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An association between kidney stone composition and urinary metabolic disturbances in children

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Abstract *Objective:* To determine kidney stone composition in children and to correlate stone fractions with urinary pH and metabolic urinary risk factors.
Patients and methods: We studied 135 pediatric patients with upper urinary tract lithiasis in whom excreted or extracted stones were available for analyses. Composition of stones was analyzed. A 24-hour urine assessment included volume, pH and daily excretions of calcium, oxalate, uric acid, cystine, creatinine, phosphate, magnesium and citrate.
Results: Calcium oxalate was the major component of 73% stones, followed by struvite (13%) and calcium phosphate (9%). Uric acid was present in almost half of stones, but in rudimentary amounts. The calcium oxalate content in calculi showed a strong relationship with calciuria, and moderate association with oxaluria, magnesuria and acidification of urine. The percent content of struvite presented reverse and lower correlations with regard to the above parameters. Calcium phosphate stone proportion had low associations with urinary risk factors.
Conclusions: Calciuria, oxaluria, magnesuria and low urine pH exerted the biggest influence on calcium oxalate content in pediatric renal stones. Relationships of urinary risk factors with calculi calcium phosphate content were of unclear significance. Urinary citrate excretion did not significantly correlate with kidney stone composition in children.

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Introduction

Evaluation of urinary stone composition is an important diagnostic step in determining the possible etiology and pathophysiologic mechanisms of stone formation. Effective crystal formation takes place when urine is supersaturated with stone-forming salts and, thus, the calculi composition should correspond with specific admixture's urine saturation [1,2].

In cases of struvite ($MgNH_4P$) and cystine stones, these associations with chronic infection of the urinary tract with urea-splitting organisms and cystinuria, respectively, are clearly shown. However, for most common calcium stones, the presence of several risk factors, including hypercalciuria, hyperoxaluria, hypocitraturia and hyperuricosuria was reported [3,4]. Moreover, the composition of most of the calculi is not homogeneous. In developed countries, calcium oxalate (CaOx) is the predominant stone constituent usually admixed with small amounts of calcium phosphate (CaP) and/or uric acid (UA), which may form the initial nidus of the CaOx stone. Only in a limited number of cases do substances different from CaOx constitute the main stone phase [5,6].

In children, the reported compositions of stones slightly differ from those in adults. They are often made of a larger number of constituents reflecting a specific complex structure. Another important feature of pediatric urinary stone disease is the prevalent proportion of cases with coincident metabolic disturbances in urine. Excretion rates of calcium, oxalate, citrate and uric acid are higher when adjusted for urine creatinine. Calcium oxalate supersaturation is similar to that in adults, but calcium phosphate supersaturation is usually higher whereas uric acid is lower because of higher urine pH at pediatric age [7–12].

In fact, only few reports to date have focused on the association between different stone components and biochemical urinary risk factors in children [10,11]. Therefore, the purpose of this study was to define the correlations between stone constituents and urinary pH, and accompanying metabolic abnormalities in urine in pediatric kidney stone formers.

Patients and methods

Study population

This retrospective study was carried out using the data of 135 patients with upper urinary tract lithiasis (71 boys, 64 girls), aged 2–18 years (median 14.6 years), treated in the University Children's Hospital in Bialystok, Poland during 2002–2011. There were two main inclusion criteria for the study: availability of the stone for chemical analysis and appropriate 24-hour urine collection. There were no other exclusion criteria if complete urinary metabolic and stone composition results were attainable. The study included 36% of urolithiasis patients registered in the hospital records during that period. In the remaining children, stones were not excreted or were unavailable because of loss/unnoticed spontaneous passage.

Calculi were obtained intact from spontaneous passage (81), open surgery (26) or fragmented form after ureterorenoscopic lithotripsy (15), extracorporeal shock wave lithotripsy (12) or percutaneous nephrolithotripsy (1). In 26 traditionally operated children, 10 had staghorn calculi and concomitant pyeloureteral junction obstruction was suspected in 11. Twenty-one patients submitted more than one stone during that time, but only primary stone analyses and urinary chemical profiles were considered in the study. Thirteen stone formers presented with urinary tract infection at admission, and the another 17 had positive history of recurrent infections of urinary system. Ten participants in the study had neurogenic bladder because of myelomeningocele.

Stone analysis and urine assessment

Composition of stones was analyzed by laboratory commercial test (DiaSys Diagnostic Systems GmbH, No 131399990351, Holzheim, Germany) assessing the presence and relative proportions of the seven most frequent natural chemical components. The stone phase was considered to be the major component if it reached at least 50% of the total calculus composition. Four to eight weeks after passing/retrieving the stones and recovery from urinary infection, if present, the 24-hour urine collections were provided while patients were on their usual diet and fluid intake. After voiding, urine samples were kept refrigerated at 4 °C and all measurements were conducted at the end of collection periods within 4 h. Urine assessment included volume, pH and daily excretions of calcium, oxalate, uric acid, cystine, creatinine, phosphate, magnesium and citrate. Urinary metabolites were assessed in an identical manner to that described in our previous publication [13]. Participants and their legal guardians gave informed consent for participation in the procedures, and the study was approved by the ethical committee of the Medical University of Bialystok.

Statistical analyses

The statistical analysis was performed by Statistica, version 10.0 PL (StatSoft Inc., Tulsa, OK, USA). Kruskal–Wallis testing was performed to evaluate differences among the predominantly CaOx, CaP and $MgNH_4P$ stone groups for a given urinary parameter, and Mann–Whitney test was used for comparisons of two groups. Differences were considered statistically significant if $p < 0.05$. Correlations between proportional stone constituents and a given urinary parameter were made using the Spearman test. The r values of correlation coefficients $\leq$0.35 were considered to represent weak a relationship, 0.36–0.67 moderate association and 0.68–1.0 strong correlation [14].

Results

Kidney stone analyses revealed that the vast majority of stones presented mixed composition. The most common chemical combinations were CaOx and CaP admixed with small amount of uric acid (38%) followed by biminerals formed of CaOx and CaP (30%). All infection stones revealed some admixture of metabolic components. Qualitative