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URINARY TUBULAR ENZYME EXCRETION IN CHILDREN WITH NEPHROLITHIASIS AND UROLITHIASIS WITH HYDRONEPHROSIS

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ABSTRACT

Objective: Nephrolithiasis and urolithiasis are recurrent conditions associated with significant morbidity and economic impact. Previous studies have suggested that cell-crystal interactions lead to tubular damage and/or dysfunction. To find further proof for these observations, a metabolic evaluation (including serum and urine biochemistry and urinary enzyme excretion) was done in children with nephrolithiasis and urolithiasis with hydronephrosis.

Patients and Methods: This study included two groups: 10 normal children (controls) and 32 children with calcium oxalate urinary tract stones. The latter group was further subdivided into those with nephrolithiasis (n=12) and urolithiasis with hydronephrosis (n=20). Levels of uric acid, oxalate, calcium, magnesium and inorganic phosphorus in 24-hour urine and serum were determined. Urinary N-acetyl-β-D-glucosaminidase (NAG), β-galactosidase (β-GAL), β-hexosaminidase (β-Hex), angiotensin converting enzyme (ACE) and gamma glutamyl transferase (γ-GT) levels were also determined colorimetrically.

Results: Increases in urinary excretion of oxalate, calcium, magnesium and inorganic phosphorus were the major abnormalities found in stone forming patients. Elevated urinary NAG, β-GAL, β-Hex and ACE levels were also noted in patients compared with controls. Urinary excretion of oxalate, NAG, β-GAL and ACE was significantly elevated in children with nephrolithiasis compared to those with urolithiasis and hydronephrosis.

Conclusion: Abnormal urine biochemistry seems to have a role in the risk for urinary-tract stone formation in children. Hyperoxaluria can induce tubular cell injury mainly in proximal tubules, which is more pronounced in children with nephrolithiasis. The tubular injury manifested by enzymuria occurs before alteration of renal functions and blood biochemistry. Urinary tubular enzymes should be screened in children with urinary tract stones.

Key words: Urinary tract stones, N-acetyl-β-D-glucosaminidase, β-hexosaminidase, β-galactosidase, gamma glutamyl transferase, angiotensin converting enzyme.

INTRODUCTION

The incidence and prevalence of urinary tract stones may be affected by genetic, nutritional, hormonal and environmental factors[1] The current prevalence of pediatric urolithiasis in Europe is low, with an estimated rate of 1-5 in 10,000 children[2]. However, it is the cause of considerable morbidity and has a high risk of recurrence[2]. Diagnosis of urinary stones is often delayed in infants and young children as they may present with non-specific symptoms. Occasionally, urolithiasis or nephrocalcinosis are detected incidentally on ultrasound or abdominal x-ray.

In most industrialized countries, about 80% of stones are composed of calcium salts

and usually occur as calcium oxalate and less commonly as calcium phosphate (apatite or brushite)[3].The remaining 20% of stones are composed of uric acid, struvite or carbonate apatite.

The mechanism of renal stone formation is still a matter of debate[4]. In experimental models, it was demonstrated that the first steps of calculi formation were associated with crystal-cell interactions, e.g. calcium oxalate crystals and/or oxalate ions[5]. These interactions may result in tubular damage and/ or dysfunction. Obviously, experimental models do not physiologically mimic human conditions, but similar histological changes were found in adult patients with stone disease or primary hyperoxaluria (HyOx)[6]. It was also reported that stone formers excrete more cell membranes and their fragments than normal individuals. This may indicate an increased turnover of tubular epithelial cells[7].

N-Acetyl-β-D-glucosaminidase (NAG), β-galactosidase (β-GAL) and β-hexosaminidase (β-Hex) are lysosomal enzymes, whereas γ-glutamyl transferase (γ-GT) and angiotensin converting enzyme (ACE) are brush border enzymes. These enzyme activities have been demonstrated in all segments of the nephron, with highest activity in the convoluted part and the beginning of the straight part of the proximal tubule. Since they have a high molecular mass, their activities in urine most probably derive only from kidney tubules. Elevation of these enzymes in the urine is considered a sign of tubular cell necrosis[8, 9].

