JOURNAL OF ENDOUROLOGY
Volume 23, Number 3, March 2009

Pp. 347–350
DOI: 10.1089/end.2008.0225

Clinical Science: Second Prize

Effect of Soda Consumption on Urinary Stone Risk Parameters

Corey M. Passman, M.D.,[1] Ross P. Holmes, Ph.D.,[1] John Knight, Ph.D.,[2] Linda Easter, R.D.,[3] Vernon Pais Jr, M.D.,[1] and Dean G. Assimos, M.D.[1]

Abstract

Background and Purpose: Fluid consumption has been demonstrated to influence kidney stone formation. Studies have shown that consumption of cola may be a risk factor for stone disease, while fluids containing citric acid may attenuate stone activity. Diet was not always controlled in these investigations, however. We undertook a study to determine the impact of three different fluids on urinary stone risk factors.
Subjects and Methods: Six healthy nonstone-forming adults were placed on a standardized metabolic diet and consumed three different types of fluid during three 5-day periods. There was a 2-day washout between each sequence. The three fluids administered during these periods were Le Bleu® water, caffeine-free Diet Coke,® and Fresca® (citrate containing). These two soda preparations were chosen to prevent the known increase in calcium excretion promoted by carbohydrates and caffeine. Twenty-four hour urine specimens were collected on days 4 and 5 of each sequence. The following urinary parameters were measured: Volume, calcium, oxalate, creatinine, uric acid, citrate, sodium, magnesium, phosphorus, sulfate, urea nitrogen, pH, and supersaturation indices. A paired *t* test was used for statistical analysis.
Results: Urinary volumes were significantly higher and supersaturation of calcium oxalate significantly lower compared with a self-selected dietary regimen. A decrease in uric acid was also seen in the Fresca cohort. There were no statistically significant differences for any of the urinary parameters.
Conclusion: There is no increased risk or benefit to consuming Fresca or caffeine-free Diet Coke compared with Le Bleu bottled water with respect to stone formation.

Introduction

The prevalence of kidney stones in the United States is increasing and is 4.1% among adult women and 6.3% for adult men.[1] In addition, recurrence will occur within 10 years of an initial event in approximately 50% of stone formers.[2] This certainly impacts the quality of life of those afflicted and promotes economic stress on the health care system of the United States, where it is estimated that 2 billion dollars are spent annually on the diagnosis and treatment of these patients.[1] Therefore, effective measures to prevent stone formation benefit patients as well as the health care system.

Dietary measures to prevent kidney stones have been shown to be effective. Borghi and colleagues[3] demonstrated that increased fluid consumption decreased the risk of stone recurrence in first-time calcium oxalate stone formers. Increased fluid consumption has also been shown to decrease the risk of incipient stone formation in 3 large epidemiologic cohorts.[4,5]

There is some debate as to which fluid is the optimal one to consume for stone prevention.[6,7] The administration of citrate-containing fluids has been recommended by a number of investigators. Wabner and Pak[8] reported that the intake of 1.2 L of orange juice daily had the same beneficial effects as the consumption of 60 mEq of potassium citrate, including an

[1]Division of Urology, Department of Surgery, and [2]General Clinical Research Center, Wake Forest University Baptist Medical Center, Winston Salem, North Carolina.
[3]Division of Urology, Department of Surgery, University of Kentucky, Lexington, Kentucky.

increased citrate excretion. Others have recommended consumption of lemonade to augment citrate excretion. Seltzer and colleagues[9] administered 2 L of lemonade daily to hypocitraturic stone formers and reported a 143% increase in citrate excretion. Kang and associates[10] and Penniston and colleagues[11] performed similar studies and reported 110% and 142 % increases in citrate excretion. In contrast, Koff and colleagues[12] and Odvina[13] reported that lemonade consumption did not significantly increase citrate excretion. The latter investigator, however, did report a significant increase in citrate excretion with orange juice intake.

