Lipoprotein(a) Levels in Hemodialysis Patients: Relation to Glucose Intolerance and Hemodialysis Duration

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Dear Sir,

Lipoprotein(a) [Lp(a)] is a plasma lipoprotein consisting of a particle similar to low-density lipoprotein (LDL), with apoprotein(a) covalently linked to apoprotein B-100 by a disulfide bridge [1]: an Lp(a) level greater than 30 mg/dl is an independent risk factor for the development of cardiovascular disease [2]. It is well known that chronic renal failure hemodialysis (HD) patients have an elevated incidence of premature atherosclerosis [3]: furthermore, recent studies have shown that increased plasma levels of Lp(a) are present both in chronic renal failure [4], in impaired glucose tolerance (IGT) [5] and in insulin-dependent diabetes mellitus [6] patients. However, no data exist concerning Lp(a) levels in HD patients with IGT or non-insulin-dependent diabetes mellitus (NIDDM) and the relation between HD duration and Lp(a) levels.

We have evaluated the lipoprotein profile [total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)] and Lp(a) levels in a group of 104 fasting patients with chronic renal failure (68 males, 36 females; mean age 57.6 ± 1.4 years) on HD treatment for 61.6 ± 5.3 months and in a group of 104 control subjects (68 males, 36 females; mean age 53.7 ± 0.8 years). Exclusion criteria were as follows: known genetic defects in lipid metabolism, liver and thyroid disease and use of drugs affecting lipid metabolism. Fifteen HD patients have IGT (according to the World Health Organization's 1985 criteria) and 7

Table 1. Clinical characteristics of HD patients

ESRD = End-stage renal disease; CGN = chronic glomerulonephritis; PKD = polycystic kidney disease; NA = nephroangiosclerosis; GN = glomerular nephropathy; CGN = patients with medical history of a wide variety of glomerular diseases without histological diagnosis.

1 Dose of HD prescribed, $Kt/v > 1$ (range: 1.04-1.17).

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Table 2. Serum concentration of lipids a Lipid profile

and Lp(a) in HD patients and in controls				
(mg/dl; means $\pm$ SEM)	TC	HDL-C	LDL-C	TG
Controls	212.2 $\pm$ 3.4	48.8 $\pm$ 1.1	137.0 $\pm$ 3.0	119.4 $\pm$ 5.4
HDpatients	181.5 $\pm$ 4.9*	35.9 $\pm$ 1.2*	109.3 $\pm$ 4.1*	190.5 $\pm$ 12.9*

b Lp(a) concentrations

Means $\pm$ SEM Range Value

≥ 30 mg/dl, %

Control patients 17.1 $\pm$ 1.5 1.1-88 20

HDpatients 30.1 $\pm$ 2.9** 1.1-111 37

IGT-NIDDM HD patients 21.7 $\pm$ 4.3 1.1-71.2 23

*p < 0.001, **p < 0.0003.

For the modified Friedewald formula, see the text.

patients have NIDDM (IGT-NIDDM group: 22 patients, 12 males, 10 females; mean age 61.9 $\pm$ 2.7 years; HD treatment for 54.6 $\pm$ 9.3 months). Data of uremic patients appear in table 1. Lp(a) levels were quantified by ELISA [Macra Lp(a), Bouty, Milan, Italy]: the intra- and interassay coefficients of variation were 4 and 8%, respectively. TC, TG and HDL-C were measured enzymatically (Boehringer, Mannheim, Germany). LDL-C was determined by the modified Friedewald formula: LDL-C = TC - HDL-C - (TG $\times$ 0.16) - [Lp(a) $\times$ 0.3]. All data are given as means $\pm$ standard error of mean (SEM). Statistical analysis was performed by Student's t test and, only for Lp(a), by the Mann-Whitney U test because Lp(a) distribution is skewed. We used Spearman's rank correlation coefficient to evaluate the degree of association between variables. Statistical significance was defined as two-tailed, p < 0.05.

Our results (table 2) confirm both lipid abnormalities and a raised Lp(a) concentration in HD patients compared to controls (30.1 $\pm$ 2.9 vs. 17.1 $\pm$ 1.5 mg/dl; p < 0.0003). The results did not appear to be affected by either gender or age. We observed no correlation between the Lp(a) level and other lipids evaluated both in HD patients and in controls. However, there is an inverse correlation between Lp(a) levels and duration (months) of HD treatment (r = -0.25; p < 0.01). This observation has not been previously reported and suggests a close relationship between the elevated Lp(a) levels and the increased cardiovascular mortality in HD patients [7]: in fact, it is possible that patients with lower Lp(a) levels are selected due to a lower incidence of cardiovascular mortality. However, in the IGT-NIDDM group, the Lp(a) concentration (21.7 $\pm$ 4.3 mg/dl) was not statistically significant compared with controls: this is at variance with data in nonuremic IGT patients [5] and in accordance with NIDDM patients receiving conservative therapy [8]. The prevalence of Lp(a) levels above 30 mg/dl was significantly higher (p < 0.01) in the HD group in respect of the IGT-NIDDM group and controls (37, 23 and 20%, respectively). At present, we can just assume the mechanism leading to normal Lp(a) levels in our IGT-NIDDM patients: good metabolic control (HbA_{1c} < 8%) and lack of albuminuria are two possible causes.

In conclusion, our study in HD patients demonstrates a prevalence of elevated Lp(a) levels, which are reduced with HD duration, and normal Lp(a) levels in the IGT-NIDDM group. These data suggest that elevated Lp(a) plasma levels may contribute to the high mortality rate from cardiovascular disease in HD patients. A long-term longitudinal study, which is currently in progress, is needed to answer this question.

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