Urol Res (1999) 27:77–81

ORIGINAL PAPER

Allen Rodgers

Effect of cola consumption on urinary biochemical and physicochemical risk factors associated with calcium oxalate urolithiasis

Received: 2 January 1998 / Accepted: 9 July 1998

Abstract Since stone formers are advised to increase their intake of fluid, the present study was undertaken to determine the effect of cola beverage consumption on calcium oxalate kidney stone risk factors. Fourteen males and 31 females provided 24-h urines before and after an acute load of cola. Relative supersaturations, activity products and empirical risk indices, ratios and quotients were calculated from urinary biochemical data to assess calcium oxalate crystal and stone formation risk. Several risk factors changed unfavourably following consumption of cola. In males, oxalate excretion, the Tiselius risk index and modified activity product increased significantly ($P < 0.05$). In females, oxalate excretion increased significantly while magnesium excretion and pH decreased significantly ($P < 0.05$). Scanning electron microscopy showed that urines obtained from both sexes after cola consumption supported calcium oxalate crystallization to a greater extent than the control urines. It is concluded that consumption of cola causes unfavourable changes in the risk factors associated with calcium oxalate stone formation and that therefore patients should possibly avoid this soft drink in their efforts to increase their fluid intake.

Key words Kidney stones · Risk factors · Fluid intake · Cola · Calcium oxalate urolithiasis

Introduction

Calcium oxalate kidney stone patients are frequently advised to increase their daily intake of fluid [2, 9, 10, 18]. Indeed, this is the only dietary modification that may be applied in all forms of urolithiasis [10]. However, while several fluids have been found to be suitable and beneficial – e.g. apple juice [18], herbal teas [2], mineral water [2, 12] – care should be exercised to avoid fluids which contain lithogenic agents and which may consequently increase the risk of stone formation. Among these are coffee, tea and alcohol [18]. A recent study has suggested that cola should be added to this list, as consumption of this soft drink resulted in magnesium and citrate excretions being decreased and oxalate excretion being increased [19]. However, this study had serious shortcomings as it was limited to only four subjects, one of whom failed to consume the required daily volume of cola while another subject had a prior history of stones. The present study was undertaken to overcome these shortcomings by extending its scope to include the investigation of multiple biochemical and physicochemical risk factors in a large group of subjects from both sexes.

A. Rodgers
Department of Chemistry, University of Cape Town,
Cape Town, South Africa 7701

Materials and methods

Subjects and urine collections

Fourteen healthy males and 31 healthy females with no prior history of urinary calculi participated in the study. All were in the age group of 20–26 years. Each subject was required to provide a 24-h urine collection under normal dietary conditions. The urine was collected in a 2.5 litre glass bottle which had been thoroughly washed with 5 M hydrochloric acid and rinsed with distilled water. No preservative was present. During the collection period, the bottle and contents were refrigerated. Thereafter, subjects were required to drink 2.0 litres of a regular carbonated cola beverage over a 24-h period during which urine was collected as described above. The consumption was effected without any change to their normal diet.

Urinalysis

Urines were tested for the presence of blood and infection (Combur 10 test strip, Boehringer Mannheim). Samples in which haematuria was detected or which were found to be nitrite positive were discarded. Thereafter, volume and pH were recorded. Urines were analysed for Na, K, Ca and Mg using a Varian 1275 Model (Australia) flame atomic absorption spectrometer. Oxalate was

determined using oxalate decarboxylase. For these analyses an ascorbate oxidase spatula was used to remove L-ascorbic acid. Citrate was determined by citrate lyase conversions to oxaloacetate. Inorganic phosphorus was determined using ammonium molybdate; creatinine was determined using picric acid and uric acid was determined using uricase. Analytical kits manufactured by Boehringer Mannheim were used for these determinations.

Metastable limit determination

Aliquots (30 ml) of each urine were pipetted into each of 10 polyethylene bottles. Successive bottles were dosed with 0.3 ml of standard aqueous sodium oxalate (NaOx) of increasing concentrations (range 0.10–1.30 mM) and incubated at 38°C for 30 min during which time they were shaken. The turbidity of the solution in each bottle was then measured using an AQUALYTIC AL 1000 turbidimeter (wavelength: 860 nm). Plots of turbidity vs sodium oxalate concentration were constructed. The calcium oxalate metastable limit (MSL) was taken as the NaOx concentration which induced a sudden increase in the turbidity (corresponding to the initiation of calcium oxalate crystallization).

