

Changes in Oxidative Stress in Renal Graft Patients Receiving Calcineurin Inhibitors: Cyclosporine Versus Tacrolimus

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OBJECTIVES

The effects of calcineurin inhibitors on oxidative stress after renal transplant are obscure. This study sought to investigate the changes in plasma oxidative stress and lipid levels in patients receiving cyclosporine or tacrolimus before and after renal transplant for 6 months.

METHODS

Twenty-one patients and 15 healthy controls were involved in our study. Twelve of the patients were treated with cyclosporine and 9 were treated with tacrolimus. Plasma malondialdehyde (MDA), nitrite/nitrate, vitamin C, vitamin E, and plasma glutathione levels, as well as total cholesterol and triglyceride levels, were evaluated before and after transplant for 6 months.

TABLES

	Patients (n=21)	Controls (n=15)	P Value
Age at transplant	33.60 ± 9.90	39.00 ± 8.30	NS
Sex ratio (% male)	76.19	46.67	NS
Dialysis duration (months)	18.00 ± 10.00		
HD/CAPD	18/3		
Total cholesterol (mmol/L)	4.42 ± 1.22	4.81 ± 0.91	NS
Triglycerides (mmol/L)	2.01 ± 1.64	1.86 ± 0.88	NS
Hemoglobin (g/L)	111.00 ± 19.00	138.00 ± 13.00	< .001
MDA (nmol/mL)	3.76 ± 0.79	3.21 ± 0.57	< .05
Nitrite/nitrate (mg/dL)	2.24 ± 0.32	2.25 ± 0.59	NS
Plasma GSH (µmol/L)	66.60 ± 23.20	43.30 ± 26.90	< .05
Vitamin C (µmol/L)	59.00 ± 8.00	59.00 ± 9.00	NS
Vitamin E (µmol/L)	11.00 ± 1.00	10.00 ± 1.00	NS

Values are expressed as means ± standard deviation

Abbreviations: CAPD, continuous ambulatory peritoneal dialysis; GSH, glutathione; HD, hemodialysis; MDA, malondialdehyde

	BT	AT30	AT90	AT180
Creatinine (µmol/L)	964.00 ± 248.00*	97.00 ± 22.00*	115.00 ± 35.00*	115.00 ± 27.00*
Total cholesterol (mmol/L)	4.42 ± 1.22†	5.61 ± 1.14†	5.77 ± 1.40†	4.84 ± 0.67
Triglycerides (mmol/L)	2.01 ± 1.64	1.70 ± 0.56	2.47 ± 1.24	1.94 ± 0.80
MDA (nmol/mL)	3.76 ± 0.79†	3.98 ± 0.74	4.38 ± 0.87†	4.28 ± 0.69†
Nitrite/nitrate (mg/dL)	2.24 ± 0.32†	2.41 ± 0.47	2.17 ± 0.36	1.90 ± 0.40†
Plasma GSH (µmol/L)	66.60 ± 23.20†	44.80 ± 14.90†	56.90 ± 19.10	52.40 ± 18.70
Vitamin C (µmol/L)	59.00 ± 8.00	54.00 ± 7.00	57.00 ± 6.00	58.00 ± 9.00
Vitamin E (µmol/L)	11.00 ± 1.00	10.00 ± 2.00	10.00 ± 2.00	10.00 ± 1.00

Values are expressed as means ± standard deviation

*P < .0001, †P < .005, ‡P < .05

Abbreviations: AT30, 30 days after transplant; AT90, 90 days after transplant; AT180, 180 days after transplant; BT, before transplant; CAPD, continuous ambulatory peritoneal dialysis; GSH, glutathione; MDA, malondialdehyde

