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Hypercalciuria in children with recurrent UTI

Mastaneh Moghtaderi: (**Corresponding author*) Associate Professor of Pediatric Nephrology, Children Medical Center Hospital, Tehran University of Medical Sciences, Tehran, Iran.
Fereshteh Roozafzay: Resident of Pediatrics, Children Medical Center Hospital, Tehran University of Medical Sciences, Tehran, Iran.
Mojtaba Fazel: Associate Professor of Pediatric Nephrology, Children Medical Center Hospital, Tehran University of Medical Sciences, Tehran, Iran.
Tahereh Khanmohamadzadeh: Stuff Nurse, Children Medical Center Hospital, Tehran University of Medical Sciences, Tehran, Iran.

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Abstract

Background and Objective: Urinary tract infection (UTI) is common in children. Recurrent UTI causes serious complications such as renal scarring, proteinuria and hypertension. Recent studies have reported that hypercalciuria may be considered a risk factor for recurrent UTI.

Methods: In this study 110 children aged 2 months to 13 years with recurrent UTI were evaluated for hypercalciuria, urinary tract anomalies and voiding dysfunction, constipation, reflux and scars of the kidney. Hypercalciuria was defined as a calcium/creatinine ratio more than 0.21 in at least two morning spot urine test. Recurrent UTI was defined as at least 3 episodes of cystitis or 2 episodes of pyelonephritis.

Findings: There were 110 children: 103 female (93.6) and 7 male (6.4). Mean age was 4.35 ± 2.05. Frequency of recurrent UTI was 2.7 times. The most common symptom was dysuria (73%), recurrent UTI (60%), and abdominal pain (44%). Hematuria was seen in 60% of patients with recurrent UTI and hypercalciuria. Mean calcium/creatinine ratio was 0.87±0.32 that detected in 37.7% of children with recurrent UTI. Familial history of hypercalciuria was detected in 13.6% of patients. Microlithiasis was detected in 83.3% of children with recurrent UTI and hypercalciuria. Patients with hypercaluria received hydrochlrotiazid for 3- 18 months (mean 8.3±3.1 months).

Conclusion:

Keywords: Hypercalciuria, Recurrent urinary tract infections, Children

Introduction

Hypercalciuria means there are high levels of calcium in the urine. This can be checked on a single urine sample, but is best checked with a 24 hour urine test (1). Increased levels of urine calcium can cause kidney stones, nephrocalcinosis, osteopenia and recurrent UTI (2). Hypercalciuria can manifest as urolithiasis, microscopic or gross hematuria, abdominal or flank pain, dysuria, frequency, urgency, urinary incontinence, and UTI (3).

UTI is common in children, 3-5% of girls and %1 of boys experience at least one episode of UTI at childhood (4). Many factors contribute to the occurrence of UTI such as vesicoureteral reflux, obstructive anomalies of the urinary tract, voiding dysfunction, constipation and hypercalciuria(5).

Recurrent urinary tract infection (UTI) as a clinical presentation of hypercalciuria was first mentioned by Heliczer in 1987(6). An entire series of mechanisms such as the reduction in renal tubular reabsorption of calcium, associated renal tubular disorders, increased intestinal calcium absorption, alternation in intestinal vitamin D receptors, primary increase in vitamin D synthesis, increased renal prostaglandin E2 production, and increased interleukin-1 and interleukin-6 production have been proposed in order to explain physiopathology of idiopathic Hypercalciuria (7). The mechanism may be related to uroepithelial injury by calcium microcrystals. It seems that irritation of the uroepithelial tissue deteriorates the normal function of the mucosal barrier against microbial pathogens (8). This study was done in children with recurrent UTI that referred to nephrology clinic. We evaluated idiopathic hypercalciuric cases by VUR,

Table 1. Sex of children with recurrent UTI.

		Frequency	Percent
Valid	Male	7	6.4
	Female	103	93.6
	Total	110	100.0

DMSA scan, voiding dysfunction and constipation also assessed. The aim of this study was evaluating the association of hypercalciuria with urinary tract infection (UTI) in children.

Methods

This is a cross-sectional study performed in the Children Medical Center Hospital, Tehran, Iran from 2012- 2015.These are 110 children 2 months to13 years of age with recurrent urinary tract infection (UTI). They are evaluated for the causes of recurrent UTI such as vesicoureteral reflux, voiding dysfunction, constipation, anatomical anomaly and hypercalciuria. Hypercalciuria was defined as a calcium/creatinine ratio more than 0.21 (according to age) in at least two morning spot urine tests. Recurrent UTI was defined as at least 3 episodes of cystitis or 2 episodes of pyelonephritis or one episode of upper urinary tract infection with one or more episodes of lower urinary tract infection. In patients who had hypercalciuria, serum calcium, phosphorus, PTH, blood urea nitrogen, serum creatinine, and blood gas analysis were investigated to differentiate idiopathic hypercalciuria from other causes of hypercalciuria.

