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ORIGINAL PAPER

Effects of vitamin E ingestion on plasma and urinary risk factors for calcium oxalate urolithiasis in two population groups having different stone-risk profiles: evidence of different physiological handling mechanisms

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Abstract It has been demonstrated that vitamin E supplementation reduces calciuria and oxaluria and that it may also prevent oxalate-mediated peroxidative injury, all of which reduce the risk of calcium oxalate urolithiasis. In view of the significant difference in stone occurrence in black (B) and white (W) South Africans, we undertook to investigate the effects of vitamin E supplementation in subjects from these two groups. Five healthy males from each group ingested one capsule (400 IU) of vitamin E daily for 60 days. Blood and 24 h urine samples were collected at baseline and on day 60; 24 h dietary questionnaires were simultaneously completed. Urine composition was determined by routine analyses. Urinary and plasma TBARS were determined using a commercially available assay kit while plasma vitamin E was determined by reverse phase HPLC. Plasma vitamin E increased significantly in W but not in B. Urinary and plasma TBARS did not increase in either group. Urinary citrate increased significantly in both groups but the percentage increase in W (169%) was greater than that in B (82%). No other urinary parameter changed significantly. The increase in plasma vitamin E in W but not in B suggests either that the mechanism by which it is packaged into chylomicrons, which are secreted into the systemic circulation, is suppressed in the latter group or that it is differentially absorbed in the two groups. Similarly, to explain the greater increase in citraturia in W compared to B, we speculate that inhibition of lipogenesis of arachidonic acid by vitamin E, ultimately leading to an increase in citraturia, occurs to a lesser extent in B than in W.

Keywords Vitamin E · Lipid peroxidation · Plasma risk factors · Urinary risk factors · Calcium oxalate urolithiasis

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Introduction

The reasons for the anomaly in the incidence of urolithiasis in South Africa's black and white populations (<1 and ~15%, respectively) are unknown in spite of previous physicochemical and biochemical investigations [1, 2]. Since hyperoxaluria is a major risk factor for calcium oxalate (CaOx) urolithiasis, investigation of factors, which affect this condition and how they might differ in the two population groups, are of interest. One such factor is the relationship between stone formation, hyperoxaluria and cellular degradation products derived from renal tubular injury [3]. The latter may be due to the production of free radicals in patients with CaOx stones [4, 5].

Cellular injury can be caused by several mechanisms, one of which is lipid peroxidation (LPO), a process in which tissue is damaged by superoxide, hydroxyl radicals or hydrogen peroxide. Exposure of renal cells to oxalate itself can also induce peroxidative injury. LPO products such as thiobarbituric acid reactive substances (TBARS), malondialdehyde (MDA) and antioxidant enzymes can be measured in urine and blood as biomarkers of cellular injury [6, 7]. Urinary *N*-acetyl-β-glucosaminidase (NAG), a tubular enzyme found primarily in the proximal tubular cells of the kidney, can also be measured and it is one of the enzymatic biomarkers for renal tubular injury [6–8].

It is well recognized that cells contain several antioxidant agents including ascorbic acid, vitamin E and thiols

which provide protection against oxidative damage [3, 9, 10]. Indeed, it has been suggested that supplementation with anti-oxidants such as vitamin E, may prevent oxalate-mediated peroxidative injury and reduce free radical damage, and hence may prevent CaOx nucleation and retention in the renal tubules [3, 11, 12]. Thus, vitamin E might be essential to protect molecules and biological systems from oxidative damage [12].

In studies involving hypertensive and hyperoxaluric patients [13] and urogenital tuberculosis patients [14], supplementation with vitamin E decreased concentration of LPO products and enhanced the antioxidant status of plasma, thereby preventing membrane injury and consequently the risk of stone formation. Supplementation also restored the biochemical and kinetic properties of urinary Tamm–Horsfall glycoprotein, a well-known inhibitor of CaOx crystallization. Previous studies have also shown that CaOx stone formers have elevated plasma TBARS [11, 15] and NAG [6] levels. In the latter study, it was shown that NAG in stone formers was positively and significantly correlated with their urinary oxalate and calcium. Moreover, it has been shown that administration of vitamin E reduced urinary excretion of oxalate and calcium in kidney stone patients [11]. All of these parameters are therefore useful indicators of stone risk.

