Urinary citrate wasting among nephrolithiasis patients associates with obesity and diabetes mellitus

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Introduction

- Metabolic syndrome including obesity, insulin resistance and diabetes increase the risk of stone disease
- Urinary citrate is thought to decrease calcium stone formation through direct inhibition of crystallization and complexing with calcium
- 24 hour urine is recommended in high risk or recurrent stone formers
- A subset of stone patients excrete very high amounts of citrate with unclear clinical implications

Objective

- Our primary objective was to identify demographic, clinical and 24H urine parameters that were associated with citrate wasting.

Methods

- All patients 1st 24-hour urine testing performed at our institution were included.
- Citrate wasting was defined as >1500mg/day of urinary citrate
- Excluded any patients on alkali therapy for a final cohort of n = 55 citrate wasters who were matched 1:3 by age and sex to other stone formers for a final cohort of n = 165
- Demographic, clinical and laboratory data were obtained using an automated data extraction tool
- Data were analyzed with chi-square for categorical variables and students' t-test for continuous variables.

Results

Table 1. Clinical and demographic characteristics of the study cohort

	Control % (n = 165)	Citrate waster % (n = 55)	p-value
Age (mean ± SD)	53.4 ± 11.6	53.2 ± 11.6	0.914
BMI (mean ± SD)	29.9 ± 7.9	35.0 ± 7.3	<0.001
Gender			
Male	67.3 (111)	67.3 (37)	
Female	32.7 (54)	32.7 (18)	
Race			
White	91.8 (15)	94.5 (52)	0.502
Non-white	8.2 (13)	5.5 (3)	
Past medical history			
Inflammatory bowel disease or Diarrhea	5.5 (9)	9.1 (5)	0.339
Hypertension	5.8 (92)	67.3 (37)	0.133
Gout	6.1 (10)	5.5 (3)	0.869
Type 2 diabetes mellitus	20.6 (34)	61.8 (34)	<0.001
Osteoporosis/immobility /hyperparathyroidism	5.5 (9)	7.3 (4)	0.62
Coronary artery disease / myocardial infarction	14.5 (24)	14.5 (8)	1.0
Cerebrovascular accident	2.4 (4)	5.5 (3)	0.267
Hyperlipidemia	61 (37.0)	22 (40.0)	0.688
Gastroesophageal reflux disease	37.0 (61)	34.5 (19)	0.746
Epilepsy/migraine	4.2 (7)	0 (0)	0.121
Medication			
Allopurinol	3.0 (5)	5.5 (3)	0.406
Hydrochlorothiazide	7.3 (12)	1.8 (1)	0.137
Stone comp			0.237
Calcium oxalate monohydrate	58.3 (73)	70.0 (28)	
Calcium oxalate dihydrate	10.6 (13)	7.5 (3)	
Brushite	0.8 (1)	0 (0)	
Struvite	0.8 (1)	0 (0)	
Hydroxyapatite	19.5 (24)	5.0 (2)	
Uric Acid	6.5 (8)	15.0 (6)	
Other	2.4 (3)	2.5 (1)	

- Citrate wasters had significantly higher mean BMI and a higher prevalence of diabetics
- Uric acid stones were more commonly among citrate wasters
- On 24-hour urine analysis, the citrate wasting group showed higher urine values of calcium, oxalate, uric acid, and sodium
- Notably, urine pH showed no difference between groups (pH 6.1, p = 0.592)

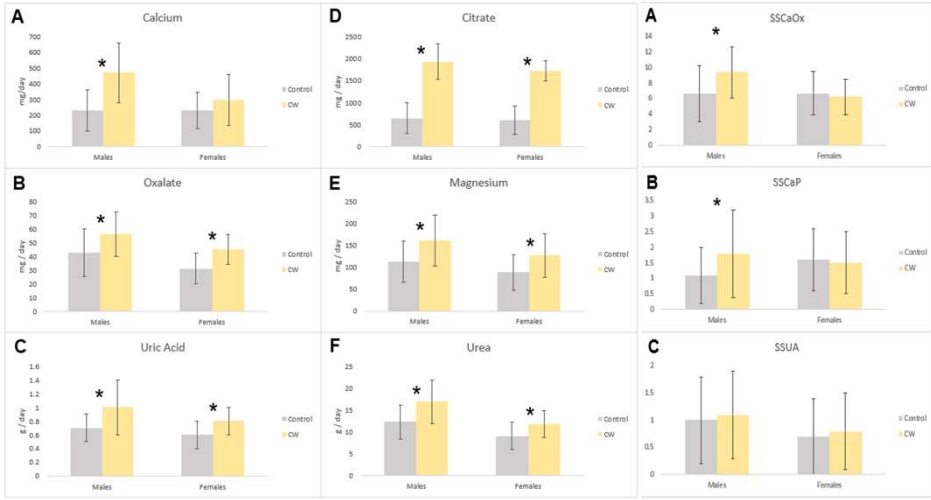

Figure 1. Comparison of mean urinary A) calcium B) oxalate C) uric acid D) citrate E) magnesium and E) urea of citrate wasters and controls by sex.
* denotes significant difference

- Supersaturation of CaOx and CaP were higher in the citrate wasting group for males only

Figure 2. Supersaturation of A) calcium oxalate B) calcium phosphate and C) uric acid in citrate wasters versus controls stratified by sex.
* denotes statistically significant difference

Conclusions

- Nephrolithiasis patients who excrete > 1500mg of urinary citrate per day are more likely to be obese and diabetic, with generally worse urinary analytes overall relating to stone recurrence risk.
- The finding of similar pH but higher uric acid stone prevalence warrants additional study.
- Further investigation is needed on the etiologic and clinical implications of these findings.

References

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