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Review Article

Pediatric Stone Disease

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Abstract

Introduction: Pediatric stone disease is one of the most common urological issues in pediatric urology practice.

Material and Methods: Analysis and evaluation of current literature about pediatric stone disease through a Pub-Med based search.

Results: In this review article we will summarize basics on pediatric stone disease and discuss recent advances both in surgical approaches and medical therapy options.

Conclusion: Pediatric stone disease management requires knowledge on pathophysiological aspects and treatment options, especially in this particular patient population.

Keywords: Pediatric stone disease; Nephrolithiasis in children; Pediatric urolithiasis; Pediatric nephrolithiasis

Introduction

Pediatric stone disease is one of the most common urological issues in pediatric urology practice. The incidence of urinary stone disease is increasing in children in last decades [1]. Treatment modalities and medical recommendations are still mainly based on studies on adult patients. In this review article we will summarize basics on pediatric stone disease and discuss recent advances both in surgical approaches and medical therapy options.

Epidemiology

Pediatric stone disease incidence increased to 50 per 100.000 adolescents during last 25 years [1]. Dietary alterations such as high sodium and carbohydrate consumption may be one of the reasons of this shift. Apart from environmental effects, some metabolic anomalies may be responsible for stone formation in children. Stone formation in children is almost equal in male and female gender, in contrast to male gender dominancy in adults [2]. Urinary stones are mostly located at the upper urinary tract. In underdeveloped countries, stone formation in bladder may be seen. Stone disease has also geographical tendencies; endemic in Turkey, Pakistan, South Asian, African and South American states [3].

Diagnosis

Non-specific symptoms such as irritability and vomiting may be the only symptoms for urinary stones in very young children. Main symptoms in older children are flank pain and heamaturia. Sole laboratory finding may be microscopic heamaturia [4]. Urinary stones may be detected incidentally or in routine radiological workup in urinary tract infections.

In children with urinary stone suspicion, Ultrasonography (USG) is a very effective and feasible imaging modality for initial evaluation. It has advantages like fast and real time imaging with its radiation-free property. Diagnostic success of USG has been widely studied and it has proven high effectiveness. Passerotti et al determined diagnostic accuracy of USG with 76% sensitivity and 100% specificity when compared with Computerized Tomography (CT) as reference test [5]. Stones that not detected with USG while CT were positive were 3 ureteral stones and 8 non-obstructive kidney stones with an average size of 2.3 mm and only one of them was larger than 5 mm. In another series, USG detected 89% of stones which requires surgical intervention [6].

While high suspicion of urinary stone stills and no definite diagnosis established with USG and X-ray radiography, CT may be considered. Non-contrast helical CT is the most sensitive imaging modality for detection of urinary stones. However, higher radiation exposure is a major drawback in children. There are some studies evaluating CT related high dose radiation and increased cancer risk. According the study of Kuhns et al, ratio of the risk for any abdominal and pelvic cancer due to a single CT examination with the aim of calculi detection may be responsible of 2-3/1000 cancers in naturally occurring over the lifetime of a child. Cumulative risk may be higher [7].

Radiograms also effective to identify radio-opaque stones. Intravenous Pyelography (IVP) may provide additional information about caliceal formation and renal functions.

American Urological Association and European Association of Urology recommend USG as a first line imaging in urinary stone suspicion [8,9]. CT may be used while stone suspicion persists with negative USG results. Urologists have to keep in mind avoiding radiation exposure in children.

Metabolic evaluation

Every child with urinary stone formation must be evaluated metabolically because of recurrence tendency of urinary stones. This evaluation must be contain detailed familial and patient history, chemical analysis of stone if the stone fragments can be obtained, metabolic laboratory evaluation; spot urine analysis, calcium/creatinine ratio.

Urine culture and 24 hr urine collection may be needed. Therapy

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recommendation will be discussed in related metabolic anomalies later on.

Treatment

Choice of treatment method depends on disease properties such as stone size, location, composition of stone and anatomical features of urinary tract. Open surgical approaches are less and less frequent by the advance of techniques in SWL and endoscopic interventions.

Shock-Wave Lithotripsy (SWL)

Extracorporeal SWL therapy can be performed in children with minimal morbidity and high success in well selected cases [10]. Usage of USG or digital fluoroscopy at focusing stones is essential to decrease radiation exposure during procedure. Number of shock waves may vary from 1800 to 2000 (up to 4000 maximum) and mean power from 14 kV to 21kV in sessions. General or dissociative anesthesia may be proper for children under age 10. Older children may need general anesthesia [11].

Stone size is the main determinative factor for success as well as risk of stonestrasse formation. The stone-free rates for <1 cm, 1-2 cm, >2 cm and overall are 90%, 80%, 60% and 80% respectively. Larger stones may need additional sessions [12].

Site of stone is another factor that affects success rate. Stones located in pelvis and upper ureter can be treated up to 90% success with SWL. Treatment success in lower caliceal stones are lower and success rate reported about 50-62% in different studies. Focusing problem is another difficulty related lowers success rate for lower ureteral stones [12].

