Treatment Response in Patients with Stones, and Low Urinary pH and Hypocitraturia Stratified by Body Mass Index

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Purpose: Obesity has been shown to be a risk factor for kidney stone formation. Obesity leads to insulin resistance which subsequently leads to low urinary pH. Low urinary pH is typically treated with potassium citrate. We determined if the response to potassium citrate for the treatment of low urinary pH and hypocitraturia varied when patients were stratified by body mass index.

Materials and Methods: We retrospectively reviewed the records of patients with urolithiasis and concomitant hypocitraturia and low urinary pH as unique abnormalities upon metabolic evaluation treated exclusively with potassium citrate. Based on body mass index the cohort was divided into the 4 groups of normal weight, overweight, obese and morbidly obese. Metabolic data were compared among the 4 groups at baseline and subsequent followup visits up to 2 years. We compared urinary pH and citrate in absolute values and the relative changes in these parameters from baseline. Similarly, we compared the rates of potassium citrate treatment failure.

Results: A total of 125 patients with hypocitraturia and low urinary pH were included in this study. Median patient age was 61 years, 80 patients were male and median body mass index was 30.4 kg/m^2. Patients with a higher body mass index tended to be younger ($p=0.010$), and had a lower urinary citrate but higher sodium, oxalate and uric acid levels. Urinary pH was similar across body mass index groups. pH values and their absolute changes from baseline were lower as body mass index increased ($p \leq 0.001$). Similarly, we noted an association between increasing body mass index category and lower urinary citrate levels accompanied by a statistically significant trend indicating lower absolute changes in citrate with increasing body mass index ($p \leq 0.001$). Potassium citrate dose was increased more frequently among the higher body mass index groups.

Conclusions: Patients with a higher body mass index presented with a lower increase in citrate excretion and urinary pH levels after they were started on potassium citrate, and they needed more frequent adjustments to their therapy.

Key Words: urolithiasis, potassium citrate, body mass index

Abbreviations and Acronyms

BMI = body mass index

Kcit = potassium citrate

Accepted for publication September 8, 2015.

No direct or indirect commercial incentive associated with publishing this article.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

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Editor's Note: This article is the fourth of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 810 and 811.

THE prevalence of nephrolithiasis has doubled during the last 1 and a half decades in the United States.[1] One of the factors believed to be responsible for this increase is the increase in obesity. Obesity has been shown to be a risk factor for kidney stone formation.[2] This association is particularly strong for females, as an obese female has nearly double the risk of stone

0022-5347/16/1953-0653/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2015.09.070
Vol. 195, 653-657, March 2016
Printed in U.S.A.

formation compared to a female with a normal BMI. One of the reasons postulated for this increased risk of stone disease in obese patients is that obesity leads to insulin resistance, which subsequently leads to a low urinary pH. A large retrospective review of nearly 5,000 patients with stones who had undergone metabolic evaluation demonstrated that as body weight increased, urinary pH decreased.[3]

Low urinary pH is associated with hypocitraturia.[4] Both abnormalities are well-known urinary lithogenic factors increasing the risk of calcium oxalate stone formation and uric acid stone formation.[5] In addition to insulin resistance there are other potential causes of low urinary pH and it is often characterized as idiopathic. It is possible that the mechanism for low urinary pH is different between obese and nonobese patients. Low urinary pH is typically treated with potassium citrate. Citrate is a known inhibitor of stone formation and Kcit also increases urinary pH.

We determined if the response to Kcit for the treatment of low urinary pH and hypocitraturia varied when patients were stratified by BMI. We also evaluated if patients with a higher BMI required more frequent dose adjustments of Kcit.

MATERIALS AND METHODS

After approval from the institutional review board we retrospectively reviewed the records of patients with urolithiasis and concomitant hypocitraturia and low urinary pH on initial metabolic evaluation treated exclusively with potassium citrate. Patients with other metabolic abnormalities such as hypercalciuria, hyperuricosuria and hyperoxaluria were excluded from analysis. Patients who were treated with medications that modified citrate level or urinary pH (thiazides, sodium bicarbonate, calcium citrate, potassium citrate) were also excluded from the study.

A search of the electronic medical records of all patients with kidney stones with a metabolic evaluation treated at our comprehensive kidney stone center was performed, identifying patients with hypocitraturia (ICD-9 275.95) or gout unspecified, which is how we code low urinary pH in our practice for billing purposes (ICD-9 274.9). The 24-hour urine samples were obtained at baseline and subsequent followup visits. In the present study metabolic data were collected at baseline, and at 3 (±1.5), 6 (±1.5), 9 (±1.5), 12 (±1.5), 18 (±3) and 24 (±3) months. Hypocitraturia and low urinary pH were defined as urinary citrate 500 mg or less (men and women) and urinary pH less than 5.6, respectively, on 2, 24-hour urine analyses. All urine samples were analyzed at the same laboratory (Litholink Corp., Chicago, Illinois).

Based on BMI the cohort was divided into 4 groups of normal weight (BMI less than 25 kg/m^2), overweight (25-29.9 kg/m^2), obese (30-34.9 kg/m^2) and morbidly obese (35 kg/m^2 or greater). Metabolic data were compared among the 4 groups at baseline and subsequent followup visits up to 2 years. We compared urinary pH and citrate in absolute values and the relative changes in these parameters from baseline. Similarly, we compared the rates of potassium citrate treatment failure, whereby failure was defined as an increase in dose or change from potassium citrate to another medication.

Data are presented as median (IQR) and number (percent) unless otherwise specified. Comparisons among the groups were conducted using the Fisher exact test and rank sum tests for categorical and continuous variables, respectively. Trend analyses to compare urinary pH, citrate level and K were performed using Cochran-Armitage and Cuzick's tests. For comparisons of changes from baseline, values were considered the first followup metabolic parameters and analyses were performed using paired nonparametric tests (signed rank tests). The statistical significance threshold was set at p=0.05 and all tests were 2-sided. Statistical analyses were performed using R v2.13 software (the R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

We reviewed records of 3,166 cases in our comprehensive kidney stone center metabolic database. A total of 125 patients with hypocitraturia and low urinary pH met the criteria and were included in the study. Patient characteristics and baseline metabolic evaluation are shown in detail in the supplementary table (http://jurology.com/). Median patient age was 61 (52–68) years, 80 (64%) were male and median BMI was 30.4 kg/m^2 (26.1–35.0). Of note, while in the entire cohort females represented 36% of the patients, among morbidly obese patients this proportion reached 53% (p=0.020). In addition, patients with a higher BMI tended to be younger (p=0.010) and have a lower urinary citrate but higher sodium, oxalate and uric acid levels. However, urinary pH was similar across BMI groups (see supplementary table, http://jurology.com/). Approximately 90% of the cohort was initially treated with 40 mEq daily potassium citrate with no notable differences across BMI groups.

Urinary pH and citrate levels at baseline and during treatment followup are depicted in the figure. Urinary pH increased from 5.4 (5.2–5.5) to 6.0 (5.5–6.6) and urinary potassium increased from 43 mEq per day (32–54) to 65 mEq (45–88) at the first followup after the initiation of potassium citrate treatment (all p <0.001). Similarly, citrate levels increased from 247 mg per day (125–355) to 534 (318–728) at first followup (p <0.001). The table shows the clinical and metabolic parameters at first followup. Median change in pH after potassium citrate treatment was 0.7 (0.2–1.2) in the entire cohort. The pH values and their absolute changes from baseline were lower as BMI increased (p ≤0.001). Similarly, we noted an association