α_1 -Microglobulin in Cadmium Poisoning

Y.		Itoh
H.		Enomoto
T.		Kawai

Department of Clinical Pathology, Jichi Medical School, Tochigi-Ken, Japan

Y. Itoh, MD, Department of Clinical Pathology, Jichi Medical School, Minami-Kawachi-Machi, Tochigi, 329-04 (Japan)

Dear Sir,

Exposure to cadmium causes renal tubular damage resulting in the increased excretion of low molecular weight proteins (LMP) in urine, but not affecting its serum level in early stage [1]. The quantitative determination of serum and urinary LMP has been, therefore, regarded as a good laboratory test for this disorder. α_1 -Microglobulin (α_1 -m) is another low molecular weight protein with a molecular weight of 33,000 daltons, could be probably handled like other LMP in renal tubules and would be expected to be useful as a new indicator of renal tubular function [2]. The present study was thus carried out to determine the variation of serum and urinary α_1 -m in patients with cadmium poisoning in an attempt to show the clinical significance of this protein in renal tubular disorders. Sera and urine were obtained from 9 patients who had been engaged in welding silver solder, and exposed to cadmium fumes for the past 4–23 years. Upon this discovery the working environments were improved, and they have been prevented from re-exposure for the past 5 years. The level of cadmium in urine is, however, still slightly elevated, ranging from 7.7 to 21 $\mu\text{g/l}$ (normal range; 0.1–8.0 $\mu\text{g/l}$). Sera and urine as controls were collected from 10 age- and sex-matched healthy adults. As soon as samples were obtained, α_1 -m in serum was measured by single radial immunodiffusion (SRID; Mancini method [3]), while that in urine was determined by enzyme immunoassay (EIA) of sandwich methods [4]. The sensitivity of SRID and EIA was 6 mg/l and 5 ng/ml, respectively and a good correlation was demonstrated between two assays ($r = 0.94$) [5]. In renal tubular disorders many kinds of constituents are increasingly excreted in the urine, and may affect EIA. Recovery tests were at first carried out by adding a known amount of purified α_1 -m to the patients urine. Recovery rates were $99.3 \pm 6.3\%$ (mean ± 1 SD) thus ruling out an effect of patients urine on EIA. On the determination of α_1 -m in con-

Fig. 1. Variation of serum and urinary α_1 -microglobulin in patients with cadmium poisoning.
= Normal range.

trols, the serum level was 18.2 ± 4.5 mg/l (mean ± 1 SD), and daily output in urine was 2.15 ± 0.72 mg. In patients serum α_1 -m concentrations were almost within the normal range (17.5–24.3 mg/l). In contrast, daily output was elevated with wide variations, reaching up to 93.2 mg/l (fig. 1). These results, showing normal serum level but increased urinary excretion of this protein, were due to renal tubular dysfunction in this disorder, and clinically demonstrated that α_1 -m is reabsorbed or catabolized in renal tubules. In

severe and/or advanced cases of cadmium poisoning the glomeruli are also affected, reducing the glomerular filtration rate (GFR) [6]. We have previously reported that the serum α i-m could more sensitively and specifically detect decreased GFR than β 2-microglobulin or creatinine because of its larger molecular size, more negative charge, and its physicochemical properties [6]. The determination of both serum and urinary α i-m can be, therefore, of great help in the more precise analysis of cadmium nephro-toxicity.

Ekström, B.; Berggard, I.: Human α i-microglobulin. *J. biol. Chem.* 252: 8048–8057 (1977).

Takagi, K.; Kin, K.; Itoh, Y.; Enomoto, H.; Kawai, T.: Human α i-microglobulin in various body fluids. *J. clin. Path.* 33: 786–791 (1980).

Takagi, K.; Koyamaishi, Y.; Itoh, Y.; Enomoto, H.; Kawai, T.: Enzyme-immunoassay of human α i-microglobulin. *Jap. J. clin. Chem.* 70:30–40(1981).

Itoh, Y.; Takagi, K.: Human α i-microglobulin. *Jap. J.clin.Path.*, (in press).

Itoh, Y.; Enomoto, H.; Takagi, K.; T. Kawai.: Clinical usefulness of serum α i-microglobulin as a sensitive indicator for renal insufficiency. *Nephron* 33: 69–70 (1983).

Acknowledgments

This study was supported by grants in aid for Scientific Research (Special Research Project on Environmental Science) from the Ministry of Education, Japan. Samples were supplied by courtesy of Kanagawa Health Service Association.

References

Piscator, M.; Petterson, B.: Chronic cadmium poisoning – Diagnosis and prevention. *Clinical chemistry and toxicology of metals*, pp. 143–155 (Elsevier/North-Holland Biochemical Press, Amsterdam 1977).