Investigation of nephrolithiasis in the West of Paraná

Investigação de nefrolitíase no Oeste do Paraná

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Abstract

Introduction: Nephrolithiasis is common and has a high rate of recurrence. **Objectives:** To assess the prevalence of the main metabolic and anatomical changes and the chemical analysis of stone found in patients with nephrolithiasis in the West region of Paraná. **Methods:** Retrospective study with 681 adult patients with nephrolithiasis. The laboratory investigation included at least two samples of 24-hour urine test with doses of calcium, uric acid, citrate, oxalate, sodium and creatinine; qualitative cystinuria, urinary pH following 12-hour fast and water restriction, urine culture and chemical analysis, when the stones were available. Renal imaging techniques included at least renal ultrasound and excretory urogram. **Results:** The metabolic changes most frequently found were: hypercalciuria (51.8%), hyperuricosuria (27.6%), and hypocitraturia (23.5%). Chemical analysis of stones showed calcium oxa late in 85.7% of the cases. The most frequently anatomical changes were renal cyst, duplicated ureter, and ureteropelvic junction obstruction. **Conclusions:** This paper served as a base for knowing the characteristics of patients with nephrolithiasis in the West area of Paraná.

Keywords: nephrolithiasis, hypercalciuria, calcium oxalate.

Resumo

Introdução: Nefrolitíase é comum e tem alta taxa de recorrência. **Objetivos:** Avaliar a prevalência das principais alterações metabólicas e anatômicas e a análise química do cálculo encontrado em pacientes com nefrolitíase na região Oeste do Paraná. **Métodos:** Foi realizado um estudo retrospectivo em 681 pacientes adultos com nefrolitíase. A investigação laboratorial incluiu pelo menos duas amostras de urina de 24 horas, com dosagens de cálcio, ácido úrico, citrato, oxalato, sódio e creatinina; cistinúria qualitativa, pH urinário após 12 horas de jejum e restrição hídrica, urocultura e análise química do cálculo, quando disponível. Técnicas de imagem renal incluíram pelo menos ultrassonografia e urografia excretora. **Resultados:** As alterações metabólicas mais frequentemente encontradas foram: hipercalciúria (51,8%), hiperuricosúria (27,6%) e hipocitratúria (23,5%). A análise química dos cálculos mostrou oxalato de cálcio em 85,7% dos casos. As alterações anatômicas mais frequentes foram: cisto renal, duplicação pieloureteral e obstrução da junção pieloureteral. **Conclusões:** Este trabalho serviu de base para o conhecimento das características de pacientes com nefrolitíase na região Oeste do Paraná.

Palavras-chave: nefrolitíase, hipercalciúria, oxalato de cálcio.

Introduction

Nephrolithiasis is a prevalent and recurrent condition, considered as one of the most common urinary tract diseases. It affects from 5 to 15% of the world population, and has a great impact on economy and health worldwide[1-3]. In spite of the advances in surgical approaches, there have not been many changes in the history of nephrolithiasis. It affects youngsters between the third and fourth decades of life[4,5], but it is also common in children[6].

Many factors are related to the susceptibility to this disease, such as: age, gender, sedentary lifestyle, occupation, geographic and climatic aspects, heredity, and anatomic and metabolic alterations[7,8].

The initial purpose of the diagnosis of renal lithiasis must be to identify metabolic alterations. Hypercalciuria, hyperuricosuria, hypocitraturia, hyperoxaluria, cystinuria and urinary infection are the main causes of calculus formation[9,10].

Calcium oxalate is the chemical compound most commonly found in kidney stones. Studies suggest that it is present in approximately 80% of the cases[11].

Anatomic factors contribute to the formation of calculus, for example, with the high insertion of the ureter into the renal pelvis and the ureteropelvic junction obstruction, and they may also contribute to calculus formation by means of deficient drainage with urinary stasis and a higher incidence of infection. Patients with anatomically abnormal kidney stones must undergo metabolic evaluation to identify risk factors, start the medical preventive therapy, and reduce the risk of relapse[12].

The objective of the present study was to demonstrate the main characteristics of patients with nephrolithiasis in the West region of Paraná.

Methods

A retrospective study carried out with 681 patients in the Nephrology Service of *Ambulatório Geral do Hospital Universitário do Oeste do Paraná*, diagnosed with nephrolithiasis from 1995 to 2010. Inclusion criteria were: spontaneous, endoscopic or surgical kidney stone elimination, and/or radiological confirmation of its presence in the urinary tract in the previous six months. The 24-hour urine test information of patients was registered with more than one sample, family history, clinical presentation, analysis of kidney stones and imaging exams.

Laboratory investigation considered two or more blood and urine samples from the 24-hour tests, including calcium, uric acid, citrate, sodium, creatinine and urinary oxalate; and calcium, uric acid, creatinine and parathormone in the blood. Qualitative cystinuria, urinary pH after a 12-hour fast and fluid restriction uroculture and kidney stone analysis were performed.

