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TRANSPLANTATION: TRANSFORMING THE LANDSCAPE TOWARDS A NEW HORIZON

Tacrolimus metabolism and impact on graft function, a single center experience.

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Introduction

Tacrolimus is part of standard immunosuppressive regimen after renal transplant. It has high inter-individual variable metabolism; genetic polymorphism has shown to significantly influence tacrolimus metabolism. Literature suggests that tacrolimus metabolism may have influence on renal graft outcome.

Method

This is a single centre, retrospective, observational cohort study from year 2000 to 2021.

Tacrolimus metabolism rate was determined by concentration: dose (C/D) ratio at third month post transplantation. Patients with Tacrolimus C/D ratio< 1 ng/ml are characterized as fast metabolizers and ≥ 1 are characterized as slow metabolizers.

Subjects' characteristic and eGFR were compared and analyzed

Results

78 subjects were included in the study. 9 of them were classified as fast metabolizers with a mean C/D ratio of 0.725.

Age, genders, race, diabetes, hypertension status, induction agent and cold ischaemic time were not associated with C/D ratio ($p > 0.05$).

Fast metabolizers had significant higher tacrolimus dose as compared to slow metabolizer; mean dose 8.06mg vs 3.82mg ($p < 0.001$)

Fast metabolizers also had lower trough levels 5.81ng/ml vs 8.23ng/ml ($p = 0.016$).

There is no statistical difference in graft function at 3, 6, 9, 12 and 24th month.

	Fast Metabolizer (n=69)	Slow Metabolizer (n=9)	p Value
Age, year	38.0 \pm 12.6	37.5 \pm 12.0	0.456
Male	6 (66.7)	39 (57.4)	0.728
Race			0.505
Malay	7 (77.8)	38 (55.9)	
Chinese	2 (22.2)	22 (32.4)	
Indian	0 (0.0)	8 (11.8)	
Induction agent			0.533
Basiliximab	4 (44.4)	42 (61.8)	
Thymoglobulin	3 (33.3)	15 (22.1)	
Unknown	2 (22.2)	9 (13.2)	
Donor			1.000
Living	5 (55.6)	38 (55.9)	
Deceased	4 (44.4)	30 (44.1)	
Cold ischemic time, minutes	195.0 (150.0-840.0)	184.5 (130.0-765.3)	0.889
Comorbidities			
Diabetes mellitus	3 (33.3)	8 (11.8)	0.113
Hypertension	8 (88.9)	50 (73.5)	0.438

78 subjects	69 fast	FK dose	FK level	eGFR	3 rd month	6 th month	12 th month
		8.06 \pm 1.85	5.81 \pm 1.60		55.5 \pm 26.1	62.5 \pm 32.1	63.9 \pm 35.9
		$p < 0.001$	$p = 0.016$		$p = 0.121$	$p = 0.473$	$p = 0.572$
9 slow	9 slow	3.82 \pm 2.04	8.23 \pm 2.87	eGFR	70.5 \pm 27.1	69.3 \pm 25.7	69.4 \pm 25.9

Conclusion

Previous literatures have demonstrated that fast tacrolimus metabolizers are associated with worse graft outcome. However, in our study there was no statistical difference in graft function observed between fast and slow metabolizers. The possible limitations include a small study population, short study duration as well as possible confounding factor of diltiazem usage.

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