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

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Dear Sir,

αm Microglobulin (αm), 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 αm); the other is an IgA-bound form (IgA-αm complex) [3]. Because of the selectivity of the glomerular basement membrane, αm found in urine is LMW αm. Clinical studies indicate that the main catabolic site for LMW αm is in the renal proximal tubules [4–6]. Another reliable double-antibody radioimmunoassay for αm, 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 αm 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 αm 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 αm level in females, leaving an average discrepancy of 1.36 mg of excreted αm 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 α,-m 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 αm in each fraction was measured by RIA. Fractionation had good reproducibility, and recovery from 80 to 85% when those fractions in which the αm concentration was below the minimum required by the test were excluded. In accordance with previously reported results [3], serum αm centered
around two main peaks, representing LMW $\alpha_{\text{rm}}$ and IgA-$\alpha_{\text{rm}}$ complex. Of the total $\alpha_{\text{rm}}$ fractions assayed, the LMW $\alpha_{\text{rm}}$-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 $\alpha_{\text{rm}}$

Table 1. Differences in urinary $\alpha_{\text{rm}}$ values between males and females

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<th>Males</th>
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<td>%</td>
<td>37.3%</td>
<td>41.1%</td>
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Table 2. Differences in $\alpha_{\text{rm}}$ 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 prefiltered 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 $\alpha_{\text{rm}}$ by the kidneys.

A further clinical study was carried out to measure the $\alpha_{\text{rm}}$ 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 $\alpha_{\text{rm}}$ 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 $\alpha_{\text{rm}}$ should be further elucidated.

As compared with $\beta_2$-microglobulin and retinol-binding protein, $\alpha_{\text{rm}}$ 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 $\alpha_{\text{rm}}$ explain the sex-related differences in the $\alpha_{\text{rm}}$ concentration in urine obtained from normal adults.

References