Data on urinary enzyme activity in children with urolithiasis are scarce[10], while there is a lot of information about tubular enzymuria in adults with urinary stone disease[11]. The aim of the present study was to evaluate renal tubular damage in children with nephrolithiasis or urolithiasis with hydronephrosis by measuring urinary excretion of tubular enzymes [NAG, β-GAL, β-Hex, γ-GT and ACE] and their relationship with major risk factors for urolithiasis [urinary oxalate, calcium, magnesium and inorganic phosphorus].

PATIENTS AND METHODS

This study included 10 non-stone forming healthy children (6 boys and 4 girls; mean age 9.3 ± 0.9 years; BMI 17.46 ± 0.72 Kg/ cm^2) who were admitted to the hospital for minor surgery unrelated to the urinary or gastrointestinal tract (control group) and 32 children with urinary tract stones (21 boys and 10 girls; mean age 8.94 ± 0.69 years; BMI 17.92 ± 0.64 Kg/cm^2) who attended the Stone Clinic at Assiut University Hospital, Egypt, for surgical intervention, and the Urology Clinic at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. The patient group was further subdivided into 12 children suffering from nephrolithiasis (7 boys and 5 girls) and 20 children suffering from urolithiasis with hydronephrosis (15 boys and 5 girls) .The clinical diagnosis of urinary tract stones was made by renal ultrasonography and/or intravenous urography (IVU). All children were symptomatic and presented for the first time with renal stone. They were admitted to the hospital one day before surgery. All stones were mixed calcium oxalate (CaOx) and calcium phosphate in different proportions as diagnosed by X-ray powder diffraction. Informed consent was obtained from the parents of all participants. The study was approved by the Local Ethical Committee of both Assiut and King Abdulaziz University Hospitals.

Exclusion criteria for patients and controls were: urinary tract infection, primary or secondary hyperparathyroidism, cystinuria >70 umol/24h, renal tubular acidosis, vesicoureteral reflux, urinary tract anomalies detected by abdominal ultrasound, renal impairment (endogenous renal creatinine clearance less than 50 mL/min/1.73 m^2)[12], chronic diarrhea states, and intake of thiazide diuretics, angiotensin converting enzyme inhibitors or glucocorticoids. None of the patients had primary hyperoxaluria. Patients with hydronephrosis caused by other factors, such as external compression by aberrant vessels, were also excluded. An additional exclusion criterion for control subject enrollment was the presence of one or more metabolic risk factors for nephrolithiasis.

Venous blood samples were collected from the antecubital area. Blood samples were sent to the central laboratories of Assiut and King Abdulaziz university hospitals for blood chemistry analysis, all were centrifuged at 3000 rpm for 10 minutes and sera were frozen at –20°C until further analysis.

Twenty-four hour urine samples were also collected at the same time, and the urine volumes were recorded. Uric acid was measured in fresh morning void following urine collection. The urine was directly poured into sampling bottles containing 10 ml 6M HCl per liter of urine for further analysis. An aliquot was stored at 20°C and analyzed within one month.

Urinary enzymes were measured in 24-hour urine specimens using a colorimetric method. Urinary NAG and β-GAL were measured by Maruhn's method[13]. Urinary activities of β-Hex[14] and γ-GT[15] were also estimated. Urinary ACE activity was determined by measuring furylacrylyl phenylalanyl glycylglycine (FAPGG) hydrolysis to furylacrylyl phenylalanine (FAP) at 334 nm[16]. All assays were performed in duplicate for each sample and expressed per gram of urinary creatinine[11].

Urine and serum levels of sodium and potassium were determined using flame photometry (Jenway Clinical PFP7), total calcium was estimated by atomic absorption/ flame emission spectrophotometry. Commercial kits (Quimica Clinica Aplicada, S.A., Spain) were used for determination of chloride by silver precipitation[17], inorganic phosphorus[18], creatinine by picric acid method[19] and uric acid by urease method[20]. Urinary oxalate was measured using the oxalate oxidase enzymatic method with a commercial assay kit (Sigma, St. Louis, Mo). Urinary levels of protein were determined enzymatically according to the method described by Henry[21].