Scanning electron microscopy (SEM)

Each pair of urines (pre-cola and post-cola) was innoculated with the same dose of NaOx at a concentration which was 10% in excess of the MSL of the former. Each urine was then filtered through a Nucleopore filter (0.2 μm, diameter: 13 mm) supported in a Sartorius membrane and filter clamp (Göttingen). The filter paper, with deposited crystals, was pasted onto an aluminium stub and was then coated with approximately 20 nm of Au/Pd in a Polaron 5100 Sputter Coater. Specimens, tilted at 35° to the collector, were examined in a Cambridge S200 scanning electron microscope operating at a nominal beam potential of 10 kV and beam current of 100 μA. Semi-quantitative estimates of particle number, sizes and aggregation were made by visual inspection and comparison of fields at approximately the same magnification.

Calculation of risk quotients

Relative supersaturation values of calcium oxalate, calcium phosphate (brushite) and uric acid were computed using the program EQUIL [20]. In addition, the empirically derived Tiselius risk index [16] and modified activity product [17] were also calculated.

Statistical method

Data were statistically treated by analysis of variance.

Results

Several urinary biochemical (Table 1) and physicochemical (Table 2) risk factors and indices were altered following the acute consumption of cola.

Table 1 Mean urinary biochemical risk factors before and after cola consumption

Biochemical risk factor	Males				Females			
	Pre-cola	Post-cola	*P*	Change	Pre-cola	Post-cola	*P*	Change
Oxalate	0.22 (0.02)	0.28 (0.02)	0.05	−	0.19 (0.01)	0.25 (0.01)	0.002	−
Magnesium	3.32 (0.47)	3.53 (0.45)	0.75		3.77 (0.31)	2.92 (0.31)	0.06	−
Phosphate	30.81 (2.25)	33.40 (2.25)	0.41		20.82 (1.51)	26.21 (1.51)	0.01	−
Calcium	4.07 (0.47)	4.01 (0.47)	0.93		2.56 (0.32)	2.26 (0.32)	0.51	
Citrate	1.99 (0.40)	2.28 (0.42)	0.62		3.14 (0.27)	2.50 (0.27)	0.10	
Uric acid	3.38 (0.21)	3.52 (0.21)	0.63		2.57 (0.14)	2.49 (0.14)	0.70	
Sodium	129.3 (15.7)	121.3 (15.7)	0.72		144.9 (10.5)	99.9 (10.5)	0.003	
Potassium	55.2 (4.4)	46.5 (4.6)	0.18		46.0 (2.9)	36.7 (2.9)	0.009	
Creatinine	14.9 (0.7)	15.0 (0.7)	0.99		9.5 (0.4)	9.9 (0.4)	0.51	
Vol (ml)	1316 (170)	1848 (170)	0.03	+	2119 (114)	2039 (114)	0.62	
pH	6.06 (0.13)	5.84 (0.13)	0.22		6.26 (0.08)	5.75 (0.09)	0.0001	−

+ Favourable change, i.e. risk of stone formation decreases; − unfavourable change, i.e. risk of stone formation increases
Excretion rates: mmol/24 h

Table 2 Mean urinary physicochemical risk factors before and after cola consumption

Physicochemical risk factor	Males				Females			
	Pre-cola	Post-cola	*P*	Change	Pre-cola	Post-cola	*P*	Change
Tiselius risk index	215 (43)	348 (43)	0.03	−	227 (30)	292 (30)	0.13	
Tiselius modified activity product	1.07 (0.13)	1.48 (0.14)	0.03	−	0.64 (0.09)	0.84 (0.09)	0.12	
Brushite relative supersaturation	1.12 (0.14)	0.68 (0.12)	0.02	+	0.33 (0.08)	0.29 (0.08)	0.70	
Uric acid relative supersaturation	1.99 (0.36)	2.04 (0.35)	0.93		0.80 (0.24)	1.81 (0.23)	0.003	−
MSL	0.75 (0.16)	0.66 (0.16)	0.67		1.22 (0.11)	1.18 (0.11)	0.82	
CaOx relative supersaturation	4.00 (0.45)	3.68 (0.45)	0.61		1.53 (0.30)	1.79 (0.31)	0.54	

+ Favourable change, i.e. risk of stone formation decreases; − unfavourable change, i.e. risk of stone formation increases
MSL metastable limit

In the SEM studies, comparisons were made of relative crystal numbers, sizes and aggregation in the pre- and post-cola urines after each had been dosed with the same concentration of aqueous sodium oxalate. An increase in any of these was interpreted as demonstrating an increase in stone-forming potential. A summary of these results is given in Table 3. In general the number and size of calcium oxalate dihydrate (COD) and trihydrate (COT) crystals were greater in the post-cola urines (Figs. 1–4). In addition, while small aggregates of COD occurred in the pre-cola specimens (Figs. 5 and 6), considerably larger agglomerates were frequently noted in the post-cola samples (Fig. 7). Another feature commonly observed in the post-cola urines was the co-existence (Fig. 8) and intergrowth (Fig. 9) of COD and COT crystals.

