Spectrum of Renal Tubular Disorders in Iraqi Children

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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 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 > 3 mg/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), and hyperuricosuria (urinary uric acid excretion over 3 mg/kg/day). Hyperuricosuria was defined as urinary uric acid excretion of greater than 55 mg/kg/day.

Results

The pattern of RTDs has been infrequently reported in the literature [1], and 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).

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

Table 1: Renal tubular disorders in sample of Iraqi children

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercalciuria</td>
<td>8</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Cystinosis</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Cystinuria</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Distal RTA</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Proximal RTA</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>XLDHR</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Hyperuricosuria (+mild hypercalciuria)</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>14</td>
<td>37</td>
</tr>
</tbody>
</table>

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. Hyperuricosuria was considered indicative of primary hyperuricosuria [6, 8, 9, 10].
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.

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


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