Increased Urinary Excretion of Urine Protein 1 Induced by L-Arginine Monohydrochloride

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β 2-microglobulin (μ m), and albumin. N-ace-tyl- β -D-glucosaminidase (NAG) activity was determined by a standard assay kit (Shionogi Co., Ltd., Osaka). Urinary arginine concentration was determined using an amino acid analyzer (Hitachi Amino Acid Analyzer, Model 835-50-501, Tokyo).

Administration of 0.25 g/kg of arginine successfully blocked the reabsorption of low molecular weight proteins in the proximal

Dear Sir,

Urine protein 1 (UPI) has a molecular weight of 14 kDa and consists of a homodimer with 7 kDa subunits joined by disulfide bonds [1]; it is quite stable in the urine. Urinary level of UPI in normal males is about five times higher than in normal females, though serum concentration shows no significant differences associated with sex. The precise mechanism accounting for this sex-related difference remains obscure [2], however, UPI, like other low molecular weight proteins, should be catabolized in the kidney. Yet, the average urinary excretion in spot urine of cadmium workers did not differ significantly from that of control workers who did not work with cadmium [3]. Male sex could prevent a minute elevation of UPI from being detected, because of the high background level from other sources.

We recently purified UPI protein from urine, prepared a monoclonal antibody, and developed a preliminary enzyme-linked immunosorbent assay (ELISA) [4]. An arginine infusion test using this assay was conducted on normal individuals to confirm that the renal tubules are the catabolic site of UPI. The goal was to increase urinary excretion of UPI above the background level.

In this test, L-arginine monohydrochloride (Morishita, Co., Ltd., Osaka) was infused in 6 male subjects for 30 min. Urine was collected every 5-10 min, and the present ELISA was used to measure UPI concentration. For comparison, a double antibody radioimmunoassay [5] and a latex agglutination photometric assay [6] were used to simultaneously measure α microglobulin (μ m),

Fig. 1. Increased urinary excretion of UPI closely parallels levels of α_1 -m and β_2 -m induced by the infusion of L-arginine monohydrochloride. renal tubules in all cases, probably with little functional change in the renal glomeruli. A typical case is shown in figure 1. Urinary excretion of UPI increased markedly with increase in level of urinary arginine but decreased as arginine levels fell. Maximum total excretion, 5,818 μ g, occurred 60 min after infusion. This is about 100 times higher than the preinfusion level. Elevation of UPI was accompanied by similar increases in levels of

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α_1 -m and β_2 -m, but not in level of albumin or NAG, which remained almost constant throughout the study. Average UPI concentration in serum, measured 7 times during the study, was $11.06 \pm 0.89 \mu\text{g/l}$ (mean $\pm$ 1 SD); coefficient of variation, 8.1%.

These experimental data strongly suggest that UPI is filtered in the glomeruli and catabolized in the renal proximal tubules, as are other proteins of low molecular weight. We recently confirmed our previous findings of a sex-related difference in concentration of this protein in normal urine: the level in males was about 10 times higher than in females (unpublished data). A previous study also demonstrated sex-related differences in urinary α_1 -m [6]. A possible common sex-related mechanism may, in fact, account for the handling of low molecular weight proteins in the kidney; but, since α_1 -m concentration was only 2 times higher in males than in females, the observed sex-related differences in UPI concentration is so prominent that the possibility of the existence of another mechanism requires investigation. The absence of any relevant sex-related difference in the serum rules out the participation of prerenal effects. Thus, excretion of UPI, either from the kidney or genitourinary organs, would appear to be the most likely explanation of this phenomenon.

This study clearly showed plasma to be a source of urinary UPI, though it neither confirmed nor ruled out other possible sources. In a study now in progress, we will attempt to use immunochemical and histologic findings to elucidate this sex-related difference by identifying the site of excretion of UPI.

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