Changing Stone Composition Profile of Children With Nephrolithiasis

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OBJECTIVE To determine if this trend toward calcium phosphate stone formation exists in children.

METHODS This is a retrospective study of medical records of 179 children managed at our medical center from 1992-2010 for whom stone analysis and other pertinent laboratory data were available. A comparison of patients managed from 1992-2000 (P1) and 2001-2010 (P2) was undertaken. Statistical analysis included nonparametric tests.

RESULTS There were no significant differences in the mean age of the 2 cohorts. During both periods, boys comprised a significantly higher proportion during the first decade of life, whereas girls comprised a significantly higher proportion during the second decade. A higher percentage of patients had calcium oxalate (CaOx) stones in P1 compared to P2 (60% vs 47%, $P = .0019$). There was a significant increase in the percentage of patients having calcium phosphate stones in P2 compared to P1 (27% vs 18.5%, $P = .008$). Twenty-seven patients had recurrent stones. A comparison of the compositions of the first and last stones of patients within this group demonstrated an increasing proportion of brushite stones (3.7% vs 11.1%, $P = .04$). Twenty-four hour urine testing results were similar for those with CaOx and calcium phosphate stones.

CONCLUSION An increasing proportion of children have calcium phosphate calculi. Brushite stones are more prevalent in children with recurrent stone events. The impetus of these shifts is not readily apparent. UROLOGY 82: 210–213, 2013. © 2013 Elsevier Inc.

Children comprise 2%-3% of the total population of kidney stone formers. Similar to adults, children forming kidney stones have a high prevalence of underlying metabolic abnormalities placing them at risk for calculogenesis.[1,2] In addition, children in industrialized countries are subject to the environmental and life style influences promoting stone formation. Some of the same medical comorbidities that are associated with kidney stone formation in adults are found in children; namely, hypertension and diabetes mellitus.[1,2]

The prevalence of calcium phosphate stones in adults in the United States over the last few decades has increased.[3,4] Furthermore, a shift from calcium oxalate (CaOx) to calcium phosphate with increasing episodes of stone recurrence has been reported.[3,5] Herein, we performed a retrospective study to determine whether similar trends are present in children.

MATERIAL AND METHODS

Study Design

We retrospectively reviewed a database of stone compositions and 24-hour urine chemistry studies at a single center. The institutional review board approved this study. Children were defined as being ≤18 years of age. Out-patient clinic and hospital records were analyzed. Body mass index data within 3 months of the stone episode were used. Overall, we reviewed the medical records of 179 patients managed from 1992-2010 (age range 0.2-18 years) for whom stone analysis data were available. A comparison of patients managed from 1992-2000 (P1) and 2001-2010 (P2) was undertaken.

Stone and Urine Collections

Stone analyses were conducted at 3 different laboratories including Beck (Indianapolis, IN), Louis C. Herring and Company (Orlando, FL), and Mandel International Stone and Molecular Analysis Center (Milwaukee, WI). Urinary parameters measured included sodium, calcium, citrate, uric acid, oxalate, potassium, phosphorus, magnesium, creatinine, and volume. The urine assays were done in our laboratory using previously described techniques.[6] Supersaturation for CaOx and calcium phosphate was estimated using the technique of Tiselius.[7] A stone was considered to be CaOx if it contained >50% of any form of CaOx. A stone was considered calcium phosphate if it contained >50% of any form of calcium phosphate. An analysis of the composition of the first stone vs the last stone among recurrent stone formers was performed.

Statistical Analysis

Urine chemistry studies were adjusted for both urinary creatinine and body weight. All statistical trends were done using GraphPad software. When needed, multivariate models were

Financial Disclosure: *The authors declare that they have no relevant financial interests.*

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Submitted: December 12, 2012, accepted (with revisions): February 18, 2013