	BT	AT30	AT90	AT180
Total cholesterol (mmol/L)	4.34 ± 1.16*, †	5.61 ± 1.09*	6.21 ± 1.66†	5.02 ± 0.78*
Triglycerides (mmol/L)	2.47 ± 1.93	1.59 ± 0.49	2.83 ± 1.37	2.13 ± 0.88
MDA (nmol/mL)	3.64 ± 0.74*	3.81 ± 0.76	4.11 ± 0.92	4.22 ± 0.75*
Nitrite/nitrate (mg/dL)	2.38 ± 0.37†	2.49 ± 0.48	2.14 ± 0.35	1.92 ± 0.34†
Plasma GSH (µmol/L)	65.40 ± 22.30†	43.20 ± 11.10†	56.30 ± 16.80	60.50 ± 19.70
Vitamin C (µmol/L)	58.00 ± 9.00	54.00 ± 7.00	57.00 ± 6.00	57.00 ± 11.00
Vitamin E (µmol/L)	11.00 ± 1.00	11.00 ± 2.00	10.00 ± 2.00	10.00 ± 2.00

Values are expressed as means ± standard deviation.

*P < .05, †P < .01

Abbreviations: AT30, 30 days after transplant; AT90, 90 days after transplant; AT180, 180 days after transplant; BT, before transplant; GSH, glutathione; MDA, malondialdehyde

	BT	AT30	AT90	AT180
Total cholesterol (mmol/L)	4.50 ± 1.37	5.61 ± 1.32	5.15 ± 0.47	4.60 ± 0.47
Triglycerides (mmol/L)	1.32 ± 0.72	1.86 ± 0.65	1.85 ± 0.72	1.69 ± 0.69
MDA (nmol/mL)	3.93 ± 0.88	4.21 ± 0.70	4.73 ± 0.69	4.37 ± 0.62
Nitrite/nitrate (mg/dL)	2.06 ± 0.12	2.32 ± 0.45	2.21 ± 0.39	1.89 ± 0.48
Plasma GSH (µmol/L)	64.20 ± 25.10*	50.30 ± 21.00	59.60 ± 24.20	42.40 ± 13.60*
Vitamin C (µmol/L)	1.05 ± 0.15	0.96 ± 0.11	1.00 ± 0.10	1.03 ± 0.04

Values are expressed as means ± standard deviation.

*P < .05.

Abbreviations: AT30, 30 days after transplant; AT90, 90 days after transplant; AT180, 180 days after transplant; BT, before transplant; GSH, glutathione; MDA, malondialdehyde

CONCLUSIONS

An enhancement in plasma MDA levels was found after transplant at 6-month follow-up. However, no significant change in vitamin C, vitamin E, nitrite/nitrate levels between patients and controls was recorded. Although both calcineurin inhibitors showed similar effects on oxidative stress, cyclosporine-treated patients had higher levels of total cholesterol and triglycerides.

RESULTS

Before the transplant, patients had higher MDA and plasma glutathione levels than did healthy controls (3.76 ± 0.79 nmol/mL vs 3.21 ± 0.57 nmol/mL; $P < .05$, and 66.6 ± 23.2 µmol/L vs 43.3 ± 26.9 µmol/L; $P < .05$). In the overall group of patients, a significant increase in MDA levels was detected 3 and 6 months after transplant (3.76 ± 0.79 nmol/mL vs 4.38 ± 0.87 nmol/mL in the third month; $P = .02$ and 3.76 ± 0.79 nmol/mL vs 4.28 ± 0.69 nmol/mL in the sixth month; $P = .04$). A significant reduction in plasma glutathione levels 1 month after transplant and nitrite/nitrate levels 6 months after transplant was found. No changes in vitamin C and vitamin E levels were detected before and after transplant. After 3 and 6 months of transplant, cyclosporine treated patients had higher levels of total cholesterol and triglycerides when compared with tacrolimus-treated patients.

REFERENCE

Akbasli AC, Keven K, Erbay B, Nebioglu S. Changes in oxidative stress in renal graft patients receiving calcineurin inhibitors: cyclosporine versus tacrolimus. *Exp Clin Transplant*. 2012 Oct;10(5):439-45.