Pais[14] demonstrated in a small cohort of healthy adult subjects that Fresca® consumption increased citrate excretion a mean of 40%. These persons were consuming self-selected diets. This sugar- and caffeine-free beverage contains potassium citrate and citric acid. It theoretically has the advantage of containing these substances and is devoid of caffeine, which increases calcium excretion, and high-fructose corn syrup present in other soda beverages. Fructose consumption is a risk factor for stone formation, which is attributed to increased oxalate, calcium, and uric acid excretion, and the promotion of insulin resistance.[15–21]

We performed a study to determine whether the consumption of Fresca augments citrate excretion and to test whether responses were different with the use of Le Bleu® bottled water or caffeine/sugar-free cola as fluid sources. The use of a cola preparation was selected because there is some evidence that such beverages increase stone activity. This study was conducted with the subjects receiving a standardized metabolic diet administered by our General Clinical Research Center (GCRC). This approach was only undertaken in two of the aforementioned studies and is considered the "gold standard" method of assessing metabolic responses to dietary intervention.

Subjects and Methods

After obtaining Institutional Review Board approval, six nonstone-forming healthy adult (two men and four women) volunteers consented to participate in the study. The mean age of the subjects was 28.8 years (range 27–32 years). The mean body mass index was 22 (range 18.4–26.9). The subjects collected two 24-hour urine specimens while consuming a self-selected diet.

Each person was then placed on a standardized metabolic diet prepared in a GCRC kitchen. The subjects were given one of three drinks (caffeine-free Diet Coke,® Fresca or Le Bleu bottled water) to consume solely over a 5-day period. All subjects drank each of the liquids separated by a 2-day washout period, the order of which was randomly assigned to the subjects at the beginning of the study. Liquid volumes were based on the volunteers' lean body weight.

The calcium content was targeted at 1000 mg/2500 kcal; sodium, 3.5 g/2500 kcal; and oxalate content, 150 mg/2500 kcal. This oxalate content is within the reported range of normal oxalate intake.[22] Diets were adjusted to within 5% of these amounts and with a ratio of calcium to oxalate in each meal >5:1. Each diet contained 15% to 16% protein, 29% to 30% fat, and 54% to 55% carbohydrate. Two 24-hour urine specimens were collected on days 4 and 5 of each study fluid. All subjects completed all arms of the study.

Table 1. Citric Acid, Oxalate, Cation, and Anion Content of Study Beverages, Mean (Standard Deviation)

	Caffeine-free Diet Coke®	*Fresca®*	*Le Bleu® Water*
Oxalate (mg/L)	<1	<1	0
Citrate (mg/L)	150 (10)	2330 (270)	0
Phosphate (mg/L)	276 (12)	<1	<10
Chloride (mg/L)	46 (3)	73 (16)	<0.1
Sodium (mg/L)	40.6 (2.1)	33 (12.6)	20.9 (3.8)
Magnesium (mg/L)	3.1 (0.6)	2.8 (0.7)	0
Potassium (mg/L)	66.5 (7)	290 (14)	0
Calcium (mg/L)	24.6 (0.1)	11.8 (3.4)	0

Twenty-four–hour urine samples were analyzed for volume, calcium, oxalate, creatinine, uric acid, citrate, sodium, magnesium, phosphorus, sulfate, pH, and urea nitrogen. All of the assays except pH were performed using a Beckman analyzer as described previously.[23] The pH was measured using an electrochemical pH meter. Oxalate was measured using an oxalate oxidase technique.[23] The citric acid, oxalate, phosphate, chloride, potassium, sodium, magnesium, and calcium contents of the beverages were measured using ion chromatography as described previously.[24] Supersaturation indices for calcium phosphate and calcium oxalate were calculated using the method of Tiselius.[25]

Statistical analysis was performed using a paired t test. P values of greater than 0.05 were considered statistically significant. Both the self-selected diet and water diet were used as separate controls in the statistical analysis.

Results

All six subjects completed all arms of the study. Table 1 demonstrates the anion, cation, and citric acid contents of the three tested beverages. Table 2 shows the mean urinary parameters for both the self-selected diet and the three different study drinks. There was a statistically significant increase in the volume of urine produced while the subjects were on the controlled metabolic diets ($P = 0.009$). Uric acid was significantly less during Fresca consumption compared with the self-selected diet phase ($P = 0.006$). Supersaturation indices for calcium oxalate showed a significant decrease when comparing Le Bleu bottled water, caffeine-free Diet Coke, and Fresca with the self-selected control group ($P < 0.05$). There was no change for the supersaturation of calcium phosphate.

