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Urinary mineral excretion among normal Taiwanese children

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Abstract. Prompted by a large population of children with renal stones seen in 20 of our country's teaching hospitals over the past 10 years, this study of urinary mineral excretion in normal children was performed. Fasting urine from 1,072 normal Taiwanese school children and 24-h urine collections from 125 children separated into three age groups were analysed for calcium (Ca), phosphate, magnesium (Mg), uric acid, sodium (Na) and creatinine (Cr). Fasting Ca/Cr ratios were not different between the sexes. Ca/Cr ratios were higher in the 17- to 18-year age group as were 24-h urinary Ca excretions. Urinary Mg/Cr ratios were higher in girls than boys and 24-h urinary Mg excretion was highest in the younger age groups. Urinary Mg excretion in Taiwanese children is 54%–86% lower than previously reported in Caucasian children. Both uric acid/Cr ratios and 24-h urinary uric acid excretion were highest in the youngest children. Urinary Na/Cr ratios and 24-h urinary Na excretion were higher in the two younger age groups. There was no correlation between 24-h urinary Ca and Na excretion.

Key words: Urinary mineral excretion – Urolithiasis – Risk factors

Introduction

Promoters of calcium urolithiasis in children include oxalate, uric acid and calcium (Ca). Inhibitors of crystalluria include citrate, magnesium (Mg), glycosaminoglycans and pyrophosphates [1, 2]. Excess or deficient urinary excretion of these constituents, in addition to urine pH and environmental temperature, may contribute to the formation of renal stones [3, 4].

The investigation of disorders of mineral metabolism in children is dependent upon comparing the urinary excretion of certain minerals with normal reference values. Since normal values for urinary mineral excretion in Taiwanese children were not available, we performed this study of mineral excretion in normal Taiwanese school children.

Methods

Normal students (1,072) from 7 to 18 years of age were randomly selected following prior informed parental consent and assent from the children. All students were subjected to physical examination and measurement of body weight, blood pressure and vital signs; Urinalysis by dipstick and routine serum biochemical analysis were also performed. Students were excluded from the study if any evidence of acute or chronic illness was detected. Prior to the study, 15 students were found to have a family history of renal stones by questionnaire (4 grandparents, 6 parents, 3 uncles and 2 siblings).

Due to the complexity of performing 24-h urine collections in all 1,072 students, 125 students in three age groups (7–8, 12–13 and 17–18 years) were selected for the collection of 24-h urine samples. These age groups were representative of elementary, junior high-school and senior high-school. To insure completeness of collections, students, teachers and their parents were given detailed instructions on the technique of timed urine collections. Incomplete or inaccurately timed urine samples were determined by careful review of the details and timing of urine collections with parents, teachers and students. Furthermore, 24-h urinary creatinine (Cr) excretion factored by weight was utilized to assess the completeness of urine collection. Only 3 24-h urine samples had to be discarded because of inaccurate collection using these criteria. The volume and pH of all urine samples was measured together with Cr, Ca, phosphorus, sodium (Na), potassium, Mg and uric acid. Ca was measured by the *O*-cresolphthalein complexone spectrophotometric method [5], phosphate by the ammonium molybdate reduction method [6], Mg by atomic absorption spectrophotometry [7], Cr by a kinetic assay [8], uric acid by the uricase peroxide method [9] and pH by the ABL-3 radiometer.

The study was approved by the Committee for Human Research of National Defense Medical Center, Taipei, Taiwan, Republic of China.

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Table 1. Fasting urinary Ca/Cr, P/Cr, Mg/Cr, uric acid/Cr and Na/Cr ratios

	All ($n = 1072$)		Boys ($n = 569$)		Girls ($n = 503$)		
	Mean ± SD	95th%	Mean ± SD	95th%	Mean ± SD	95th%	P
Ca/Cr (mg/mg)	0.068±0.057	0.171	0.069±0.062	0.171	0.067±0.051	0.172	NS
P/Cr (mg/mg)	0.321±0.177	0.63	0.318±0.19	0.634	0.325±0.159	0.626	NS
Mg/Cr (mg/mg)	0.020±0.012	0.043	0.019±0.011	0.039	0.022±0.013	0.046	<0.01
Uric acid/Cr (mg/mg)	0.065±0.062	0.19	0.066±0.062	0.197	0.063±0.059	0.188	NS
Na/Cr (mg/mg)	2.015±1.350	4.651	2.047±1.393	4.788	1.969±1.299	4.618	NS

NS, Not significant; Ca, calcium; Cr, creatinine; P, phosphate; Mg, magnesium; Na, sodium

