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Hypocitraturia in patients with urolithiasis

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Abstract

The urinary citrate/creatinine ratio was evaluated in 25 children with idiopathic calcium urolithiasis and 24 controls. The mean (SD) urinary citrate/creatinine ratio in controls and patients was 0·510 (0·205) and 0·181 (0·076), respectively, a statistically significant difference. In neither group was there a relation between age and urinary citrate excretion.

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The urinary inhibitors of crystal nucleation, growth, and aggregation play an important part in urolithiasis.[1] Such inhibitors are presumed to afford protection against stone formation in normal individuals. Possible inhibitors include pyrophosphate, magnesium, citrate, and glycosaminoglycans.[2–5] Citrates and glycosaminoglycans are the most important and almost completely account for urinary inhibiting activity.[6] Decreased urinary citrate excretion is a common finding in calcium stone formers,[7–15] but the physiological disturbance that leads to hypocitraturia in patients without metabolic abnormalities still remain unclear. In children, hypocitraturia is present in renal tubular acidosis.[16] However, little information is available concerning urinary citrate excretions in various forms of childhood nephrolithiasis.[17–19]

We have attempted to establish whether the differences previously described between controls and adult stone formers are also present in children with idiopathic urolithiasis.

Methods

Twenty four hour urine samples were collected after an overnight fast from 25 calcium stone formers (15 girls and 10 boys) with a mean (SD) age of 6·2 (2·4) years and from 24 controls (10 girls and 14 boys) with a mean (SD) age of 6·8 (3·5) years. Written consent was obtained from parents.

All subjects had normal renal function, as evaluated by endogenous creatinine and absence of proteinuria or urinary tract infection. Patients with known physiological or metabolic disorders were excluded from this study. Urinary calcium, magnesium, and oxalate concentrations and pH are listed in table 1. The children had a normal diet for the two weeks before investigation.

Urine specimens were kept at 4°C in plastic containers with added penicillin G and streptomycin sulphate.[20]

Citrate determination was with a commercially available kit based on the citrate lyase technique.[21] Calcium and magnesium determinations were performed by atomic absorbtion spectrophometry (Perkin-Elmer) and oxalate determinations by an enzymatic method.

The Student's *t* test was used to search for significant differences comparing control and patient groups.

Results

The results are summarised in table 2. In control subjects, we found no significant difference between girls and boys (the mean (SD) urinary citrate/creatinine ratio were 0·590 (0·19) and 0·451 (0·21) respectively. However, in the patient group, the urinary citrate/creatinine ratio was reduced, 0·181 (0·076), and the difference between patients and controls was significant ($p<0·001$).

There was no correlation of age with urinary citrate/creatinine ratio in either group.

Discussion

The pathogenesis of idiopathic nephrolithiasis involves an imbalance between promoting and inhibiting factors of calcium crystal growth and aggregation in urine. Urinary citrate, in particular, is important in inhibiting calcium oxalate[6] and calcium phosphate crystals.[22]

There have been numerous reports showing that urinary citrate is low in adult patients with nephrolithiasis,[7–15] but information is scanty concerning urinary excretion of citric acid in paediatric idiopathic urolithiasis. Baggio *et al* reported that, in contrast to observations in adults, urinary citrate excretion was normal in children with idiopathic urolithiasis.[17] Miller and Stapleton found normal urinary citrate excretion in children with either type of hypercalciuria or idiopathic calcium oxalate stones. The urinary citrate/creatinine ratio in seven

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*Table 1 Mean (SD) urinary ratios of calcium, magnesium, and oxalate to creatinine and urinary pH values in controls and patients**

	Calcium/creatinine ratio	*Magnesium/creatinine ratio*	*Oxalate/creatinine ratio*	*pH*
Controls (n=24)	0·250 (0·065)	0·125 (0·032)	0·012 (0·003)	6·9 (0·5)
Patients (n=25)	0·225 (0·040)	0·140 (0·027)	0·115 (0·006)	7·2 (0·3)

*There was no significant difference between patients and controls for any of the ratios or the pH.

Table 2 Mean (SD) urinary citrate/creatinine ratios in controls and patients

	Citrate/creatinine ratio
Controls (n=24)	0·510 (0·20)
Girls (n=10)	0·590 (0·19)
Boys (n=14)	0·451 (0·21)
Patients (n=25)	0·181 (0·076)*

*There was a significant difference between patients and controls: $p<0·001$.

healthy children was reported as 0·439 by Miller and Stapleton.[18] However, Norman *et al* reported that the urinary citrate/creatinine ratio in girls was 0·681 and in boys 0·457.[23] We found similar results to Norman *et al* with the same method. There was no correlation of urinary citrate excretion with age; this agrees with the findings of Miller and Stapleton.[18]

Our findings differ from those of Baggio *et al*,[17] but they did not take the citrate/creatinine ratio into consideration and Miller and Stapleton examined only a limited number of specimens. Neither group used any preservative during the collection of urine specimens, and it is known that bacteria can use citrate as a carbon source.[20] Many urine specimens will contain bacteria and the citrate concentration decreased after collection and analysis of the samples.

We conclude that because it is possible to treat calcium oxalate urolithiasis with thiazides and potassium citrate, estimating urinary citrate excretion is essential in children with urolithiasis.

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