Discussion

Our results demonstrated that there were no differences in urinary stone risk parameters between the three fluid regimens. There were significant increases, however, in urinary volume and reductions in the calcium oxalate saturation indices on all three regimens relative to those collected during the self-selected diet. These were most likely because of dietary control and increased fluid consumption during all three regimens.

An increase in citrate excretion did not occur with the consumption of Fresca. This could be because of the citric acid content of this beverage, which we measured to be 2.33 g/L, an amount that is similar to several lemonade preparations but

Table 2. 24-Hour Urine Results, Mean (Standard Deviation) Broken Down by Drink Regimens*

	Self-selected	*Water*	*Cola*	*Fresca®*
Volume (mL)[a]	1679.1 (817.6)	2314 (481.9)	2595.8 (188.8)	2500 (358.6)
Sodium (mmol/d)	167.1 (93.9)	97.7 (40.5)	102.3 (39.7)	108.2 (40.8)
Potassium (mmol/d)	73.6 (30.5)	61.9 (19.0)	63.5 (15.6)	63.2 (14.0)
Calcium (mg/d)	143.3 (65.2)	133.7 (60.4)	143.9 (70.0)	137.5 (72.1)
Magnesium (mg/d)	73.5 (34.8)	82.3 (16.5)	91.3 (19.0)	92.4 (13.6)
Creatinine (mg/d)	1540.1 (682.1)	1383.2 (422.5)	1488.1 (437.2)	1417.2 (403.4)
Citrate (mg/d)	617.6 (271.5)	608.2 (305.8)	620.2 (356.9)	630.9 (325.3)
Phosphate (mg/d)	831.6 (458.0)	1005.6 (179.9)	1049.5 (244.5)	1029.5 (309.9)
Uric acid (mg/d)[b]	641.8 (217.7)	543.4 (164.5)	519.5 (239.5)	516.8 (202.7)
Urea nitrogen (mg/d)	10605.4 (4144)	11336.6 (2525.5)	11415 (2849.5)	11184.5 (3192.9)
Oxalate (mg/d)	30.9 (10.9)	25.6 (7.2)	26.2 (7.5)	24.4 (6.2)
pH	6.11 (0.39)	5.92 (0.26)	5.83 (0.25)	6.06 (0.39)
AP(CaOx)[c]	0.807 (0.305)	0.448 (0.225)	0.427 (0.240)	0.390 (0.221)
AP (CaP)	0.958 (1.68)	0.280 (0.354)	0.198 (0.274	0.463 (0.606)

*Tiselius indices for calcium oxalate (AP[CaOx]) and calcium phosphate (AP[CaP]) are also provided.
[a]Significant increase in the urinary volumes when comparing self-selected diets with the three treatment protocols ($P = 0.0009$).
[b]Significant decrease in uric acid excretion when comparing Fresca ingestion with the self-selected diet ($P = 0.006$).
[c]Significant decrease in supersaturation index of calcium oxalate during Le Bleu® bottled water, caffeine-free Diet Coke,® and Fresca regimens compared with self-selected diet ($P < 0.05$).

much lower than lemon, lime, grapefruit, or orange juice.[25] The form of citrate present in the beverages could also have been influential. The assay used did not discriminate between citric acid and potassium citrate; the latter form is thought to augment citrate excretion while the other does not.[13] This is hypothesized to be because of the hydrogen proton present in citric acid negating the benefits of citrate.[13] Potassium citrate, which has a different accompanying cation, provides an alkali load whereas citric acid does not because of the hydrogen cation. Alkali load enhances urinary citrate excretion by reducing renal tubular reabsorption and metabolism of citrate. Other organic acids found in fluids, in the presence of potassium, may produce a similar response, however.

Hönow and associates[26] placed subjects on a metabolic diet and assessed the impact of consumption of three different fluids (grapefruit juice, apple juice, and orange juice) on urinary parameters. Urine citrate increased and the supersaturation of calcium oxalate decreased from baseline to a similar degree on all three regimens. The potassium content of all three beverages was similar, while the citrate content of grapefruit and orange juice was robust compared with a negligible amount in apple juice. It is feasible that other organic acids present in apple juice combined with an adequate amount of potassium to produce an alkali load similar to that of the other juices.

