Which Factors Account for Increased Serum Laminin Levels in Patients with Chronic Renal Diseases?

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Dear Sir,

It has been suggested that the increased levels of laminin observed in patients with renal disease may indicate changes in glomerular basement membrane metabolism [1]. However, to date, little is known about the factors determining serum levels of laminin in these patients. In this study, we determined the serum levels of laminin P1, a pepsin-resistant fragment of laminin with a molecular weight of 300 kD, by a specific competitive radioimmunoassay (Behring Werke, Germany, intra- and interassay variation coefficients 3.6 and 5.8%, respectively), in a sample of 60 nondiabetic patients with different forms of active, primary, biopsy-proven chronic renal diseases with or without renal failure. We analyzed the relationship between laminin P1 levels and the following variables: age, blood pressure, serum creatinine, endogenous creatinine clearance, type of histological injury, degree of renal sclerosis, serum lipid profile, proteinuria and ethanol intake.

The study group comprised 60 patients (38 M, 22 F average age: 49 years (range 20-77 years). The etiology of renal disease was as follows: minimal change disease (n = 10), idiopathic focal sclerosis (n = 10), mesangial proliferative glomerulonephritis with IgA deposits (n = 10), membranous nephropathy (n = 10), membranoproliferative glomerulonephritis (n = 10) and chronic interstitial nephritis (n = 10). No patient suffered from chronic hepatic disease. Ethanol intake (grams ethanol/day) was recorded in all patients.

Thirty patients (50%) were hypertensive and were taking antihypertensive drugs (enalapril n = 20, amlodipine n = 12, furosemide n = 19, atenolol n = 16). In the 12 months preceding the study, no patients was treated with either immunosuppressive or lipid-lowering agents. Reference values were obtained from a matched control group.

Table 1 shows serum laminin levels in a study group classified according to histological criteria and in healthy controls. Values are mean (1 SD). Comparisons among means were done by the Kruskal-Wallis test followed by the Mann-Whitney U test. Correlation analyses were done by the Spearman-rank correlation test. A p value less than 0.05 was considered significant. Bonferroni correction was applied when multiple comparisons were made.

In healthy controls, serum laminin correlated weakly with age ($r:0.25$, $p = 0.02$) and ethanol intake ($r:0.33$, $p = 0.01$). Serum laminin levels were meaningfully higher in patients with membranous nephropathy, mesangial proliferative glomerulonephritis and membranoproliferative glomerulonephritis. In patients with minimal change disease, focal glomerulosclerosis and interstitial nephropathy, levels of laminin **PI** were not significantly different from those in healthy controls. Within a given histological group, there was little variation in serum laminin levels. Laminin **PI** levels did not correlate with age, blood pressure, ethanol intake, serum creatinine, endogenous creatinine clearance, serum lipids nor with the degree of glomerular or interstitial sclerosis.

Laminin is an 850,000-dalton protein which localizes at the lamina rara of basement membranes where it develops both structural and biologic functions. The factors determining serum laminin levels are not known at present. In healthy people, laminin levels increase with age, ethanol intake and pregnancy [2-4]. In pathological states, increased laminin levels have been described in patients with chronic renal and hepatic diseases and in some neoplastic disorders [1, 4-6]. Factors favoring laminin increase in these disorders are not known. Either increased synthesis or reduced hepatic catabolism might occur but none of these mechanisms can be proved. In our patients, serum laminin levels were independent of both age and ethanol intake. An accumulation of laminin as a consequence of renal failure is not likely since most patients with histological forms associated with increased laminin levels had serum creatinine less than 1.5 mg/dl and, in the whole group, no correlation between laminin and endogenous clearance of creatinine was found. Moreover, no patient had a secondary kidney disease nor a chronic hepatic disease to account for the increase in serum laminin. Since the only factor determining serum laminin was the kind of histological injury, we argue that increased laminin levels may transduce both mesangial and basement membrane expansion. Further study is needed to address the long-term prognostic value of increased serum laminin levels in these patients.

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Table 1. Clinical characteristics of the patients classified in histological groups

MC: Minimal change disease; FGS: focal glomerulosclerosis; MES: mesangial proliferative; MN: membranous nephropathy; MP: membranoproliferative; INT: interstitial nephropathy; CG: control group; SCr: serum creatinine; HBP: high blood pressure; PROT: 24-hour protein excretion; TC: total cholesterol; TG: triglycerides; Lam **PI**: laminin **PI**. Values are means $\pm$ SD. * $p < 0.001$ vs. the other groups. Differences among laminin values in patients with MES, MN and MP were not significant.

References

- Horikoshi S, Koide H: Serum laminin **PI** fragment concentration in renal diseases. *Clin Chim Acta* 1991;196:185-191.
- Pietschmann P, Scherthaner G, Schnack CH, Gaube S: Serum concentrations of laminin **PI** in diabetics with advanced nephropathy. *J Clin Pathol* 1988;41:929-932.

Van Zanten RAA, van Leeuwen RE, Wilson JHP: Serum procollagen type III N-terminal peptide and laminin PI fragment concentrations in alcoholic liver disease and primary biliary cirrhosis. Clin Chim Acta 1988;77:141-146.

Würz H, Crombach G: Radioimmunoassay of laminin PI in body fluids of pregnant women, patients with gynecological cancer and controls. Tumor Biol 1988;9:37-46.

Gressner AM, Tittor W: Serum concentrations of laminin and aminoterminal propeptide of type III procollagen in relation to the portal venous pressure of fibrotic liver diseases. Clin Chim Acta 1986;16:249-258.

Gressner AM, Tittor W, Kropf J: The predictive value of serum laminin for portal hypertension in chronic liver diseases. Hepatogas-troenterology 1988;35:95-100.

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