Table 2. Fasting urinary Ca/Cr, P/Cr, Mg/Cr, uric acid/Cr and Na/Cr ratios

Age	7–10 years ($n = 345$)		11–14 years ($n = 340$)		15–18 years ($n = 387$)	
	Mean ± SD	95th%	Mean ± SD	95th%	Mean ± SD	95th%
Ca/Cr (mg/mg)	0.055±0.044	0.142	0.044±0.038	0.101	0.106±0.066*	0.213
P/Cr (mg/mg)	0.439±0.162**	0.75	0.308±0.134***	0.595	0.218±0.159	0.379
Mg/Cr (mg/mg)	0.027±0.015***	0.0521	0.02 ±0.001***	0.041	0.015±0.007	0.03
Uric acid/Cr (mg/mg)	0.110±0.079**	0.238	0.047±0.031	0.099	0.037±0.034	0.096
Na/Cr (mg/mg)	2.974±1.587***	5.879	1.725±1.002***	3.728	1.348±0.703	2.571

*P <0.05 vs. 7–10 years and 11–14 years;
**P <0.05 vs. 11–14 years and 15–18 years;
***P <0.05 vs. 15–18 years

Table 3. Urinary Ca, P, Mg, uric acid, Na and Cr excretion (24 h)

Age	7–18 years ($n = 125$)		7–8 years ($n = 44$)		12–13 years ($n = 35$)		17–18 years ($n = 46$)	
	Mean ± SD	95th%	Mean ± SD	95th%	Mean ± SD	95th%	Mean ± SD	95th%
Ca (mg/kg)	2.065±1.211	4.51	1.86 ±1.16	4.15	1.68 ±1.06	4.21	2.57±1.23*	5.03
P (mg/kg)	12.46±4.63	20.86	15.87±4.03*[2]	22.74	13.75±3.05*[3]	18.87	8.13±2.2	12.44
Mg (mg/kg)	0.464±0.243	0.954	0.510±0.255*[3]	0.948	0.596±0.264*[3]	1.053	0.315±0.09	0.485
Uric acid (mg/kg)	3.194±1.787	6.891	3.72 ±2.12*[4]	8.37	2.22 ±1.22	5.15	3.43 ±1.51	6.98
Na (mEq/kg)	2.18 ±0.76	3.52	2.22 ±0.61*[3]	3.39	2.69 ±0.84*[3]	4.48	1.75 ±0.54	3.01
Cr (mg/kg)	21.46±3.32	25.65	18.05±2.19	22.52	21.63±2.03*[5]	24.93	24.66±0.87*	25.78

*P <0.05 vs. 7–8 years and 12–13 years; *[2]P <0.05 vs. 12–13 years and 17–18 years; *[3]P <0.05 vs. 17–18 yeras; *[4]P <0.05 vs. 12–13 years; *[5]P <0.05 vs. 7–8 years

Statistical analysis. Significance of difference between the sexes was evaluated by Student's t-test with P <0.05 considered significant, differences among age groups by analysis of variance and Scheffe's test and correlation coefficients by Pearson's method.

Results

In the past 30 years, 9,936 patients (adults and children) with renal stones have been followed in the urology clinic of the National Taiwan University Hospital (NTUH). The ratio of males to females was 2.5:1. Only 625 (6.3%) of these patients were less than 20 years of age and 105 (1%) were less than 16 years of age. An analysis of 1,200 renal stones from 9,936 stone patients at NTUH urology clinic revealed that 72% were Ca oxalate, 10% were Ca phosphate and 18% Mg ammonium sulphate or struvite.

Ca excretion

Fasting urinary Ca/Cr ratios for 569 boys, 503 girls and all study subjects combined are shown in Table 1 and for three separate age groups in Table 2. Urinary Ca/Cr ratios were not different between the sexes and were significantly higher in 15- to 18-year-old subjects; 24-h urinary calcium excretion (Table 3) was also significantly higher in 17- to 18-year-old subjects.

Phosphate excretion

Fasting urinary phosphate/Cr ratios for all children (Table 1) and for separate age groups (Table 2) showed a progressive decrease with increasing age. The same trend was observed with 24-h urinary phosphate excretion (Table 3).

Mg excretion

Fasting urinary Mg/Cr ratios (Table 1) were significantly higher in girls than boys and were significantly higher in the two younger age groups than in 17- to 18-year-old children (Table 2). Similarly, 24-h urinary Mg excretion was significantly higher in the two younger age groups (Table 3).

Uric acid excretion

Fasting urinary uric acid/Cr ratios were not different between the sexes (Table 1). Both fasting uric acid/Cr ratios (Table 2) and 24-h urinary excretion of uric acid (Table 3) were significantly higher in younger children than in the two older age groups.

Na excretion

Fasting urinary Na/Cr ratios were not different between the sexes (Table 1). Both fasting urinary Na/Cr ratios (Table 2) and 24-h urinary Na excretions were significantly higher (Table 3) in both younger age groups compared with the older age group. There was no correlation between 24-h urinary Ca and urinary Na excretion ($r = 0.04139$, $P = 0.6481$).

Discussion

Some urinary risk factors known to contribute to stone formation are urine pH and volume and the concentrations of Ca, Na, uric acid, citrate, Mg and oxalate [2]. Variations in these risk factors may occur with age, gender, dietary and fluid intake, environment, urinary tract pathology and various metabolic disorders [10]. Excess or deficient excretion of some of these urinary constituents may lead to abnormal crystal formation and subsequently to stone formation.