The lack of deleterious changes in stone risk factors with consumption of caffeine-free Diet Coke is consistent with the epidemiologic findings of Curhan and colleagues.[4,6,7] They reported that the intake of sugar- and caffeine-free cola reduced stone risk compared with caffeine- and sugar-containing cola, which increased stone risk. Rodgers reported that consumption of the latter promoted unfavorable changes in urinary stone risk parameters, including increased oxalate excretion, a lowering of urine pH, and an increase in the relative supersaturation indices.[27] Weiss and coworkers[28] reported that such cola consumption reduced magnesium and citrate excretion and increased oxalate excretion.

One of the proposed mechanisms for increased oxalate excretion is that cola has a high oxalate content.[29] We demonstrated, however, using more contemporary and accurate techniques, that the oxalate content of the cola beverage used in this study was low. The latter findings may be because of increased calcium excretion promoted by sucrose, fructose, and caffeine consumption.[15–17,30] In addition, as previously stated, fructose consumption is reported to increase oxalate and uric acid excretion as well as promote insulin resistance.[18–21,31–33] The latter is associated with a reduction in urinary pH and increased risk of uric acid stone formation.[34–36]

A limitation of this study is that these responses were not assessed in stone-forming subjects. It is possible that such subjects could have a different response.

Conclusion

This study demonstrates that Fresca does not augment citrate excretion while having no other deleterious effects on stone risk parameters. Similar results were found with caffeine-free Diet Coke and water. This study also demonstrates the importance of controlling other dietary factors in such studies.

Disclosure Statement

No competing financial interests exist.

References

1. Pearle MS, Calhoun E, Curhan GC. Urolithiasis. In: Litwin MS, Saigal CS, eds. Urologic Diseases in America. Washington, DC: NIDDK, 2007, p 283–319.
2. Ljunghall S, Danielson BG. A prospective study of renal stone recurrences. Br J Urol 1984;56:122–124.
3. Borghi L, Meschi T, Amato F, Briganti A, Novarini A, Giannini A. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: A 5-year randomized prospective study. J Urol 1996;155:839–843.

4. Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med 1993;328: 833–838.
5. Taylor EN, Stampfer MJ, Curhan GC. Dietary factors and the risk of incident kidney stones in men: New insights after 14 years of follow-up. J Am Soc Nephrol 2004;15:3225–3232.
6. Curhan GC, Willett WC, Rimm EB, Spiegelman D, Stampfer MJ. Prospective study of beverage use and the risk of kidney stones. Am J Epidemiol 1996;143:240–247.
7. Curhan GC, Willett WC, Speizer FE, Stampfer MJ. Beverage use and risk for kidney stones in women. Ann Intern Med 1998;128:534–540.
8. Wabner CL, Pak CY. Effect of orange juice consumption on urinary stone risk factors. J Urol 1993;149:1405–1408.
9. Seltzer MA, Low RK, McDonald M, Shami GS, Stoller ML. Dietary manipulation with lemonade to treat hypocitraturic calcium nephrolithiasis. J Urol 1996;156:907–909.
10. Kang DE, Sur RL, Haleblian GE, Fitzsimons NJ, Borawski KM, Preminger GM. Long-term lemonade based dietary manipulation in patients with hypocitraturic nephrolithiasis. J Urol 2007;177:1358–1362.
11. Penniston KL, Steele TH, Nakada SY. Lemonade therapy increases urinary citrate and urine volumes in patients with recurrent calcium oxalate stone formation. Urology 2007;70: 856–860.
12. Koff SG, Paquette EL, Cullen J, Gancarczyk KK, Tucciarone PR, Schenkman NS. Comparison between lemonade and potassium citrate and impact on urine pH and 24-hour urine parameters in patients with kidney stone formation. Urology 2007;69:1013–1016.
13. Odvina CV. Comparative value of orange juice versus lemonade in reducing stone-forming risk. Clin J Am Soc Nephrol 2006;1:1269–1274.
14. Pais VJ. The effects of Fresca consumption on urinary citrate excretion. In: New England Section of the American Urological Association. 2001.
15. Milne DB, Nielsen FH. The interaction between dietary fructose and magnesium adversely affects macromineral homeostasis in men. J Am Coll Nutr 2000;19:31–37.
16. Koh ET, Min KW. Fructose precipitates calcium phosphate in the kidneys of female rats fed magnesium-deficient diets. Magnes Res 1991;4:171–176.
17. Koh ET, Reiser S, Fields M. Dietary fructose as compared to glucose and starch increases the calcium content of kidney of magnesium-deficient rats. J Nutr 1989;119:1173–1178.
18. Holmes RP, Assimos DG. Glyoxylate synthesis, and its modulation and influence on oxalate synthesis. J Urol 1998;160:1617–1624.
19. Daly M. Sugars, insulin sensitivity, and the postprandial state. Am J Clin Nutr 2003;78:865S–872S.
20. Thorburn AW, Storlien LH, Jenkins AB, Khouri S, Kraegen EW. Fructose-induced *in vivo* insulin resistance and elevated plasma triglyceride levels in rats. Am J Clin Nutr 1989;49: 1155–1163.
21. Nguyen NU, Dumoulin G, Henriet MT, Regnard J. Increase in urinary calcium and oxalate after fructose infusion. Horm Metab Res 1995;27:155–158.
22. Holmes RP, Kennedy M. Estimation of the oxalate content of foods and daily oxalate intake. Kidney Int 2000;57:1662–1667.
23. Holmes RP, Goodman HO, Hart LJ, Assimos DG. Relationship of protein intake to urinary oxalate and glycolate excretion. Kidney Int 1993;44:366–372.
24. Penniston KL, Nakada SY, Holmes RP, Assimos DG. Quantitative assessment of citric acid in lemon juice, lime juice, and commercially-available fruit juice products. J Endourol 2008;22:567–570.
25. Tiselius HG. Aspects on estimation of the risk of calcium oxalate crystallization in urine. Urol Int 1991;47:255–259.
26. Hönow R, Laube N, Schneider A, Kessler T, Hesse A. Influence of grapefruit-, orange- and apple-juice consumption on urinary variables and risk of crystallization. Br J Nutr 2003;90:295–300.
27. Rodgers A. Effect of cola consumption on urinary biochemical and physicochemical risk factors associated with calcium oxalate urolithiasis. Urol Res 1999;27:77–81.
28. Weiss GH, Sluss PM, Linke CA. Changes in urinary magnesium, citrate, and oxalate levels due to cola consumption. Urology 1992;39:331–333.
29. Smith LH, Van Den Berg CJ, Wilson DM. Nutrition and urolithiasis. N Engl J Med 1978;298:87–89.
30. Massey LK, Sutton RA. Acute caffeine effects on urine composition and calcium kidney stone risk in calcium stone formers. J Urol 2004;172:555–558.
31. Rofe AM, James HM, Bais R, Conyers RS. Hepatic oxalate production: The role of hydroxypyruvate. Biochem Med Metab Biol 1986;36:141–150.
32. Rofe AM, James HM, Bais R, Edwards JB, Conyers RA. The production of (14C) oxalate during the metabolism of (14C) carbohydrates in isolated rat hepatocytes. Aust J Exp Biol Med Sci 1980;58:103–116.
33. Fox IH, Kelley WN. Studies on the mechanism of fructose-induced hyperuricemia in man. Metabolism 1972;21:713–721.
34. Maalouf NM, Cameron MA, Moe OW, Sakhaee K. Novel insights into the pathogenesis of uric acid nephrolithiasis. Curr Opin Nephrol Hypertens 2004;13:181–189.
35. Maalouf NM, Cameron MA, Moe OW, Adams-Huet B, Sakhaee K. Low urine pH: A novel feature of the metabolic syndrome. Clin J Am Soc Nephrol 2007;2:883–888.
36. Sakhaee K, Maalouf NM. Metabolic syndrome and uric acid nephrolithiasis. Semin Nephrol 2008;28:174–180.

Address reprint requests to:
Corey Passman, M.D.
Department of Urology
Wake Forest University Baptist Medical Center
Medical Center Blvd.
Winston Salem, NC 27157

E-mail: cpassman@wfubmc.edu

Abbreviation Used

GCRC = General Clinical Research Center