Statistical Analysis

Values are expressed as mean ± standard error of the mean (SEM). Statistical significance was determined by one-way analysis of variance (ANOVA) or unpaired student t-test using SPSS software (Chicago III, USA). Pearson's correlation method was used to determine the correlation between tubular enzymes and the major urinary risk factors for stone formation.

RESULTS

When comparing the stone forming children to controls there was a significant decrease in 24-hour urine volume, and a significant increase in the 24-hour urinary excretion of uric acid, creatinine, oxalate, calcium, magnesium and phosphate (Tables 1 and 2). There were no significant differences between patients and controls regarding the 24-hour urinary excretion of protein, sodium, potassium, and chloride.

There was a significant increase in the urinary excretion of NAG, β-GAL, β-Hex and ACE in the stone forming children compared to controls.However, γ-GT did not show any significant difference between patients and controls (Table 2).

There were increased serum levels of urea and creatinine in the patients compared to the controls, but no significant difference was found in the other serum parameters (Table 3).

Compared to the controls there was a significant increase in the 24-hour urinary excretion of uric acid, creatinine, oxalate, magnesium and phosphorus in nephrolithiasis and urolithiasis patients with hydronephrosis (Table 4). Urinary oxalate excretion was significantly elevated in the patients with hydronephrosis compared to those with nephrolithiasis.

There was a significant increase in urinary excretion of NAG, β-Hex and ACE in nephrolithiasis and hydronephrosis patients compared to the controls (Table 5). β -GAL was significantly elevated in nephrolithiasis patients compared to the controls, but γ-GT did not show any significant difference

Table 1: Urinary chemistry profile in control group and children with urinary tract stones

Parameters	Controls (n=10)	Pediatric stone formers (n=32)	Significance
Urine Volume (L)	0.11±0.00	0.85±0.04	P<0.000
Uric acid (g/24hr)	0.44±0.05	2.15±0.11	P<0.000
Protein (g/24hr)	0.20±0.02	0.29±0.05	p>0.05
Creatinine (mg/24hr)	1.37±0.24	575.60±31.24	P<0.000
Oxalate (mg/24hr)	17.90± 0.74	55.91±4.43	P<0.000
Calcium (mg/24hr)	151.30±28.22	211.30±13.80	p<0.05
Magnesium (mg/24hr)	123.40±6.22	205.70±12.75	p<0.001
Inorganic phosphorous (mg/24hr)	536.90±52.31	905.70±43.38	p<0.000
Sodium (mEq/24h)	138.40±16.41	150.50±12.86	p>0.05
Potassium (mEq/24h)	68.77±4.98	105.9±10.82	p>0.05
Chloride (mEq/24h)	139.50±11.62	194.10±15.59	p>0.05

Data are expressed as mean ± SEM.
P: Significance versus control, using unpaired student "t" test.

Table 2: Urinary enzyme levels in control group and children with urinary tract stones

Parameters	Controls (n=10)	Pediatric stone formers (n=32)	Significance
NAG (U/g Creatinine)	7.58±0.71	12.86±1.14	p<0.05
β-GAL(U/g Creatinine)	9.16±0.84	15.96±1.16	p<0.01
β-Hex(U/g Creatinine)	5.47±0.38	9.97±0.47	p<0.000
ACE(U/g Creatinine)	38.20±4.88	216.30±37.63	p<0.05
γ-GT (U/g Creatinine)	2.57±0.39	3.90±0.39	p>0.05

N-acetyl-β-D-glucosaminidase (NAG), β-galactosidase (β-GAL), β-hexosaminidase activity (β-Hex), angiotensin converting enzyme (ACE), gamma glutamyl transferase (γ-GT)

Table 3: Serum chemistry profile in control group and children with urinary tract stones

Parameters	Controls (n=10)	Pediatric Stone (n=32)	Significance
Urea (mg/dl)	26.40±1.77	48.38±1.86	p<0.000
Uric acid (mg/dl)	6.18±0.85	6.75±0.39	p>0.05
Creatinine(mg/dl)	0.86±0.06	1.24±0.04	p<0.000
Inorganic phosphorus(mg/dl)	5.42±0.21	5.56±0.24	p>0.05
Soduim (mEq/L)	149.60±2.36	146.10±3.91	p>0.05
Potassium(mEq/L)	4.25±0.07	6.51±0.63	p>0.05
Chloride(mEq/L)	88.25±3.73	89.31±3.18	p>0.05
Calcium(mg/dl)	9.92±0.98	11.81±0.59	p>0.05
Magnesium(mg/dl)	1.07±0.09	1.31±0.07	p>0.05

Data are expressed as mean ± SEM.

