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URINARY CALCIUM EXCRETION OF CHILDREN LIVING IN THE EAST REGION OF TURKEY*

*Mukadder Ayşe Selimoğlu MD**, Handan Alp MD***, Hürol Bitlisli MD*****
*Zerrin Orbak MD**, Meltem Energin MD**, Cahit Karakelleoğlu MD****

SUMMARY: Selimoğlu MA, Alp H, Bitlisli H, Orbak Z, Energin M, Karakelleoğlu C. (Department of Pediatrics, Atatürk University Faculty of Medicine, Erzurum, Turkey). Urinary calcium excretion of children living in the east region of Turkey. Turk J Pediatr 1998; 40: 399-404.

We screened 1647 randomly selected Turkish primary school children to detect the prevalence of hypercalciuria. Ninety-seven children had hypercalciuria, with a prevalence of 5.88 percent. Mean Uca/Ucr ratio was 0.135 ± 0.108; mean Uca/Ucr value for girls was 0.139 and for boys 0.130 ($p > 0.05$). Mean Uca/Ucr of boys with hypercalciuria was 0.341 ± 0.09 and of girls 0.327 ± 0.08 ($p > 0.05$). Of these 97 children, all investigations could be completed in only 40 and these cases were considered to be idiopathic. Twelve children (21%) had a family history of consanguinity and 17 (29.8%) of renal stones. The relation between blood parathormone and Uca/Ucr ratio was not statistically important ($p > 0.05$). *Key words: hypercalciuria, prevalence, children.*

Idiopathic hypercalciuria is characterized by a urinary calcium excretion exceeding 4 mg/kg/day or by a calcium/creatinine ratio exceeding 0.21, and is one of the most common causes of renal stones at any age[1-5]. Excretion of abnormal amounts of calcium interferes with the metabolism of calcium, parathormone, 1.25 dihydrocholecalciferal and calcitonin, and increases the risk of stone formation[2, 5-9]. Although urolithiasis is endemic in Turkey, epidemiological and etiogenic investigations are not satisfactory[7]. This study was performed to screen 1647 Turkish primary school children living in the east region of Turkey for hypercalciuria and to determine its prevalence.

Material and Methods

We included 1647 randomly selected Turkish primary school children in this study. Since it has been demonstrated that 24-hour calcium excretion is best represented by second morning urine, these samples were collected[4]. Urine calcium (Uca) and creatinine (Ucr) concentrations were determined by the O-Cresolphthalein and Jaffe methods, respectively, on a Hitachi-717 autoanalyzer[4]. In children with a Uca/Ucr ratio above 0.21, parameters were restudied; those

* From the Department of Pediatrics, Atatürk University Faculty of Medicine, Erzurum.

** Assistant Professor of Pediatrics, Atatürk University Faculty of Medicine.

*** Associate Professor of Pediatrics, Atatürk University Faculty of Medicine.

**** Research Assistant in Pediatrics, Atatürk University Faculty of Medicine.

with high levels recorded again were considered as having hypercalciuria. These students were asked to complete a questionnaire providing information on history of urinary tract infections, renal stones, hematuria, abdominal pain, dysuria, polyuria, pollakuria, day and night enuresis, polydipsia and renal stones or renal disease in their families. Ninety-seven children with hypercalciuria were invited to hospital for further investigations. Weight, height and blood pressure measurements were recorded. Specific gravity, pH and protein were measured, and urine culture, microscopic examination, as well as tests to determine blood urea nitrogen, creatinine, uric acid, calcium, phosphate, alkaline phosphatase, sodium, potassium and parathormone levels were performed. Abdominal radiography and ultrasonography were performed. For statistical analysis, Student's t test and regression analysis were used.

Results

Of 1647 primary school children, 847 (51.5%) were boys and 800 (48.5%) were girls. Ninety-seven children had hypercalciuria (prevalence 5.88%). Mean Uca/Ucr ratio was 0.135 ± 0.108; mean Uca/Ucr value of girls was 0.139 and of boys 0.130 ($p > 0.05$). Table I shows the number of each age group and the mean Uca/Ucr values, no statistical difference was detected ($p > 0.05$). Figure 1 shows the relation between age and Uca/Ucr ratio ($r = 2.601$, $p < 0.005$). Figure 2 shows percentile curve of Uca/Ucr values. Of 97 cases with hypercalciuria, 63 (65%) were boys and 34 (35%) were girls. Mean Uca/Ucr of boys was 0.341 ± 0.09 and of girls 0.327 ± 0.08 ($p > 0.05$). Of these children, 57 accepted the invitation to hospital; all investigations could be completed. In only 40 (25 boys and 15 girls). Figure 3 includes the clinical symptoms of the 57 children. Twelve children (21%) had a family history of consanguinity; 17 (29.8%) of renal stones. Weight, height and blood pressure values were within normal limits. In the 40 cases, aside from Uca/Ucr ratios, no abnormality was detected in other parameters. These cases were considered to be idiopathic. The relation between blood parathormone and Uca/Ucr ratio was not statistically important ($p > 0.05$). Abdominal radiograms and ultrasonographs (14 cases) were normal.

