Association between Trough Mycophenolic Acid Concentration and Clinical Events in Live Donor Kidney Transplant Recipients

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Introduction

Mycophenolate mofetil (MMF), is used as maintenance immunosuppressant in solid organ transplantation along with tacrolimus and steroid. Therapeutic drug monitoring of MMF is recommended due to large inter-patient variabilities and strong association between drug exposure and clinical events. The present study was conducted to assess the correlation between trough mycophenolic acid (MPA) concentration and clinical outcomes in live donor kidney transplant recipients.

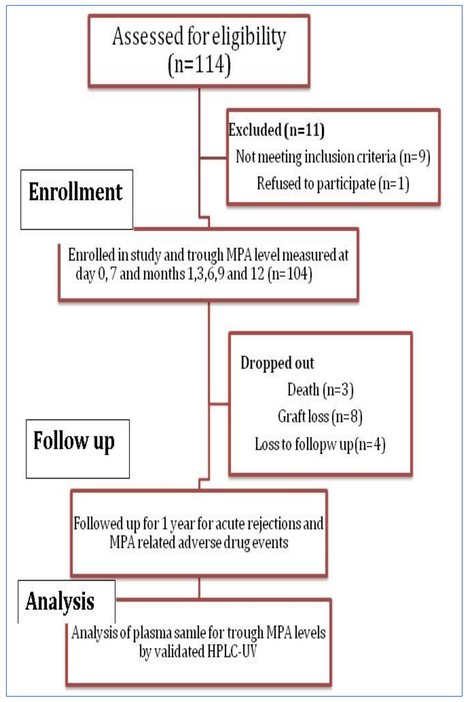
Material and Method

This is single centre non-randomized longitudinal prospective open-label study.

Between January 2014 to August 2014, 104 patients underwent live donor kidney transplantation at Muljibhai Patel Urological Hospital, Nadiad.

MPA trough levels were monitored on days 0 and 7 and months 1, 3, 6, 9 and 12.

Total MPA level was measured in plasma by validated High-Performance Liquid Chromatography with UV detector (HPLC-UV). The linearity of the method was evaluated by processing a seven-point calibration curve range from 0.5 mg/l to 6 mg/l (r^2= 0.993).



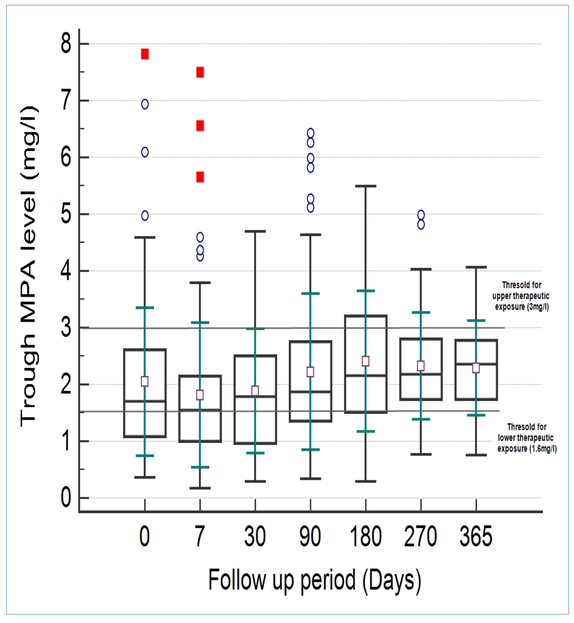
Overview of screening, enrollment, and follow-up of the patients

Results

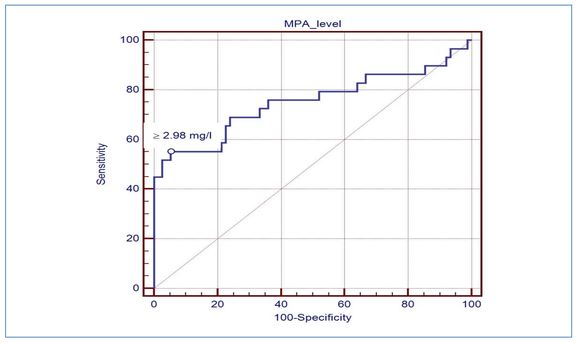
The mean age of the patient was 38, and there were 88 (78.8%) male and 22 (21.2%) female patients in the study cohort.

The native kidney disease was undetermined (47.1%) in the majority of patients while 25 (24%) patients of living donor renal allograft recipient had diabetic kidney disease.

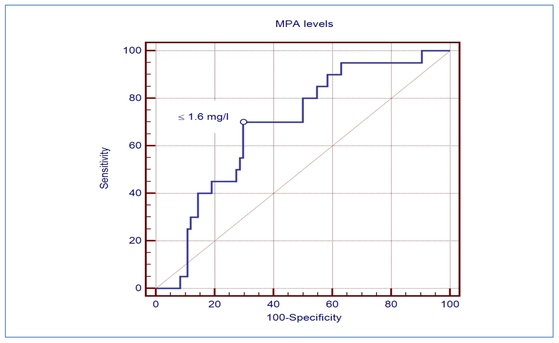
Patient and graft survival among study population was 96.2% and 93.3% respectively after 12 months of follow up period.



Box and whisker plot shows the median, interquartile range, outlier (o) and mean value (□) and extreme value ( ) of the trough MPA level over different follow up visits



ROC curve obtained for trough MPA level to discriminate between patients with and without leucopenia



ROC curve obtained for trough MPA concentration to discriminate between patients with and without acute rejection

Results of logistic regression analysis concerning the association between trough MPA level and clinical events

Clinical events	OR	95% CI	P value
Acute rejection			
MPA level	0.35	0.14 to 0.90	0.0290
Leucopenia			
MPA level	1.83	1.25 to 2.67	0.0018
ATG	3.70	1.37 to 9.96	0.0097
Infection			
Induction	3.82	1.01 to 14.50	0.0489
MPA level	1.84	1.09 to 3.09	0.0223
GI adverse events			
MPA level	2.32	1.16 to 4.63	0.0169
MMF/EC MPS dose	1.01	0.99 to 0.99	0.0437

Incidence of drug-related clinical events in accordance with targeted trough level range with MPA level

Clinical events	Total no. of patients (%)	MPA trough level (mg/l)		
		<1.6	1.6-3	> 3
Rejection	19 (18.3)	9	9	1
Infection	37(35.6)	9	19	9
Leucopenia	29(27.9)	5	8	16
Anemia	45(43.3)	7	35	3
GI adverse events	10(9.6)	0	4	6
Thrombocytopenia	6(5.8)	1	4	1

Conclusion

The study can be concluded with that trough MPA concentration below 1.6 mg/l might be associated with increase risk of graft rejection episodes, whereas concentration above a threshold of 3 mg/l during post transplant period might be responsible for increase incidence of MPA related adverse events such as leucopenia and GI AEs.

References

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