

Conversion to Tacrolimus in Hyperlipidaemic Patients

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Introduction

Present and future problems of kidney transplantation

- Chronic rejection
- Cardiovascular morbidity and mortality
- Malignancies and infections caused by immunosuppression

Advantages of Tacrolimus vs. Cyclosporine

- Reduced incidence of acute rejection
- Improved lipid metabolism
- Comparable nephro- and neurotoxicity
- Comparable incidence of hypertension
- No differences in the incidence of infections

Objectives

- Is there an improvement of lipid metabolism under tacrolimus in kidney transplantation ?
- If so, does tacrolimus has a long-term lower risk of cardiovascular morbidity and mortality, without increasing the incidence of infections and/or rejections after conversion of the baseline immunosuppressive regimen from cyclosporine to tacrolimus ?

Inclusion Criteria

- Follow-up time after kidney transplantation longer than 6 months
- Stable kidney function in the last 3 months
- Elevated mean arterial blood pressure or blood pressure controlled with antihypertensive medication
- Pre-prandial cholesterol ≥ 250 mg %
- Pre-prandial triglyceride ≥ 150 mg %
- Serum creatinine ≥ 1.5 mg %

Patient Characteristics

• Number of patients	n = 47	male n = 27	female n = 20
• Mean age at time of conversion	44 [25-74] years		
• Original renal disease			
• Chronic glomerulonephropathy	n = 37		
• Chronic pyelonephropathy	n = 6		
• Inherited nephropathy	n = 4		
• Mean body weight (bw) in kg			
• Before	68.5		
• Cyclosporine	72.7		
• Tacrolimus	72.4		
• Immunosuppressive dose (average mg/kg bw)			
• CSA 3.2	• Tac 0.1		
• AZA 1.2	• AZA 1.2		
• Pred 0.07	• Pred 0.07		

Monitoring

- Imx II
- Blood samples:
 - Once a week during first 4 weeks
 - Every 2 weeks during 2nd month
 - Once monthly thereafter
- Always pre-prandial
- LDL and HDL determinations: pre-conversion, at M 6 and M 24
- Blood pressure: every visit and 3xd by the patient himself
- Kidney function with each blood sample

Side Effects

	CSA	Tacrolimus
• Hirsutism	18/47 (38%)	0/47 (0%)
• Gingivahyperplasia	12/47 (26%)	0/47 (0%)
• Alopecia	0/47 (0%)	10/47 (21%)
• Itching + Diffuse Joint pain	0/47 (0%)	28/47 (60%)
• Tremor	39/47 (83%)	40/47 (85%)
• Hypertension treated with:		
• Ca-Antagonist	47/47 (100%)	47/47 (100%)
• ACE Inhibitor	45/47 (96%)	30/47 (64%)
• Beta blocker	21/47 (45%)	16/47 (34%)

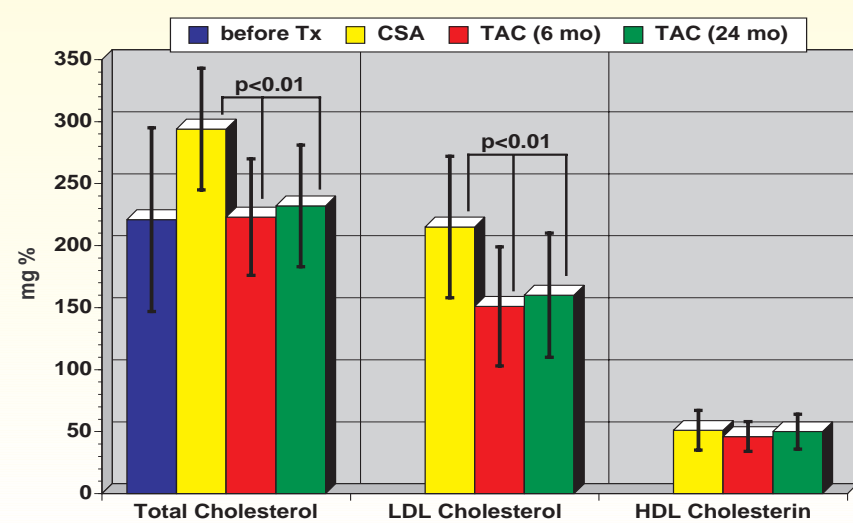
No Side Effects

- Blood count
- Liver enzymes
- Enzymes (CK; Amylase; Lipase)
- Protein metabolism
- Serum electrolytes
- Status of coagulation
- Rejection
- Serious infection

