

Hypercalciuria and recurrent urinary tract infections among children in Zahedan, Iran

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Abstract

Objectives: To evaluate the association of idiopathic urinary tract infection (UTI) and hypercalciuria in Iranian children.

Methods: Seventy children with episodes of UTI, and 70 healthy controls were studied. Random urine calcium-creatinine ratio (UCa/Cr) and plasma calcium were measured.

Results: Hypercalciuria was found significantly higher ($p < 0.05$) in UTI patients (30%) than normal subjects (11.4%). The results showed that frequency of hypercalciuria is higher in females (42.9%) than males (17.1%).

Conclusion: The investigation of urinary calcium excretion in children with recurrent UTI is recommended (JPMA 58:624; 2008).

Introduction

The term 'idiopathic hypercalciuria' (IH) was originally used to describe the association of elevated urinary calcium excretion with a normal serum calcium level in patients with calcium containing renal stones. It is one of the most-common metabolic abnormalities in humans and is present in approximately 60% of individuals with nephrolithiasis. Idiopathic hypercalciuria (IH) in adults is recognized as a cause of urolithiasis. If IH is symptomatic, the symptoms are haematuria, renal colic, or obstructive uropathy with or without infection. In children, IH has been linked to the spectrum of urinary symptoms including haematuria, pyuria, dysuria, recurrent urinary infections, abdominal or suprapubic pain, proteinuria, and the frequency-urgency syndrome.¹

Pediatricians frequently have faced one or more of an array of lower urinary tract symptoms without obvious cause. Idiopathic hypercalciuria is believed to be the cause of a variety of urinary tract complaints in clinical paediatrics, including urinary frequency, urgency, and/or dysuria, often associated with gross or microscopic haematuria.² Hypercalciuria is an important and common

risk factor in the formation of renal stones.³ Recurrent urinary tract infection (UTI) as a clinical presentation of hypercalciuria was first mentioned by Heliczer in 1987.⁴ An entire series of mechanisms such as the reduction in renal tubular reabsorption of calcium, associated renal tubular disorders, increased intestinal calcium absorption, alteration 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.^{3,5,6}

The aim of this study was to evaluate the association of hypercalciuria with urinary tract infection (UTI) in children.

Patients and Methods

Seventy children, referred for investigations after a documented urinary tract infection, were enrolled in the study. There were 35 males and 35 females. The control group was children without any disease (36 males and 34 females). Urinary calcium excretion is best measured in a 24-hour collection. However, such collections are difficult to obtain in children and many investigators have used the

urinary calcium/creatinine ratio (UCa/Cr) as an alternate measurement. The use of the UCa/Cr as a measure of urinary calcium excretion was first proposed by Nordin⁷ Ghazali and Barratt have found that there was a strong positive correlation between the UCa/Cr and the 24-hour urine calcium excretion.⁸ In this study, UCa/Cr was used as an indicator of urinary calcium excretion. Normal range of UCa/Cr in infants (7 months) is less than 0.8 (mg/mg) and in children 0.20. The UCa/Cr greater than 0.2 in children and greater than 0.8 in infants is considered as hypercalciuria.

Serum levels of calcium and urinary calcium and creatinine concentrations were determined by spectrophotometric analysis using commercial kits.

Statistical analysis was performed using the SPSS 11.0 software. Data were expressed as mean ± standard deviation; descriptive analyses were performed for the calculation of frequencies.

Results

In this study 70 UTI patients (35 Male, 35 female) and 70 controls (36 Male, 34 Female) were enrolled. In table 1; age, UCa/Cr and plasma calcium of case and control

shown in table 2 the frequency of hypercalciuria in females (42.9%) was statistically higher than males (17.1%) in UTI patients (p<0.05).

Out of 70 UTI patients, 40 (57.1%) had lower urinary tract infection and 30 patients (42.9%) had upper urinary tract infection. The frequency of hypercalciuria was not statistically significant between lower and upper urinary tract infection (p>0.05). (Table 3)

Discussion

In the present study high frequency of hypercalciuria (30%) in children with UTI was observed. UCa/Cr ratio for hypercalciuric individuals was 0.55 ± 0.60 mg/mg (range; 0.20-3.10) and for normal calciuria was 0.11 ± 0.08 mg/mg (range; 0.01-0.58). A Venezuelan study by Lopez et al reported the incidence of hypercalciuria to be 32% among patients with recurrent UTI. They found an association between hypercalciuria and UTI.⁹ Biyikli et al found that 43% of children with UTI had hypercalciuria.³ They observed that the mean UCa/Cr ratio for hypercalciuric patients was 0.50 ± 0.21 mg/mg (min: 0.24, max: 2.60). The mean urinary UCa/Cr ratio for the rest of the study population, those without hypercalciuria was 0.10±/0.04

Table 1: The characteristic of UTI patients and control subjects.

