Metabolic Evaluation and Medical Management Of Pediatric Urolithiasis

Essasy

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In Urology

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(1) Introduction and aim of the work

Approximately 7% of urolithiasis occurs in children younger than 16 years ***(Davis, 2004)***. Generally the incidence of stone disease in children is about 2-3 %. Pediatric patients tend to form stones in a recurrent pattern, with rates of recurrence of 6.5% – 44% ***(Erbagci et al., 2003)***. This tendency as well as the destructive nature of stone formation can quickly lead to progressive decline in renal function in the fragile pediatric kidney.

Several factors help us to understand the incidence and the prevalence of pediatric urolithiasis. These factors may be extrinsic factors which include geography, climate, diet, fluid intake and exercise. And intrinsic factors which include genetic, race, age, sex, weight, prematurity, and oxalobacter formigenes ***(Anderson, 1993).***

The etiology of urolithiasis in children is largely unknown, though anatomic genitourinary abnormalities, metabolic abnormalities and urinary tract infection are usually coexistent in this population ***(Minevich, 2001)***. In a study by Chang et al., 41% of children with stones had a metabolic abnormality ***(Chang, 2008).***

The goal of a metabolic evaluation is to identify any physiologic or pathologic factors that could be responsible for active stone formation. All children should have comprehensive metabolic evaluation which includes medical history, physical examination, laboratory study and imaging study. Any evaluation should be able to identify associated metabolic disorders responsible for recurrent stone disease. These metabolic problems include renal tubular disorders, Enzyme disorders, Hypercalcaemia, hypercalciuria, hyperuricosuria, and Hypocitriuria ***(Pak et al, 2003).***

After treating the acute stone episode, it is of critical importance to collect a 24-hour urine sample in order to determine a stone-risk profile and to rule out any subtle metabolic abnormalities. The urine collection is evaluated for volume, pH, calcium, uric acid, creatinine, sodium, oxalate, citrate, and cystine ***(Pramod, 2007)***.

The medical treatment is based on the chemical composition of the stone and the biochemical abnormalities causing its formation ***(Share, 2004)***. Initial management is always to increase fluid intake. Dietary modification is a mandatory part of effective therapy. The child should be referred to a dietician to assess accurately the daily intake of calcium, animal protein, and sodium ***(Borghi et al., 2002).***

Aim of the work

In this study we will revise and discuss the metabolic evaluation that should be done for pediatric patients presented with urinary stones, also we will discuss the different protocols used for prophylaxis and treatment of pediatric urolithiasis.

(2) Epidemiology and risk factors

It is important to define the terms incidence and prevalence of stone disease to ensure proper comparisons between epidemiological studies. The incidence of stone disease is defined as the number of new stone patients in a given population over a defined period of time (usually a year). Prevalence is defined as the number of stones present in a screened population at a particular point in time.

Several factors help us to understand the incidence and the prevalence of urolithiasis. These factors may be extrinsic factors which include geography, climate, diet, fluid intake and exercise. And intrinsic factors which include genetic, race, age, sex, weight, prematurity, and oxalobacter formigenes ***(Anderson, 1993*).**

2.1. Extrinsic factors:

2.1.1. Geographical factors:

The prevalence of urinary calculi is higher in those who live in mountainous, desert and tropical areas. The high incidence areas are British Isles, Scandinavian countries, Mediterranean countries, Northern India, Northern Pakistan, Northern Australia, Central Europe and China. The low incidence areas are Central

America, South America, most of Africa and those areas of Australia populated by aborigines ***(Mani and Martin, 2007).***

Pediatric urolithiasis is endemic to certain developing countries such as Turkey, India, and Thailand, and until recently was a relatively rare condition in the Western Hemisphere. The incidence in the USA has been increasing over the past decade, possibly due to changing dietary and physical activity patterns in the pediatric population. In the USA, urinary stone disease accounts for 1:1000 to 1:7600 hospital admissions, whereas in countries where stone disease is endemic the incidence is approx 1:1000 to 1:3000 hospital admissions ***(Stapleton, 1989).***

The bladder stones are common among the poor, while upper urinary tract stones are common in the developed and civilized areas ***(Ramell, 2000).***

The different racial and ethnic groups living in the same area and sharing the same physical environment may demonstrate striking difference in the frequency of stone disease ***(Angwafo et al., 2002).***

2.1.2. Climate:

Hot climate plays apart in the etiology of stone formation. It induces dehydration which leads to a low urine volume per day with subsequent increased stone incidence ***(Coward et al., 2003).***

Parry and Lister suggested that increased exposure to sunlight causes increased production of 1, 25-dihydroxyvitamin D_3 and increased urinary calcium excretion. This may cause a higher incidence of urolithiasis during the summer months ***(Mani and Martin, 2007).***

Prince and Scardino show a relationship between environmental temperature and seasonal incidence of urinary stone disease. The peak incidence occurred in July, August, and September ***(Mani and Martin, 2007).***

There is no significant seasonal variation with calcium oxalate or calcium phosphate stones, while the incidence of uric acid stones are increased significantly during summer and autumn, and that of infectious stones are decreased significantly during spring and summer ***(Baker and colleagues, 1993).***

It was postulated that the increase in uric acid stones was due to the fall in urine volume during summer combined with a reduction in urinary pH. In support of this, a recent review of over (280 000) 24 h urine test results in the United States demonstrated that urinary volumes fall significantly in men, but not in women, during summer. This was associated with a fall in urinary pH and an increase in the supersaturation of uric acid ***(Parks, 2003).***

2.1.3. Diet:

The dietary intake of various foods and fluids has a significant effect on the incidence of urinary calculi. Ingestion of excessive amounts of purines, oxalates, calcium, phosphate, and other elements often results in excessive excretion of these components in urine ***(Freeman, 1998).*** The pathological role of diet rich in protein, refined carbohydrates and sodium in stone formation have become evident, while the effect of alimentary calcium and oxalate is still debatable ***(Trinchieri, 1996).***