Children with neurologic bladder, sever hydronephrosis, posterior urethral valve (PUV) and renal failure were excluded from this study.

All demographic, clinical and laboratory findings were collected in an organized forms. They were evaluated and fallowed up for ongoing 6 - 36 months. We presented our plan to the research ethics committee of Tehran University of Medical Sciences and they approved our study; also, informed consent form was taken from parents.

Results

There were 110 children, 103 female (93.6) and 7 male (6.4). Mean (SD) age was 4.35 ±2.05 (ranging 2 months to 13 years). Frequency or recurrent UTI was 2.7 times. The mean calcium/creatinine ratio was 0.87±0.32 (range: 057-4.20) that detected in 37.7% of children with recurrent UTI. The most common symptom was dysuria (73%) recurrent UTI (60%), and abdominal pain (44%). Voiding dysfunction and constipation were seen in 70.9% of these patients. Hematuria considered in 47.7% of patients with recurrent UTI and was seen in 60% of patients with recurrent UTI and hypercalciuria. Microlithiasis was detected in 8.3% of children with recurrent UTI and hypercalciuria. Sterile pyuria was seen in 5.4% of patients with recurrent UTI and hypercalciuria. Results of sonography and DMSA and VCUG are showed in the following Tables. The patients with hypercalciuria received hydrochlorothiazide for 3- 18 months (mean 8.3±3.1 months). After management of hypercalciuria and microlithiasis with increasing fluid intake, salt restricted diet, hydrochlorothiazide and polycitra k decreased the rate of hypercalciuria (mean calcium/creatinine 0.29± 0.31) and microlithiasis, but there were no direct relation between decrease of hypercalciuria and recurrent UTI.

Discussion

In the present study high frequency of hypercalciuria (37.7%) in children with recurrent UTI was observed. Urine calcium/Cr ratio for hypercalciuric individuals was 0.87 ± 0.32 mg/mg (range:

Table 2. Result of sonography.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NL	83	75.5	79.0	79.0
	Ab NL	22	20.0	21.0	100.0
	Total	105	95.5	100.0	
Missing	System	5	4.5		
Total		110	100.0		

Table 3. Results of DMSA.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NL	16	14.5	39.0	39.0
	Ab NL	25	22.7	61.0	100.0
	Total	41	37.3	100.0	
Missing	System	69	62.7		
Total		110	100.0		

Table 4. Results of VCUG.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NL	33	30.0	55.9	55.9
	I	7	6.4	11.9	67.8
	II	15	13.6	25.4	93.2
	III	2	1.8	3.4	96.6
	4	2	1.8	3.4	100.0
	Total	59	53.6	100.0	
Missing	System	51	46.4		
Total		110	100.0		

057-4.20). In a study performed in Zahedan, Iran by Sadeghi and colleagues rate of hypercalciuria in children with recurrent UTI was similar to our study (30% versus 37.7%)(9). In a study done in Tabriz, Iran by Mortazavy et al, rate of hypercalciuria in children with recurrent UTI was 47.5% that was higher than that of our study (10). In a study done by Gheissari et al in Esfahan, Iran hypercalciuria was significant in male children with UTI and under 6 years old (8). A Venezuelan study by Lopez et al reported the incidence of hypercalciuria to be 32% among patients with recurrent UTI (11). Biyikli et al in Turkey showed that 43% of the patients with recurrent UTI had hypercalciuria (12). In a study by Vachvanichsanong et al, recurrent UTI was accompanied by hypercalciuria in 31.4% of the patients (13). In a study by Stojanociv et al, 44% of the patients with recurrent UTI had hypercalciuria (14). The results of the 4 aforementioned recent studies were similar to our study.

We found no association between recurrent UTI and hypercalciuria. After treatment of hypercalciuria using procedures such as adequate fluid intake and salt restriction and hydrochlorothiazide, rate of UTI did not decrease. Kaminska et al showed that treatment of hypercalciuria reduced the episodes of UTI in 43.6% of the patients (15). In a study done by Yosefi et al in Iran treatment of idiopathic hypercalciuria did not prevent recurrent UTI (16). The different results among the above studies may be due to different causes of recurrent UTI such as VUR, constipation, voiding dysfunction, and hypercalciuria. Also, one patient may have multiple etiologies. Management of hypercalciuria alone cannot prevent recurrent UTI.

Conclusion

This study showed that hypercalciuria was common in children with recurrent UTI. In children with recurrent urinary tract infection with any underline disease and anatomic anomaly, evaluation of hypercalciuria is recommended.

Conflicts of interest: None declared.

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