

Idiopathic Hypercalciuria in Children With Vesico Ureteral Reflux and Recurrent Urinary Tract Infection

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Purpose: Our aim was to determine association of vesicoureteral reflux (VUR) and idiopathic hypercalciuria in children with recurrent and single episode of urinary tract infection (UTI).

Materials and Methods: The study group consisted of 45 children with VUR and recurrent UTI, and 2 control groups: 45 normal healthy children (control group 1) and 45 children with VUR and single episode of UTI (control group 2). Idiopathic hypercalciuria was defined as urine calcium to creatinine ratio more than 0.8 (mg/mg) in infants younger than 1 year old, and more than 0.2 (mg/mg) in older children (without any detectable causes for hypercalciuria).

Results: The study group consisted of 26 (57.8%) girls and 19 (42.2%) boys, with the mean age of 41.14 ± 22.1 months. Nine (20%) subjects had hypercalciuria. The control group 1 composed of 22 (48.9%) girls and 23 (51.1%) boys, with the mean age of 43.98 ± 16.23 months. In this group, 6 subjects (13.3%) with hypercalciuria were detected. The control group 2 composed of 23 (51.1%) girls and 22 (48.9%) boys, with the mean age of 39.96 ± 24.2 months. In group 2, 7 subjects (15.6%) with hypercalciuria were detected.

Conclusion: Comparison between such results was not statistically significant. Despite reports of different studies about accompanying of hypercalciuria with recurrent UTI with or without anatomical abnormalities, according to the present study, idiopathic hypercalciuria is not a major contributing factor to recurrent UTI in children with VUR.

Keywords: vesico ureteral reflux, hypercalciuria, recurrent urinary tract infection

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INTRODUCTION

Urinary tract infection (UTI) is known as one of the most frequent diseases in pediatric medicine. Due to its harmful effects on the renal tissue, UTI's importance is undeniable.⁽¹⁻³⁾

There are many factors that can predispose occurrence of UTI, including anatomic abnormalities, vesico ureteral reflux (VUR), dysfunction of the bladder, etc. Another factor that is suggested as a facilitating cause of recurrent UTI is idiopathic hypercalciuria (IH).⁽⁴⁻¹⁰⁾

Idiopathic Hypercalciuria is a common disorder in children and can present with a range of clinical manifestations such as hematuria, voiding dysfunction, abdominal pain, flank pain, nephrolithiasis, and osteoporosis.⁽¹¹⁾

Micro crystals of calcium oxalate, which cause trauma and damages to the mucosa of the lower urinary tract, can lead to voiding dysfunction and recurrent UTI. According to some reports, VUR

is one of the facilitative factors of UTI, but the latest researches have showed that VUR has been detected in less than 50% of subjects with recurrent UTI.^(12,13)

Until the roles of such etiological factors for UTI are fully understood, complete prevention of the upper urinary tract infection and scarring is unlikely. Study of non anatomic problems, such as hypercalciuria (with or without VUR) as predisposing factors of the recurrent UTI, gained its importance. In the present study, we have tried to determine association of vesicoureteral reflux and idiopathic hypercalciuria in children with recurrent and single episode of urinary tract infection.

MATERIALS AND METHODS

This case control study was carried out between October 2007 and April 2008 in Shahid Motahari Pediatric Hospital in Urmia, Iran. The study group composed of 45 children older than 2 months and younger than 6 years with VUR who were also suffering from recurrent UTI (presence of more than 2 UTI attacks during 6 months).

Exclusion criteria were:

1. Children with secondary VUR (neurogenic bladder, bladder obstruction, and other detectable bladder abnormalities).
2. Children who have been hospitalized for a long time because of a special illness like major fracture in extremities or who have been bed rest for a long time.
3. Children who received corticosteroids or diuretics in the last month, or high dose calcium and vitamin D in the last 6 months.
4. Children with renal dysfunction and low glomerular filtration rate.

Two control groups were selected for this study:

Control group 1: Healthy children that were

selected among those who referred to health centers of the city, without any special disease.

Control group 2: Children with VUR, but with single UTI.

The control groups were matched with the subjects, regarding the age and sex.

Thereafter, the calcium to creatinine ratio was measured from the second morning urine sample by professional laboratory technicians. All laboratory studies were performed by only one laboratory technician who was expert in investigation of urine calcium level using the auto-analyzer device (standard Hitachi 9/2, Model 2006).

Idiopathic hypercalciuria was defined as urine calcium to creatinine ratio more than 0.8 (mg/mg) in infants younger than 1 year old, and more than 0.2 (mg/mg) in older children (without any detectable causes for hypercalciuria).⁽¹¹⁾

Voiding cystourethrography was the standard for diagnosing VUR and grading was defined according to the International Reflux Grading system.

Eventually, the one-way Anova test was used for evaluation of the mean age of control and study groups, chi-square test for analyzing data and logistic regression test for omitting the confounder's variables effects. *P* values less than .05 were considered statistically significant.

RESULTS

The study group consisted of 26 (57.8%) girls and 19 (42.2%) boys, with the mean age of 41.14 ± 22.1 months. Nine (20%) subjects with hypercalciuria were detected (Tables 1 and 3). In logistic regression analysis after entering confounder variables such as age and sex, no variable was detected in the final model.