In previous studies, subjects from South Africa's black and white population groups have responded differently to different supplemental challenges [16–18]. As such, an investigation of their relative responses to an anti-oxidant is warranted. The present study was therefore undertaken to measure the levels of LPO biomarkers and other risk factors for CaOx stone formation in subjects from the two ethnic groups, and to investigate the effects of vitamin E ingestion on these parameters, with a view to gaining new insights, which might explain the differences in stone forming propensities between the two population groups.

Materials and methods

Subjects

Healthy South African black ($n = 5$) and white ($n = 5$) males (aged 18–30 years) were recruited from the student cohort of the University of Cape Town. The study was approved by the research and ethics committee of the university. All of the subjects signed informed consent documents prior to participation. Studies were performed in accordance with the ethical standards as originally laid down in the 1964 Declaration of Helsinki and updated in October 2001. The number of subjects corresponds to that investigated in similar studies [19–21]. In the present study, the subjects were matched for age and body mass index (BMI). Subjects were excluded if they were taking any medication or supplements, which might affect vitamin E metabolism (such as warfarin, dalteparin sodium, enoxaparin sodium), if they had high blood pressure and/or diabetes or if they had a family history of kidney stone disease.

Study design

Subjects were instructed to ingest one vitamin E capsule (DL-α-tocopheryl acetate, 400 IU) [Vitalfarm (Pty) Ltd, Cape Town, South Africa] per day immediately after their evening meal for 60 days [14, 20, 22]. We selected this dosage as previous studies using similar levels have detected effects on plasma and urinary risk factors [11, 14, 22, 23]. The duration of the trial was based on two previous scientific studies that investigated the effect of vitamin E (200 mg, 298 IU) on renal stone risk factors in urogenital tuberculosis patients [14, 22]. Alpha tocopherol was selected for this study (as opposed to other analogues of vitamin E) because it has been reported as having the highest biological and antioxidant activity [24]. Nevertheless, we recognized that since the product used in our study was a racemic mixture, only about 50% of the administered amount would be bioavailable.

Following an overnight fast (12 h), venous blood samples (5 ml) were collected in EDTA tubes from each subject at baseline (day 0) and on day 60. 24 h urine samples were collected on the same days. Subjects were instructed to continue taking their free and unrestricted regular diet for the duration of the study so that their habitual intake of macronutrients was maintained throughout the study period [25]. 24 h dietary food records were collected on the days on which blood and urine samples were drawn.

Analytical methods

Dietary intake was assessed using the FoodFinder 2 computer software programme [26]. 24 h urine samples were tested for haematuria and nitrite using urinalysis test strips (Medi Test Combi 5 N, Macherey–Nagel, Düren). All urines tested negative. Urine pH (pH 211 microprocessor pH meter, Hanna Instruments, Cape Town, South Africa) and volume were routinely measured. 24 h urine composition values for calcium, oxalate, citrate, magnesium, sodium, potassium, urate, phosphate and creatinine values were determined as previously described [27].

Blood samples were stored in the dark and on ice until they were processed within 1 h of collection. They were centrifuged at 3,000 rpm for 10 min [21, 28] using a Labofuge 200 centrifuge (Heraeus Sepatech, Germany). It has been recommended that at least one of the biomarkers (TBARS, MDA or isoprostanes) be determined when

evaluating oxidative stress in humans and its association with disease [29]. Plasma vitamin E has been used as an additional measure [14, 22]. In the present study, we determined urinary and plasma TBARS (MDA equivalents) using a spectrophotometric method (Spectronic Unicam Helios, Cambridge, England) based on a commercially available assay kit (OXI-TEK TBARS assay kit, Zeptometrix, Buffalo, New York), while plasma vitamin E was measured using reverse phase HPLC [30].

Statistical methods

Data were statistically analysed using repeated measures ANOVA (STATISTICA version 8.0) and were considered statistically significant if $p \leq 0.05$.

