Calcineurin Inhibitor-Free Regimens in Pediatric Heart Transplant Recipients – Outcomes of Empiric Transition to Sirolimus

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Introduction: Mammalian Target of Rapamycin (mTOR) inhibitors including sirolimus have been successfully used in adult heart transplant patients to attenuate graft arterial vasculopathy (CAV) and calcineurin inhibitor (CNI) nephrotoxicity. Of interest in pediatric patients is the potential offered by mTOR inhibitors to decrease morbidity related to CAV, CNI related nephrotoxicity and PTLD. Here, we report our updated experience with transition to sirolimus in a CNI-free regimen in pediatric heart transplant patients.

Materials and Methods: We retrospectively reviewed all pediatric heart transplant patients with attempted transition from a CNI to a sirolimus regimen. Patients were also treated routinely with an anti-metabolite medication with or without steroids.

Results and Discussion: We identified 31 patients (mean age at transplant 8.3 years, 55% male) for whom transition was attempted. Transition trials occurred a mean of 30 months post-transplant. Eight patients discontinued sirolimus due to side effects (pneumonitis, aphthous ulcers, diarrhea or proteinuria). All patients with a history of Fontan and protein losing enteropathy (PLE, N = 3) developed significant proteinuria while on sirolimus, requiring discontinuation. Twenty-three of 31 patients (mean age at transplant 7.6 years, 65% male) successfully completed transition to a CNI-free protocol, over a mean of 71 days. Follow-up was available for a mean of 4.3 years post-conversion. No patients were diagnosed with CAV during this short-term follow-up. There was no significant difference between the rate of rejection while taking CNIs (prior to transition) relative to the rate when on the CNI-free regimen (p = NS). Glomerular filtration rate increased from 79 mL/min/1.73m2 pre-transition to 89 mL/min/1.73m2 post-transition and further to 94 mL/min/1.73m2 at latest follow-up. However, this trend did not reach statistical significance.

Conclusion: In this cohort of pediatric heart transplant patients, a sirolimus-based, CNI-free immunosuppressive regimen was not associated with increased rejection rate. All patients with PLE before transplant developed proteinuria on sirolimus. Transition to sirolimus in a CNI-free regimen for pediatric heart transplant patients was effective in most and has the potential to improve graft and patient survival.

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	n = 27
Age at transplant (years)	7.8
Female	13 (48%)
Time to sirolimus initiation (months)	34
Successful conversion	18 (67%)
Time for conversion (days)	69
Follow up time (years)	4.4

3 patients on Siro and tacro – all with rejection episodes.

One other had rejection and is only on tacro

5 others were for side effects only without rejection episodes