The excessive animal protein intake has been shown to lead to an increase in urinary excretion of calcium and uric acid, and a decrease in urinary citrate. Additionally, a recent study suggests that a diet rich in animal protein leads to an increase in urinary oxalate excretion in recurrent idiopathic calcium stone formers ***(Nguyen et al., 2001).***

The excessive sodium intake has been linked to increased urinary calcium excretion, and thus to increased calcium stone formation. Increases in sodium intake of 100 mmol may produce an increase in urinary calcium of 1 mmol ***(Cappuccio et al., 2000).***

An epidemiological study has reported that the lower the potassium intake, below 74 mEq/d, the higher the relative risk for stone formation ***(Curhan et al., 1993).*** Such an effect can be

ascribed to an increase in urinary calcium and a decrease in urinary citrate induced by a low potassium intake ***(Lemann et al., 1991).***

The dietary oxalate is responsible for only 10% to 15% of total urinary oxalate ***(Hodgkinson, 1977)***. Urinary oxalate excretion increases after the ingestion of oxalate-rich foods such as spinach ***(Strenge et al., 1981)***. A case-control study from Newfoundland examined tea consumption in stone-formers but found no evidence to support the suggestion that tea drinking is a risk factor for calcium oxalate urolithiasis ***(Churchill et al., 1985).*** As will be discussed later caffeine - by its diuretic effect- may even have a protective effect ***(Curhan et al., 1998).***

Prospective studies show that high dietary calcium intake reduces the risk of kidney stones, possibly by reducing gut absorption of oxalate ***(Siener et al., 2003).*** The restriction of dietary calcium may increase the risk of stone formation by enhancing dietary oxalate absorption and urinary oxalate excretion ***(Massey et al., 1993)***. One of the determinants of urinary oxalate excretion is intestinal oxalate absorption. Intestinal oxalate absorption is influenced by the oxalate-to-calcium ratio of the diet. If dietary calcium is restricted, Enhanced absorption of "free" oxalate will occur, because oxalate that is bound to calcium is not absorbed ***(Giannini et al., 1993).***

The relationship between stone disease and sugar consumption is more controversial. Increased dietary sugar can increase urinary calcium excretion ***(Thom et al., 1978).***

2.1.4. Fluid intake*:*

Increasing water intake and increasing urine output decrease the incidence of urinary calculi in those patients who are predisposed to the disease. Yet two factors are involved in the relationship between water intake and urolithiasis which are the volume of water ingested and the mineral or trace element content of the water supply ***(Shuster et al., 1982).***

The hardness and mineral composition of water affect stone risk remains controversial. As the calcium content of drinking water increases, calcium excretion increases but oxalate excretion falls. Water with a large amount of bicarbonate may increase citrate excretion, and magnesium content may favorably alter citrate and magnesium excretion. Based on these findings, there is still no definite evidence that hard water, rich in calcium and magnesium, is more lithogenic than soft water ***(Agreste et al., 1999).***

A very recent epidemiological study based on food-frequency questionnaires has examined the effects of particular beverages on risk of symptomatic kidney stones. Consumption of

tea, caffeinated and decaffeinated coffee was associated with a reduction of risk of 8 to 10%, while wine decreased the risk by 59%. Conversely, grapefruit juice ingestion was associated with a 44% increased risk for stone formation. The authors speculated that the protective effects of coffee, tea and wine were caused by urinary dilution, determined by the ability of caffeine and alcohol to inhibit antidiuretic hormone. Therefore, the decreased risk for decaffeinated coffee might have been conferred by another mechanism. The adverse effects of grapefruit juice remained unexplained, since other citrus juices, like orange and lemon, may prevent and not stimulate stone formation due to their high citrate content. In summary, these results must still be interpreted with caution until adequate long-term randomized trials of dietary interventions are performed ***(Curhan et al., 1998).***

2.1.5. Exercise:

Excessive sweating may contribute to stone formation. Moderate physical exercise lowers urinary pH and citrate excretion due to a mild metabolic acidosis ***(Sakhaee et al., 1987).*** Although the total excretion of stone-forming salts decreases, the greater decrease in urine volume results in an increase in urinary calcium oxalate stone and the concentration of undissociated uric acid (secondary to an increase in total uric acid concentration and a fall in urinary pH) ***(Borghi et al.,1993).***

2.2. Intrinsic factors:

2.2.1. Genetic*:*

Several disorders that cause renal stones are hereditary. Familial renal tubular acidosis (RTA) is associated with nephrolithiasis and nephrocalcinosis in almost 70% of patients ***(Lloyd, 1996).*** Cystinuria is a homozygous recessive disease, and the genes that cause it have been cloned ***(Lloyd, 1996).*** Similarly, xanthinuria and dihydroxyadeninuria are rare hereditary disorders that cause renal stones ***(Lloyd, 1996)*** .Mutations in the CLCN5 gene, coding for a chloride channel, have been seen in patients with the X-linked hypercalciuric kidney stone syndromes, Dent's disease (disorder of the proximal tubules that is characterized by hypercalciuria, nephrocalcinosis, kidney stones, renal failure, and rickets), X-linked recessive nephrolithiasis, and X-linked recessive hypophosphatemic rickets ***(Lloyd, 1996).***

In pediatric patients with nephrolithiasis, 73% had family history of kidney stones in at least one first-order or second-order relative, as opposed to a prevalence of 22% in a control population of pediatric renal and urologic patients. The prevalence of nephrolithiasis in the family history of the patients with hypercalciuria was 69% ***(Polito et al., 2000).***