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Hypercalciuria in children with monosymptomatic nocturnal enuresis

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Abstract *Objective:* The aim of this study was to measure the 24 h urinary calcium content in children with monosymptomatic nocturnal enuresis (MNE) and compare with those in healthy children to investigate whether there is any relation with enuresis and hypercalciuria.
Material and methods: This study included 120 children and adolescents with MNE aged between 7 and 14 years. Eighty age- and sex-matched healthy children served as a control group. To determine urinary calcium excretion, 24 h urine samples were collected. The children with enuresis were divided into two sub-groups as hypercalciuric and normocalciuric groups according to the amount of urinary calcium excretion.
Results: Hypercalciuria was found in 27 (23%) of the MNE patients compared with two (4%) of continent children ($p < 0.001$). In addition, the mean 24 h urine calcium/body weight ratio was higher in the enuresis group than in the control group, 2.94 ± 2.42 versus 1.59 ± 1.72, respectively ($p = 0.002$). When the children with enuresis were divided into two groups as normokalsiuric and hypercalciuric, the hypercalciuric children were younger and the majority of this group were boys..
Conclusions: Our study showed that hypercalciuria is common in children with MNE, so we suggested measuring urine calcium levels in NE patients. However, further studies are needed to clarify the relationship between hypercalciuria and NE in larger series..

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Introduction

Nocturnal enuresis (NE) is a common problem in childhood and early adolescence. It is defined as intermittent incontinence, regardless of the presence or absence of concomitant daytime symptoms. Monosymptomatic NE (MNE) is bedwetting occurring without any daytime incontinence or urological symptoms. The excretion of large amounts of urine at night (nocturnal polyuria), lack of increment in plasma vasopressin at night, uninhibited nocturnal detrusor muscle contractions, and lack of arousal mechanisms have been proposed as pathogenic factors in this multifactorial condition. The causes of nocturnal polyuria in enuresis include sodium homeostasis, arginine vasopressin secretion, sympathetic and parasympathetic nervous system interactions, and, recently, renal calcium excretion [1–4].

Hypercalciuria has been claimed to be important in the pathogenesis of enuresis. Although several studies have shown that the frequency of hypercalciuria in pediatric enuresis patients is more than that in continent children, others could not establish a connection between hypercalciuria and NE [3–8]. The main purpose of this study was to evaluate calcium excretion in children with MNE and healthy continent children. An additional aim was to put forth the demographic and biochemical differences in enuretic children with and without hypercalciuria.

Methods

A total of 120 children aged 7–14 years with MNE were enrolled in the study. Enuretic children were selected from patients newly diagnosed according to the International Children Continence Society recommendations. Inclusion criteria for children with enuresis were enuresis frequency, at least three nights weekly; the lack of daytime symptoms such as incontinence, urgency, and frequency; the lack of clinical or laboratory signs suggestive of an underlying disease other than MNE; unremarkable clinical examination; and normal urine analysis. Our exclusion criteria were the presence of vesicoureteral reflux, urinary tract anomalies, chronic kidney disease, diabetes insipidus, diabetes mellitus, mental retardation and active neurological disease, history of urinary tract infection during the last month, nutrition with ketogenic diet, any treatment with corticosteroids, or diuretics in the last month, or high-dose vitamin D in the last 6 months. Eighty age- and gender-matched healthy children served as the control group.

Children were asked to collect their urine in separate containers for daytime and night-time urine samples during 2 days and nights at weekends. All collections were performed without restrictions in the quantity or quality of fluid intake. Daytime urine collections were obtained following spontaneous voiding. Night urine collections were collected by a Uridome in boys and an adhesive Assura device in girls. The collected urine was preserved in the refrigerator and delivered to us within a maximum of 48 h. The daytime, nighttime and 24 h urine volume and calcium excretion levels were measured separately in the urine samples collected on 2 consecutive days for each patient. The average of two samplings was calculated for study.

Table 1 Demographic features of enuretic and continent children and their mothers.

	Enuretic group ($n = 120$)	Controls ($n = 80$)	p
Children			
Age (year)	8.79 ± 2.24	8.61 ± 2.04	0.693
Boys, *n* (%)	76 (63%)	48 (60%)	0.789
Weight (kg)	28.0 ± 7.5	29.2 ± 7.7	0.866
Height (cm)	129 ± 13	131 ± 12	0.721
Mothers			
Age (year)	32.5 ± 5.9	32.9 ± 5.2	0.688
Married, *n* (%)	112 (93%)	75 (94%)	0.904
Employed/unemployed, *n* (%)	24(20)/96(80)	17 (21)/63 (79)	0.674
Duration of education (year)	7.4 ± 1.9	7.1 ± 1.7	0.685

Urine was measured and stored at −20 °C until analysis. The expected normal bladder capacity for age was calculated by the formula 30 + (30 × age in years) = volume (mL). An average nocturnal urine output on wet nights exceeding 130% of expected bladder capacity for age was used to define nocturnal polyuria.

Biochemical parameters included serum urea, creatinine, fasting blood sugar, electrolytes, alkaline phosphatase and parathyroid hormone (PTH), urinalysis, and culture. Serum samples were analyzed simultaneously using commercial kits on an Abbott C-16000 (Abbott-Laboratories, Abbott Park, IL, USA) autoanalyzer. Calcium levels in urine were measured using the spectrophotometric method. Hypercalciuria was defined as excess urinary calcium excretion greater than 4 mg/kg/day measured in a 24 h urine collection or urinary calcium/creatinine (Ca/Cr) ratio greater than 0.21 while taking a normal daily diet. The patients were divided into hypercalciuric and normocalciuric groups based on urinary calcium levels.

The local Research Ethics Committee approved this study protocol. Written informed consent was obtained from children older than 12 years and from the parents of all subjects. Our examinations of the patients conformed to good medical and laboratory practices and the recommendations of the Declaration of Helsinki on Biomedical Research Involving Human Subjects.

Quantitative results were expressed as mean or median. The Student *t*, Mann–Whitney *U* and chi-square tests were used for comparison between patients and controls and between patient subgroups according the data distribution pattern and/or sample size. Statistical analyses were done using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). A p value less than 0.05 was considered significant.

Results

One hundred and twenty enuretic (76 boys) and 80 continent (48 boys) children were included in the study. The mean ages of the children with MNE and controls were 8.79 ± 2.24 years and 8.61 ± 2.04 years, respectively. There was no significant difference in the gender, age,