High Urinary Levels of Human Growth Hormone in Children with Renal Tubular Dysfunction

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Dear Sir,

Serum proteins with a molecular weight of less than 50,000 daltons pass freely through the renal glomeruli, but in normal individuals the filtered protein is almost completely reabsorbed by the proximal tubules. The major condition for low molecular weight proteinuria is impairment of proximal tubular protein uptake, such as occurs in Lowe syndrome and Fanconi's syndrome, but the protein absorption mechanism is not clear. The concentration of these proteins in endocytosomal vesicles in tubular cells is greater than the concentration in tubular fluid [1]. A certain degree of selectivity for uptake takes place, and it must depend on the charge or molecular size [2]. However, it is uncertain whether there are specific receptors on the luminal membrane. Among these low molecular weight proteins, peptide hormones [for example, growth hormone (HGH), insulin, etc.], immunoproteins [for example, β 2-microglobulin (β 2-MG)], enzymes (for example, lysozyme) are important. The estimate of the mean HGH production in normal subjects ranges from 500 to 875 μ g/day, and about 0.01–0.001% of that amount is excreted in the urine [3]. Thus, the concentration of HGH in normal urine is very low indeed. Hashida et al. [4] reported levels of HGH in urine determined by a highly specific and sensitive sandwich enzyme immunoassay. Urinary excretion of HGH was also studied in normal children, and it has been suggested that this technique might be useful, not only for the diagnosis of acromegaly, but to detect renal tubular dysfunction [6].

We studied urine HGH and β 2-MG in children with renal dysfunction. This study included 205 normal controls (age 3–12 years), 12 children with renal tubular dysfunctions (age 5–15 years) and 18 children with nephrotic syndrome (age 3–18 years). Five children with renal dysfunction had Lowe syndrome, 5 had Fanconi's

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Fig. 1. Urinary HGH levels: a= Normal controls (3–5 years); b= nephrotic syndrome; c= tubular dysfunction; Δ= asymptomatic low molecular weight proteinuria.

syndrome and 2 had asymptomatic low molecular weight proteinuria. Using the sandwich immunoassay, urine HGH levels in normal children were found to be 13.8 ± 8.8 pg/mg creatinine (cr) in males and 16.7 ± 9.4 pg/mg cr in females at ages 3–5 years, 12.9 ± 9.1 pg/ mg cr in males and 14.7 ± 10.6 pg/mg cr in females at ages 6–8 years, and 15.5 ± 8.99 pg/mg cr in males and 15.8 ± 10.09 pg/mg cr in females at ages 9–12 years. In children with tubular dysfunction, urine HGH levels were significantly higher, ranging from 8.5×10^2 to 2.5×10^5 pg/mg cr (3.29×10^2 – 3.73×10^4 pg/ml; fig. 1). HGH levels in children with nephrotic syndrome were also elevated (3.6 to 2.4×10^2 pg/mg cr). Urine β 2-MG levels in children with renal tubular dysfunction ranged from 6.8×10 to 1.2×10^5 μ g/l. The assay method for β 2-MG was a radioimmunoassay by the double-antibody

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method (Daiichi Radioisotope Co., Ltd.). We noted a close correlation between urine HGH and β 2-MG levels in these patients (correlation coefficient $r = 0.69$, $p < 0.05$). Similarly, Kato et al. [5] reported a good correlation in renal disease.

The fact that there is a good correlation between the β 2-MG level and the HGH level demonstrates that the measurement of HGH in urine is a very useful marker of renal tubular dysfunction.

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