0090-4295/13/$36.00
http://dx.doi.org/10.1016/j.urology.2013.02.033

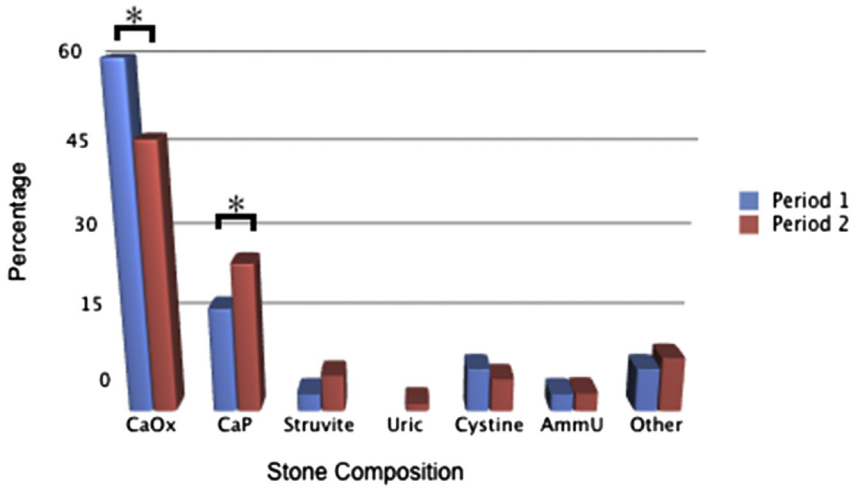

Figure 1. Demonstrates significant (*) decrease in calcium oxalate (CaOx) from period 1 (1992-2000) to period 2 (2001-2010) and a significant (*) increase in calcium phosphate between those same periods. (Color version available online.)

used adjusting for age. Statistical analysis primarily included nonparametric chi-square and *t* test. Statistical significance was set at $P < .05$.

RESULTS

One hundred seventy-nine pediatric stone cases were identified from 1992-2010 (28 boys and 28 girls in P1, and 59 boys and 64 girls in P2). The overall mean age 10.9 ± 5.1 SD in years of manifestation did not differ between the periods (10.6 ± 5.4 years in P1 and 11.1 ± 5.0 years in P2, $P = .6$). There were no statistically significant differences in ages among the same gender between P1 and P2. Mean age of boys was 9.2 ± 5.5 years (± SD) for P1 and 10.0 ± 5.0 years for P2 ($P = .5$). Mean age for girls was 12.0 ± 5.0 years for P1 and 11.9 ± 4.8 years ($P = .96$). There was a statistically significant difference between age at presentation between genders for both periods combined (boys 9.8 ± 5.1 years and girls 11.9 ± 4.8 years, $P = .004$). When broken down among periods, the differences approached statistical significance for P1, girls 12.0 ± 4.9 years and boys 9.2 ± 5.5 years ($P = .06$), and was significant for P2, girls 11.9 ± 4.8 years and boys 10.0 ± 5.0 years ($P = .03$). The mean BMI for P1 was 18.1 ± 4.6 and 22.0 ± 7.0 ($P = .04$). The latter data were available for 41 patients in P1 and 42 in P2.

Boys comprised a higher proportion of the patients who developed stones during the first decade of life, with a boy:girl ratio of 1.6:1 for both periods, 1.9:1 for P1 and 1.5:1 for P2. In contrast, girls comprised a higher proportion of the patients who developed stones during the second decade of life, with a boy:girl ratio of 1:1.7 for both periods, 1:1.7 for P1 and 1:1.8 for P2.

There were significant differences in type of calcium stone compositions between P1 and P2. A higher percentage of patients had CaOx stones in P1 compared to P2 (60% vs 47%, $P = .0019$). There was a significant increase in the percentage of patients having calcium phosphate stones in P2 compared to P1 (27% vs 18.5%, $P = .008$). There were no significant gender differences in stone composition ($P = .7$ for CaOx, $P = .33$ for calcium phosphate). There were no statistically significant differences in other stone compositions between P1 and P2. In addition, there were no statistically significant differences in stone compositions in patients less than or greater than 10 years in age. The breakdown of stone compositions is displayed in Figure 1.

Twenty-seven patients had recurrent stones. The composition of the initial stone was calcium phosphate in 33% of this cohort and 37% for the last stone analyzed ($P = .67$). The compositional data for the recurrent group are shown in Figure 2. A subset analysis based on the form of calcium phosphate demonstrated that the percent with brushite increased from 3.7% for the first stone to 11.1% for the last stone analyzed as brushite stones ($P = .04$).

Twenty-four hour urine testing was performed in 62 children with calcium containing stones (49 CaOx and 13 calcium phosphate). There were no statistically significant differences in the urinary parameters of patients with CaOx stones compared with patients with calcium phosphate stones. Furthermore, there were no differences in urinary parameters between P1 and P2.

DISCUSSION

The results of this study demonstrate that there has been a shift in stone composition of pediatric stone formers over the past 2 decades with calcium phosphate becoming more prevalent. Gender did not influence this trend in our study. This is consistent with adult studies. Parks et al[4] reported that, in an adult cohort of 1201 patients, the percentage of calcium phosphate in stones increased from 1970-2003. They noted that this trend occurred in both genders but it was more prominent in women. This group reported that the supersaturation of calcium phosphate, urine pH, and calcium excretion were higher in patients with calcium phosphate stones as compared to CaOx