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Prevalence, diagnosis and treatment in urolithiasis

Monika Kusz[1], Adam Alzubedi[2], Joanna Popiołek[3], Michał Konopelko[4]

1. Department of Paediatric Nephrology, Medical University of Lublin
2. Department of General and Transplant Surgery and Nutritional Treatment, Medical University of Lublin
3. Department of Cardiology, Cardinal Waszynski Hospital in Lublin,
4. Chair and Department of Hygiene, Medical University of Lublin,

Correspondence: Monika Kusz, Department of Paediatric Nephrology, Medical University of Lublin Ul. A. Gębali 6, 20-093 Lublin, Tel. 504429544. E-mail: moniakusz@gmail.com

Abstract

Kidney stone disease is one of the most common disorders and can be considered a disease systmetic. It occurs in about 5-20 % of all population. Due to the chemical composition of deposits there are several types of kidney stones including calcium oxalate, calcium phosphate, uric acid, magnesium-amonium, phosphate, cysteine. Nephrolithiasis is more common in men than in women. Kidney stones are formed as a result of the crystallization of minerals and their salts.
The cause of stone formation in the kidneys also contributes some drugs (such as corticosteroids), hyperparathyroidism, osteoporosis, long-term treatment of peptic ulcer with alkalizing preparations, overdose of vitamin D and improper diet. The most important in treatment of renal colic is relieving pain. Sometimes it is enough to administer analgesics, but sometimes it is necessary to administer strong opioid drugs. Effective medical treatments including thiazide, potassium citrate, acetohydroxamic acid can prevent new stone formation in most patients.

Keywords: urolithiasis, hypercalciuria, nephrolithiasis, kidney stones,

Epidemiology

Nephrolithiasis is one of the most frequent diseases in the world. The prevalence is estimated between 5 to 10 % of all cases and calcium nephrolithiasis occurs 70 to 85 % of all cases. Epidemiology. About 25 % of patients experience recurrent stone formation. [1] The urinary stone formation is a common disease and increasing from 3,8% in 1976-1980 to 8,4 % in 2007 to 2010.[2]

There are a lot of genes which are associated with calcium kidney stones. Adenylyl cyclase gene *(ADCY10)* have been linked to bone loss and I is related to asoprtive hypercalciuria in kidney stone patients. [3] CLDN14 gene encodes for tight junction claudin-14 have been linked to reduced BMD at the hip. [4]

Pathogenesis

Around 75 % of all patients with urolithiasis develop calcium stones, most of them are composed of calcium oxalate.[5] Uric acid, calcium phosphate, struvite and cystine stones can be distinguished. Oxalte stones is the second most common stone. The mechanism is unclear but may be closely related to diet. Cystines stones can form in people who suffer form cystinuria. This disorder runs in families, both men and women. Uric acid stoned are more common in men than women. They can occur with gout or chemotherapy. Struvite stones are mostly found in women who have urinary tract infection.

Two theories regarding calcium stone formation are identify. One of them concern the supersaturation of the urine by stone-forming constituents such as oxalate, calcium, uric acid which involve in the [process of crystal formation. It is believed that these aggregates increase slowly in size over the time. [5]

The second theory begins in the renal medullary interstinum and then pushed at the renal papilla, forming the Randall's plaque. It's usually composed of calcium and phosphorus. What is more, vitamin D play an important role in calcium and phosphorus metabolism, therefore, 25-hydroxyvitamind D3 and the active form, 1,25 dihydroxyvitamin D3 are pivotal in stone formation. Hypercalciuria is considered to be one of the most common metabolic disorder in patients with urolithiasis.[6]

