Noninvasive Diagnosis of Tubular Damage by the Use of Urinary Chondroitin-4-Sulfate/Heparan Sulfate Ratio

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Dear Sir,

The diagnosis of tubular damage by routine methods is very limited. Clinical symptoms are very often rare or absent. The loss of concentration ability, alterations in the acid base balance are not sensitive enough to detect tubular lesions early. Sophisticated methods have been described to diagnose the tubular lesions: enzyme determinations and the quantitation of low molecular weight proteins in urine are some of them. Until now the best method for routine diagnosis is the use of the polyacrylamide gel electrophoresis of native urine. The only disadvantage is that this method gives qualitative results and the sensitivity of the observer's eye presents the semi-quantitative estimation. Scanning of the gels is an appropriate but time-consuming possibility for quantification. This was one of the reasons for developing another noninvasive method which takes less time for quantification. We performed parallelly protein electrophoresis on polyacrylamide gels and acid glycosaminoglycan electrophoresis on cellulose acetate in order to compare the newly developed acid glycosaminoglycan (AGAG) separation to the standardized protein gels.

20 patients with established diagnosis of tubulointerstitial nephritis (TIN) were compared to 20 healthy persons and 20 patients with glomerular diseases. The polyacrylamide gel electrophoresis (PAGE) was run on a standard electrophoresis apparatus (Pharmacia/Uppsala) on 8% SDS-polyacrylamide gel run for 6 h at 135 mA at room temperature and stained with Coomassie Blue. Electrophoresis on cellulose acetate for AGAG was performed after the method of Hopwood and Harrison [1]. The ratio of quantified chondroitin-4-sulfate and heparan sulfate was calculated. Healthy subjects showed a mean CS/HS ratio of 3.8 ± 0.4 . Patients with glomerular diseases showed values of 3.7 ± 0.3 and patients with TIN showed a low ratio of means = 1.5 ± 0.5 .

All patients with TIN and a low CS/HS ratio showed on polyacrylamide gel electrophoresis the tubular pattern of low molecular weight proteins.

The normal distribution of AGAG along the nephron shows the predominant presence in the proximal and distal tubular system. In the glomerulus only the glomerular basement membrane contains traces of heparan sulfate covalently linked to collagen type IV [2].

AGAG are not filtered into urine from serum which means that urinary AGAG are derived from the tubular system. The presence of acid glycosaminoglycans in urine thus indicates damage of this part of the nephron.

Though also the urinary total AGAG excretion is higher in patients with tubular damage, this is not a specific finding which can be used for diagnosis, as in some other instances as, e.g. in diabetes mellitus the concentration of total AGAG can be increased. The electrophoretic separation of chondroitin-4-sulfate and heparan sulfate makes the test valuable for the evaluation

of tubular lesions. Thus, the CS/HS quotient can be used as an alternative, quick, easy, semiquantitative corresponding method for /to protein electrophoresis on polyacrylamide gel.

References

Hopwood, J.; Harrison, J.R.: *Analyt. Biochem.* 119: 120–127 (1982).