Discussion

The tables show that in males, consumption of cola induced unfavourable changes in three important risk factors. First, oxalate excretion is widely regarded as being one of the most crucial determinants of calcium oxalate urolithiasis [1]; thus an increase in this variable is of critical significance. Second, since the Tiselius risk index [16] and the Tiselius modified activity product [17] both take into account the synergistic effects of Ca, Mg, oxalate and citrate, an increase in its value is also a powerful indicator of stone risk.

Two factors changed favourably in males. These were urinary volume (Table 1) and the relative supersaturation of brushite (Table 2). As far as the latter is concerned, brushite has been mooted as the nidus of calcium oxalate calculi [8]; hence lowering of its supersaturation may have a bearing on decreasing the risk of forming stones of this type. Similarly, an increased urinary volume is an indicator of reduced risk [11]. However, despite these effects, the three unfavourable changes mentioned earlier are more likely to have a greater influence on the overall risk.

In females, five risk factors were unfavourably altered as a result of cola consumption. Of these, oxalate excretion, which has already been commented upon, was the only factor that changed in both sexes; all other changes occurred uniquely in either males or females. Of the other unfavourable changes, low magnesium levels have been associated with increased calcium oxalate crystalluria and stone formation [14], while the increase in the relative supersaturation of uric acid and the raised phosphate excretion are noteworthy as there is much empirical evidence suggesting a link between calcium oxalate urolithiasis and urate on the one hand [13] and phosphate on the other [7]. The decrease in pH represents an increased risk of stone formation [3] because inhibition of calcium oxalate crystal growth decreases with decreasing pH even though calcium oxalate solubility increases at lower pH values [15].

Table 3 Summary of changes in the degree of crystallization following cola consumption: SEM observations

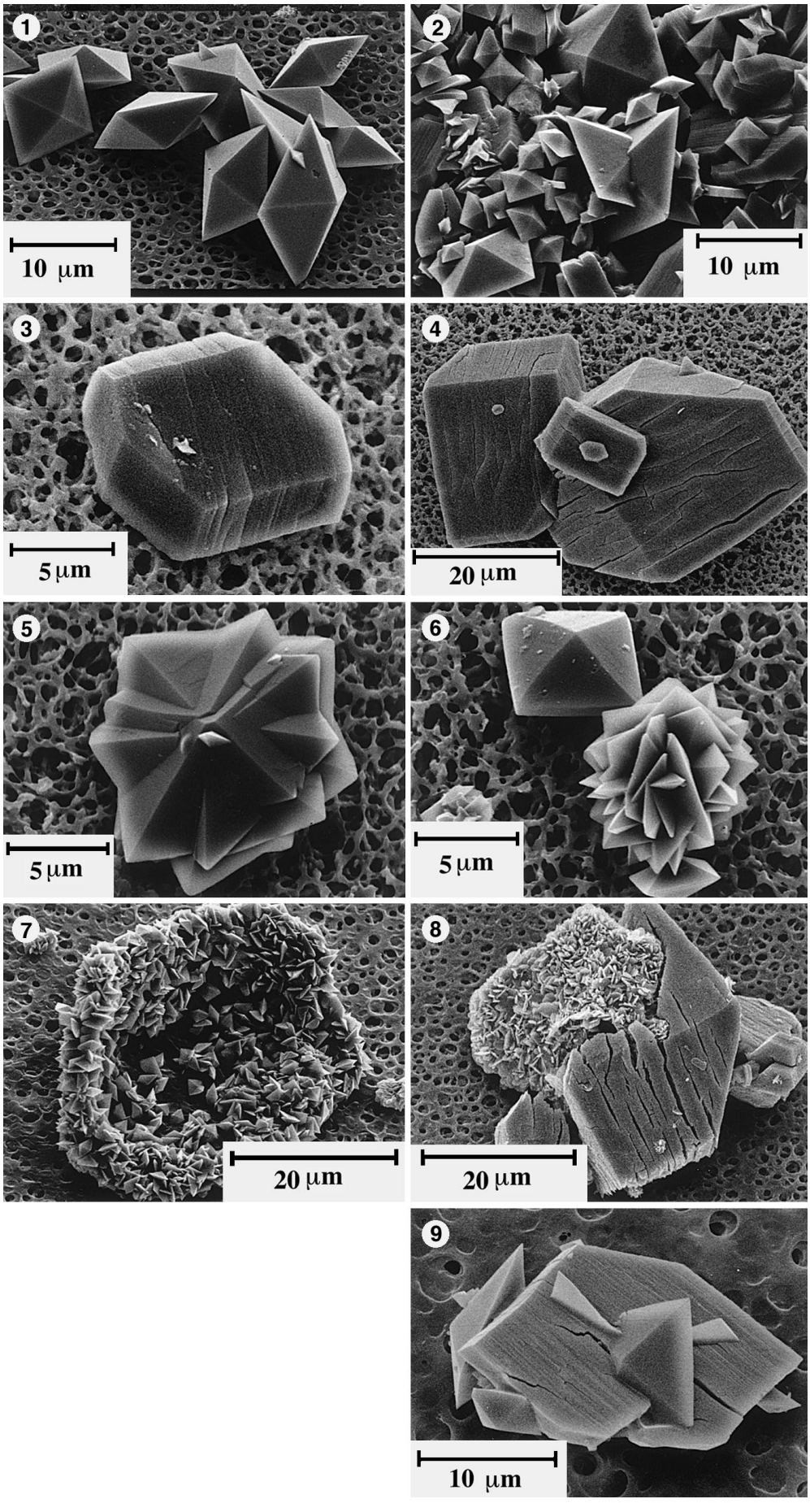
Degree of crystallization	Number of males	Number of females
Increased	5 (35.7%)	16 (51.6%)
Decreased	3 (21.4%)	5 (16.1%)
No change	6 (42.9%)	10 (32.3%)