Data of 381 patients shows 76.7% stone-free status after SWL therapy [13]. History of ipsilateral stone treatment was related to stone-free status. Stone location was a significant variable for stone-free status, but only in girls. Age and stone burden were two other significant factors in multivariate model [13]. Nomograms are also generated for clinicians in counseling the parents of children with urolithiasis and in recommending treatment [13].

Stone related complications like steinstrase and renal colic, transient hydronephrosis, dermal ecchymosis, urinary tract infection, sepsis and heamoptysis is possible with SWL treatment. Advances in SWL machines resulted in smaller focal zone and less energy deliver with the result of less morbidity such as pulmonary trauma [12].

Percutaneous nephrolithotripsy

Larger urinary stones may not be treated with SWL therapy alone. PCNL can be used as a monotheraphy or as an adjacent to other modalities like SWL. PCNL is effective and safe. Development of small caliber instruments allows usage of PCNL procedure with less morbidity with the high stone-free rate like in adult patients [14]. After single session, stone free-rates vary 86.9% to 98.5%. PCNL therapy has high success up to %89 even in staghorn stones [15].

One of the biggest PCNL series which is published in 2013 focused on complications in pediatric population of this procedure, show that it's safe and effective [16]. Postoperative stone-free rate was 81.6% and there were 359 complications in 334 rental units (27.7%). There were 118 intraoperative and 241 postoperative complications. Stone history, positive urine culture, operative time, length of hospitalization, treatment success, punctured calyx and location of stone were factors effecting complications rates in univariate analysis. Operative time, sheath size, mid calyceal puncture and partial staghorn formation were related with complication rates in multivariate analysis [16].

Miniaturized PCNL (mini-perc) through 13-14 F sheaths is more popular in recent years. Mini-perc technique offers high success rate comparable with wide sheats and decreases transfusion rate [17]. There are also reports on usage off mini-perc for upper ureteral stones. Also a micro-perc technique described and it is another option with a 4.85 F sheath use and with no stone extraction but in-situ laser defragmentation and left for spontaneous passage. Tubeless PCNL is another modification under study [18].

Ureterorenoscopy

URS is effective, with a high stone-free rate (up to 90%) in children with ureteral stones [19]. Data compiled from 660 seasons shows 8.4% complication rate. Operative time, age, institutional experience, orifice dilation, stenting and stoneburden were related with complication rate on univariate analysis. Operative time was the only statistical parameter effecting complication rate on multivariate analysis [19].

Ureteroscopy technique for children is similar to procedure in adult patients. Guide wire usage recommended. Balloon dilatation to ureterovesical junction and routine stenting is controversial. Hydrodistansion is also effective [20].

Different kinds of lithotripsy techniques are available including pneumatic, laser and ultrasonic [21]. URS is a safe and effective procedure for treatment of ureteral stones and serious complications like stricture formation and reflux are rare with adequate instrument usage and gentle surgical approach [22].

Flexible URS is also available as an option for treatment of ureteral and renal stones as well as stones located in lower calices [21]. Retrograde access through the ureter is the most commonly reported problem in studies. Stenting and waiting for passive dilatation before the procedure may be helpful.

Open, laparoscopic stone surgery

Large stones and obstructed systems are candidates for open surgery. In case of orthopedic limitations that are not allowing positions for endoscopic procedures, open approaches may be needed. Laparoscopy is another choice. Requirement of adequate equipment for children differ from the adults.

Bladder stones can be managed by endoscopic or open surgical techniques.

Urinary stones by their compositions

Calcium stones: Calcium oxalate and calcium phosphate are most commonly found chemical formation in calcium stones. Two main factors are supersaturation and decreased inhibitors in urine [23,24].

Hypercalciuria is defined as increased extraction of calcium in the urine. Calcium extraction more than 4 mg/kg/day in 24 hr urine in a child weighing less than 60 kg is considered as hypercalciuria [25]. 5 mg/kg/day is the upper limit for infants younger than 3 months [25].

Hypercalciuria may be in idiopathic (primary) or secondary form. When laboratory and metabolic evaluation fails to identify the cause of increase calcium extraction this situation called idiopathic hipercalciuria. Secondary hypercalciuria may be result of increased bone resorption (hyperparathyroidism, hyperthyroidism, immobilization, acidosis, metastatic disease) or gastrointestinal hyperabsorbtion (hypervitaminosis D) [26].

When hypercalciuria suspected in a child, first step laboratory test must be measurement of urinary calcium-to-creatinine level. Normal calcium-to-creatinin ratio is less than 0.2. If this results higher than 0.2, a second measurement must be obtained. Calcium extraction more than 4 mg/kg/day (0.1 mmol/kg/day) in 24-hour urine collection will be considered as hypercalciuria. Neonates and infants have higher calcium excretion and lower creatinine levels than older children [25]. After the statement of 'hypercalciuria', laboratory analysis should be extended with the evaluation of serum bicarbonate, creatinine, alkaline phosphatase, calcium, magnesium, pH, parathyroid hormone. Also calcium, phosphorus, sodium, magnesium, citrate, oxalate levels must be evaluated in 24 hr urine. P^H level measurement must be made in fresh void urine.