Table I: Mean Uca/Ucr Values of Each Age Group

Age (Years)	Mean Uca/Ucr
6 (n = 28)	0.138 ± 0.121
7 (n = 255)	0.145 ± 0.111
8 (n = 287)	0.138 ± 0.121
9 (n = 376)	0.131 ± 0.104
10 (n = 402)	0.128 ± 0.121
11 (n = 299)	0.130 ± 0.098

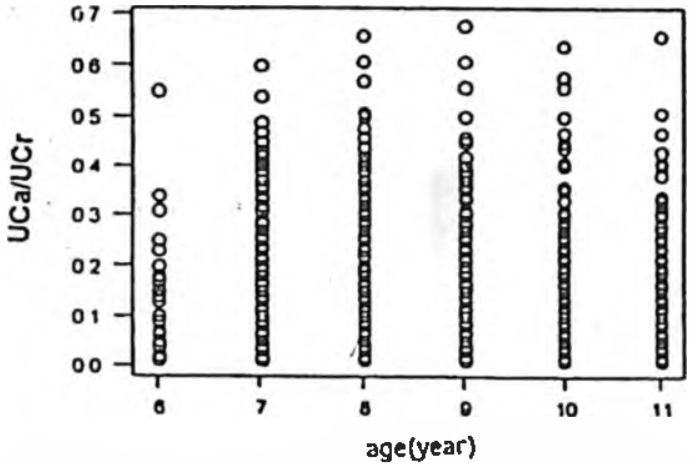

Fig. 1: Correlation between age and Uca/Ucr value.

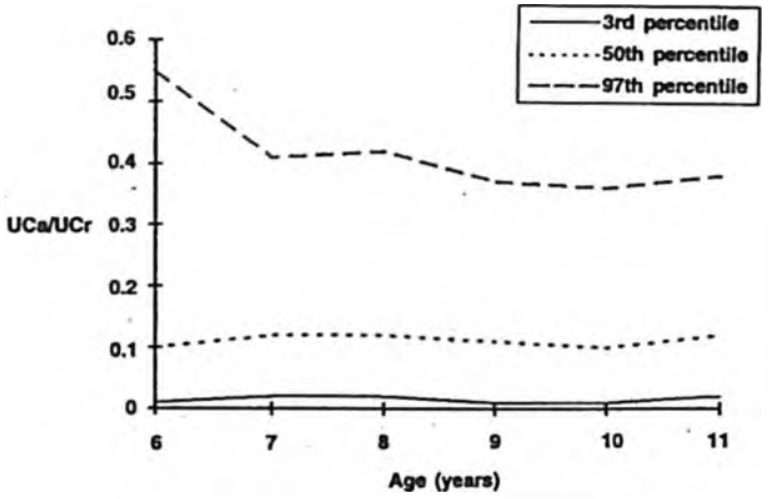

Fig. 2: Percentile curve of Uca/Ucr value.