It is of interest to speculate as to which components of cola might be giving rise to the altered urinary risk factors, in particular the hyperoxaluria. An obvious candidate is sucrose. However, although sucrose has been reported as increasing calcium and oxalate excretions [4], two recent studies have shown that oxaluria increases after an oral glucose load and decreases after fructose ingestion [5] but that no change occurs after sucrose ingestion [6]. Thus, the chemical structure of the sugar in cola would appear to have an influence on the level of oxaluria which it might induce. The important point, however, is that irrespective of its composition, consumption of this beverage has been shown in the present study to cause hyperoxaluria.

It might also be argued that the altered urine chemistry arises simply as a result of the increased fluid intake. In a previous study on the effects of mineral and tap water ingestion, the latter did indeed induce a decrease in brushite relative supersaturation and an increase in urinary volume in males but had no effect on oxalate excretion or the Tiselius risk index [12]. Thus, although the favourable changes in males can be attributed to the raised fluid intake, the unfavourable changes cannot be similarly explained and must therefore be due to the ingestion of cola per se. In females, oxalate excretion *decreased* after tap water ingestion [12], unlike the increase observed after cola consumption in the present study, indicating that the latter is the culprit. On the other hand magnesium excretion decreased in both studies suggesting that the raised fluid intake is the causal factor in this instance. The other changes observed after cola consumption did not occur after tap water consumption [12] and can therefore be attributed to the former.

The different response patterns of males and females to the cola load may be due to the latter group altering their normal diets (despite our instructions not to do so) to compensate for the increased calorie intake associated with the cola protocol. Such non-compliance might also explain the decreases in sodium and potassium excretion, observed in the post-cola urines of this group.

Notwithstanding the urine analysis, SEM was performed on each specimen thereby permitting a qualitative and semi-quantitative assessment to be made of their potential to support calcium oxalate crystallization. While it is recognized that crystal features observed using this technique may be dependent on pre-treatment procedures involved in their isolation, and that such observations are merely empirical as opposed to providing real proof of any effect, we nevertheless believe


1
10 μm
2
10 μm
3
5 μm
4
20 μm
5
5 μm
6
5 μm
7
20 μm
8
20 μm
9
10 μm

◀

Fig. 1 Calcium oxalate dihydrate (COD) crystals observed in the pre-cola urine of a male subject (×3620)

Fig. 2 COD and calcium oxalate trihydrate (COT) crystals observed in the post-cola urine of the same subject as in Fig. 1. Note the heavier deposition of crystals in Fig. 2 (×3500)

Fig. 3 Single COT crystal observed in the pre-cola urine of a female subject (cross-section ~ 8μm; ×4200)

Fig. 4 COT crystals observed in the post-cola urine of the same subject as Fig. 3. Note the larger size of two of the crystals relative to the one in Fig. 3 (cross-section ~15 μm; ×3800)

Fig. 5 Aggregate of intergrown COD crystals observed in the pre-cola urine of a male subject (cross-section ~ 10μm; ×3950)

Fig. 6 Single and aggregated COD crystals observed in the pre-cola urine of the same subject as in Fig. 5 (cross-section of aggregate ~ 5μm; ×3800)

Fig. 7 Large aggregate of COD crystals observed in the post-cola urine of the same subject as in Figs. 5 and 6 (cross-section of aggregate ~ 23μm; ×2450)

Fig. 8 Co-existence of a COD aggregate and a COT crystal observed in the post-cola urine of a female subject (×2600)

Fig. 9 Intergrowth of a COD and a COT crystal observed in the post-cola urine of a female subject (×3350)

that our SEM data provide compelling evidence in support of our biochemical and physicochemical data.

