Increased Lipoprotein (a) Levels in Subjects with Chronic Renal Failure on Hemodialysis

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Dear Sir,

It is already known that chronic renal failure on hemodialytic treatment is associated with an elevated incidence of premature atherosclerosis [1]. A close relationship between the lipid abnormalities documented in uremia [2] and the increased cardiovascular mortality of these patients has been suggested [3]. Recently, the role of Lp(a), lipoprotein discovered by Berg [4] in 1963, in the development of atherosclerosis has been revalued [5]. The structure of Lp(a) is very similar to that of low-density lipoproteins (LDL): both contain apo B-100 as major protein, but only Lp(a) contains apo(a), a protein structurally very close to plasminogen [6]. Although the metabolic function of Lp(a) is still unknown, it seems to be linked to lipoprotein metabolism as well as to the fibrinolytic system [7]. Plasma levels are strongly regulated by a genetic trait [8] but renal diseases seem to be associated with increased levels of Lp(a) [9, 10].

We have evaluated the apolipoprotein profile [total cholesterol (TC), triglycerides (TG), HDL-cholesterol (HDL-C), apo A-I and B] and Lp(a) levels, after an overnight fast, in a group of 45 subjects with chronic renal failure on hemodialytic treatment (26 males, 19 females, aged 55.6 ± 12.9 years, BMI 25.2 ± 2.2 , age of dialysis 4.1 ± 2.7 years) and in a group of normal subjects matched for age, gender, body weight and fasting TC and TG levels as controls. None of them, patients or controls, was affected by diseases (diabetes, obesity, liver diseases) or used drugs affecting the lipid metabolism. TC and TG were quantified by enzymatic methods, HDL-C after precipitation of apo-B-containing lipoproteins by PTA/magnesium chloride, apo A-I and apo B by the nephelometric method and Lp(a) levels by RIA. Because the Lp(a) distribution is highly skewed, statistical analysis for this parameter was performed by both the Mann-Whitney U test and by Student's t test after log transformation of values. We have observed that patients with chronic renal failure on hemodialytic therapy showed levels of HDL-C and apo A-I lower and levels of Lp(a) always significantly higher than controls, even if they were matched for fasting lipid levels (table 1). Therefore, the prevalence of subjects with Lp(a) levels above 25 mg/dl was significantly higher in patients with chronic renal failure (53% vs. 18%; $p < 0.01$; data not shown). These data agree with the report of Parra et al. [9] who found, in subjects

with chronic renal failure treated with hemodialysis, levels of Lp(a) increased threefold in comparison with normolipidemic controls. However, patients studied by these authors showed higher triglyceride levels in comparison with controls (respectively 2.5 ± 1.47 and 1.11 ± 0.39 mmol/l). We have previously demonstrated that the apolipoprotein profile in patients affected by hypertriglyceridemia secondary to chronic renal failure is different from that of subjects with primary type IV hyperlipoproteinemia [11]. Although we have studied patients and controls matched for fasting lipids, Lp(a) levels were significantly increased in chronic renal failure, and plasma concentrations of Lp(a) were not different from those in the report of Parra et al. [9] (median of Lp(a) 31.5 vs. 28.5 mg/dl in uremic patients and 9.4 vs. 7.1 mg/dl in controls); therefore, the prevalence of Lp(a) levels above 25 mg/dl was significantly higher in uremia. Karadi et al. [10] have suggested an enhanced synthesis of Table 1. Lipids, apolipoprotein and Lp(a) levels in 45 patients with chronic renal failure on hemodialytic therapy (CRF) and in 45 normal controls (C)

All the values are expressed as mg/dl, mean $\pm$ SD. *p < 0.01; **p < 0.001, Student's t test; ***p < 0.003, Mann-Whitney U test. a Median. b Transformed log values.

Lp(a), together with apo-B-100-containing particles, in nephrotic syndrome but the mechanism underlying the increase in this lipoprotein in plasma of patients with uremia on hemodialysis is not clear. However, elevated levels of Lp(a) could raise the risk for cardiovascular disease on patients with chronic renal failure on hemodialytic treatment.

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