Accumulation of Low Molecular Weight Proteins in Patients Treated with Repeated Hemodialysis

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Dear Sir,

Treatment of patients with end stage renal disease (ESRD) with repeated hemodialysis does not prevent the accumulation of peptides and low molecular weight proteins (LMWP) in the plasma of patients [1]. Little is known so far how LMWPs are cleared from plasma in patients with renal failure. The recent findings of β_2 -microglobulin in amyloid deposits in ESRD patients [2] focused the attention on the importance of LMWPs for the pathogenesis of amyloidosis related to prolonged maintenance hemodialysis therapy. We determined the concentrations of acid ribonuclease, alkaline ribonuclease, β_2 -microglobulin and retinol-binding protein and assessed the correlations between concentrations of these proteins in 34 ESRD patients treated with repeated hemodialysis from 3 to 72 months.

Acid and alkaline ribonuclease activity was determined by their enzyme activities [3], and retinol-binding protein concentrations were determined by a radial diffusion method, β_2 -Microglobulin was determined by the EIA Boehringer Enzygnost test.

The obtained results showed, as expected, that serum concentrations of all studied LMWP levels were manifold increased in ESRD patients when compared to healthy controls: the increase was 11-fold for alkaline ribonuclease (2.52 ± 0.66 in ESRD patients vs. 0.23 ± 0.105 in healthy controls); 8.7-fold for the activity of acid ribonuclease (0.297 ± 0.0298 U/l in ESRD patients vs. 0.034 ± 0.0067 in healthy controls); 40-fold for the concentration of retinol-binding protein ($1,820.4 \pm 516.7$ mg/l in ESRD patients vs. 45.0 ± 15 mg/l in healthy controls) and 28-fold for the concentration of β_2 -micro-globulin (51.74 ± 7.90 mg/l in ESRD patients vs. 1.85 ± 0.65 mg/l in healthy controls). The accumulation of the individual LMWPs studied, expressed as the multiple of the mean for the control group, was different. Neither were correlations found between concentrations of the studied proteins, except for activities of acid and alkaline ribonucleases ($r = 0.469$ at $p > 0.05$), nor between concentration levels of studied LMWPs and the time of treatment of patients with maintenance hemodialysis.

The obtained results seem to suggest that in patients with renal failure individual LMWPs are removed from plasma and catabolized by mutually unrelated mechanisms. There is evidence that some amounts of these proteins are removed by the liver [4]. But the rate of liver ingestion of ribonuclease from plasma was only 5% of its renal filtration and catabolism. There is no information on protein composition of ESRD amyloid. Its formation in ESRD

patients maintained on prolonged treatment with hemodialysis shows that at least some of the LMWPs tend to accumulate in tissues producing the amyloid tumors. The recent findings of lysozyme and two other proteins in amyloid-like renal stones [5] suggest that β_2 -microglobulin is only one amongst many small molecular weight glycoproteins which precipitate in amyloid deposits. So far, it is unknown whether the amyloid deposits are produced upon exceeding certain critical protein concentration levels only, or rather some specific mechanisms are to be involved in the process. One could suggest that tissue deposition is just a substitute for renal filtration and catabolism of these proteins, and the effective removal of LMWPs seems to be the only procedure to prevent amyloid deposit formation.

References

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