ORIGINAL ARTICLE

Spectrum of Renal Tubular Disorders in Iraqi Children

Aamir Jalal Al Mosawi

Abstract

Objectives of study: The pattern of renal tubular disorder (RTDs) has been infrequently reported in the literature. In Germany the three most frequent disorders were cystinosis, X-linked hypophosphatemic rickets (XLHR), and idiopathic hypercalciuria. This study was undertaken to determine the pattern of RTDs in Iraqi and Arab children as it is not known.

Methods: From June 2000 to April 2007, 42 children with suspected RTD were evaluated to determine the type of tubulopathies.

Results: Ages at referral ranged from 8 months to 14 years (mean 4.8 years). There was evidence of RTD in only 37 patients; 23 males (62 %) and 14 females (38 %). Their ages at referral ranged between 8 months and 14 years (Mean 4.8 years). In 4 patient with oculo-cerebro-renal syndrome, there was no evidence of RTD and one has patient have hyperoxaluria which was not a RTD. Seven types of RTDs were identified. The three most common disorders were: idiopathic hypercalciuria (35 %), cystinosis (21.6 %) and renal tubular acidosis RTA (21.6%) Four of the patients with RTA have proximal RTA, and four have distal RTA. Four of the patients with hypercalciuria have also significant hyperoxaluria > 3mg / kg/ day.

Conclusion: Common RTDs in Iraqi children are idiopathic hypercalciuria, cystinosis and RTA and differs from those reported elsewhere

Introduction

The pattern renal tubular disorder (RTDs) has been infrequently reported in the literature [1], and the pattern of RTDs in Iraqi and Arab children is not known.

Methods and Materials

From June 2000 to April 2007, 42 children with suspected RTD were evaluated to determine the type of tubulopathy. Ages at referral ranged from 8 months to 14 years (Mean 4.8 years). Investigations for RTD included urinalysis, serum electrolytes (potassium, chloride, sodium), serum calcium and phosphorus, serum bicarbonate, renal function tests (blood urea and serum creatinine), bone radiographs (usually of the left wrist), and a renal ultrasound for most patients. Patients with urolithiasis were also investigated with 24-hour urinary examination for calcium, uric acid, and oxalate. Cyanide nitroprusside and monospot tests were performed for cystinuria. Patients with a history or evidence of proximal RTA underwent slit lamp examination of the eyes to exclude cystinosis. The diagnosis of proximal RTA was based on the association of vitamin D-resistant rickets, hyperchloremic acidosis, hypokalemia and urine pH below 5.5. The diagnosis of distal RTA was based on the association of nephrocalcinosis, acidosis and hypokalemia. Fanconi syndrome was diagnosed by the features of proximal RTA with glycosuria and aminoaciduria. The diagnosis of cystinosis was based on pathognomic corneal cystine deposition. The diagnosis of X-linked hypophosphatemic rickets (XLHR) was based on persistent hypophosphatemia (serum phosphorus < 2 mg), hyperphosphaturia (urinary phosphate 2.8 g / 24 h, upper limit of normal 200 mg/24 h). The diagnosis of idiopathic hypercalciuria was made by finding normal serum calcium and no other obvious secondary cause for the hypercalciuria. [2, 3, 4, 5, 6]. In patients with urolithiasis, hypercalciuria was defined as urinary calcium excretion of greater than 4 mg/kg/day. Hyperuricosuria was defined as urinary uric acid excretion of greater than 55 mg/kg/day, and hyperoxaluria was defined as urinary oxalate excretion over 3 mg/kg/day or 50 mg/1.73/m^2/day. A level of hyperoxaluria > 80mg/1.73m^2/day was considered indicative of primary hyperoxaluria [6, 8, 9, 10].

Results

Seven types of RTDs were identified (Table 1) in 37 patients [23 males (62%) and 14 females (38 %)]. The three most common disorders were idiopathic hypercalciuria (35 %), cystinosis (21.6%), and RTA (21.6%). Four of the patients with RTA had proximal RTA, and four had distal RTA. Four of the patients with hypercalciuria also had significant hyperoxaluria (> 3 mg /kg/ day). Bone disease (renal rickets) occurred in 14 patients (32.4%), including eight patients with cystinosis, four patients with proximal RTA, and two patients with X-linked dominant hypophosphatemia (XLH). Significant bone deformities were evident in seven patients (17 %); three with proximal RTA, and two each with cystinosis and XLH. Proximal RTA was the most frequent cause of rickets in this sample of children. Six (16.2 %) patients with cystinosis developed chronic renal failure. Long-term follow-up was not possible for many of the patients. Urolithiasis or nephrocalcinosis were found in 23 patients (62 %), including 18 patients with stones. Six patients had surgery prior to referral, and two of them had at least one lithotripsy session. The etiological causes of urolithiasis/nephrocalcinosis, in the observed order of frequency, were hypercalciuria, cystinuria, and distal RTA. Hypercalciuria was responsible for approximately half the cases of stones (52%). Two patients had hyperuricosuria and associated hypercalciuria presenting with bilateral infantile urolithiasis.

