min/1.73 m2 before and after the switch respectively p=o.45

Patients characteristics	N=34
Male/Female	21/13
Mean age	44 years
First graft	30
Living donor	33
Mean duration after transplantation (M)	16
Mean T0 before the switch	7.05 +/- 2.2 ng/ml
Mean T0 after the switch	6.91 +/- 2.08 ng/ml





Self reported compliance was very high (more than 95%) with the two formulations but patients expressed preference for the once daily tacrolimus.

CONCLUSION

Switching from tacrolimus twice daily to tacrolimus once daily formulation leads to slightly, clinically non significant, decrease in trough levels of the drug, but does not decrease intrapatient variability.

Patients may have a preference for the once daily formulation but don't report an increase in their compliance.

Larger studies are needed to better evaluate the effect of both drug formulations on intrapatient variability.

References:

High intrapatient variability of tacrolimus concentration predicts accelerated progression of chronic histologic lesions in renal recipients. Vanhove T, AJT Oct 2016
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