Laboratory methods and reference values adopted for the 24-hour urine test samples were: calcium, atomic absorption spectrophotometry (< 4.0 mg/kg), uric acid, enzymatic uricase method (> 15 mg per kg), citrate, enzymatic method of citrate-lyase (> 320 mg), sodium, ion selective method (<150 mEq), creatinine, alkaline picrate method (> 1,000 mg) and urine volume, volumetric measurement in a Becker collector for visual analysis.

For the plasma dosage, the methods of choice were: calcium, colorimetric method (8.5 to 10.5 mg/dL), uric acid, colorimetric method with uricase (2.0 to 7.0 mg/dL), creatinine, alkaline picrate method (0.7 to 1.4 mg/dL) and parathormone, intact molecule assay. For the examinations with isolated urine samples, the methods were: qualitative cystinuria, sodium nitroprusside test, and measurement of urinary pH by means of reactive strips with red methyl and blue bromothymol indicator systems. Decreased urine volume was considered when at least one of the samples presented less than 15 mL/kg/day[9,13.] To perform chemical analysis, the colorimetric method was used[3,11].

Anatomical changes were considered as being fully investigated in cases in which kidney imaging exams were performed, including renal ultrasound and excretory urography.

Fisher's exact test and $\chi 2$ were used to compare the variables, being considered as statistically significant $p<0.05$. This study was approved by the Human Research Ethics Committee of *Universidade Estadual do Oeste do Paraná* (UNIOESTE).

Results

Out of the 1,450 medical files studied (mean age of 39.5 ± 12.9 years), 781 patients were female (54.7% with a positive family history); 681 concluded metabolic investigation (mean age of 39.1 ± 10.6 years; 54.9% were female); 388 met the inclusion criteria for anatomical change (mean age of 39.0 ± 24.0 years; 53.9% were female); and 126 were submitted to kidney stone chemical analysis (mean age of 40.6 ± 10.9 years; 50% were female).

From the 681 patients who concluded metabolic investigation, at least one change was found in 638 of them (93.7%), and some patients presented more than one change. Metabolic changes were: hypercalciuria in 51.8% of the patients; hyperexcretion of uric acid in 27.6%; hypocitraturia in 23.5%; low urine volume in 19.8%; urinary tract infection in 13.5%; hyperoxaluria in 8.0%; hyperparathyroidism in 5.6%; renal tubular acidosis in 0.7%; and cystinuria in 0.7%. When metabolic disorders were compared between genders, hyperexcretion of uric acid was more frequent in men, and urinary tract infection in women ($p <0.05$; Table 1).

Table 1 Metabolic alterations found in 681 patients suffering from nephrolithiasis according to gender

Metabolics alterations	Male (n = 307)		Female (n = 374)		p-value
n	N	%	N	%	
Hypercalciuria	178	58.0	175	46.8	0.004#
Hypocitraturia	74	24.1	86	23.0	0.734#
Hyperuricosuria	117	38.1	71	19.0	< 0.001#
Low urine volume	53	17.3	82	21.9	0.129#
Hyperoxaluria	27	8.8	27	7.2	0.449#
Urinary infection	11	3.6	81	21.7	< 0.001#
Hyperparathyroidism	16	5.2	22	5.9	0.704#
Renal tubular acidosis	4	1.3	1	0.3	0.181*
Cystinuria	3	1.0	2	0.5	0.662*
Without detected alterations	20	6.5	23	6.1	0.846#
Total	503		570		

 # $\chi 2$, * Fisher's exact test

Calcium oxalate calculi were found in 85.7% of the cases. Hypercalciuria and hyperuricosuria were the most associated metabolic disorders in patients with calcium oxalate and uric acid (60%). Table 2 shows the chemical analysis performed when the kidney stones were available.

Anatomical changes were found in 33.5% of the 388 analyzed patients. Renal cyst, complete or incomplete ureteral duplication and ureteropelvic junction obstruction were the most frequent ones. Table 3 describes these alterations.

Discussion

Nephrolithiasis is a highly prevalent and recurrent disease, and also one of the most common urinary tract disorders[12]. Besides, it is an avoidable cause of morbidity and represents a high cost to society[14]. Men present a greater risk of having kidney stones, with rates up to four times higher when compared to women. The condition affects mainly youngsters. In this study, men are prevalent (61.2%), with mean

Table 2 Chemical analysis of urinary calculus in 126 patients

Chemical composition	N	%
Calcium oxalate	108	85.7
Calcium carbonate	55	43.7
Uric acid	27	21.4
Ammonia	20	15.9
Calcium phosphate	10	7.9
Cystine	1	0.79
Magnesium	3	2.4
Total of chemical compounds	224	

Table 3 Anatomical changes in 153 patients

Anatomical changes	Total	%
Renal cyst	55	35.9
Pyeloureteral duplication	28	18.3
UPJ Stenosis	15	9.8
Single kidney	11	7.2
Atrophic kidney	9	5.9
Medullary sponge kidney	10	6.5
Polycystic kidneys	6	3.9
Pelvic kidney	4	2.6
Neurogenic bladder	3	1.9
Renal ptosis	3	1.9
Horseshoe kidney	4	2.6
Bad renal rotation	2	1.3
Calyceal clubbing	1	0.7
Dilatation of the ureter	1	0.7
Stenosis of the distal ureter	1	0.7
Polycystic horseshoe kidney	1	0.7
Kidney tumor	1	0.7
Total of alterations	155	

UPJ: ureteropelvic junction.

age of 32.2 years, which is in accordance with literature[15-17]. The prevalence of caucasians is also observed (85%), but this is in accordance with the general population of the West of Paraná. In 96.5% of the patients at least one metabolic disorder was found. The most frequent metabolic changes were hypercalciuria (51.8%), hyperexcretion of uric acid (27.6%) and hypocitraturia (23.5%), result that is similar to other studies[18,19].