In 15- to 18-year-old children fasting urinary Ca/Cr ratios and 24-h urinary Ca excretion were statistically greater than in the two younger age groups. Increased urinary Ca excretions in the 17- to 18-year-old children may represent a potential risk factor for the increased prevalence of renal stone formation in Taiwanese children 16–20 years of age. Of interest, a dietary survey in 1980 among junior high-school students in Taipei [11] revealed that the daily Ca intake was 64% of the recommended daily allowance (RDA) in girls and 83% of RDA in boys. A more recent survey [12] of 552 households in 12 Taiwan districts has again demonstrated that daily Ca intake is still only 81.9% of RDA. In each of our arbitrarily assigned age groups, especially the 17–18 age group, the 95th percentile for 24-h urinary Ca excretion was increased above the normal excretion of 4 mg/kg per day quoted in other population studies [13–15]. Urinary Na excretion does not appear to be a factor in the increased urinary Ca excretion in the older children, since Na excretion was lowest in 17- to 18-year-old children who had the highest Ca excretion. Whether this unexpected finding relates to a different Ca requirement, increased gastrointestinal absorption or decreased renal resorption of Ca in the 17–18 age group cannot be answered by this study. Increased Ca excretion in this age group may also be related to low Mg excretion.

Fasting Mg/Cr ratios and 24-h urinary Mg excretions were significantly higher in the 7–10 and 11–14 age groups when compared with the 15–18 age group. Urinary Mg/Cr ratios also were higher in girls than in boys. However, 24-h urinary Mg excretion and fasting Mg/Cr ratios are 54%–86% lower in Taiwanese children at all ages when compared with Mg excretion in Caucasian children [16–18]. The role of Mg as an inhibitor of urolithiasis is an unsettled issue. Urinary Mg excretion in patients with Ca oxalate stones has been shown to be lower [19], not different [20] or lower only in females [21]. To our knowledge no studies to date have addressed the specific question of low urinary Mg excretion relative to renal stone formation in pediatric populations. Further investigation of dietary fibre, protein, Ca, Na and Mg intake and urinary factors such as urinary citrate and oxalate excretion, which may affect Mg excretion in Taiwanese children, is indicated.

Fasting uric acid/Cr ratios in the 7–10 age group and 24-h uric acid excretion in the 7–8 age group were significantly increased when compared with the two older age groups. This decline in uric acid excretion with age has been previously described in Caucasian children [22].

Based upon the findings in this study, we speculate that the high urinary Ca excretion and low urinary Mg excretion in the 17- to 18-year-old group may be potential risk factors explaining the increased prevalence of urolithiasis in Taiwanese children 16–20 years of age.

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Literature abstracts

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A missense mutation in the hypoxanthine phosphoribosyltransferase gene in a pediatric patient with hyperuricemia

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We have identified a mutation in the gene coding for the enzyme hypoxanthine phosphoribosyltransferase in a pediatric patient with hyperuricemia and nephrolithiasis. The mutation is a nucleotide substitution causing an amino acid substitution in the hypoxanthine phosphoribosyltransferase protein. In this patient, fibroblasts but not lymphocytes showed resistance to 6-thioguanine, and reduced enzyme activity was detected in lymphocytes. These results are consistent with the intermediary phenotype associated with partial hypoxanthine phosphoribosyltransferase enzyme deficiency. Altogether, six males in this family suffered from hyperuricemic symptoms, and small differences in phenotype were seen.

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Effect of dietary fish oil on renal function and rejection in cyclosporine-treated recipients of renal transplants

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Background. Dietary fish oil exerts effects on renal hemodynamics and the immune response that may benefit renal-transplant recipients treated with cyclosporine. To evaluate this possibility, we studied the effect of fish oil on renal function, blood pressure, and the incidence of acute rejection episodes in cyclosporine-treated recipients of renal transplants.

Methods. In a randomized, double-blind trial, 33 recipients of first cadaveric kidney transplants who were treated with cyclosporine and prednisolone ingested 6 g of fish oil daily during the first postoperative year (the fish-oil group), whereas another 33 renal-graft recipients treated with cyclosporine and prednisolone ingested 6 g of coconut oil daily for three months, after which time it was stopped (the control group).

Results. One year after transplantation, the fish-oil group had higher median values than the controls for glomerular filtration rate (53 vs. 40 ml per minute per 1.73 m^2, P = 0.038) and effective renal plasma flow (214 vs. 178 ml per minute per 1.73 m^2, P = 0.023) and lower mean arterial pressure (103 vs. 118 mm Hg, P = 0.0011). The cyclosporine doses in the two groups were similar. The cumulative number of rejection episodes was 20 in the controls, as compared with 8 in the fish-oil group (P = 0.029). Oneyear graft survival also tended to be better in the fish-oil group (97 vs. 84 percent, P = 0.097).

Conclusions. The daily administration of 6 g of fish oil during the first postoperative year has a beneficial effect on renal hemodynamics and blood pressure in renal transplant recipients treated with cyclosporine. Although the fish-oil group had significantly fewer rejection episodes than the control group, graft survival at one year was not significantly better in the fish-oil group.