Risk factor

Urolithiasis is a multifactorial disease. Genetic and environmental factors have effects on onset and severity urolithiasis. Plenty of environmental factors are responsible for high prevalence of urolithiasis. Obesity, diabetes, metabolic syndrome may strongly associate with calcium and uric acid formers.[7] A low fluid intake which subsequently high concentrations of stone-forming solutes in the urine. Moreover, high dietary salt, oxalate and protein presumably have been associated with urine composition to promote stone formation. Oxalobacter formigenes is an important bacterium which reduce oxalate absorption the large intestine.[8] Urease-producing organism such as Proteus species, which responsible for recurrent urinary tract infections associated with high urine ph, are crucial factors for struvite stones. [9] Moreover, some gastrointestinal operations such as jejuno-ileal bypass or bariatric surgery ale associated with hyperoxaluria and calcium oxalate stones. There are plenty of medications which are involved in stone formation. Indinavir, atazanavir, acetazolamide, triamterene, sulfa drugs including sulfasalazinem sulfadiazine and topiramate are distinguished.[2]

What is more some genetic factor are initial in development in kidney stone formers. More than 50% of all patients with urolithiasis have first-degree relative with stones.

Occupational statues such as teachers or pilot are in the risk group of kidney stones because of low-fluid intake. Disease such as myelomas, inflammatory bowel diseases - ulcerative colitis and Crohn's disease, sarcoidosis could predispose to evaluate nephrolithiasis. Anatomical

alterations such as congenital vesicoureteral refluxes, urinary tract diverticula, horseshoe kidneys, sponge kidneys, stenosis -checks-ureteral and pyeloureteral junction, secondary to urological surgeries could contribute to urolithiasis. [10]
Hypercalciuria is defined as the excretion of urinary calcium over 250 mg per 24 h in women and 300 mg per 24 h in men [11] . The mechanisms which are responsible for HC is increased gut calcium absorption. Normally intestinal calcium absorption rises with dietary intake, around 25 % of dietary calcium is absorbed. Whereas, around 30 % of dietary calcium is absorbed in patients with idiopathic hypercalciuria. [6]

Clinical manifestations
The intermittent pain often begins suddenly in lumbar region and radiates into the pelvis and external genitals. The renal colic is described as one of the strongest pain sensations comparable to pain at delivery. Nausea, vomiting and sweating may be observed. Microhematuria or grosshematuria are present usually. [12]

Imaging studies
Intravenous pyeolography (IVP) was on of the first diagnostic procedure of choice in diagnosis of renal colic, but because of higher radiation exposure, low sensivity and potential contrast reactions is no longer acceptable tool for visualizing stones. It is contraindicated in patients with contrast medium allergy, pregnant women and impaired renal function. [13]
Currently the gold standard for the diagnosis of urolithiasis is computed tomography (CT). Superior sensitivity around 96-100%, specificity and accuracy of 96-98% are main advantages responsible for choosing this procedure.[13] Moreover it provide information about the stone composition, extent of obstruction, renal anatomy.[14] Calcium stones are radio-opaque, whereas uric acid stoned are never opaque. Cystine and struvite stones are usually radio-opaque. What is more CT is faster and safer than IVP because it does not required any contrast.
In patients with suspection of nephrolithiasis the acceptable initial form is ultrasonography. Magnetic resonance is not appropriate for detection of stones. Ultrasound is an imaging modality that uses high frequency sound waves and it is useful for detecting and locating renal stones especially in children. This technique detect all types of stones except for stones located in ureter. [15]

Laboratory studies
All cases of recurrent urolithiasis required metabolic evaluation to determine the etiology. 24-h urine collection is recommended by National Institutes of Health Consensus Development Conference on the Prevention and Treatment of Kidney Stones.[2] The basic evaluation warrant include serum electrolytes, creatine, calcium, phosphorus, uric acid, blood urea nitrogen. Parathyroid hormone level, 25-OH vitamin D, 1,25 hydroxyvitamin D may be appropriate for patients mainly with hypercalcemia.

Treatment
Medical intervention including treatment by drug therapy or surgical removal depending upon stone size ,shape, type and location.
For relieving pain non steroidal anti-inflammatory drugs (NSAIDs) and opioids provide the most effective analgesia. The first line treatment should be started with an Diclophenac sodium, Indomethacin, Ibuprofen. The second line is hydromorphine, pentazocine, tramadol. The third line is spasmolytics.[12] Both the categories of drugs are equally effective. The main

drawback of NSAIDs are potential gastrointestinal and renal side effects, while opioid cause nausea, vomiting.

