Sex Differences in Urinary Alpha-1-Microglobulin Value in Normal Individuals

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Dear Sir,

α₁-Microglobulin (α₁m), a brown-colored low-molecular weight (LMW) glycoprotein of 30 kD, has unique physicochemical properties and suppresses leukocyte migration [1,2]. Two molecular forms are found at varied ratios in serum: one is a free form (LMW α₁m); the other is an IgA-bound form (IgA-α₁m complex) [3]. Because of the selectivity of the glomerular basement membrane, α₁m found in urine is LMW α₁m. Clinical studies indicate that the main catabolic site for LMW α₁m is in the renal proximal tubules [4–6].

Another reliable double-antibody radioimmunoassay for α₁m, based on a previously established radioimmunoassay method [7], has been developed recently. Its sensitivity is 20 ng/ml, and the assay time when undiluted samples are used is only 2 h. In the course of evaluating this assay, we coincidentally discovered a sex-related difference in the α₁m value in normal urine. Thus, we investigated it in some detail.

Serum and 24-hour stored urine specimens obtained from 17 normal males and females ranging from 20 to 30 years of age were paired. The quantity of α₁m excreted during a 24-hour period was greater in males than in females (p < 0.01; table 1). On a simple anatomical basis, the correction for body surface area gave only an 18% increase in the α₁m level in females, leaving an average discrepancy of 1.36 mg of excreted α₁m per day. Similar results were obtained when kidney weight was corrected for, leaving about a 7% increase, indicating that the differences are accounted for by physiological variation. Prefiltered load of serum LMW α₁m on the kidneys was analyzed chromatographically. Each pooled-serum sample was diluted five times with 0.05 M phosphate buffer (pH 7.2), gel-filtered on Superose 6 and Superose 12 using FPLC system (Pharmacia, Sweden), and the concentration of α₁m in each fraction was measured by RIA. Fractionation had good reproducibility, and recovery from 80 to 85% when those fractions in which the α₁m concentration was below the minimum required by the test were excluded. In accordance with previously reported results [3], serum α₁m centered...
around two main peaks, representing LMW $\alpha'\text{m}$ and IgA-$\alpha'\text{m}$ complex. Of the total $\alpha'\text{m}$ fractions assayed, the LMW $\alpha'\text{m}$ fractions accounted for 37.3% of the total in males, and 41.1% in females. Despite significant differences in serum concentration ($p < 0.05$), the absolute quantity of LMW $\alpha'\text{m}$

Table 1. Differences in urinary $\alpha'\text{-m}$ values between males and females

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<th>Males</th>
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<td>$\alpha'\text{-m}$</td>
<td>37.3%</td>
<td>41.1%</td>
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Table 2. Differences in $\alpha'\text{-m}$ values in spot urine from 6- to 7-year-old school children and from 13- to 15-year-old junior high-school students

was almost the same in males and females. Since the 24-hour creatinine clearance was almost the same, the prefilttered load on the kidneys varied little. These facts appeared to indicate that differences in the urinary value reflect a difference in the physiological handling of $\alpha'\text{m}$ by the kidneys.

A further clinical study was carried out to measure the $\alpha'\text{m}$ value in spot urine collected at medical check-ups in an elementary school and a junior high school. No sex-related difference was found in the $\alpha'\text{m}$ concentration in school children aged 6–8 years. However, a significant difference ($p < 0.05$) in the concentration was found in samples obtained from high-school students 13–15 years old (table 2). This may indicate that a sex-related physiological development plays an important role in the appearance of this difference, and that hormonal effects on the renal handling of $\alpha'\text{m}$ should be further elucidated.

As compared with $\beta_2$-microglobulin and retinol-binding protein, $\alpha'\text{m}$ is present in normal urine at relatively high concentrations and stable in urine of low pH [7]. Furthermore, its urinary level is less influenced by pre-renal variation than that of other LMW proteins. These characteristics of $\alpha'\text{m}$ explain the sex-related differences in the $\alpha'\text{m}$ concentration in urine obtained from normal adults.

References