Hyperoxaluria in Kidney Stone Formers Treated With Modern Bariatric Surgery

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Purpose: Nephrolithiasis and renal failure secondary to severe hyperoxaluria were complications of jejunoileal bypass for obesity, leading to the discontinuation of this procedure in the United States in 1980. Bariatric procedures currently in use have not been adequately evaluated for this complication.

Materials and Methods: We compared 24-hour urine chemistry studies of 132 patients with nephrolithiasis who had undergone bariatric surgery with the urine chemistry studies of patients who had undergone jejunoileal bypass, those with routine kidney stones and normal subjects. The primary aim was to determine if hyperoxaluria developed in patients who underwent bariatric surgery and had kidney stones as had been seen with jejunoileal bypass.

Results: Patients who have undergone modern bariatric surgery had an adjusted mean urine oxalate excretion of 83 mg per day compared to 39 mg per day for routine kidney stone formers and 34 mg per day for normal subjects ($p < 0.001$ for both comparisons), but not quite as high as that found in patients treated with jejunoileal bypass (102 mg per day, $p < 0.001$). Urine supersaturation of calcium oxalate, the main driving force for calcium oxalate stone formation, was higher in patients treated with bariatric surgery compared to routine kidney stone formers and normal subjects ($p < 0.001$ for both comparisons).

Conclusions: Hyperoxaluria is the most significant abnormality of urine chemistry studies in patients with kidney stones who have undergone bariatric surgery. Many of these patients have a degree of hyperoxaluria that could lead to kidney failure. Further studies are required to determine the prevalence of this problem in patients who have undergone bariatric surgery.

Key Words: obesity, oxalates, gastric bypass, jejunoileal bypass, urinary calculi

Obesity is a major public health problem in the United States. Data from the National Health and Nutrition Examination Survey have shown BMI in the United States continues to increase and, in particular, extreme obesity (BMI greater than 40) has increased by 80% from 1988 to 1994, to 1999 to 2000.[1] People with morbid obesity have a marked increase risk of type II diabetes, hypertension, sleep apnea, hyperlipidemia, cardiovascular disease and osteoarthritis.[2] The risk of death also increases significantly when BMI is greater than 35.[3] Diet restrictions and exercise programs can lead to weight loss but the results are seldom sustained, with re-accumulation of the lost weight being the norm.[4] Due to the lack of effectiveness of diet and exercise programs in producing sustained significant weight loss, gastrointestinal surgical interventions have become increasingly popular as a means to lose weight. The number of bariatric procedures performed in the United States increased 5-fold from 1998 to 2002.[5]

Jejunoileal bypass was the first commonly used surgical procedure used to treat obesity. Over time complications of JI bypass became apparent including liver failure, arthritis, kidney stones and renal failure.[6] Severe hyperoxaluria from over-absorption of dietary oxalate was the cause of the nephrolithiasis and renal failure.[7,8] Due to the high rate of serious side effects the Food and Drug Administration placed a moratorium on the procedure in 1979. Approximately 25,000 JI bypasses were performed before the Food and Drug Administration ban, many of which required surgical reversal to stave off irreversible damage such as liver and renal failure.[8]

Newer surgical techniques have replaced JI bypass for treatment of obesity. Restrictive procedures such as gastric banding limit the amount of food a person may eat at any given time by reducing the size of the gastric reservoir.[9] Other procedures combine some level of gastric resection with bypass of variable amounts of small intestine, such as Roux-en-Y gastric bypass and biliopancreatic diversions.[10,11] Although there have been reports on the long-term complications of these procedures such as cholelithiasis and vitamin deficiencies,[12,13] little attention has been focused on potential renal complications of these procedures. Here we report markedly increased urine oxalate excretion in patients with kidney stones who have undergone modern bariatric surgery.

Submitted for publication February 22, 2006.

Supported by Grants R44DK059086 and PO1DK56788 from the National Institutes of Health.

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† Financial interest and/or other relationship with Litholink Corp.

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DOI:10.1016/j.juro.2006.09.033

MATERIALS AND METHODS

Data for the analysis were obtained from Litholink Corp. and the University of Chicago Kidney Stone Clinic. Litholink is a clinical laboratory specializing in the measurement of urine chemistry studies for patients with kidney stones. As part of the disease management program, a medical history is obtained from patients during a telephone interview with a patient care representative. Patients are specifically asked if they have had weight reduction surgery and if they have, was the surgery JI bypass or a modern procedure such as gastric banding or gastric bypass. For the purposes of this analysis we did not attempt to separate the various bariatric procedures currently in use. The date of bariatric surgery and the date of the first stone event were also recorded. Data were queried from the Litholink database and stripped of patient identifiers. The institutional review board (Western Institutional Review Board, Olympia, Washington) classified the protocol as exempt.