Parameters Groups	No.	Age (Years)		Urine Ca+2/Creatinin (mg/mg)		hypercalciuria	Normal calciuria
		Range	Mean ± SD	Range	Mean±SD		
UTI patients	70	0.2-11	3.52 ± 2.98	0.03-1.95	0.23 ± 0.27	21 (30%)	49 (70%)
Control	70	0.2-12	3.35 ± 3.15	0.01-3.10	0.18 ± 0.38	8(11.4%)	62(88.6%)

groups are shown. Hypercalciuria was found in 30% (21/70) of UTI patients, while in normal subjects there was 11.4% (8/70). The frequency of hypercalciuria was significantly higher in UTI patients than normal subjects (p<0.05). As

Table 2: Frequency of hypercalciuria in male and female UTI patients and normal subjects.

Groups	Sex		Total
	Male	Female	
Hypercalciuria	6 (17.1%)	15 (42.9%)	21 (30%)
Normal calciuria	29 (82.9%)	20 (57.1%)	49 (70%)
Total	35 (100%)	35 (100%)	70 (100%)

Table 3: Frequency of hypercalciuria in upper and lower tract infection.

Groups	Location		Total
	Lower UTI	Upper UTI	
Hypercalciuria	13 (32.5%)	8 (26.6%)	21 (30%)
Normal calciuria	27 (67.5%)	22 (73.3%)	49 (70%)
Total	40 (100%)	30 (100%)	70 (100%)

mg/mg (min: 0.01, max: 0.18)³ Our findings are in agreement with those obtained by Biyikli et al and Lopez et al^{3,9} The frequency of idiopathic hypercalciuria is 3-9% among children.¹⁰ We found that in normal subjects the frequency of hypercalciuria is 11.4%. The results show that idiopathic hypercalciuria is common among children. Stapleton et al assessed urinary calcium excretion in 83 consecutive children with gross or microscopic haematuria in whom the presence of proteinuria or urinary-tract infection had been excluded; they found that 23 children had hypercalciuria.¹¹

The frequency of hypercalciuria is higher in females (42.9%) than males (17.1%) in UTI patients. Idiopathic hypercalciuria must be diagnosed and treated with care in order to reduce consequences such as haematuria, abdominal pain, urinary stone formation and possible bone involvement. Signs and symptoms such as urgency and urinary incontinence, suprapubic pain and nocturnal enuresis may result from renal hyperexcretion of calcium.⁵ In 1981, two groups simultaneously reported an association

between IH and recurrent gross haematuria in the absence of demonstrable nephrolithiasis.^{12,13} Therapy in all children consisted of increased fluid intake and reduction in diet sodium and oxalate.¹⁴

Idiopathic hypercalciuria (IH) in adults is recognized as a cause of urolithiasis. If IH is symptomatic, the symptoms are haematuria, renal colic, or obstructive uropathy with or without infection. In children, IH has been linked to the spectrum of urinary symptoms including haematuria, pyuria, dysuria, recurrent urinary infections, abdominal or suprapubic pain, proteinuria, and the frequency-urgency syndrome. Haematuria may appear prior to the appearance of stones, and thiazide therapy prevents stone formation by decreasing urinary calcium excretion.¹

It is possible that hypercalciuria may play a predisposing role for recurrent UTI in children by promoting the formation of microcrystals which damage the uroepithelium.⁹

However, HC represents a common symptom of various underlying disorders, which proves that the etiology of HC is heterogeneous. Mutations in the gene coding for the renal tight junction protein claudin 16 causes familial hypomagnesaemia with hypercalciuria.¹⁵

In conclusion, hypercalciuria is not a rare finding among UTI patients in Iranian children and the frequency of hypercalciuria is higher in females than males. We suggest the investigation of urinary calcium excretion in children with recurrent UTI. If untreated, hypercalciuria may lead to nephrolithiasis.

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