The decrease in urine volume is considered to be a cause of nephrolithiasis. In countries with hot climate, extrarenal losses and low fluid ingestion may also contribute to the formation of calculi. In the present study, a decrease in urine volume was observed in 13.8% of the patients, result that is much lower than the rates found in the countryside of the state of Sao Paulo, where the climate is warmer; in this region, the index was 77%[20].

Hypercalciuria was the cause of more than 50% of metabolic disorders in adults, and from 53 to 75% in children[21]. It is possible that there is a strong genetic component, with autosomal dominant interaction[22]. It is a result of the mutations in genes that are direct or indirectly involved with the renal tubular transport of calcium, among them, CLCN5, CLCNKB and WNK kinases. CLCN5 gene mutations are related to the so called Dent's Disease. Hypercalciuria may be associated with hypophosphatemia due to mutations in phosphorus /sodium cotransporter proteins, encoded by the NPT2a gene[23-25]. In children with hypercalciuria, the prevalence of renal lithiasis in the family ranges from 46 to 49%[26-28].

Idiopathic hypercalciuria is a heterogeneous disorder that includes absorptive, renal and resorptive forms[29-31]. A hypersodic diet must be taken into account for the pathogenesis of hypercalciuria[32]. In this study, hypercalciuria was the prevalent metabolic change. In the West of Paraná, the ingestion of milk and dairy products is not expressive; meanwhile, the ingestion of salt and protein is frequent, which probably contributes to the occurrence of hypercalciuria[10].

Hypocitraturia is a metabolic abnormality found in 20 to 60% of the patients with nephrolithiasis[28,33,34]. In this study, such change was observed in 23.5% of the metabolic disorders. Tefekli *et al.*[35] referred to hypocitraturia as the most prevalent metabolic risk factor in children and adults with renal lithiasis (60.6%). Since the etiology of hypocitraturia is multifactorial and directly related to the consumption of animal protein, promoting acid overload, its incidence varies in the different studied regions[36].

Hyperuricosuria results from the frequent ingestion of purines or high endogenous production. Low fluid ingestion and urinary pH below 5.5 favor the precipitation in acidic urine[28,37]. Hyperuricosuria was detected in 27.6% of the metabolic disorders observed in patients. It is believed that the hyperprotein diet in the region should be a risk factor. National literature observes such disorder in 18 to 76% of the cases[20]. In this study, hyperuricosuria was more frequent in male patients.

Hyperoxaluria is a rare disorder, and it was observed in approximately 1% of the studied patients[5]. In this study, such disorder was found in 8% of the patients. Infected calculi are a consequence of the microbial proliferation that changes the chemicals found in urine. Urease positive microorganisms produce ammonia and bicarbonate that can cause struvite precipitation, forming Staghorn calculus in the collector system[2]. In the present study, urinary tract infection was more frequent in female patients; however, there is no information about the incidence of Staghorn calculus.

Daudon *et al.*[38] found a male prevalence among patients with calcium oxalate calculi and uric acid; a female preponderance for patients with calcium phosphate and struvite calculi; and an increasing prevalence of uric acid calculi with age in both genders. Chemical analyses demonstrated that calcium oxalate is the most common component found in kidney stones[39]. Calcium oxalate calculi were also found in 85.7% of the cases in this study.

Calculus is more common in patients with anatomic disorders. The prevalence of kidney stones in patients with renal cyst, autosomal dominant polycystic kidney disease, medullary sponge kidney, ureteropelvic junction stenosis and pyeloureteral duplication exceeds that of kidney stones in the general population, which suggests that malformation disorders favor calculus formation. Urine stasis with delay in carrying crystals increases the risk of urinary tract infections[40,41]. The most frequent anatomical changes in the present study were renal cysts and reteropelvic junction obstruction in ureteral duplication.

Nephrolithiasis has been associated with hypertension, obesity and diabetes mellitus. The prevalence of cardiovascular events among kidney stone agents has recently been recognized. There is historical evidence of the diet influence on calculus. A medically controlled diet and changes in lifestyle are essential to reduce the prevalence of nephrolithiasis and cardiovascular risks[42].

This paper was the base for the knowledge of the metabolic profile of patients with lithiasis of the West region of Parana, Brazil. The most frequent metabolic alterations were hypercalciuria, hypocitraturia and hyperuricosuria.

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