Table 1: Renal tubular disorders in sample of Iraqi children

	Males	Females	Total
Hypercalciuria	**8**	**5**	**13 (35%)**
Cystinosis	**4**	**4**	**8 (21.6%)**
Cystinuria	**2**	**2**	**4**
Distal RTA	**4**		**4**
Proximal RTA	**2**	**2**	**4**
XLDHR	**2**	**0**	**2**
Hyperuricosuria (+mild hypercalciuria)	**1**	**1**	**2**
Total	**23**	**14**	**37**

In one patient with proximal RTA, an annual routine ultrasound showed unexpected bilateral nephrocalcinosis. The serum calcium level in this patient did not reach the upper limit of normal (11 mg/dL), but 24 hours urinary calcium excretion was 5.6 mg/dL/day. Seven of the 21 patients with urolithiasis/nephrocalcinosis showed significant growth retardation (growth parameters at or below the third centiles), including two patients with hypercalciuria, four patients with distal RTA and one patient with proximal RTA. The remaining 14 patients in this group had growth parameters between the 10th to the 70th centiles. Patients with hypercalciuria and cystinuria generally had better growth parameters than patients with RTA or cystinosis. Eleven patients with urolithiasis/nephrocalcinosis had a family history of stone disease, including four patients with distal RTA (two pairs of brothers), and seven with hypercalciuria including two sets of siblings. Extra-renal (ocular) abnormalities were found in nine patients, including eight with cystinosis and one patient with idiopathic hypercalciuria and a unilateral convergent squint.

Seven patients (6 males and 1 female) with ultrasonographically proven renal or ureteral stones were enrolled in a clinical study investigating the possibility of using essential oil terpenes in the management of childhood urolithiasis. Four children had hypercalciuria and three had hyperoxaluria, distal renal tubular acidosis, and Hyperuricosuria associated with hypercalciuria. Their ages ranged from 10 months to 5 years. They received traditional treatments for the underlying metabolic abnormalities, such as hypocalciuric diuretics for hypercalciuria. The children received these therapies for a period ranging from 10 days to 16 weeks. All patients achieved a stone-free state without the occurrence of any adverse effects [11, 12] by addition of essential oil terpenes to their traditional therapies. During this period of observation three patients died; one (with cystinosis) from uremia, and two (each with cystinosis and proximal RTA) from pneumonia.

Discussion

The pattern of childhood renal tubular disorders in Iraqi children is different in many aspects from the reported patterns throughout the world. The three most frequently encountered renal tubular disorders in this small sample of Iraqi children were idiopathic hypercalciuria, RTA and cystinosis. These findings differ from those of a German study that included a larger number of patients and who reported the three most frequent disorders as cystinosis, XLHR, and idiopathic hypercalciuria [1]. XLHR, which was the second most common disorder in the German study, was among the least common disorders in our study. Forty-two percent of the German patients developed CRF, compared to 16.2 % in our study. The lower number of patients developing CRF can well be attributed to the shorter period of observation. The percentages of patients having nephrocalcinosis and urolithiasis were similar - around 57% in both studies. Significant bone deformities occurred in six patients (18%) and in 28% in the German study as the result of the higher incidence of XLHR which was the second most common disorder in the German study, was among the least common disorders in our study. Forty-two percent of the German patients developed CRF, compared to 16.2 % in our study. The lower number of patients developing CRF can well be attributed to the shorter period of observation. The percentages of patients having nephrocalcinosis and urolithiasis were similar - around 57% in both studies. Significant bone deformities occurred in six patients (18%) and in 28% in the German study as the result of the higher incidence of XLHR.