Results

Dietary analysis

Mean nutrient intakes were the same on day 0 and day 60 (Table 1). Intergroup comparisons at baseline showed that moisture, energy, total protein, calcium and magnesium were significantly lower in blacks than in whites, while oxalate was significantly higher in the former group. All of these differences were maintained at day 60 except that of oxalate ($p = 0.064$).

Plasma vitamin E

There were no intergroup differences in mean plasma α-tocopherol levels at baseline ($p = 0.272$) or on day 60 ($p = 0.1153$) (Fig. 1). With-in group levels increased significantly in white subjects (from 10.22 ± 0.77 to 20.72 ± 4.13 mg/l, $p = 0.0047$) after vitamin E supplementation. An increase was also observed in black subjects (from 9.48 ± 1.09 to 15.14 ± 1.83 mg/l) but it did not achieve significance ($p = 0.0689$).

Urinary and plasma TBARS

Urinary TBARS excretions (mmol/24 h) and concentrations (mmol/24 h/L) are given in Table 2 while plasma TBARS levels (nmol/ml) are shown in Fig. 2. There were no statistically significant within-group or inter-group differences for any of these parameters at baseline or on day 60.

Table 1 Mean dietary intakes (SE) of black and white subjects before and after vitamin E ingestion

Nutrients	Black (B)		*p* values	White (W)		*p* values	B versus W, *p* values	
	Baseline	Day 60		Baseline	Day 60		Baseline	Day 60
BMI (kg/m^2)	25.30 (0.83)	n/a	n/a	25.81 (1.11)	n/a	n/a	0.7263	n/a
Energy (kJ)	8,720 (847)	8,922 (839)	0.7360	13,815 (2,133)	14,133 (1,589)	0.5970	0.0364*	0.0332*
Moisture (g/day)	1,870 (347)	1,729 (435)	0.3150	3,287 (432)	3,303 (501)	0.9072	0.0476*	0.0317*
Total protein (g/day)	86 (4.2)	87 (7.2)	0.8190	121 (6.5)	116 (5.0)	0.2630	0.0018*	0.0057*
Total fat (g/day)	104 (19)	103 (19)	0.7659	111 (9.6)	109 (11)	0.6598	0.7828	0.7975
Carbohydrate (g/day)	325 (26)	311 (23)	0.5141	339 (23)	350 (19)	0.6074	0.6858	0.2601
Fibre (g/day)	25.10 (2.98)	22.62 (2.89)	0.2444	27.00 (3.86)	29.37 (4.90)	0.2635	0.7285	0.2344
Total sugar (g/day)	36.91 (7.93)	38.56 (7.85)	0.4453	60.44 (7.85)	60.75 (8.79)	0.8851	0.0733	0.0880
Oxalate (mg/day)	262 (57)	251 (49)	0.1399	119 (34)	120 (31)	0.7903	0.0492*	0.0646
Calcium (mg/day)	659 (47)	683 (43)	0.6062	1,151 (85)	1,088 (65)	0.1907	0.0002*	0.0001*
Magnesium (mg/day)	274 (16)	280 (15)	0.6236	381 (24)	372 (9.9)	0.4809	0.0001*	0.0030*
Phosphate (mg/day)	1,817 (268)	1,670 (253)	0.1099	1,999 (302)	1,977 (253)	0.7941	0.6453	0.4435
Potassium (mg/day)	2,835 (578)	2,846 (573)	0.8447	3,550 (383)	3,497 (397)	0.3661	0.3342	0.3766
Sodium (mg/day)	2,769 (218)	2,738 (202)	0.6613	3,641 (858)	3,609 (873)	0.6518	0.3565	0.3569
Vitamin A (RE/day)	1,031 (181)	1,050 (165)	0.5381	1,157 (211)	1,140 (226)	0.5870	0.6627	0.7556
Vitamin B6 (mg/day)	2.56 (0.37)	2.44 (0.39)	0.4170	2.83 (0.40)	2.80 (0.30)	0.8650	0.6199	0.4965
Vitamin C (mg/day)	121 (31)	122 (31)	0.7629	105 (13)	103 (12)	0.6286	0.6580	0.5806
Vitamin D (μg/day)	3.32 (1.04)	3.30 (1.04)	0.4740	4.00 (1.15)	4.00 (1.16)	0.9454	0.6733	0.6643
Vitamin E (μg/day)	9.88 (1.38)	8.97 (1.00)	0.3024	11.88 (0.99)	10.92 (0.90)	0.2824	0.2205	0.2296