P: Significance versus control, using unpaired student "t" test.

Table 4: Urinary chemistry profile in subgroups of children with urinary tract stones .

Parameters	Control (n=10)	Nephrolithiasis (n=12)	Urolithiasis with hydronephrosis (n=20)
Uric acid (g/24hr)	0.44 ± 0.05	2.00 ± 0.10 p<0.001	2.24 ± 0.16 p<0.001 *p>0.05
Protein (g/2hr)	0.20 ± 0.02	0.26 ± 0.09 p>0.05	0.31 ± 0.05 p>0.05 *p>0.05
Creatineine (mg/24hr)	1.37± 0.24	510.10 ± 35.42 p<0.001	614.90 ± 43.53 p<0.001 *p>0.05
Oxalate (mg/24hr)	17.90 ± 0.74	44.15 ± 2.40 p<0.05	62.96 ± 6.51 p<0.001 *p<0.05
Calcium (mg/24h)	151.30 ± 28.22	205.20 ± 28.28 p>0.05	215.00 ± 14.47 p>0.05 *p>0.05
Magnesium (mg/24hr)	123.40 ± 6.22	192.30 ± 28.45 P<0.05	213.70 ± 11.60 P<0.01 *p>0.05
Inorganic Phosphorous (mg/24hr)	536.90 ± 52.31	882.90 ±55.38 P<0.01	919.40 ± 61.82 P<0.001 *p>0.05
Sodium (mEq/24h)	138.40 ± 16.41	150.90 ± 15.85 p>0.05	150.30 ± 18.56 p>0.05 *p>0.05
Potassium (mEq/24h)	68.77 ± 4.98	120.50 ± 20.55 p>0.05	97.20 ± 12.18 p>0.05 *p>0.05
Chloride (mEq/24h)	139.50 ± 11.62	186.60 ± 23.20 p>0.05	198.60 ± 21.09 p>0.05 *p>0.05

p: Significance versus control, using one way ANOVA
*p: significance versus nephrolithiasis using unpaired student t-test

compared to the controls in both groups of patients. Urinary NAG, β-GAL and ACE excretion was significantly elevated in patients with nephrolithiasis compared to those with urolithiasis and hydronephrosis (Table 5).

Serum levels of urea and creatinine were elevated in the nephrolithiasis and hydronephrosis patients, while serum magnesium was elevated in the hydronephrotic patients compared to controls (Table 6). In the hydronephrotic patients serum urea was elevated compared to the patients with nephrolithiasis.

In patients with nephrolithiasis there was a positive correlation between urinary NAG and each of β-GAL (r=0.99, p<0.000) and β-Hex (r=0.98, p<0.000) and between β-GAL and β-Hex (r=0.97, p<0.000).

In the patients with hydronephrosis there was a positive correlation between urinary NAG and each of β-GAL (r=0.95, p<0.000), β-Hex (r=0.98, p<0.000) and ACE (r=0.60, p<0.01) and between β-GAL and each of β-Hex (r=0.99, p<0.000) and ACE (r= 0.59, p<0.000) and between β-Hex and ACE (r=0.63, p<0.01).

