BANTAO Journal 2020; 18(1): 14-17

BJ
BANTAO Journal

Original article

Influence of Nephrolithiasis and Urinary Tract Infections on the Renal Function in Autosomal Dominant Polycystic Kidney Disease

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Abstract

Introduction. The prevalence of nephrolithiasis is considerably greater in patients with autosomal dominant polycystic kidney disease than in the general population. The anatomic factors leading to increased intrarenal obstruction, conditioning cyst growth, followed by renal tubular stasis alongside metabolic disorders, are important and may predispose stone formation. Presence of urinary tract infections in patients with adult polycystic kidney disease can influence the progression of the disease.

Methods. Forty patients with autosomal dominant polycystic kidney disease, mean age 43.2±11.8 years, 19 males and 21 females, underwent echosonography and computed tomography scan to evaluate the prevalence of nephrolithiasis in polycystic kidneys. Routine blood analysis and urine samples, including 24h urine collections were done. Patients were also evaluated from the aspect of urinary tract infection. Criteria for the presence of urinary tract infection were: more than 10 leucocytes in the urine sediment and positive urine culture.

Results. Renal stones were detected in 17 out of 40 patients (42.5%). The morphologic data presented patients with autosomal dominant polycystic kidney disease and nephrolithiasis had more renal cysts and larger predominant cyst size than patients without nephrolithiasis ($p<0.05$). Renal function expressed by creatinine clearance was also different between the 2 groups of patients (73.2±8.7 in patients with nephrolithiasis, and 96.8±7.6 in patients without nephrolithiasis). Twenty-four hours urine analysis showed that patients with nephrolithiasis had significantly lower urine volumes and levels of uric acid. Kaplan-Meier's statistical analysis demonstrated that the worsening of the renal disease depends on the presence of urinary infections in these patients. Comparing the 2 groups of patients (with and without infections), we found that patients with infections had worse renal survival ($p<0.05$). Three patients had urinary tract obstruction, ureterolithiasis with hydronephrosis, with diminished creatinine clearance, but after deopstruction and elimination of the calculi, the renal function was improved.

Conclusion. Nephrolithiasis is an important factor in further progression of renal damage in patients with autosomal dominant polycystic kidney disease accelerating its decline, especially followed by urinary tract infections.

Key words: polycystic kidney disease, nephrolithiasis, urinary tract infections

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary disease, which leads to terminal stadium of chronic renal failure and treatment with renal replacement therapy [1-3]. The disease is on the 4th place among kidney disorders, leading to chronic haemodialysis treatment. With 8-10% of these patients in haemodialysis units, adult polycystic kidney disease takes important place considering the other kidney diseases [3-5]. It is a genetic disorder characterized by formation of cysts in the kidneys. Symptoms caused by cyst formation in the kidneys include high blood pressure, pain on the sides of the body between the last rib and the hip (flank pain), hematuria and progressively loss of kidney function. In most patients, ADPKD eventually progresses to end-stage renal disease, requiring renal replacement therapy, either dialysis or renal transplantation. The disease itself is not simply a kidney disorder and other organ systems of the body can potentially be affected by the development of cysts. The specific symptoms present in each person depend on the specific organ systems involved. The liver, pancreas, the arachnoid membrane of the spinal cord and brain, the prostate, and the glands of the male reproductive tract that produce fluid that is part of semen (seminal vesicles) may become involved. Abnormalities affecting the cardiovascular system may also occur in individuals with ADPKD [2, 3].

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The prevalence of nephrolithiasis is considerably greater in patients with autosomal dominant polycystic kidney disease than in the general population [6-8]. The anatomic factors, such as cyst growth, renal tubular stasis and metabolic disorders, are important and may predispose to stone formation [7, 9-11]. Renal ultrasound may under detect nephrolithiasis, but computerized tomography, provides an excellent technique for distinguishing renal calculi from cyst calcifications in patients with ADPKD [1, 3, 12, 13].
This study aimed to assess the frequency of the presence of renal stones in patients with ADPKD, as well as to detect factors that contribute to stone formation, but also to find the influence of nephrolithiasis and urinary tract infection on the progression of the disease.