n/a Not applicable

* Significance at $p \leq 0.05$

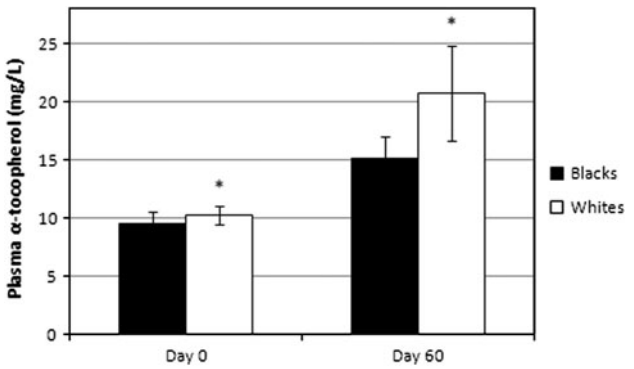

Fig. 1 Mean plasma α-tocopherol in *black* and *white* subjects before and after vitamin E ingestion. *Significance at $p < 0.05$

24 h Urine composition

Intergroup comparisons at baseline revealed that urinary calcium, magnesium and RS CaOx were significantly lower in black subjects (Table 2). All of these differences were maintained at day 60, except that for magnesium ($p = 0.0873$). Following supplementation with vitamin E, urinary citrate increased significantly in both groups. All other urinary variables remained unchanged at day 60.

Discussion

Intergroup comparisons of dietary data at baseline confirmed previously reported differences: moisture, energy, total protein, calcium and magnesium were significantly lower [31], while oxalate was significantly higher [2] in black subjects. Our observation that mean nutrient intakes were the same for both groups on day 0 and day 60 is interpreted as confirming the absence of any confounding dietary factors.

It is well-recognized that vitamin E is a major lipid soluble antioxidant in humans and that it plays an important role in protecting cell membranes [32]. Both endogenous and exogenous components contribute towards the antioxidant defense system. However, exogenous dietary components are insufficient to deliver the amount of antioxidants required to reduce oxidative stress [33]. Therefore, supplementation is necessary. Indeed, it is the most convenient way to acquire large doses of vitamin E [34].

In the present study, plasma vitamin E increased significantly in the white group after a 60-day supplementation period. Elevated levels of this antioxidant are associated with the prevention of membrane injury and consequently, the risk of stone formation [22]. Our observation of a favourable increase in the level of plasma α-tocopherol in the white group is in agreement with previous studies that have shown enhancement of plasma antioxidant status following vitamin E ingestion [14, 22]. There is evidence that vitamin E is transported in plasma lipoproteins and is incorporated into lipid bilayers of biological membranes where it determines oxidative susceptibility [35]. Thus, after its intestinal absorption, it is packaged into chylomicrons, which are secreted into the systematic circulation [36]. Since we did not observe a similar increase in plasma vitamin E in our black subjects, we suggest that the latter process occurs to a lesser extent in this group than in their white counterparts, but large cohorts' studies in both population groups are necessary before any such conclusions can be drawn. It is also plausible that the observed difference in the increase in the plasma level of vitamin E could be a consequence of its differential absorption by subjects from the two ethnic groups who participated in this study.

We also observed that urinary TBARS values did not change in either race group following vitamin E supplementation (400 IU, one capsule per day, 60 days). Although this parameter was investigated by Kosugi and co-workers [37] after administering vitamin E (447 IU, three capsules per day, 50 days), their study involved only four subjects. As such, their findings, in which urinary TBARS decreased in two subjects but remained unchanged in the other two, cannot be cited as being indicative of any trend. On the other hand, in a study by Cadenas and co-workers [23] involving 21 healthy subjects, a 27% decrease was observed in urinary TBARS following vitamin E ingestion (149 IU, one capsule per day, 30 days). Since these studies as well as ours, differ with respect to the number of subjects investigated, their gender, the dosage of vitamin E, duration of the trial and the analytical techniques which were used, comparison of results are not meaningful.

