Idiopathic hypercalciuria: presentation of 471 cases

Maria Goretti M. G. Penido, José Silvério S. Diniz, Maria Lúcia S. F. Moreira, Ana Luiza F. Tupinambá, Anderson França, Bruno H. Andrade, Marcelo F. de O. Souto

Abstract

Objective: to analyze the clinical history and evolution of children and adolescents with IH, emphasizing some of their peculiar features.

Methods: we followed 471 patients with IH at an outpatient clinic. Patients were submitted to the following protocol: abdominal X-ray, kidney and urinary tract ultrasonography; urinary ionogram, blood gas and biochemical analyses; 24-hour urine for measurement of calcium and other electrolytes and creatinine; urinalysis, urine culture and phase-contrast microscopy; second morning urine collected after fasting for measurement of calcium and creatinine.

Results: at the time of diagnosis, 6% of the patients were infants, 15% pre-school children, 55% school children, and 24% adolescents; 56% of them were boys. Clinical and laboratory findings were: 47% had hematuria and abdominal pain, 31% had isolated hematuria, 14% isolated abdominal pain, and 8% had urinary tract infection, nocturnal enuresis, suprapubic pain or urethralgia, or the frequency/urgency syndrome with urinary incontinence. Hypercalciuria was associated with urolithiasis in 56% of patients. There was association with hyperuricosuria in 18.5% of the cases, and hypocitraturia in 8.5% of the cases. Evolution was poor for 33% of the patients, with recurrence of nephrolithiasis, persistence of hematuria, and abdominal pain.

Conclusions: IH must be diagnosed and treated with criteria in order to reduce consequences such as hematuria, 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.


Introduction

Idiopathic Hypercalciuria (IH) is a metabolic change defined as an increased calcium urinary excretion in the presence of normocalcemia, whose clinical manifestation varies in adults and adolescents. Microscopic hematuria, macrohematuria episodes, unusual abdominal pain, and dysuria are the most commonly reported clinical symptoms. However, authors have observed other signs and symptoms associated with hypercalciuria such as nocturnal and/or diurnal enuresis, urinary urge incontinence, and suprapubic pain or urethralgia. Sometimes, the urinary elimination of blood clots is observed. A whole 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-1α and interleukin-6 production have been proposed in order to explain the physiopathology of IH.9,10

The possibility of multiple etiological mechanisms decharacterizes idiopathic hypercalciuria as a benign condition. Today, it is regarded as complicated not only because it predisposes calculus formation but also due to other consequences such as bone demineralization.11,12

We know that bone mass is most frequently accumulated during childhood, reaching its maximum during adolescence. This bone mass acquisition must occur without any interference so that an optimal peak bone is attained. Any interference in bone mass acquisition may be a determining factor for osteoporosis or fracture risks in adulthood.13,14

Therefore, treatment should not be exclusively concerned with reducing the urinary excretion of calcium. An active intervention in bone mass acquisition should be carried out in order to minimize deleterious effects of its reduction in adulthood.

The present study aims at investigating the history, manifestation and clinical evolution of idiopathic hypercalciuria in children and adolescents, by pointing out peculiarities presented by these patients and stressing the importance of a treatment for reducing the morbidity of this metabolic alteration.

Patients and methods

A group of 471 patients with idiopathic hypercalciuria were selected and submitted to specialized evaluation at the Saudade outpatient clinic of Pediatric Nephrology affiliated with the Health Secretariat of Belo Horizonte, and at the outpatient clinic of Pediatric Nephrology of Hospital das Clínicas (Universidade de Minas Gerais School of Medicine). These patients came from the city and suburban districts of Belo Horizonte and other towns in the State of Minas Gerais and, very few of them from the State of Espírito Santo and southern Bahia. Although patients’ family income was not surveyed, their average monthly income ranged between two and three minimum wages (180 to 270 U.S. dollars). The patients were followed up over 15 years (on average 10 years ± 2.73) at outpatient clinics. The study included patients who satisfied the criteria for idiopathic hyperuricosuria diagnosis and who did not suffer from endocrinopathies, nephropathies, other urinary tract or metabolic diseases which could predispose hypercalcemia and/or secondary hypercalciuria; with no current or recent (past 2 months) treatment with calcium, vitamin D or any drugs that act upon calcium metabolism; diurnal and nocturnal vesicourethral sphincter control; no idiopathic hypercalciuria treatment for at least one year. The diagnosis of idiopathic hypercalciuria was based on the urinary excretion of calcium equal or higher than 4mg/kg/24h.1,15,16