Material and methods

In order to evaluate the nephrolithiasis in polycystic kidney disease, 40 patients with autosomal dominant polycystic kidney disease, mean age 43.2±11.8 years, 19 males and 21 females, underwent echosonography and computed tomography scan. Considering the different morphology of the kidneys in adult polycystic kidney disease, we analyzed the impact of the cyst number, the cyst diameter and the renal volume, on the presence of nephrolithiasis in these patients. The clinical and laboratory evaluation included routine blood analysis, urine samples, and 24h urine collections for all the patients. Moreover, the presence of urinary tract infection was studied, which commonly is associated with nephrolithiasis. The presence of urinary tract infection was confirmed with finding of over 10 leucocytes in urine sediment, with confirmed positive urine culture. The diagnosis of ADPKD was mainly done by abdominal and renal ultrasound using HDI and 3 to 5 MHz covex-array transducer based on criteria established by Ravine [14]. The diagnostic criteria for individuals who have a 50% risk of developing ADPKD include:

- At least two unilateral cysts in one kidney or one bilateral cyst in both kidneys in individuals younger than age 30.
- At least two cysts in each kidney in individuals between 30 and 59 years.
- At least four cysts in each kidney in individuals 60 years old or older.

CT scan was performed in patients with suspected calculi, not detected clearly by ultrasonography, and where was needed to distinguish the calculi from calcification of the cysts. Urinary tract infections were detected during the period of 3 years follow up.

Statistical analysis

All the statistical analyses were performed with the SPSS software (Statistical Package for the Social Sciences, version 19.0, SPSS Inc, Chicago, IL, USA). Results were expressed as mean ± standard deviation. Categorical data were compared between groups by the chi-square test and parametric data with regular distribution by t-test. Kaplan-Meier's estimate was used to evaluate survival with "end point" on the creatinine clearance 60 ml/min equal to stage 3 chronic kidney disease.

Results

The presence of nephrolithiasis was identified in 17 out of 40 ADPKD patients (42.5%). The collected data were compared between the two groups of patients, presented on the following tables. Table 1 and 2 presents respectively laboratory findings of serum and urine of patients with and without nephrolithiasis.

Table 1. Median values of serum parameter

Parameter	Pts with NL*	Pts without NL	P Value
Creatinin clearance (ml/min)	73.2±8.7	96.8±7.6	0.67
Sodium (mmol/l)	142±3.6	138±4.2	0.83
Potassium (mmol/l)	4.3±2.4	3.8±1.4	0.52
Calcium (mmol/l)	2.4±0.9	2.1±0.5	0.33
Uric acid (μmol/l)	258±11.2	167±7.1	0.19

*NL-nephrolithiasis

Median values of the creatinine clearance were 73.2±8.7 ml/min, in patients with nephrolithiasis, and 96.8±7.6 ml/min in patients without calculi. Uric acid as important factor for composing calculiwas 258±11.2 μmol/l in patients with nephrolithiasis, and 167±7.1 μmol/l in those without calculi. The electrolyte status was as follows; in the group of patients with nephrolithiasis: Na 142±3.6; K 4.3±2.4; Ca 2.4±0.9 mmol/l, and in the group of patients without nephrolithiasis: Na 138±4.2; K 3.8±1.4; Ca 2.1±0.5 mmol/l.
The values for the urinary parameters are presented in Table.2. In patients with renal calculi we found that Na was 146.7±28.1, K 42.5±13.8, Ca 3.7±1.5 mmol/l, and the uric acid 2.63±0.96 mmol/l. On the contrary in the other group of patients without nephrolithiasis Na was

Table 2. Values of urinary parameters

Parameter	Pts with NL*	Pts without NL	P Value
Na (mmol/l)	146.7±28.1	142.2±32.5	0.78
K (mmol/l)	42.5±13.8	38.8±14.1	0.26
Ca (mmol/l)	3.7±1.5	2.9±1.6	0.14
Uric acid (mmol/l)	2.63±0.96	3.99±1.05	0.46

*NL- nephrolithiasis

142.2±32.5, K 38.8±14.1, Ca 2.9±1.6 mmol/l, and also uric acid 3.99±1.05 mmol/l.
In table 3 are the morphologic data of the polycystic kidneys in patients with nephrolithiasis and without nephrolithiasis. Cysts number in patients with nephrolithiasis varies from minimum 30 to up to 40, but in