Plasma TBARS values also did not change significantly in either race group following vitamin E ingestion. This is in agreement with a study by Mol and co-workers [38] in which no consistent or significant change was observed following vitamin E ingestion in healthy controls (600 IU, 4 weeks). On the other hand, our result contradicts that of Sakuma and co-workers [39] who observed a significant decrease in plasma TBARS following vitamin E supplementation (300 IU, 4 weeks). As mentioned previously, drawing conclusions based on different observations in these studies is tenuous because of fundamental differences in their respective protocols, particularly with regard to the number of subjects. Clearly, statistical power increases with increases in the latter variable.

Despite the absence of statistical significance in the present study, plasma TBARS tended to be higher in black subjects than in white subjects. Interestingly, higher values for this parameter have been reported in healthy African Americans compared to whites [40]. These observations are counterintuitive in view of the lower stone incidence in

Table 2 Mean urine parameters (SE) from 24 h urines of black and white subjects before and after vitamin E ingestion

Parameter	Black (B)		*p* values	White (W)		*p* values	B versus W, *p* values	
	Baseline	Day 60		Baseline	Day 60		Baseline	Day 60
pH	6.70 (0.27)	6.77 (0.17)	0.5660	6.29 (0.03)	6.35 (0.05)	0.6374	0.1042	0.0957
Volume (ml/24 h)	1,588 (148)	1,719 (122)	0.2084	1,453 (93)	1,596 (112)	0.1736	0.4449	0.4854
Citrate (mmol/24 h)	2.71 (0.52)	4.94 (0.43)	0.0017*	1.96 (0.23)	5.27 (0.65)	0.0001*	0.2905	0.6369
Oxalate (mmol/24 h)	0.21 (0.02)	0.24 (0.02)	0.5608	0.23 (0.03)	0.28 (0.03)	0.2431	0.6384	0.2394
Calcium (mmol/24 h)	2.22 (0.43)	2.72 (0.28)	0.2506	4.43 (0.76)	4.56 (0.60)	0.7432	0.0170*	0.0386*
Magnesium (mmol/24 h)	2.02 (0.13)	2.01 (0.12)	0.9738	3.11 (0.57)	2.99 (0.48)	0.8030	0.0609	0.0873
Sodium (mmol/24 h)	222.2 (43)	273.16 (32)	0.2256	208.52 (74)	213.86 (48)	0.8940	0.8548	0.4342
Potassium (mmol/24 h)	47.56 (7.1)	58.10 (10)	0.1617	55.06 (21)	68.76 (19)	0.0800	0.7406	0.6391
Urate (mmol/24 h)	2.68 (0.49)	3.32 (0.41)	0.2098	4.08 (0.73)	4.28 (0.54)	0.6813	0.1015	0.2464
Creatinine (mmol/24 h)	14.64 (1.40)	15.08 (1.20)	0.4869	16.90 (1.27)	17.08 (1.08)	0.7732	0.2306	0.2845
Phosphate (mmol/24 h)	20.98 (6.01)	27.88 (3.55)	0.3802	31.16 (4.48)	38.80 (5.19)	0.3338	0.1609	0.1344
u-TBARS (mmol/24 h)	0.1128 (0.010)	0.1185 (0.011)	0.3350	0.1291 (0.011)	0.1320 (0.009)	0.6157	0.2145	0.3730
u-TBARS (mmol/24 h/L)	0.0728 (0.008)	0.0688 (0.004)	0.6266	0.0914 (0.012)	0.0849 (0.009)	0.4282	0.1563	0.2172
RS CaOx (COM)	5.31 (0.64)	5.34 (0.53)	0.9233	6.88 (0.05)	6.76 (0.12)	0.6971	0.0243*	0.0375*
RS brushite	7.16e−9 (1.59e−9)	7.13e−9 (1.27e−9)	0.9669	3.37e−9 (0.16e−9)	3.72e−9 (0.32e−9)	0.6140	0.0270*	0.0422*
RS uric acid	1.60 (1.33)	1.13 (0.81)	0.3462	3.25 (0.22)	2.85 (0.39)	0.4134	0.1814	0.1665
Tiselius risk index	157 (28)	176 (11)	0.7240	227 (60)	236 (21)	0.8613	0.1772	0.2416

