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

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Dear Sir,

αₐᵢₘ, 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 αₐᵢₘ); the other is an IgA-bound form (IgA-αₐᵢₘ complex) [3]. Because of the selectivity of the glomerular basement membrane, αₐᵢₘ found in urine is LMW αₐᵢₘ. Clinical studies indicate that the main catabolic site for LMW αₐᵢₘ is in the renal proximal tubules [4–6].

Another reliable double-antibody radioimmunoassay for αₐᵢₘ, 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 αₐᵢₘ 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 αₐᵢₘ 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 αₐᵢₘ level in females, leaving an average discrepancy of 1.36 mg of excreted αₐᵢₘ 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 αₐᵢₘ 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 αₐᵢₘ in each fraction was measured by RIA. Fractionation had good reproducibility, and recovery from 80 to 85% when those fractions in which the αₐᵢₘ concentration was below the minimum required by the test were excluded. In accordance with previously reported results [3], serum αₐᵢₘ centered...
around two main peaks, representing LMW αm and IgA-αm complex. Of the total αm fractions assayed, the LMW αm 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 αm

Table 1. Differences in urinary α-m values between males and females

Table 2. Differences in α-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 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 αm by the kidneys.

A further clinical study was carried out to measure the αm 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 αm 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 αm should be further elucidated.

As compared with β2-microglobulin and retinol-binding protein, αm 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 αm explain the sex-related differences in the αm concentration in urine obtained from normal adults.

References