The control group 1 consisted of healthy children without VUR and UTI, composed of 22 (48.9%)

Table 1. Demographic findings

Title	Number	Mean age	Girl	Boy	P
Healthy control group	45	43.98 ± 16.23	48.9%	51.1%	.095
Single UTI and VUR	45	39.96 ± 24.2	51.1%	48.9%	.083
Recurrent UTI and VUR	45	41.14 ± 22.1	57.8%	42.2%	.880

Table 2. VUR Grading and Hypercalciuria

Title	VUR Number (Percent)					Hypercalciuria	P
	1	2	3	4	5		
VUR Grade	1	2	3	4	5
Single UTI and VUR	...	20 (44.4%)	22 (48.9%)	3 (6.7%)	...	7	.690
Recurrent UTI and VUR	8 (18%)	18 (40%)	13 (29%)	5 (11%)	1(2%)	9	.450

Table 3. Hypercalciuria (in case and control groups)

Title	Recurrent UTI and VUR	Single UTI and VUR	Healthy Control Group	Odds Ratio	P
Number	45	45	45
Hypercalciuria	17.8%		13.2%	1.35	.507
Hypercalciuria (Number)	...	15.6% (7.0)	13.2%	1.18	.450
Hypercalciuria	20.0% (9.0)	...	13.2% (6.0)	1.54	.690
Hypercalciuria	20.0% (9.0)	15.6% (7.0)	...	1.28	.890

girls and 23 (51.1%) boys, with the mean age of 43.98 ± 16.23 months. In this group, 6 subjects (13.3%) with hypercalciuria were detected (Tables 1 and 3). The control group 2 consisted of children with primary VUR, but without recurrent UTI (single UTI), composed of 23 (51.1%) girls and 22 (48.9%) boys, with the mean age of 39.96 ± 24.2 months. In the control group 2, 7 subjects (15.6%) with hypercalciuria were detected (Tables 1 and 3).

DISCUSSION

In the present study, the rate of hypercalciuria in the study group was 1.54 folds more than control group 1 ($P = .690$) and 1.35 folds more than control group 2 ($P = .890$). In fact, the prevalence of hypercalciuria among subjects with VUR and recurrent UTI did not have significant differences in comparison with the healthy subjects and single UTI. Also, comparison between control groups 1 and 2 was not significant ($P = .450$). Therefore, when the rate of hypercalciuria in children with VUR (in both study group and control group 2) and healthy subjects were compared, there was not any significant differences ($P = .507$).

The pathophysiologic mechanism of hypercalciuria as a facilitative factor to recurrent UTI can be explained by the damage and trauma that can occur to the epithelial cells of the urinary tract mucosa due to micro crystals formation. Such damage can interfere with the natural defiance of uroepithelial cells, and on the other side, the dysfunction of the bladder can be occurred as a predisposing factor for recurrent UTI.⁽⁸⁻¹⁰⁾

A few studies have been reported on the accompanying of hypercalciuria in children with VUR. In a study in Iran, the prevalence of hypercalciuria in children with UTI and in healthy control group was reported to be 34% and 8%, respectively.⁽⁵⁾ Vachvanichsanong and colleagues⁽⁶⁾ reported that 85% of hypercalciuric patients with recurrent UTI did not demonstrate anatomical abnormalities of the urinary tract. This study has advocated the investigation of urinary calcium excretion in children with recurrent UTI, but without anatomical abnormalities.

In a study by Biyikli and associates,⁽⁷⁾ the accompanying of hypercalciuria with UTI was detected in 43% of children. The age of the study group was more than 5 years and their results showed that 37.5% of hypercalciuric patients had predisposing urinary tract abnormality, including urolethiasis. Moreover, there had been a statistically significant difference between hypercalciuric children with UTI and control group.

In other study carried out by Lopez and colleagues,⁽⁹⁾ the children with UTI and without any anatomic abnormality who were also suffering from hypercalciuria were treated to eliminate hypercalciuria. In 95% of children, after treatment of hypercalciuria, no UTI was detected; hence, it was concluded that hypercalciuria can be as a predisposing factor for recurrent UTI.

There are a few studies in which hypercalciuria has been studied in children with VUR. Garcia and colleagues reported the prevalence of

hypercalciuria and VUR in the study group and control group to be 18.7% and 15.1%, respectively (not significant differences).⁽¹⁴⁾ In other study by Noe and coworkers on 46 children with VUR,⁽¹⁵⁾ the prevalence of hypercalciuria was studied. It was concluded that the prevalence of hypercalciuria in children with VUR was 58.6%, which was significantly more than healthy children. It is important to say that children with urolithiasis were included in this study, which naturally increased the rate of hypercalciuria. In our study, the prevalence of hypercalciuria in children with recurrent UTI and VUR has not significant differences in comparison with control groups (VUR with single UTI and healthy children).

There are some important points about our study in comparison with other studies, which may have its own effects on our results, including the sample size, selection of patients without urolithiasis, and local high prevalence of hypercalciuria.

CONCLUSION

Despite reports of different studies about accompanying of hypercalciuria with recurrent UTI with or without anatomical abnormalities, according to the present study, idiopathic hypercalciuria is not a major contributing factor to recurrent UTI in children with VUR.

CONFLICT OF INTEREST

None declared.

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