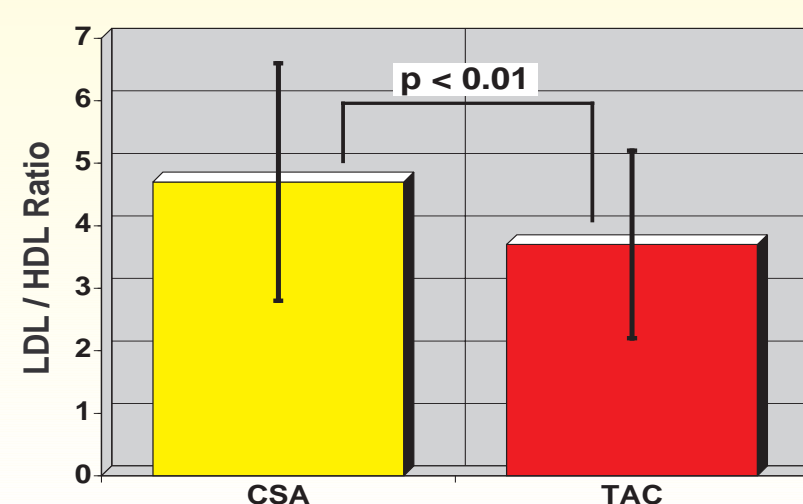
Results

- 42 patients finished 2 year follow-up
- Mean tacrolimus dose could be reduced from 0.1 mg/kg/d to 0.05 mg/kg/d
- Concomitant immunosuppression remained the same
- No rejection episodes after conversion
- No serious infections
- 5 patients reconverted to CyA due to alopecia

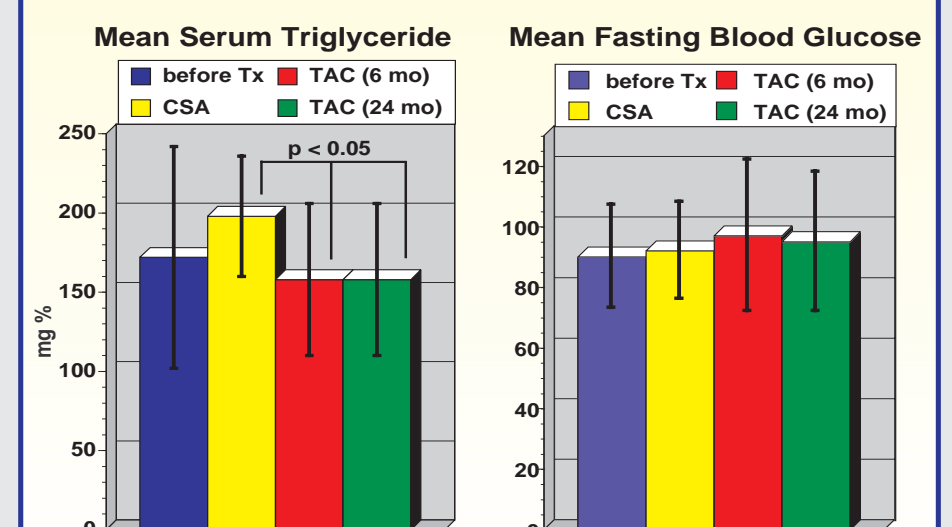
Results 1



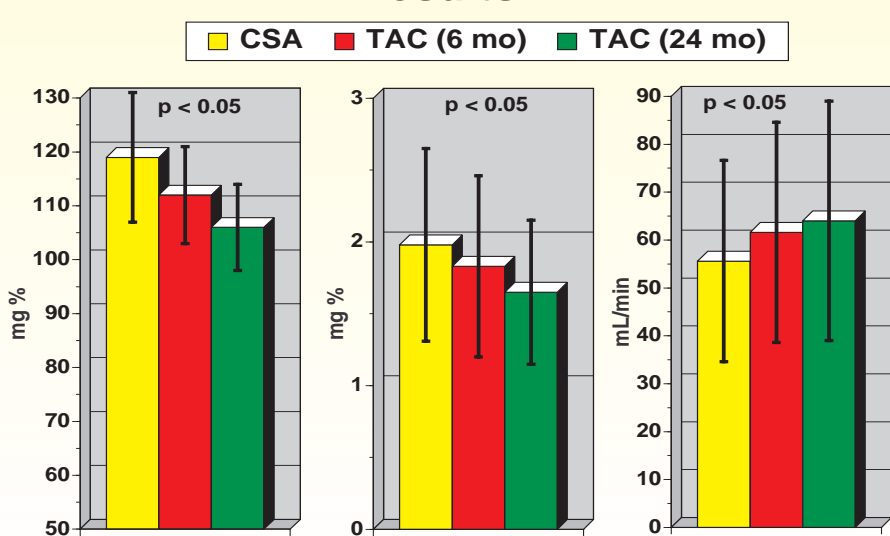
Results 2



Results 3



Results 4



Conclusions (1)

- CyA induced reversible atherogenic changes in lipid metabolism that are not seen under tacrolimus.
- The better control of hypertension and the significant better kidney function under tacrolimus in contrast to CyA might be related to lower vasoconstrictive effect of tacrolimus.
- Common cosmetic side effects like gingival hyperplasia and hirsutism seen under CyA, do not appear under tacrolimus.
- The alopecia seems to be induced by the withdrawal of CyA.

Conclusion (2)

- The reduced atherogenic potency and the lower vasoconstrictive action of tacrolimus in comparison to CyA, without a higher incidence of acute rejection nor of infections favours tacrolimus as the first line immunosuppressive regimen after kidney transplantation.
- The use of tacrolimus may concur with the long-term aim to reduce chronic rejection and cardiovascular morbidity and mortality in kidney transplantation.