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

Y.	Yoshihisa	Itoh
T.	Tadashi	Kawai

Department of Clinical Pathology, Jichi Medical School, Minami-Kawachi-Machi, Tochigi, Japan

Yoshihisa Itoh, Department of Clinical Pathology, Jichi Medical School, Minami-Kawachi-Machi, Tochigi-Ken 329-04 (Japan)

Dear Sir,

α_1 -Microglobulin (α_1 m), 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 α_1 m); the other is an IgA-bound form (IgA- α_1 m complex) [3]. Because of the selectivity of the glomerular basement membrane, α_1 m found in urine is LMW α_1 m. Clinical studies indicate that the main catabolic site for LMW α_1 -m is in the renal proximal tubules [4-6].

Another reliable double-antibody radioimmunoassay for α_1 m, 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 α_1 m 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 α_1 m 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 α_1 m level in females, leaving an average discrepancy of 1,36 mg of excreted α_1 m per day. Similar

Supported partly by a grant-in-aid from the Ministry of Education for Scientific Research (Project No. 62480435) and a research grant from the Tochigi Association for Preventive Nephrology (1988). A radioimmunoassay kit (AMG RIA) was supplied from Shionogi & Co., Ltd. (Osaka, Japan). The authors are grateful to the staff of the Serological Diagnostic Section in the Department of Clinical Laboratory, Jichi Medical School, and Kanagawa Yobo Igaku Kyokai (Yokohama, Japan) for supplying sera.

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_1 -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 α_1 -m in each fraction was measured by RIA. Fractionation had good reproducibility, and recovery from 80 to 85% when those fractions in which the α_1 m concentration was below the minimum required by the test were excluded. In accordance with previously reported results [3], serum α_1 m centered

around two main peaks, representing LMW α_2 -m and IgA- α_2 -m complex. Of the total α_2 -m fractions assayed, the LMW α_2 -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 α_2 -m

Table 1. Differences in urinary α_2 -m values between males and females

122

Itoh/Kawai

Table 2. Differences in α_2 -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 α_2 -m by the kidneys.

A further clinical study was carried out to measure the α_2 -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 α_2 -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 α_2 -m should be further elucidated.

As compared with β_2 -microglobulin and retinol-binding protein, α_2 -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 α_2 -m explain the sex-related differences in the α_2 -m concentration in urine obtained from normal adults.

References

- Ekström, B.; Peterson, P.A.; Berggård, I.: A urinary and oracid acid glycoprotein of low molecular weight: Isolation and some properties. *Biochem. biophys. Res. Commun.* 5: 1427–1433 (1975).
- Åkerström, B.; Lögdberg, L.: α_2 -Microglobulin glycopeptides inhibit antigen-specific stimulation of human peripheral blood leukocytes. *Scand. J. Immunol.* 20:559–563 (1984).
- Vincent, C; Bouic, P.; Revillard, J.P.: Complexes of α_2 -micro-globulin and monomeric IgA in multiple myeloma and normal sera. *Mol. Immunol.* 22:663–673 (1985).
- Itoh, Y.; Enomoto, H.; Kawai, T.: α_2 -Microglobulin in cadmium poisoning. *Nephron* 55:211–212 (1983).
- Kusano, E.; Suzuki, M.; Asano, Y.; Itoh, Y.; Takagi, K.; Kawai, T.: Human α_2 -microglobulin and its relationship to renal function. *Nephron* 47:320–324(1985).
- Itoh, Y.; Cooper, E.H.; Stavlienic, A.; Cvoriscec, D.: Urinary α_2 -microglobulin in surveys of Balkan endemic nephropathy. *Biomédecine* 4:341–344 (1986).
- Itoh, Y.; Nishino, H.; Enomoto, H.; Kawai, T.: A double antibody radioimmunoassay for human α_2 -microglobulin. *Clin. Chim. Acta* 755:221–226 (1986).