Diabetic Kidney Stone Formers Excrete More Oxalate and Have Lower Urine pH Than Nondiabetic Stone Formers

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Abbreviations and Acronyms

BMI = body mass index

CaP = calcium phosphate

SS = supersaturation

Submitted for publication September 18, 2009.

Study received institutional review board approval.

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† Financial interest and/or other relationship with Boston Scientific, PercSys and Ravine Group.

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For another article on a related topic see page 2419.

Purpose: The epidemiological relationship between nephrolithiasis and type 2 diabetes mellitus is well-known. Patients with diabetes mellitus are at increased risk for nephrolithiasis and those with nephrolithiasis are at risk for diabetes mellitus. We examined 24-hour urine composition in stone formers with and without diabetes mellitus.

Materials and Methods: We retrospectively reviewed a database of 462 stone forming patients to examine the relationship between hypertension and 24-hour urine composition. Multivariate linear regression models were adjusted for age, race, gender, body mass index, hypertension, relevant medications and 24-hour urine constituents.

Results: On univariate analysis diabetic patients had significantly greater urine volume than nondiabetic patients (2.5 vs 2.1 l daily, $p = 0.004$). Those with diabetes mellitus also excreted less daily potassium (61.1 vs 68.8 mEq, $p = 0.04$), phosphate (0.84 vs 1.0 gm, $p = 0.002$) and creatinine (1405.5 vs 1562.8 mg, $p = 0.03$), and had significantly lower daily urine pH (5.78 vs 6.09, $p < 0.001$) and CaP supersaturation (0.49 vs 1.20, $p < 0.001$) than nondiabetic patients. On multivariate analysis compared to patients without diabetes mellitus those with type II diabetes mellitus had significantly lower urine pH (−0.34, 95% CI −0.48 to −0.21) and significantly greater urine oxalate (6.43 mg daily, 95% CI 1.26 to 11.60) and volume (0.38 l daily, 95% CI 0.13 to 0.64).

Conclusions: Results show that of stone formers patients with type II diabetes mellitus excrete significantly greater urinary oxalate and significantly lower urine pH than those without diabetes mellitus. These findings are important for treating nephrolithiasis since they may influence dietary counseling, medical management and stone prevention.

Key Words: kidney, nephrolithiasis, diabetes mellitus, oxalates, hydrogen-ion concentration

Diabetes mellitus and nephrolithiasis are 2 common causes of morbidity of which the incidence appears to be increasing.[1,2] Several studies demonstrated a relationship between diabetes mellitus and nephrolithiasis, suggesting a common physiological pathway. Population based cohort studies showed that patients with diabetes mellitus are at significantly increased risk for nephrolithiasis.[3,4] To date metabolic studies of the relationship between diabetes mellitus and nephrolithiasis have focused on the increased prevalence of uric acid calculi secondary to low urine pH in patients with diabetes mellitus.[5–8] We compared 24-hour urine chemistry in diabetic and nondiabetic stone formers.

0022-5347/10/1836-2244/0
THE JOURNAL OF UROLOGY®

Vol. 183, 2244-2248, June 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.02.007

MATERIALS AND METHODS

Study Design

We retrospectively reviewed a 24-hour urinalysis database at a tertiary care academic medical center metabolic stone clinic. Patients 18 years old or older who presented for the initial metabolic stone assessment were identified and included in the study. Electronic medical records and 24-hour urine composition data were analyzed. BMI was calculated in kg/m^2 from self-reported patient height and weight values at 24-hour urine collection. Stone analysis was done using infrared spectroscopy. Patients were categorized as having diabetes mellitus if they met 2 criteria, including 1) they had type II diabetes mellitus listed in the medical history of the electronic medical record and 2) they were on antiglycemic medication (oral hypoglycemics with or without insulin). Patients were excluded from study when BMI or medical history was not available or 24-hour urine collections were deemed to be inadequate, including 24-hour urine creatinine less than 800 mg in men and less than 600 mg in women.

Urine Collection

Patients underwent 24-hour urinalyses which were processed by Litholink®. Standard urinary parameters were evaluated, including sodium, Ca, citrate, creatinine, uric acid, oxalate, potassium, phosphorus, magnesium, sulfate, pH and urine volume. The SS ratio of Ca oxalate, CaP and uric acid was calculated using the iterative computer program EQUIL2.

Statistical Analysis

We included only a single 24-hour urinalysis in analysis. In patients for whom more than 1, 24-hour urinalysis was available only the first urinalysis was used. Univariate analysis was done with Student's t test. Values are shown as the mean ± SD. Multivariate linear regression was adjusted for possible confounders, including age, gender, race, BMI, hypertension, thiazide and/or potassium citrate use and 24-hour urine chemistry (volume, pH, Ca, citrate, creatinine, oxalate, magnesium, phosphate, potassium, sodium, sulfate and uric acid). All tests were 2-sided with significance considered at $p < 0.05$. The 95% CI was calculated for all regression coefficients. All analysis was done with JMP® 8.0.