As contrast to the urine chemistry studies of patients who have undergone bariatric surgery, urine chemistry study data for patients who have undergone JI bypass, routine stone formers and normal nonstone formers were obtained from the University of Chicago Kidney Stone Clinic. Routine stone formers were defined as all patients with kidney stones without history of intestinal resection or inflammatory bowel disease, hyperparathyroidism or cystinuria. The results of patients who underwent JI bypass have been published previously.[14] University of Chicago data for routine stone formers were used in preference to those of Litholink since all subjects were directly interviewed by one of the authors and we can be assured that no subjects with enteric hyperoxaluria from bowel disease or bariatric surgery would be included in the group. Data from all categories of stone formers included only urine samples collected before the start of active treatment to prevent stones. If a subject had multiple urine collections performed for initial evaluation, the results were averaged so each subject is represented only once in the analysis.

The Litholink laboratory and the University of Chicago Kidney Stone Laboratory are replicates of each other. All assays are performed in the same manner and the laboratories share urine samples 3 times per year to ensure that the results from the laboratories are comparable. Urine pH was measured using a pH electrode. Oxalate and citrate were measured enzymatically using oxalate oxidase and citrate lyase, respectively. Calcium, magnesium, uric acid, creatinine, phosphorous, sodium, potassium and ammonium were measured using a Beckman autoanalyzer (Beckman Instruments, Brea, California). Urine supersaturation of calcium oxalate was calculated using the iterative computer program, Equil II.[15]

Univariate analysis was performed comparing modern bariatric surgery to JI bypass, routine stone formers and normal subjects. Comparisons were not made among all the groups because the question being addressed in this study was related to stone risk factors in patients who have undergone bariatric surgery. Oxalate excretion and SS CaOx were not normally distributed as assessed by the Kolmogorov-Smirnov test, so the nonparametric Kruskal-Wallis test was used in preference to t tests for all comparisons.

For the multivariate analysis general linear models were constructed for the principle variables of interest including urine oxalate excretion, SS CaOx, urine calcium excretion, urine volume, urine pH and urine citrate excretion. Gender and body weight were included in all models. There was no interaction of gender and patient type in multivariate models so the genders were not separated in the general linear models. For oxalate, calcium, and citrate excretions and urine volume we included urine creatinine excretion to adjust for lean body mass and completeness of collection. For SS CaOx and urine pH only gender was included in the model. In all instances we used the model to compare the 4 groups using post hoc pairwise analysis with Scheffe correction. In the single case of urine calcium concentration we limited our comparison to a simple test between bariatric and JI bypass. All data are presented as mean ± SEM.

RESULTS

Patients

A total of 132 patients (104 females, 28 males) were identified in the Litholink database as having undergone modern bariatric surgery. Subjects who had identified themselves as having undergone JI bypass or bariatric surgery before 1980 were excluded from analysis. The average time from bariatric surgery to initial stone event was 3.6 ± 5.4 years. Only 1 subject had kidney stones which predated the bariatric surgery. There were 27 patients who underwent JI bypass (10 females, 17 males), 2,048 routine stone formers (718 females, 1,330 males) and 168 normal subjects (72 females, 96 males) in the analysis.

Univariate Analysis

The various patient groups had significantly different gender composition ($p < 0.001$ for all groups compared to bariatric surgery) so all comparisons were made across the groups but within the same gender (see table). The most significant difference in the measured stone risk factors was in oxalate excretion. Patients treated with bariatric surgery had oxalate excretions that were 2 to 3 times higher compared to stone formers and normal subjects of the same gender, and were not significantly different than those found in patients who had undergone JI bypass (fig. 1). SS CaOx was higher in female patients treated with bariatric surgery than in the female stone formers and normal subjects, and the same trend was present for men but the difference did not reach statistical significance. Calcium excretion was lower in the bariatric group than male and female stone formers but not different than JI bypass or normal groups (fig. 2). Urine pH was also lower in bariatric cases than stone formers and normal subjects, although urine citrate was reduced only in the female bariatric cases. Neither urine volume nor creatinine differed among the groups.

Multivariate Analysis

Compared to normal and stone forming subjects oxalate excretion is significantly increased in patients treated with modern bariatric surgery (adjusted mean values 83 ± 2 vs 39 ± 0.4 and 34 ± 1 mg per day, bariatric, stone formers, normals, respectively, $p < 0.001$, both comparisons, fig. 1). Patients treated with JI bypass as a group have higher urine oxalate excretion than those treated with bariatric surgery