Table 5: Urinary enzyme levels in subgroups of children with urinary tract stones

Parameters	Control (n=10)	Nephrolithiasis (n=12)	Urolithiasis with hydronephrosis (n=20)
NAG (U/g Creatinine)	7.58 ± 0.71	16.32 ± 2.57* P<0.01	10.78 ± 0.71* P<0.05 *p<0.05
ß-GAL(U/g Creatinine)	9.16 ± 0.84	19.67 ± 2.47* P<0.01	13.73 ± 0.83* p>0.05 *p<0.05
ß-Hex(U/g Creatinine)	5.47 ± 0.38	10.86 ± 0.89 P<0.001	9.44 ± 0.51 P<0.001 *p>0.05
ACE(U/g Creatinine)	38.20± 4.88	381.20± 31.47 P<0.001	117.40 ± 16.87 P<0.001 *p<0.05
γ-GT (U/g Creatinine)	2.57 ± 0.39	3.91 ± 0.67 p>0.05	3.89 ± 0.49 p>0.05 *p>0.05

p: Significance versus control, using one way ANOVA
*p: significance versus nephrolithiasis using unpaired student t-test.
N-acetyl-β-D-glucosaminidase (NAG), β-galactosidase (β-GAL), β-hexosaminidase activity (β-Hex), angiotensin converting enzyme (ACE), gamma glutamyl transferase (γ-GT)

Table 6: Serum chemistry profile in subgroups of children with urinary tract stones

Parameters	Control (n=10)	Nephrolithiasis (n=12)	Urolithiasis with hydronephrosis (n=20)
Urea (mg/dl)	26.40 ± 1.77	45.17 ± 1.46 P<0.001	50.31± 1.31 P<0.001 *P<0.05
Uric acid (mg/dL)	6.18 ± 0.85	7.80 ± 0.53 p>0.05	6.13 ± 0.50 p>0.05 *p>0.05
Creatinine (mg/dL)	0.86 ± 0.06	1.31 ± 0.09 P<0.001	1.20 ± 0.05 P<0.01 *P>0.05
Inorganic phosphorus (mg/dL)	5.42 ± 0.21	5.48 ± 0.22 p>0.05	5.61 ± 0.37 p>0.05 *p>0.05
Sodium (mEq/L)	149.60 ± 2.36	144.70 ± 5.40 p>0.05	146.90 ± 5.44 p>0.05 *p>0.05
Potassium (mEq/L)	4.25 ± 0.07	6.57 ± 0.56 p>0.05	6.48 ± 0.96 p>0.05 *p>0.05
Chloride (mEq/L)	88.25 ± 3.73	85.32 ± 2.57 p>0.05	91.70 ± 4.83 p>0.05 *p>0.05
Calcium (mg/dL)	9.92 ± 0.98	10.45 ± 0.68 p>0.05	12.63 ± 0.80 p>0.05 *p>0.05
Magnesium (mg/dL)	1.07 ± 0.09	1.14± 0.07 p>0.05	1.41 ± 0.09 P<0.05 *p>0.05

P: Significance versus control, using one way ANOVA.
*P: significant versus nephrolithiasis using unpaired student "t" test.

DISCUSSION

The normal urinary environment is inhibitory to crystallization. Occasional crystals are internalized by the renal epithelial cells and sequestered by lysosomes or externalized into the interstitium to be handled by the inflammatory cells[22]. The effects of urinary tract obstruction on renal function have been clarified in animal studies. During chronic unilateral obstruction, both the renal blood flow and glomerular filtration rate are reduced, and a compensatory increase in these parameters occurs in the contralateral normal kidney. In adult patients with idiopathic stone formation, the renal functions are found to be normal, but enzymuria may occur[23].

The results of the present study revealed normal protein levels in the urine of nephrolithiasis and urolithiasis in children. However, an increased protein excretion in urolithic rats as well as in stone formers has been reported previously[24]. In consistence with others[12] we found a higher oxalate, uric acid, magnesium and inorganic phosphorus excretion in children with nephrolithiasis and urolithiasis than in controls. In contrast to our results, other investigators[12,25] did not report any change in urinary inorganic phosphorus or uric acid excretion in calcium stone forming children.

Urinary enzymes originate in the kidneys, and many of them can be traced back to specific segments and cellular components of the renal tubules. Therefore, abnormal changes in urinary enzyme levels can indicate tubular dysfunction and the specific tubular segments that are involved. It is well established that calcium oxalate urolithiasis is associated with a greater than normal urinary excretion of brush border [neutral endopeptidase (NEP), γ-GT, ACE] and lysosomal enzymes (NAG and GAL). NAG and GAL have been demonstrated in all segments of the nephron, with highest activity in the convoluted part and the beginning of the straight part of the proximal tubule[25].