Medical expulsive therapy (MET) allow to pass sized distal ureteral calculi from urinary tract. Alpha-adrenergic blockers also reduce the number of recurrent colic. [12] 2 L in urine volume per day has been crucial to reduce the incidence of stone forming. Thiazide diuretic decrease urinary calcium are the main therapy for patient with hypercalciuria. There are some factors predisposing to reduce urinary citrate excretion such as hypokalemia, metabolic acidosis, excessive protein intake, hypomagnesemia, infections, androgens, starvation, acetazolamide.

Many protective factor could be distinguished to avoid stone disease. Greater fluid intake, normocalcemic diet (1000-1200mg/day) are considered one of the most important factors. [11] Dietery animal proteins may produce metabolic acidosis, which is known risk factor for bone resorption and may develop osteopenia or osteoporosis. The Women's Health Initiative involve 83,000 women. Studies have shown that the dietary intake of fruits, fiber and vegetables reduce the incident of kidney stones. [16] Moreover both caffeinated or decaffeinated coffee, tea, wine ,orange juice all decrease risk of stone formation.[17]

What is more in men with body mass index (BMI) less than 25kg/m2, high intake of vitamin C (more than 1000mg/d) observed increase risk of urolithiasis. It is not observed in women.

treatment procedures, such as extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy, and ureteroscopy [18].

A low urinary- citrate excretion (less than 320mg/day) cause kidney stones in up to 2/3 of cases. Citrate decrease urinary supersaturation of calcium salts by forming soluble complexs with calcium ions which inhibit crystal growth and aggregation.

The treatment for urolithiasis is multiple. It's according to the size of the stone, its location and the age of the patient.

Complications – recurrent urinary tract infections – risk of pyelonephritis and urosepsis, urinary obstruction – inflammation of the kidney hydronephrosis. Acute kidney injury

Extracorporeal shock-wave lithotripsy (ESWL) is successfully used for stone removal in patients with stones with diameters below and above 20 mm. The results of ESWL showed stone free rates from 66-99% for smaller stones and around 45-60% for larger stones. [19] The main complications after ESWL are hydronephrosis, pain, fever, urosepsis, severe haematuria, renal haematoma, steinstrasse. The contraindications are pregnancy, bleeding disorders and abdominal aneurysm.

Percutaneous nephrolithotomy (PCNL) is the gold standard for managing large and complex renal stones. PCNL is a minimal invasive technique, involves direct fragmentation of the kidney stone through a small incision made in the flank through which a nephroscope is passed directly into the kidney. This method carries a risk of complications such as bleeding, infections or urinary fistulas. [20]

Ureterorenoscopy (URS) has dramatically changed the management of ureteral calculi. It is a procedure in which a small telescope is inserted through the urethra and bladder into the ureter or kidney. It is used to diagnose and treat a stones in the urinary tract. Thanks to improvement of ureteroscopes the success rate under sedation analgesia is around 88-97 %. The complications of URS is very low. The most common are sepsis, stricture, uretral injury and urinary tract infection.

Three techniques are currently available (Table 1**).**

Open surgery has been used less and less often since the development of the previously mentioned techniques. Now it constitutes less than 1- 5,4 % % of all interventions.[21] The disadvantages include longer hospitalization, convalescence, increased requirements for blood

transfusion. The indications for open stone surgery during the past 20 years has changed. The indications for this method for stone removal include: complex stone burden, failure in treatment with ESWL,PCNL, morbid obesity, skeletal deformity, fixed deformities of hips and legs, anatomical abnormalities such as infundibular stenosis, stone in the caliceal diverticulum, obstruction of the ureteropelvic junction, stricture, non-functioning kidney, non-functioning lower pole, stone in an ectopic kidney where ESWL may be difficult or impossible, cystolithotomy for giant bladder calculus. [22]

Primary therapeutic method	Indications
Extracorporeal shock wave lithotripsy (ESWL).	Stone size < 2 cm; upper uretral stone
Ureteroscopy (URS)	Stone size < 2 cm; lower uretral stone
Percutaneous removal or lithotripsy	Stone size > 2 cm; complex calculus, cystine stone

Table 1. Approach to treatment of a stone according to stone size

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