

DE NOVO DEVELOPMENT OF HYPERCHOLESTEROLAEMIA AND INCREASED HDL-CHOLESTEROL: APOPROTEIN A-I RATIO IN PATIENTS WITH CHRONIC RENAL FAILURE FOLLOWING KIDNEY TRANSPLANTATION

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Summary

Lipid profiles were studied in 27 kidney transplant patients with stable renal function during long term follow-up and 18 haemodialysis patients. Hypertriglyceridaemia resolved after kidney transplantation. In contrast, hypercholesterolaemia developed and persisted in transplant patients. HDL-CHL temporarily elevated at 1–5 years post-transplant compared to decreased values during haemodialysis. HDL-CHL:Apo.A-I ratio became elevated post-transplant, although no variation in Apo.A-I values was observed between either groups. It is suggested that qualitative and quantitative changes of HDL particles develop after grafting.

Introduction

Alterations in lipid metabolism, notably hypertriglyceridaemia and reduced high density lipoprotein (HDL)-cholesterol (CHL), are known to exist in chronic renal failure patients both before and after starting haemodialysis [1–5]. Since the effect of transplantation on lipid metabolism is still a matter of debate we studied lipid profiles in transplant patients with stable renal function during long term follow-up.

Materials and methods

Twenty-seven kidney transplant (25 living-related and two cadaveric) patients (19 males and eight females) and 18 patients on maintenance haemodialysis at Kitasato University Hospital were studied (Table I). Haemodialysis patients with poor control and transplant patients with steroid-induced diabetes mellitus, liver dysfunction (serum glutamic pyruvic transaminase ≥ 35 Karmen units per ml) or within one year after grafting were excluded.

Fasting blood was obtained for the measurement of serum triglycerides (TG)

TABLE I. Clinical profile of haemodialysed patients with chronic renal failure and transplant recipients

	CRF on HD†	Transplant recipients	
		1–5 years	5 years
Number of patients	18	15	12
Male/Female	10/18	9/6	10/2
Age, years	35 ± 7.4‡	32 ± 6.1	35 ± 5.9
Cr, mmol/L	1.32 ± 0.28	0.10 ± 0.02*	0.12 ± 0.02*

† Patients with chronic renal failure on maintenance haemodialysis

‡ Mean ± SD

* $p < 0.001$, vs CRF on HD

(autoanalyser), cholesterol (CHL) (autoanalyser), free fatty acids (FFA) (enzyme method), phospholipids (PL) (enzyme method), HDL-CHL (heparin-Ca-Ni precipitation method), Apo.A-I (rocket immunoelectrophoresis) and lecithin-cholesterol acyltransferase (LCAT) (Nagasaki-Akanuma's autosubstrate method).

Statistical analysis was performed employing Student's unpaired t-test.

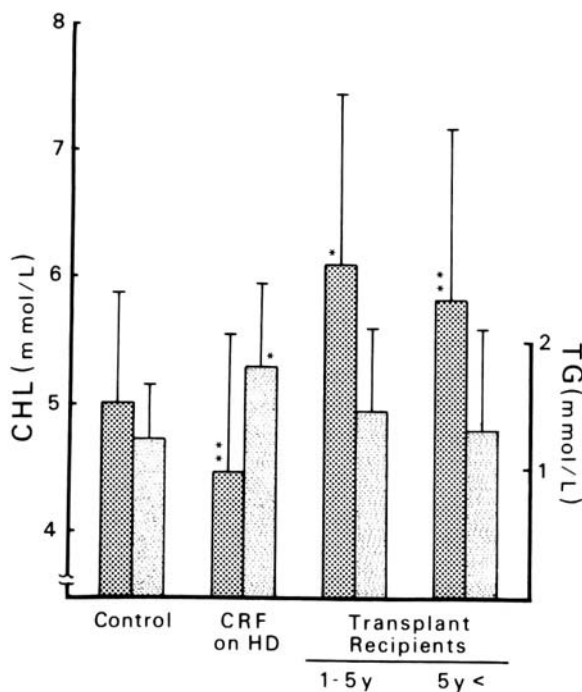


Figure 1. CHL and TG values in dialysed and post-transplant patients: * $p < 0.001$ versus control; ** $p < 0.01$ versus control. Stippled column represents CHL; shaded column represents TG; central bar 1SD

Results

Hypertriglyceridaemia, which was a characteristic feature in haemodialysis patients, resolved after kidney transplantation (Figure 1). In contrast, hypercholesterolaemia newly developed and persisted following transplantation (Figure 1). Elevation in FFA was only observed in transplant patients at 1–5 years (Table II). PL was significantly elevated in patients both at 1–5 years and more than five years post-transplant. HDL-CHL, which was significantly decreased during haemodialysis, temporarily elevated at 1–5 years post-transplant and returned to normal thereafter (Table II).

