Serum Lipoprotein (a) Concentration Is Increased in Moderate Renal Failure

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Table 1. Concentrations of serum lipids, lipoproteins including Lp(a), apolipoprotein B, plasma albumin and urine albumin in groups with different GFRs

Dear Sir,

Lipoprotein (a) (Lp(a)) consists of an LDL particle linked by a disulfide bridge to apolipoprotein (a) [1], a glycoprotein which has structural homologies with plasminogen [2]. Increased serum concentrations of Lp(a) have been shown to be a strong, independent risk factor for the development of atherosclerosis in the general population [3] and in hemodialysis patients [4]. Moreover, Lp(a) has been found in atherosclerotic lesions in arterial walls, implying pathogenetic significance [5]. There are several reports of increased serum concentrations of Lp(a) in advanced renal failure: in predialytic patients [6], in hemodialysis patients [6-11], and in CAPD patients [10-13]. Less is known about serum Lp(a) concentrations earlier in renal failure. Lipid, lipoprotein including Lp(a), and apolipoprotein concentrations were analyzed in serum from 72 patients with a wide range of glomerular filtration rates (GFRs). The patients were divided into three GFR groups: a reference group (67-107 ml/min), patients with moderate renal failure (36-63 ml/min), and patients with severe renal failure (6-32 ml/min). Factors other than renal insufficiency, known to influence lipoprotein metabolism, were strictly excluded (diabetes, endocrine disease, obesity, liver disease, active inflammatory disease, malignancy, treatment with lipid-lowering agents, steroids or cyclosporin). Patients with urine albumin concentrations exceeding 500 mg/l (50 mg/dl) and/or signs of moderate-severe inflammatory activity in the plasma protein pattern were excluded.

Serum Lp(a) concentrations were measured with a radioimmunoassay with reagents from Pharmacia, Uppsala, Sweden. The results were expressed as median/range and nonparametric statistical tests were applied.

GFR was estimated by a single sample method with iohexol as a marker [14, 15]. Plasma iohexol concentrations were analyzed by high-performance liquid chromatography.

The results of the Lp(a) analyses are shown in table 1. As estimated by the Kruskal-Wallis test, the variance between the groups was significantly different. Serum Lp(a) concentrations were significantly increased in moderate and severe renal failure as compared with the reference group, and they were inversely correlated with GFR ($r = -0.33$, $p = 0.005$). A trend was observed in the renal failure groups towards an increase in the number of subjects with serum Lp(a)

concentration > 300 mg/l (30 mg/dl) as estimated by $2 \times 3 \chi^2$ test (3/24 in the reference group, 9/26 in moderate renal failure, 8/22 in severe renal failure). The range of serum Lp(a) concentrations was similar in all groups.

Concentrations of serum lipids, lipoproteins and apolipoprotein B, plasma albumin and urine albumin are shown in table 1. There were significant correlations between serum concentrations of Lp(a) and total cholesterol ($r = 0.27$, $p = 0.025$), LDL cholesterol ($r = 0.31$, $p = 0.009$) and apolipoprotein B ($r = 0.25$, $p = 0.043$). On the other hand, there were no correlations between serum concentrations of Lp(a) and concentrations of serum triglycerides, serum HDL cholesterol, plasma albumin and urine albumin.

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This study demonstrates that serum Lp(a) concentrations are significantly increased relatively early in renal failure. This probably contributes to the increase in atherosclerotic disease observed in predialytic patients. Moreover, this finding offers at least a partial explanation of the elevated serum Lp(a) concentrations reported in kidney transplant recipients [16], a patient category with moderately reduced GFR.

Serum Lp(a) concentrations are under strict genetic control and strikingly resistant to environmental influence [17]. However, serum Lp(a) concentrations are elevated in the nephrotic syndrome [18] and in advanced renal failure, CAPD patients in particular [10-13]. Consequently, it has been suggested that protein losses, inducing a general increase in hepatic protein synthesis, might play an important part in determining serum Lp(a) concentration in renal disease. The patients in the present material were practically devoid of factors known to disturb lipid metabolism. Most relevantly, they had normal plasma albumin concentrations and very modest urinary albumin excretion. In spite of this, the concentrations of Lp(a) were elevated already in moderate renal failure and correlated inversely with GFR, indicating that renal failure per se is a pathogenic factor.

The results imply that uremia, by unknown mechanisms, causes an increase in serum Lp(a) concentrations, which is superimposed on the genetic influence, an important determinant at all levels of renal function. Possibly, this increase is caused by a posttranscriptional change in the phenotypic expression [17]. The direct correlation between serum concentrations of Lp(a) and LDL cholesterol probably reflects the common origin of the lipoproteins.

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