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Secondary Hyperparathyroidism, Decreased Hepatic Triglyceride Lipase, Elevated Intermediate Density Lipoprotein and Atherosclerosis in Hemodialysis Patients

Dear Sir,

Cardiovascular mortality is higher in dialysis patients than the nonuremic population. This has been taken to indicate that dialysis patients have accelerated atherosclerosis [1]. We have recently revealed that atherosclerosis in hemodialysis patients is advanced morphologically, showing a greater intima media thickness in the carotid and femoral arteries in dialysis patients than healthy control subjects by high-resolution B mode ultrasonography [2]. Lipoprotein abnormality is one of the major risk factors for atherosclerosis in the general population, and recent studies [3–6] reemphasize the importance of triglyceride-rich lipoproteins such as partially lipolyzed very low density lipoprotein (VLDL) and intermediate density lipoprotein (IDL). These lipoprotein classes are significantly elevated in patients with chronic renal failure [7–9]. To under-

stand the mechanism behind the increased IDL level in uremic patients, we examined factors responsible for the elevated IDL concentration in chronic renal failure patients.

The subjects were 24 hemodialysis patients, 42 peritoneal dialysis patients and 25 healthy controls. Their age and gender were comparable between the groups. Lipoproteins were measured by 1-step ultracentrifugation [8]. Lipoprotein lipase (LPL) and hepatic triglyceride lipase (HTGL) protein masses were measured in postheparin plasma by a sandwich enzyme immunoassay [10]. We previously reported elsewhere [8] that the IDL cholesterol level was markedly elevated in the hemodialysis (13.6 ± 1.4 mg/dl, mean $\pm$ SE) and peritoneal dialysis patients (22.4 ± 1.5 mg/dl), as compared with the control level (5.3 ± 1.1 mg/dl). LPL was not significantly different between the three

groups, whereas HTGL was significantly lower in both hemodialysis (557 ± 96 ng/ml) and peritoneal dialysis patients (720 ± 61 ng/ml) than control subjects ($1,259 \pm 134$ ng/ml).

Table 1 summarizes the data by a univariate analysis of IDL cholesterol. VLDL cholesterol correlated positively to IDL cholesterol. LPL showed a weak positive relation with IDL cholesterol with a borderline significance. In contrast, HTGL was in a significant inverse relationship with IDL cholesterol. These univariate results are all consistent with the metabolic cascade of IDL; IDL is generated from VLDL via the action of LPL, and it is further metabolized by the action of HTGL. Then, we tried to find independent associations of the IDL cholesterol level with these factors by a multiple regression analysis (table 2). The results indicate

Table 1. Simple regression analysis of factors associated with IDL cholesterol

Variable	r	p value
VLDL cholesterol	0.463	0.0001
LPL	0.208	0.0838
HTGL	-0.291	0.0146

Simple regression analysis was performed to examine the correlation of IDL cholesterol with other variables in the 91 total subjects. r = Correlation coefficient.

Table 2. Multiple regression analysis of factors determining IDL cholesterol level

Dependent variable	β	p value	R ²
VLDL cholesterol	0.460	0.0001	
LPL	0.278	0.0001	
HTGL	-0.334	0.0001	0.348 (p = 0.0001)

Factors determining IDL cholesterol were evaluated by multiple regression analysis in the 91 total subjects. β = Standard partial regressin coefficient; R² = multiple coefficient of determination.

that all of the VLDL cholesterol, LPL and HTGL levels significantly and independently related to the IDL cholesterol level.

These data provide clinical evidence that a decreased HTGL level is an important determinant of IDL accumulation in chronic renal failure. We previously reported that a decrease in HTGL was closely associated with a low ionized calcium concentration and elevated parathyroid hormone [8]. Therefore, we speculate that impaired calcium homeostasis and secondary hyperparathyroidism reduce the HTGL enzyme, increase the IDL level, and presumably accelerate atherogenesis in chronic renal failure. In support of this, the parathyroid hormone level was shown to be an independent risk factor of femoral atherosclerosis in hemodialysis patients [2]. To date, however, no published data are available that show the atherogenic role of IDL in patients with chronic renal failure. We are currently working to clarify this point.

References

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Announcement

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