The three most frequent disorders associated with urolithiasis in this sample of Iraqi children were idiopathic hypercalciuria, cystinuria, and distal RTA. This differs from Tunisian studies reporting cystinuria as the most frequent RTD associated with urolithiasis [13, 14]. However, the results of this study were similar to a British study reporting that the two most common RTDs in children with urolithiasis were hypercalciuria (57%), and cystinuria (23%) [15]. Nephrolithiasis occurs mainly in distal RTA. Major risk factors for Nephrolithiasis include alkaline urine and hypercalciuria. Patients with proximal RTA had a significantly lower urinary pH and urinary excretion, and renal stone formation is uncommon. The major protection from renal stone formation in proximal RTA results from a reduction in renal excretion of calcium [16, 17, 18]. In this series, a patient with classical hereditary proximal RTA unexpectedly developed bilateral nephrocalcinosis, which was detected by renal ultrasound. The patient's serum calcium was normal. However, 24 h calcium excretion was 5.6 mg/kg, providing an explanation for the occurrence of nephrocalcinosis [17]. Although this association of proximal RTA, urolithiasis, and hypercalciuria is rare, it has been described [19].

References

1. Haffner D, Weinfurth A, Manz F, Schmidt H, Bremer HJ, Scharer K . Long-term outcome of pediatric patients with hereditary tubular disorders. Nephronn 1999; 83 (3):250-260.

2. Sayer JA, Pearce SH. Diagnosis and clinical biochemistry of inherited tubulopathies. Ann Clin Biochem 2001; 38:459-470.

3. Donckerwolke RA. Diagnosis and treatment of renal tubular disorders in children. Pediatr Clin N Am 1982; 29:895-905.

4. Postlethwaite RJ. Renal tubular disorders. In: Postelthwaite RJ ed. Clinical Pediatric Nephrology. 1980; 238-252.

5. Watson A .Renal tubular disorders.In: Campbell AGM, McIntosh Ed Forfar Textbook of paediatrics 5th Ed Churchil Livingstone 2004; 944-949.CD-ROM

6. Barratt TM, Duffy PG. Nephrocalcinosis and urolithiasis. In: Pediatric Nephrology, 4thEdn Barratt TM, Avner ED, Harmon WE Eds, NY, USA Williams &Wilkins 1999; 933–945.

7. Ghazali S, Barratt TM. Urinary excretion of calcium and magnesium in children. Arch. Dis. Child 1974; 49: 94–101.

8. Moxey-Mims MM, Stapleton FB. Hypercalciuria and nephrocalcinosis in children. Curr. Opin. Pediatr 1993; 5: 186–190.

9.Nash MA. Urolithiasis. In: Pediatric Kidney Disease. Edelmann Jr CM (Ed), MA USA Little Brown and Company 1978; 1170–1176.

10. Barratt TM, Kasidas GP, Murdoch I, et al.Urinary oxalate and glycolate excretion and plasma oxalate

concentration. Arch. Dis.Child 1991; 66: 501–503.
11. Al-Mosawi AJ.A possible role of essential oil terpenes in the management of childhood urolithiasis.Therapy 2005; 2:243-247. 12. Idiopathic hyeruricosuria, hypercalciuria and infantile renal stone disease: new association and therapeutic approach. Therapy (London) 2006:3(6): 755-757.
13. Kamoun A, Daudon M, Abdelmoula J, Hamzaoui M,et al. .Urolithiasis in Tunisian children: a study of 120 cases based on stone composition. Pediatr Nephrol 1999; 13(9):920-925 14. Kamoun A, Daudon M, Kabaar N, Dhaoui R, et al. Etiologic factors of urinary lithiasis in Tunisian children. Prog Urol. 1995; 5(6):942-5. 15. Coward R J M, Peters C J, Duffy P G, Corry D et al. Epidemiology of paediatric renal stone disease in the UK. Arch Dis Child 2003; 88:962-965 16. Buckalew VM Jr. Nephrolithiasis in renal tubular acidosis. J Urol 1989; 141(3 Pt 2):731-7. 17. Uribarri J, Oh MS, Pak CY. Renal stone risk factors in patients with type IV renal tubular acidosis. Am J Kidney Dis 1994; 23(6):784-7.
18. Brenner RJ, Spring DB, Sebastian A, McSherry EM,etal Incidence of radiographically evident bone disease, nephrocalcinosis, and nephrolithiasis in various types of renal tubular acidosis. N Engl J Med. 1982; 22; 307(4):217-21. 19. Ito H, Kotake T, Suzuki F . Incidence and clinical features of renal tubular acidosis in urolithiasis. Urol Int.1993 ;50(2):82-5.

E-published: September 2008.

From: Department of Pediatrics, University Hospital in Al Kadhimiyia, Iraq

Address for Correspondence: Aamir Jalal Al Mosawi, Head – Pediatrics, University Hospital in Al Kadhimiyia PO Box: 70025, Iraq. Email: almosawiAJ@yahoo.com