RESULTS

We analyzed the records of 462 patients, of whom 46 (9.9%) had type II diabetes mellitus and 416 (90.1%) did not. Diabetic patients were older (mean age 60.4 ± 9.8 vs 51.0 ± 13.3 years, $p < 0.001$), and had greater BMI (mean 30.2 ± 8.4 vs 26.6 ± 5.4 kg/m^2, $p = 0.005$), a greater incidence of hypertension (63.0% vs 26.4%, $p < 0.001$) and greater thiazide use (21.7% vs 9.1%, $p = 0.02$) than nondiabetic patients. The diabetic group also included a greater proportion of females (54.4% vs 39.2%, $p = 0.05$, and males 45.7% vs 60.8%) and a greater ratio of Asian/Pacific Islander to white patients (39.1% vs 17.5%) than the nondiabetic group (60.9% vs 82.5%, $p = 0.001$). There was no difference in potassium citrate use between diabetic and nondiabetic patients (9.6% and 10.9%, respectively, $p = 0.79$).

On univariate analysis diabetic stone formers excreted a greater volume than nondiabetic stone formers (2.5 ± 0.9 vs 2.1 ± 1.0 l daily, $p = 0.004$). Diabetic stone formers also had lower 24-hour urine phosphate (0.84 ± 0.32 vs 1.00 ± 0.36 gm, $p = 0.002$), potassium (61.1 ± 22.4 vs 68.8 ± 31.4 mEq, $p = 0.04$), creatinine (1405.5 ± 467.2 vs 1562.8 ± 475.1 mg, $p = 0.03$), pH (5.78 ± 0.48 vs 6.09 ± 0.54, $p < 0.001$) and SSCaP (0.49 ± 0.59 vs 1.20 ± 1.03, $p < 0.001$, table 1). There were no other differences between the 2 groups.

Multivariate linear regression revealed that compared with nondiabetic stone formers diabetic patients excreted significantly more daily oxalate (6.43 mg, 95% CI 1.26 to 11.60) and volume (0.38 l, 95% CI 0.13 to 0.64). Diabetic patients also had significantly lower daily urine phosphate (−0.11 gm, 95% CI −0.18 to −0.04) and pH (−0.34, 95% CI −0.48 to −0.21). There were no other differences between the 2 groups (table 2).

Subgroup analysis was performed in the diabetic group. Stone composition analysis in diabetic patients showed 100% Ca oxalate monohydrate in 18, 100% CaP in 4, 100% uric acid in 2, mixed Ca oxalate and CaP in 6, and mixed uric acid and Ca oxalate monohydrate with a greater than 50% uric acid component in 4. The remaining 12 diabetic patients did not have stone analysis available for review. Of stones with known composition 82.3% in patients with diabetes mellitus were 100% Ca and the remaining 17.7% were purely or mostly uric acid. Table 3 shows univariate analysis of 24-hour urine composition in diabetic patients with available stone analysis. Those with Ca stones excreted sig-

Table 1. *Univariate analysis of 24-hour urine chemistry by diabetes mellitus status*

	Mean ± SD No Diabetes	Mean ± SD Type II Diabetes	p Value
Ca (mg)	214.5 ± 119.0	183.1 ± 110.6	0.07
Oxalate (mg)	42.1 ± 17.7	48.1 ± 22.9	0.09
Citrate (mg)	575.6 ± 355.9	534.5 ± 441.6	0.54
Uric acid (gm)	0.70 ± 0.23	0.73 ± 0.23	0.30
Sodium (mmol)	169.8 ± 73.9	194.9 ± 87.0	0.07
Potassium (mEq)	68.8 ± 31.4	61.1 ± 22.4	0.04*
Magnesium (mg)	108.5 ± 42.6	106.4 ± 43.4	0.76
Phosphate (gm)	1.00 ± 0.36	0.84 ± 0.32	0.002*
Sulfate (mmol)	44.9 ± 16.9	45.4 ± 16.7	0.85
Creatinine (mg)	1,562.8 ± 475.1	1,405.5 ± 467.2	0.03*
pH	6.09 ± 0.54	5.78 ± 0.48	<0.001*
Vol (l)	2.1 ± 1.0	2.5 ± 0.9	0.004*
SS:			
Ca oxalate	7.12 ± 3.98	5.84 ± 4.39	0.06
CaP	1.20 ± 1.03	0.49 ± 0.59	<0.001*
Uric acid	0.99 ± 0.97	1.15 ± 0.89	0.27

* $p < 0.05$.