Recommendation of increased fluid intake and dietary modifications is essential. A dietician consultation may be beneficial with the determination of calcium and sodium intake in children at this stage. Uncontrolled, long and excessive calcium restriction may be harmful for children. Hydrochlorothiazide prescription at a dosage of 1-2 mg/kg/day may be beneficial to treat hypercalciuria [27]. In case of low citrate levels with hypercalciuria, citrate therapy may be useful [28].

Hypocitraturia: Citrate has an inhibitor role for urinary stone formation by binding to calcium and inhibiting aggregation of calcium oxalate and calcium phosphate crystals [29]. Hypocitraturia may be associated with any metabolic acidosis, distal tubuler acidosis or diorrhoeal syndromes. High protein and salt intake may cause low urinary citrate levels [30]. Hypocitraturia exists approximately 60% of children with nephrolithiasis [31].

In a prospective cohort study, Sarica et al showed that potassium citrate therapy reduces stone formation and decreases growth of residual fragments after SWL therapy [32]. In another study, Tekin et al observed 1 mEq/kg potassium citrate therapy divided into 3 doses after meals decreases stone recurrence in children between age 1 and 15 who have history of calcium based stones and hypocitraturia [33]. Potassium citrate therapy may be also useful after PCN therapy for calcium oxalate stones.

There is no long –term study with potassium citrate therapy in children addressing any side effects or complications. Potassium citrate should be used with caution in hyperkalemia and chronic renal failure situations.

Hyperoxaluria may be result of increased dietary intake, enteric hyperabsorption (e.g. short bowel syndrome) or a congenital metabolical error. In some cases, liver enzymes responsible of oxalate metabolism may be deficient, resulting calcium oxalate stone formation in kidneys. Most common form of hyperoxaluria is 'idiopathic mild hyperoxaluria'. Increased fluid intake, restriction in oxalate intake and normal calcium intake recommended. Pyridoxine is useful in reducing urine oxalate levels, especially in primary hyperoxaluria [34].

Uric acid stones: Hyperuricosuria is the main cause of urinary uric acid stone formation. Hyperuricosuria defined as uric acid output more than 10 mg/kg/day. Uric acid formation mainly effected by acidic pH of urine. Uric acid solubility reduced at pH level under 5.8. Therefore alcalinisation of urine is an effective method to prevent uric acid stone formation. Idiopathic Hyperuricosuria and secondary Hyperuricosuria because of metabolical disorders and myeloproliferative diseases may be another cause [35]. Uric acid stones are non-opaque. Renal USG and CT may required for diagnosis. Citrate prescription is helpful for urine alcalinisation with the aim of urine pH level between 6 to 6.6. If citrate therapy fails, allopurinol is an additional medication choice. Allopurinol must be used cautiously because of side effect risks like as rash, diarrhea, eosinophiliae in patients with chronic renal failure [36].

Cystine stones: Cystinuria is an incompletely recessive autosomal disorder [37]. Reabsorption fail of four basic amino acides; cystine, ornithine, lysine and arginine is resulted with cystine stone formation in urine. Cystine stone formation eases at pH level under 7.0. Other metabolic alterations such as hypercalciuria, hypocitraturia and hyperuricosuria may seen with cystinuria resulted with stones formation in mix chemical properties [38].

Cystine stones are fairly opaque in X-ray. Fragmentations of cystine stones are also difficult with SWL therapy. Reducing cystine saturation in urine and increasing solubility is the main targets in medical therapy. Potassium citrate use is suitable with the purpose of urine alcalinasition. Alpha mercaptopropiionyl glycine may help to reduce cystine levels [39]. Gastrointestinal side effects such as alteration in taste and odeur, fever, rash can be seen.

Surgical techniques such as PCNL are safe and effective for children with cystine stones [40]. Additional endoscopic procedures will help to achieve higher stone-free status. Even after medical treatments following surgical procedures, stone recurrence and regrowth rates are high, which emphasize there is no definite adequate treatment to avoid recurrence for good [40].

Dietary Modification Recommendations

Dietary modifications may decrease stone formation in children dramatically [41]. There are several studies on low protein and low salt diet reduces stone formation in adults with recurrent stone formation and hypercalciuria. Pediatric patient population differs from adults with child's basic need during growth. Decreased fluid intake is a major factor for urinary stone formation [42]. Consumption of drinks with high fructose levels, calcium and oxalate extraction in urine increases with a higher risk of stone formation [43]. Also there is a competition between sodium and calcium at nephrons and high sodium intake increases calcium levels in urine.

Decreasing or limiting calcium intake is not recommended. On contrary, low calcium intake may increase bone resorption and higher urine calcium. Diet on high animal protein results increased urine calcium and decreased urine citrate [41]. There are some studies in favor of decreased stone formation with low protein diets in adults, but protein limitation cannot be recommend to children who are still growing.

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