* Significance at $p \leq 0.05$

blacks relative to whites both in South Africa [2] and in North America [41]. On the other hand, it is consistent with our finding of an increase in plasma α-tocopherol levels in the white group but not in the black group on day 60, as this biomarker serves as a sensitive indicator of vitamin E status in biological fluids [42].

The results of other prospective, controlled human trials of the effect of vitamin E ingestion on lipid peroxides such as TBARS are inconsistent. While reduction (normalization) of plasma TBARS and/or MDA has been observed in hyperoxaluric kidney stone patients [11] and in healthy subjects [39, 43], as well as reduction of urinary TBARS in healthy subjects [23, 44], similar changes have not been observed in other studies [37, 38, 45].

The most widely used indicator of LPO is TBARS [46] because they have all been implicated in the potential

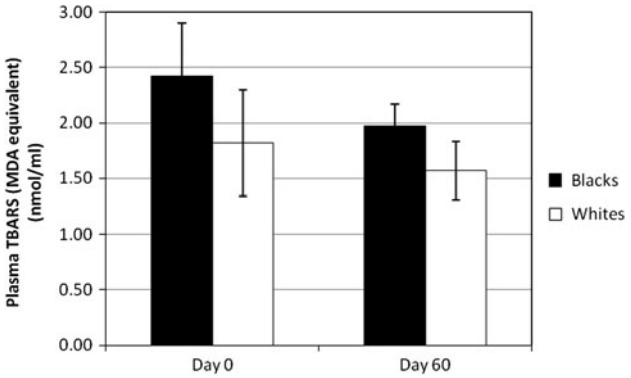

Fig. 2 Mean plasma TBARS in *black* and *white* subjects before and after vitamin E ingestion

pathways linking oxidation to pathologic processes [47]. Nevertheless, it has been recommended that more than one marker be used to provide a better estimate of oxidative stress [48] One such marker could be urinary $F_{2\alpha}$-isoprostanes [43]. These, as well as MDA are two different metabolic end products of oxidative injury. Measuring any one of them will indicate oxidative stress. Quantification of the latter will require HPLC techniques to separate interfering compounds [49, 50].

It is therefore recommended that future studies on the effects of vitamin E ingestion should additionally investigate urinary $F_{2\alpha}$-isoprostanes (prostaglandin-like compounds produced by reactive oxygen species-catalysed peroxidation of arachidonic acid, largely independent of cyclooxygenase activity), as they have been reported as being superior markers of LPO than MDA-TBARS [43].

At baseline, intergroup comparisons of mean 24 h urine composition confirmed previously reported differences: urinary calcium, magnesium and RS CaOx were significantly lower in black subjects [16, 31]. This is consistent with the lower incidence of stone formation in the black population. However, our observation that urinary calcium and oxalate did not change after vitamin E supplementation is in contrast with other studies. A reduction in these parameters has been reported in hyperoxaluric kidney stone patients (298 IU, 90 days) [11] and in urogenital tuberculosis patients (298 IU, 60 days) [14, 22] following ingestion of vitamin E. In another study on the effect of vitamins C and E on biomarkers of oxidative stress, the authors [51] demonstrated that baseline values are important when determining whether decreases per se have occurred or not. They commented that values are only likely to decrease if they are not already low. We suggest that a similar argument can be invoked in the present study to explain our observation of no change in urinary calcium and oxalate after vitamin E ingestion, since our subjects were normo-calciuric and normo-oxaluric.

