Renal Function after Transplantation of the Liver and Intestine

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin vid Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, fredagen den 12 februari 2010 kl 9.00

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Avhandlingen baseras på följande delarbeten

I. Herlenius G, Fistouris J, Olausson M, Felldin M, Bäckman L, Friman S.

Early renal function post-liver transplantation is predictive of progressive chronic

Early renal function post-liver transplantation is predictive of progressive chronic kidney disease.

Scand J Gastroenterol. 2008 Mar; 43(3):344-9

II. Herlenius G, Fägerlind M, Krantz M, Mölne J, Olausson M, Gäbel M,Friman V, Oltean M, Friman S.

Chronic kidney disease--a common and serious complication after intestinal transplantation.

Transplantation. 2008 Jul 15; 86(1):108-13.

III. Herlenius G, Hansson S, Krantz M, Olausson M, Kullberg-Lindh C, Friman S

Stable long term renal function after pediatric liver transplantation.

Pediatric Transplantation. In press

IV. Herlenius G, Felldin M, Gustafsson B, Olausson M, Bäckman L, Nordén G, Friman S.

Conversion from calcineurin inhibitor to either MMF or sirolimus improves renal function in liver transplant recipients with chronic kidney disease- results of a prospective randomized trial

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ABSTRACT

Background: Chronic kidney disease (CKD) after liver (LT) or intestinal (IT) transplantation may decrease patient survival. Calcineurin inhibitors (CNI) play a major role in its development.

<u>Aims</u>: Describe long term renal function and risk factors for developing CKD in adults and children after LT and IT. Investigate if CNI discontinuation in adults after LT improves renal function.

<u>Methods</u>: GFR was measured (GFRm) with either Iohexol or 51-Cr EDTA-clearance in both adults and children at different intervals before and after LT and IT.

Results: After LT in adults (n=152) (I), GFRm decreased with 42% after 10 years. Prevalence of CKD increased over time: 12% at 5 years and 29% at 10 years. Eight patients (5%) required renal replacement therapy (RRT). Baseline GFRm correlated poorly with late renal function. GFRm at 3 months post-LT correlated well with GFRm at 5 years and GFRm below30 ml/min/1.73m2 at 3 months was a risk factor for CKD at 5 years. After IT (II) CKD was almost universal. RRT was required in 20% of the patients. Calculated GFR (MDRD equation) overestimated GFRm with 30-40%. Children (n=36) undergoing LT (III) stabilized their renal function after an initial decline. None required RRT. Age above 2 years at LT, hepatic malignancies or metabolic liver diseases as the cause for LT were risk factors for developing CKD. A CNI discontinuation protocol (IV) in 25 adult patients with severe CKD was used with either mycophenolate mofetil (MMF) (n=13) or sirolimus (SRL) (n=12). Baseline GFRm (n=25) was 31+/-8 ml/min/1.73m2. At 3 months GFRm (n=23) increased to 40+/-10 ml/min/1.73m2 (p=0.0001). There was no significant difference when comparing the MMF and the SRL study arms. Patients (n=8) with baseline GFRm below 30 ml (CKD stage IV) increased GFRm at one year with 63% (p=0.003). Patients in the SRL group presented a higher incidence of oral ulcerations and hypertriglyceridemia. Two deaths were reported both probably unrelated to the change in immunosuppression. No biopsy proven rejection episodes occurred.

Conclusion: CKD is a frequent complication after LT and IT. Early renal function may identify patients at risk of developing CKD. CNI discontinuation under the protection of either MMF or SRL was safe and GFRm increased significantly under the observational period.

Keywords: adult liver transplantation, pediatric liver transplantation, intestinal transplantation, multivisceral transplantion, immunosuppression, calcineurin inhibitors, glomerular filtration rate, renal function, nephrotoxicity, chronic kidney disease, renal replacement therapy, mortality