In agreement with others[10,11,26,27], our study showed a significant increase in the urinary excretion of NAG and β-GAL in oxalate stone forming children compared to controls. The levels of NAG and GAL were more significantly elevated in patients with nephrolithiasis when comparing them to those with hydronephrosis. In contrast, Huang, et al.[11] reported elevated urinary NAG and GAL in adult patients with hydronephrosis compared to those with nephrolithiasis. Increased urinary NAG in children with renal calculi has been reported to be related to tubular injury[10]. However, Kavukcu et al.[26] reported that the urinary NAG level was not affected unless the calciuria level was very high. Balla et al.[10] hypothesized that NAG may be a useful parameter for the follow-up of tubular damage in patients with stone disease.

Regarding brush border enzymes, we reported a significant elevation in ACE activities in oxalate stone forming children compared with controls; they were more elevated in nephrolithiasis children compared to those with hydronephrosis. These results were consistent with those obtained by Baggio et al.[8] who reported elevated urinary ACE activities in both children with hydronephrosis and nephrolithiasis. Other studies have provided evidence for the activation of the renin-angiotensin system during the development of tubulointerstitial lesions of CaOx crystals[27]. Reduction of angiotensin production by inhibiting angiotensin-converting enzyme as well as blocking the angiotensin receptor reduced crystal deposition and ameliorated the associated inflammatory response. Khan[22] has recently shown that CaOx crystal deposition in rat kidneys activates the renin-angiotensin system and increases renin expression in the kidneys and serum.

On the other hand, urinary activity of γ-GT did not show any significant changes in stone forming patients compared with controls. In contrast to our study, El-Sharabasy[28] reported elevated urinary γ-GT activity in calcium oxalate stone formers. Huang et al.[11] reported a decrease in brush border enzyme [neutral endopeptidase (NEP)] excretion in adult patients with urolithiasis and hydronephrosis

compared with controls and nephrolithiasis patients. Because the amount of urinary NEP may reflect the proportion of brush borders remaining intact at the apical end of the proximal tubules, Nortier et al.[29] suggested that the reduction of NEP enzymuria could reflect the atrophy of renal proximal tubules which is more apparent in patients with hydronephrosis.

These results suggest that the renal tubules of the nephrolithiasis and urolithiasis patients with hydronephrosis may become impaired, although the renal function tests (plasma creatinine and blood urea nitrogen) and blood biochemistry are still within normal limits. Furthermore, Huang et al.[11] combined the results on the excretion patterns of lysosomal and brush border enzymes and found that other tubular segments apart from the proximal tubules may contribute to the enhanced urinary excretion of β-GAL and NAG in stone disease.

The mechanism that leads to the local release of tubular enzymes in humans with stone disease is not quite clear. From the study of an animal model and cell culture, it appears that both calcium oxalate crystals and oxalate are injurious to renal epithelial cells, and the toxicity of oxalate is associated with lipid peroxidation of the cellular membrane[30] This process may lead to brush border injury or even cellular death, with enzymuria as a sign of tubular necrosis and, indirectly, as a marker of disease activity. However, the study of Verkoelen et al.[31] revealed that there was no measurable damaging effect on Madin-Darby canine kidney (MDCK) monolayers induced by either calcium oxalate saturated solution or by the solution including calcium oxalate crystals, unless obstruction has occurred. There is no evidence to suggest that the visible renal or ureteral stones could cause renal tubular damage[11]. Scheid et al.[32] found that a toxic effect of oxalate on LLC-PKI cells (a line of renal epithelial cells) is both time and concentration dependent.

Our results indicate that only proximal tubule damage could be detected in children with calcium oxalate (CaOx) stones. However, both proximal and distal renal tubule damage has been found in chronic hyperoxaluric rats[33]. Humans with renal CaOx calculi had a much lower urinary oxalate concentration than did the experimental hyperoxaluric rats[33]. Oxalate is secreted along the entire length of the proximal tubule[33], which may be the first part to be damaged when the oxalate concentration becomes high enough to have a toxic effect on the kidney, and damage to the distal tubule occurs only when the concentration becomes higher. Huang et al.[33] found that urinary μ-glutathione-S-transferase (μ-GST) had a statistically significant, positive, linear correlation with urinary oxalate, which implied that the damage to the distal tubule was also influenced by the concentration of urinary oxalate, but this damage was not prominent enough to be statistically significant compared with the level in the controls.