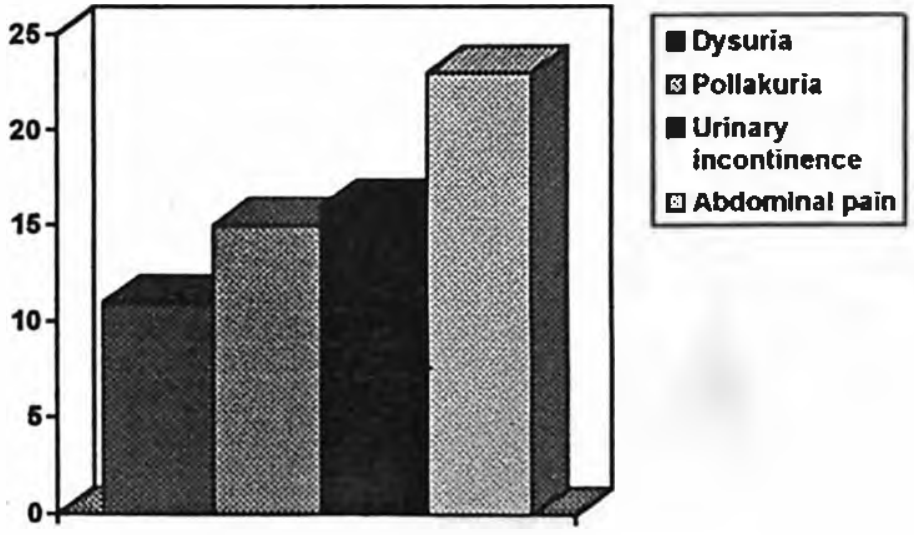

Fig. 3: Symptoms of children with hypercalciuria.

Discussion

Asymptomatic idiopathic hypercalciuria was first reported in 1978[10-12]. In literature, the prevalence is reported to be 2.9-6.2 percent[9, 10, 12, 13]. Our hypercalciuria prevalence was 5.88 percent, which is similar to that of Moore et al.[12]. The prevalence in Ankara and İstanbul were reported as 4.2 and 2.5 percent, respectively[9, 10]. The differences between regions of Turkey may speculatively be attributed to different water calcium concentrations. While the mean Uca/Ucr values of girls and boys were similar to those of Ghazali et al.'s[4], they were higher than those reported by others[12, 14]. This higher mean Uca-Ucr value may be the cause of endemic urolithiasis in Turkey[7].

Consistent with findings of other studies, except that of Moore et al.[12], was found that mean Uca/Ucr values did not differ with sex and age[4, 13-16].

We analyzed urinary samples for calcium content while the children were on an unrestricted diet. Several studies demonstrated that restriction of diet did not influence the results, but oral calcium loading did[4, 9, 12, 13, 17]. Distinguishing between renal and absorptive subtypes of hypercalciuria is important because of their different management. This distinction was made with an oral calcium loading test established by Pak et al.[17]. The variation in Uca/Ucr levels between samples from the same individual obtained at different times is helpful in the diagnosis of subtypes of hypercalciuria. Pak et al.[16] and Stapleton et al.[13] demonstrated in their studies that mean fasting value of Uca/Ucr was lower in absorptive hypercalciuria, but in renal hypercalciuria, there was no difference in the value following a meal. Forty children with hypercalciuria were considered to be renal subtype since there was no difference in the Uca/Ucr values after a meal.

Hypercalciuria may lead to resorption of calcium from bones resulting in secondary hyperparathyroidism. Coe et al.[18] and Moore et al.[19] found hyperparathyroidism in 2/3 and 42 percent, respectively, of cases with idiopathic hypercalciuria. In contrast, Stapleton et al.[2] found no hyperthyroidism among their cases with hypercalciuria. Our parathormone results were consistent with those of Stapleton et al.[2].

It has been stated that idiopathic hypercalciuria (IHC) may be familial with autosomal dominant trait[10, 11, 16, 20, 21]. In the study of Coe et al.[16], 26 of 73 relatives of nine patilents with hypercalciuria also had hypercalciuria. Likewise, Beilin and Clayton[22], Stapleton[2], and Carvera et al.[21] reported hypercalciuria in siblings and parents of children with hypercalciuria. Buckalew et al.[23] detected IHC in 13 of 64 members of a family. In 1988, Buyan et al.[20] described two forms of IHC, familial and non-familial. They stated that the familial form is inherited as autosomal dominant. In their study, urolithiasis was reported in 26.3 percent of the family members of patients with IHC[20]. We found urolithiasis in 29.8 percent

of first-and second-degree relatives of children with hypercalciuria. All these results suggest that children with hypercalciuria may unfortunately develop urolithiasis in the future.

Management of IHC is still controversial. Drug therapy is not recommended unless dysuria, recurrent gross hematuria, polyuria, recurrent urinary tract infection or urolithiasis is present. In most patients, adequate fluid intake and sodium restriction are sufficient[3, 5, 11, 19, 21, 22, 24, 25]. Because of the absence of the symptoms mentioned above in our cases, we also recommended only fluid intake.

Idiopathic hypercalciuria must be considered an important entity because of its onset in childhood, of its being asymptomatic in 80-90 percent of patients and of the risk of stone formation. Early diagnosis and management may reduce the incidence and morbidity, particularly in countries like Turkey where urolithiasis is endemic[7].