TABLE II. Serum lipid levels of haemodialysed patients with chronic renal failure and transplant recipients

	Normal control	CRF on HD	Transplant recipients	
			1–5 years	5 years
HDL-CHL, mmol/L	1.38 ± 0.27 (313)	0.83 ± 0.31*	1.61 ± 0.49**	1.51 ± 0.53 (12)
FFA, mEq/L	0.44 ± 0.10 (43)	0.40 ± 0.17 (18)	0.54 ± 0.16**	0.47 ± 0.19 (12)
PL, g/L	1.99 ± 0.28 (75)	1.84 ± 0.33 (18)	2.31 ± 0.40*	2.26 ± 0.33* (12)

Number of cases studied in brackets. * $p < 0.001$ vs normal control; ** $p < 0.01$ vs normal control

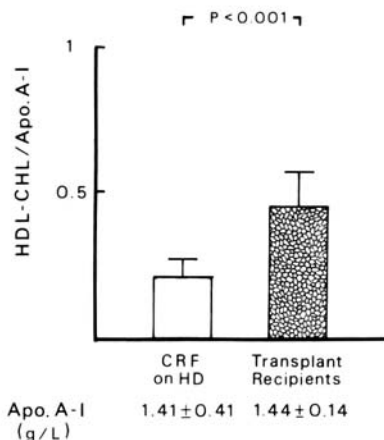


Figure 2. HDL-CHL : Apo.A-I ratio and Apo.A-I values in dialysed and post-transplant patients

Apo.A-I values and HDL-CHL : Apo.A-I ratio were compared before and after kidney transplantation (Figure 2). Apo.A-I remained constant, while the HDL-CHL : Apo.A-I ratio became elevated post-transplant. LCAT activities, which were decreased in dialysis patients became elevated after transplantation compared to both haemodialysis patients ($p < 0.001$) and normal controls ($p < 0.01$, Figure 3).

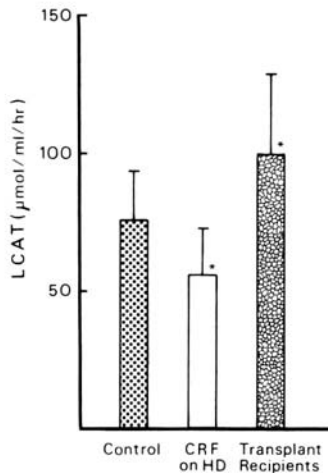


Figure 3. LCAT activity in dialysed and post-transplant patients. * $p < 0.01$ versus control

Discussion

Lipid abnormalities, such as hypertriglyceridaemia and reduced HDL-CHL, have been observed in CRF patients [1–5]. Post-transplant improvement in hypertriglyceridaemia observed in this study is in contrast to other reports [1–5]. Hypercholesterolaemia developed and persisted after kidney transplantation, although it showed a tendency to decrease after more than five years. Hyperlipidaemia after grafting may be due to impaired VLDL-TG removal caused by decreased lipoprotein lipase activity [6]. In addition, steroid administration may contribute by promoting insulin resistance [5,7].

HDL values in CRF patients both before and after grafting have been reported by several authors [8–14]. HDL-CHL, which is considered as one of the antiatherogenic factors, increased above normal after kidney transplantation. Total CHL values also increased in the present study. LCAT activities likewise became elevated together with the increase in CHL.

Apo.A, the major HDL apoprotein, has recently been studied after grafting [12–14]. No effect of transplantation was observed in our patients on Apo.A-I, which constitutes one of the major components of Apo.A, showing similar values before and after grafting. In conclusion, it may be suggested that qualitative and quantitative changes of HDL particles appear after grafting when compared to the CRF stage.

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