Notwithstanding that changes in urinary calcium and oxalate did not occur after vitamin E administration in the present study, urinary citrate increased in both race groups. Elevated citrate excretion has been reported in hyperoxaluric kidney stone patients [11] and in urogenital tuberculosis patients [14, 22]. According to Khan [7], urinary citrate is involved in maintaining endogenous antioxidants and indeed citrate is widely regarded as a protective factor with regard to stone formation [52]. Intriguingly, the percentage increase in citrate excretion was higher in whites (169%) than in blacks (82%), suggesting a greater sensitivity in the former group towards vitamin E.

Although the increase in urinary citrate following vitamin E ingestion is in itself notable, and in agreement with previously reported results, it is the significantly greater percentage increase in whites that is of particular interest. The mechanism by which vitamin E ingestion increases citraturia is not obvious. According to Goetzl [53] and Panganamala and Cornwell [54] higher concentrations of vitamin E (α-tocopherol) exert a suppressive effect on both the fatty acid release and lipoxygenation of arachidonic acid. This is consistent with its role as a hydroperoxide scavenger. A hypothetical mechanism has been previously suggested, by which inhibition of lipogenesis decreases cellular consumption of citrate thereby making more plasma citrate available to filter through the glomerulus, ultimately leading to an increase in citraturia [17]. We speculate that the same mechanism might be occurring in the present study and that this effect might be suppressed in the black group compared to their white counterparts. This is consistent with our general view that the two race groups respond differently to different supplemental challenges [16, 27, 31].

Although citraturia increased in both groups, no changes were observed in RS CaOx and the Tiselius risk index (TRI) following vitamin E ingestion in either group. The reason for this apparent anomaly is not obvious. It is probably related to other changes in urine composition values, which were statistically too small to have been detected individually, but which had a collective influence on the RS and TRI values.

Studies have revealed that oxidative damage is more closely related to hyperoxaluria and crystalluria than to tissue crystal deposits and that the process of membrane damage is greatly increased with progressive crystal deposition [12, 55]. As stated earlier, NAG is a lysosomal enzyme found primarily in the proximal tubular cells of the kidney and is one of the most sensitive marker enzymes for renal tubular injury [7, 8]. Previous studies have reported that it is significantly and positively correlated with urinary oxalate [7, 56]. However, since changes in urinary oxalate did not occur in either group in the present study, NAG was not determined.

The present study has demonstrated that vitamin E ingestion elicited different responses in subjects from the

two race groups. This is consistent with several previous studies in which dietary supplements were administered to healthy subjects from the same groups [16–18, 31]. However, the responses observed in the present study are counterintuitive. Firstly, since plasma vitamin E has been associated with a lower risk of stone formation, the absence of intergroup differences in this determinant at baseline is unexpected. It suggests that antioxidant protection from this source probably does not contribute to the rarity of stone disease in the black group. Moreover, we speculate that the absence of a significant increase in this determinant after supplementation with vitamin E for 60 days possibly indicates a sufficiency of other antioxidants in the relatively stone-free black group.

Secondly, as mentioned previously, the tendency towards higher plasma TBARS in blacks than in whites is also puzzling, albeit that differences were not statistically significant. Of interest is whether these differences are clinically significant. We speculate that perhaps TBARS levels in relatively stone-free groups do not arise from the same pathogenic aetiology as in stone-formers and are therefore not clinically significant.

The causes of differential effectiveness of vitamin E in epidemiological, clinical and experimental studies have not been clearly defined [57, 58]. Some authors have speculated that it might be related to variations in the nature and dosage of vitamin E, the duration of the therapy, the stage and nature of various diseases including stone formation amongst participants, the age of patients and their degree of renal insufficiency [43]. We agree with all of these assertions but suggest that the present study has indicated that ethnicity of participants is also a determining factor. Although the influence of gender was not investigated in the present study, it might be of interest to do so in future.

From a clinical point of view, our findings of a favourable and significant increase in the urinary excretion of citrate coupled with an increase of plasma α-tocopherol levels in both groups support the notion of a protective role for vitamin E ingestion in calcium oxalate urolithiasis. As such, clinicians may wish to offer this as a conservative intervention in the management of this disease. However, caution should be exercised, as undesirable side effects have been attributed to prolonged administration of vitamin E in a daily dose greater than 300 mg (447 IU) [59].

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