REFERENCES

1. Coe FL, Favus MJ. Disorders of stone formations. In: Brenner RFC (ed). The Kidney (3rd ed). Philadelphia: WB Saunders; 1986: 1402-1442.
2. Stapleton FB, Noe HN, Roy S3d, Jerkins G. Hypercalciuria in children with urolithiasis. Am J Dis Child 1982; 136: 675-678.
3. Hymes LC, Warshaw BL. Idiopathic hypercalciuria. Renal and absorptive subtypes in children. Am J Dis Child 1984; 138: 176-180.
4. Ghazali S, Barrat TM. Urinary excretion of calcium and magnesium in children. Arch Dis Child 1974; 49: 97-101.
5. Stapleton FB, Roy S3d, Noe HN, Jerkins G. Hypercalciuria in children with hematuria. N Engl J Med 1984; 310: 1345-1348.
6. Bianchi G, Vezzoli G, Cusi D, et al. Abnormal red-cell calcium pump in patients with idiopathic hypercalciuria. N Engl J Med 1988; 319: 897-901.
7. Akıncı M, Esen T, Tellaloğlu S. Urinary stone disease in Turkey: an updated epidemiological study. Eur Urol 1991; 20: 200-203.
8. Remzi D, Bakkaloğlu MA, Erkan İ, Özen HA. Pediatric urolithiasis. Turk J Pediatr 1984; 26: 43-49.
9. Çalışkan S, Erkan T, Sever L, Arısoy N. İstanbul'da çocuklarda hiperkalsiüri taraması. İst Çocuk Klin Derg 1992; 27: 36-38.
10. Buyan N, Saatçi Ü, Bakkaloğlu A, Beşbaş N. Okul çocuklarında asemptomatik hiperkalsiüri: epidemiyoloji ve patogenez. Çocuk Sağ Hast Derg 1989; 32: 43-50.
11. Heiliczer JD, Canonigo BB, Bishof NA, Moore ES. Noncalculi urinary tract disorders secondary to idiopathic hypercalciuria in children: Pediatr Clin North Am 1987; 34: 711-718.
12. Moore ES, Coe FL, McMann BJ, Favus MJ. Idiopathic hypercalciuria in children: prevalence and metabolic characteristics. J Pediatr 1978; 92: 906-910.
13. Stapleton FB, Noe HN, Jerkins G, Roy S3d, Urinary excretion of calcium following an oral calcium loading test in healthy children. Pediatrics 1982; 69: 594-597.
14. Bulusu L, Hodgkinson A, Nordin BE, Peacock M. Urinary excretion of calcium and creatinine in relation to age and body weight in normal subjects and patients with renal calculus. Clin Science 1970; 38: 601-612.

15. Esbjömer E, Jones IL. Urinary calcium excretion in Swedish children. Acta Paediatr 1995; 84: 156-159.

16. Coe FL, Parks JH, Moore ES. Familial idiopathic hypercalciuria. N Engl J Med 1979; 300: 337-340.

17. Pak CY, Kaplan R, Bone H, et al. A simple test for the diagnosis of absorptive and renal hypercalciuria. N Engl J Med 1975; 292: 497-500.

18. Coe FL, Canterbury JM, Firpo JJ, Reiss E. Evidence for secondary hyperparathyroidism in idiopathic hypercalciuria. J Clin Invest 1973; 52: 134-141.

19. Moore ES, Langman CB. Hypercalciuria in clinical pediatrics: a review. Clin Pediatr 1984; 23: 135-137.

20. Buyan N, Saatçi Ü, Bakkaloğlu A, Beşbaş N. Familial idiopathic hypercalciuria. Turk J Pediatr 1988; 30: 145-151.

21. Cervera A, Corral MJ, Gomez Campdera FJ, et al. Idiopathic hypercalciuria in children. Classification, clinical manifestatilon and outcome. Acta Paediatr Scand 1987; 76: 271-278.

22. Beilin LJ, Clayton BE. Idiopathic hypercalciuria in a child. Arch Dis Child 1964; 39: 409-414.

23. Buckalew VM, Parvis ML, Shulman MG, et al. Hereditary renal tubular acidosis. Report of a member kindred with variable clinical expression including idiopathic hypercalciuria. Medicine 1974; 53: 229.

24. Pak CY, Ohata M, Lawrence EC. Hypercalciuria: causes, parathyroid functions and diagnostic criteria. J Clin Invest 1974; 54: 378-400.

25. Kher KK. Urinary stone disease. In: Kher KK, Makker SP (eds). Clinical Pediatric Nephrology. MacGraw Hill Inc., Health Professions Divisilon; 1992: 699-719.