Thus the present study has shown that consumption of cola unfavourably altered several key biochemical and physicochemical kidney stone risk factors in the urine of male and female subjects. Despite the fact that these changes occurred within the normal ranges, the subtle shifts in their values tended towards creating a milieu more conducive to stone formation. As such, we believe that urolithiasis patients should be made aware of this and should possibly be advised to avoid consumption of large volumes of this soft drink when implementing the universal kidney stone strategy of increasing their fluid intake.

Acknowledgements The author wishes to thank the South African Medical Research Council, the South African Foundation for Research and Development and the University of Cape Town (Research Committee and Cooper Lowveld Bequest) for the award of research funds.

References

1. Borsati A (1991) Calcium oxalate nephrolithiasis: defective oxalate transport. Kidney Int 39: 1283
2. Hesse A, Siener R, Heynick H, Jahnen A (1993) The influence of dietary factors on the risk of urinary stone formation. Scanning Microsc Int 7: 1119
3. Hesse A, Tiselius HG, Jahnen A (1997) Urinary stones diagnosis, treatment and prevention of recurrence. Karger, Basel, p 45
4. Lemann J, Piering WR, Lennon EJ (1969) Possible role of carbohydrate-induced calciuria in calcium oxalate kidney stone formation. N Engl J Med 280: 232
5. Nguyen NU, Damoulin G, Wolf JP, Berthelay S (1989) Urinary calcium and oxalate excretion during oral fructose or glucose load in man. Horm Metab Res 21: 96
6. Nguyen NU, Henriet MT, Damoulin G, Widmer A, Regnard J (1994) Increase in calciura and oxaluria after a single chocolate bar load. Horm Metab Res 26: 383
7. Ohman S, Larsson L, Tiselius HG (1992) Clinical significance of phosphate in calcium oxalate renal stones. Ann Clin Biochem 29: 59
8. Pak CYC, Chu S (1973) A simple technique for the determination of urinary state of saturation with respect to brushite. Invest Urol 11: 211
9. Pak CYC, Sakhaee K, Crowther C, Brinkley L (1980) Evidence justifying a high fluid intake in treatment of nephrolithiasis. Ann Int Med 93: 36
10. Pak CYC, Smith LH, Resnick MI, Weinerth JL (1984) Dietary management of idiopathic calcium urolithiasis. J Urol 131: 850
11. Robertson WG, Peacock M (1983) Review of risk factors in calcium oxalate urolithiasis. World J Urol 1: 114
12. Rodgers A (1997) Effect of mineral water containing calcium and magnesium on calcium oxalate urolithiasis risk factors. Urol Int 58: 93
13. Ryall RL, Marshall VR (1990) The investigation and management of idiopathic urolithiasis. In: Wickham JEA, Buck AC (eds) Renal tract stone metabolic basis and clinical practice. Churchill Livingstone, Edinburgh, pp 307–331
14. Scott R (1990) The role of trace metals in renal stone disease. In: Wickham JEA, Buck AC (eds) Renal tract stone metabolic basis and clinical practice. Churchill Livingstone, Edinburgh, pp 103–113
15. Tiselius HG (1981) The effect of pH on the urinary inhibition of calcium oxalate crystal growth. Br J Urol 53: 470
16. Tiselius HG (1982) An improved method for the routine biochemical evaluation of patients with recurrent calcium oxalate stone disease. Clin Chim Acta 122: 409
17. Tiselius HG (1991) Aspects on estimation of the risk of calcium oxalate crystallization in urine. Urol Int 47: 255
18. Vahlensieck W (1986) Review: The importance of diet in urinary stones. Urol Res 14: 283
19. Weiss GH, Sluss PM, Linki CA (1992) Changes in urinary magnesium, citrate and oxalate levels due to cola consumption. Urology 39: 331
20. Werness PG, Brown CM, Smith LH, Finlayson B (1985) EQUIL 2: a basic computer programme for the calculation of urinary saturation. J Urol 134: 1242