A total of 471 patients, 264 (56%) males and 207 (44%) females, were studied. 264 (56%) of them were whites, 174 (37%) non-whites, and skin color was not informed in 33 (7%) patients. The disease started to develop between the ages of 8 months and 17 years; 28 (6%) of the patients were infants, 71 (15%) were preschool children, 259 (55%) were school-age children and 113 (24%) were adolescents. Most patients, 221 (47%), initially presented hematuria associated with abdominal pain; 146 (31%) had isolated hematuria; 66 (14%) reported isolated abdominal pain and 38 (8%) suffered from urinary tract infection, nocturnal enuresis, suprapubic pain or urethralgia or the so-called urge syndrome with urinary frequency/urgency and/or incontinence. The family samples for determining calcium, uric acid, citrate, phosphate, magnesium, oxalate, creatinine, and qualitative cystine levels; two second morning fasting urine samples collected for determining the calcium/creatinine ratio values, uric acid and urinary pH obtained through gas analysis; one urine sample for microscopic sediment examination, urine culture and antibiogram, uncentrifuged Gram-stained urine specimen and phase-contrast microscopy; two blood samples for determining calcium, phosphorus, alkaline phosphatase, uric acid, magnesium, and creatinine levels; one blood sample for determining sodium, potassium, chloride, urea, parathormone, venous blood gas analysis and hemogram; two stool samples for parasitological examination, renal and urinary tract ultrasonography, and plain abdominal x-ray. A 50% v/v hydrochloric acid solution per liter was used to preserve the 24-hour urine sample collected for determining calcium, citrate, magnesium, phosphate, oxalate, creatinine levels, and qualitative cystine; sodium bicarbonate P.A. 5g per liter was used to preserve the 24-hour urine sample collected for determining bicarbonate content.

A value equal or higher than 80% was considered for the diagnosis of dysmorphic erythrocytes, which was assessed through phase-contrast microscopy.

After the diagnosis of hypercalciuria was confirmed, the patients were initially treated as follows: increased water intake; diet adjustment according to gender and age group, in which a normal calcium, normoprotein, normosodic and normocaloric diet was followed; administration of potassium citrate at 0.5 to 1.0 mEq/kg/24h. Purines were just restricted from the diet in the presence of idiopathic hyperuricosuria.

Hydrochlorothiazide was used at 0.5 to 1.0 mg/kg/24h in those cases which did not present improved clinical or laboratory results as to calcium hyperexcretion. The patients were treated within a minimum period of six months.

The study was approved by the Ethics Committee of the Universidade Federal de Minas Gerais School of Medicine.

Results

A total of 471 patients, 264 (56%) males and 207 (44%) females, were studied. 264 (56%) of them were whites, 174 (37%) non-whites, and skin color was not informed in 33 (7%) patients. The disease started to develop between the ages of 8 months and 17 years; 28 (6%) of the patients were infants, 71 (15%) were preschool children, 259 (55%) were school-age children and 113 (24%) were adolescents. Most patients, 221 (47%), initially presented hematuria associated with abdominal pain; 146 (31%) had isolated hematuria; 66 (14%) reported isolated abdominal pain and 38 (8%) suffered from urinary tract infection, nocturnal enuresis, suprapubic pain or urethralgia or the so-called urge syndrome with urinary frequency/urgency and/or incontinence. The family
Idiopathic hypercalciuria is a disease genuinely linked to heredity. In a single family, we usually find more than an individual with the same metabolic change. Following this trend, nephrolithiasis is also related to heredity; our study revealed the presence of nephrolithiasis among patients’ relatives in more than 50% of cases. Similarly, urinary stone formation occurred in more than 50% of patients, corroborating the fact that IH is a risk factor for stone formation, as described in other studies.

The study of erythrocyte morphology through phase-contrast microscopy revealed an isomorphic pattern in 71% of patients. The other patients presented a dysmorphic erythrocyte pattern, according to the findings of Vaibich et al. (1992).

The literature recommends the following treatment for IH: high intake of water, diet adjustment in terms of sodium and proteins, prescription of potassium citrate and thiazide diuretics. All patients in this study were submitted to the same treatment, where 67% showed considerable improvement, with favorable response, presenting normal calciuria, eliminating hematuria and abdominal pain, preventing the formation of new stones and the expansion of the existing ones, also eliminating urge syndrome, nocturnal enuresis, suprapubic pain and urethralgia. 33% of patients did not show satisfactory improvement, presenting recurrence of symptoms, especially after interrupting or reducing medication. Three types of responses to the specific idiopathic hypercalciuria treatment were observed: 1) 23% of patients responded to medication in the first two months of treatment and did not present hyperexcretion of calcium and its associated symptoms ever again; 2) 51% responded to medication during the first two months but had recurrence of hyperexcretion of calcium and its associated symptoms ever again; 3) 26% responded to medication in the first two months, but presented hyperexcretion of calcium and associated symptoms two months after the completion of treatment, having to take the medication again. All patients followed the recommended treatment.

As mentioned before, IH may cause bone mass reduction in children and adults. Unfortunately, bone mass evaluation was not performed on all the patients who participated in our study. As a result, the analysis was not possible.

Conclusively, IH is a metabolic change with some characteristics typical of children and adolescents. Signs and symptoms such as urinary urgency and incontinence, suprapubic pain, nocturnal enuresis and urethralgia may be associated with urinary hyperexcretion of calcium, in the presence or absence of urinary tract infection. This metabolic change must be treated and followed up closely as it can result in problems other than hematuria, abdominal pain and urinary stone formation.

References

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Correspondence:
Dra. Maria Goretti M.G. Penido
Rua Tomé de Souza, 1292 - apto 101 – Lourdes
CEP 30140-131 – Belo Horizonte, MG, Brazil
Phones: +55 31 225.2885 / 284.3451
Fax: +55 31 241.4466
E-mail: gabrielp@gold.com.br