In the present study, in patients with nephrolithiasis, we found a positive correlation between urinary NAG and each of β-GAL and β-Hex. Also, in patients with hydronephrosis, we found a positive correlation between urinary NAG and each of β-GAL and β-Hex. Although an increased urinary NAG excretion was reported in children with nephrocalcinosis, a correlation between the urinary NAG/Cr and calcium or oxalate excretion was not observed in stone forming children by us and others[34]. Such a relationship was, however, recently found in rabbits with experimental hypercalciuria and histologically proven nephrocalcinosis[34] In contrast, Huang et al.[33] found a positive correlation between urinary oxalate level and GAL and NAG urinary levels in adult patients with renal calcium oxalate stones.

In conclusion, abnormal urine biochemistry seems to have a role in the risk of urinary stone formation in children. The mechanism of cell damage in these conditions seems to be complex and needs further investigation. Nephrolithiasis and urolithiasis with hydronephrosis in children both result in proximal tubular injury of the kidney, which may be the consequence of the metabolic activity of the disease. The destruction is more pronounced in children with hydronephrosis. NAG, GAL

and ACE could be useful parameters to monitor the activity of urinary tract stones and the degree of renal tubular damage before impairment of kidney functions occur, but this needs to be proven in long-term follow-up studies.

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RESUME

EXCRETION URINAIRE DES ENZYMES TUBULAIRES CHEZ LES ENFANTS AVEC NEPHROLITHIASES ET UROLITHIASES AVEC HYDRONEPHROSE

Objectif : Nephrolithiases et urolithiases sont souvent associées à une morbidité et un impact économique considérables. Il a été démontré que les interactions cellule-cristaux mènent à des dégâts et/ ou dysfonctionnements tubulaires. Pour trouver des arguments supplémentaires et consolider ces observations, une évaluation métabolique, y compris sérum et biochimie des urines et enzymes urinaires a été réalisée chez les enfants avec nephrolithiases et urolithiases avec hydronéphrose.

Patients et méthodes : Cette étude a inclus deux groupes principaux. Groupe (1) 10 enfants normaux inclus, et groupe (2) 32 enfants inclus avec des lithiases d'oxalate de calcium des voies urinaires. Le 2ème groupe a été subdivisé en outre en 2 sous-groupes; nephrolithiases (n=12) et urolithiases avec hydronéphrose (n=20). Les niveaux d'acide urique, oxalate, calcium, magnésium et phosphore inorganique dans les urines de 24 heures et sérum ont été déterminés. Un dosage urinaire de la N-acetyl-β-D-glucosaminidase (NAG), β-galactosidase (β-GAL), l'activité β-hexosaminidase (β-Hex), angiotensin converting enzyme (ACE), gamma glutamyl transferase (γ-GT), les niveaux ont aussi été déterminés par des moyens colorimetriques.

Résultats : L'augmentation de l'excrétion urinaire d'oxalate, calcium, magnésium, phosphore inorganique étaient caractères anormaux majeurs trouvés chez les patients présentant des lithiases. Des taux urinaires élevés de NAG, β-GAL, β-Hex, ACE ont aussi été notés chez les patients comparés avec les contrôles. L'excrétion urinaire d'oxalate, NAG, β-GAL, ACE était élevée considérablement chez les patients présentant des nephrolithiases comparé aux enfants avec urolithiases et hydronéphrose.

Conclusion : La biochimie de l'urine anormale paraît avoir un rôle dans la forte fréquence de lithiases chez les enfants. L'hyperoxalurie peut induire principalement des lésions cellulaires tubulaires qui sont plus prononcés chez les enfants avec nephrolithiases. La lésion tubulaire manifestée par une enzymurie se produit avant les modifications de la fonction rénale et de la biochimie du sang. Les enzymes tubulaires urinaires devraient être recherchées chez les enfants avec lithiases des voies urinaires.

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