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DASH Diet and Change in Serum Uric Acid over Time

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Abstract

The Dietary Approaches to Stop Hypertension (DASH) diet lowers serum uric acid (SUA) levels compared to the typical American (control) diet. However, the time required for the DASH diet to take effect is unknown. We analyzed data from a parallel arm, randomized-controlled trial in pre-hypertensive or hypertensive adults (N=103), comparing the effects of DASH or a control diet on SUA measured at 30, 60, and 90 days. Effects were examined overall, and within stratified subgroups based on baseline SUA status (SUA ≥ 6 mg/dL vs <6 mg/dL). The mean age of participants was 51.5 ± 9.7 years, 55% were women, 75% were black, 42% were obese, and 34% had hypertension. Twenty-four of the 103 (23%) participants had a baseline SUA ≥ 6 mg/dL. Overall, compared to the control, DASH lowered SUA by 0.5 mg/dL at 30 and 90 days. Among participants with baseline SUA ≥ 6 mg/dL, DASH lowered SUA by 0.8 and 1.0 mg/dL at 30 and 90 days respectively. These findings demonstrate that the DASH diet reduces SUA within 30 days, with a sustained effect at 90 days, which is informative for healthcare providers counseling patients on time course expectations for uric acid reduction in response to dietary modification.

Gout is a major cause of inflammatory arthritis affecting approximately 8 million US adults [1]. Uric acid is a well-established causal determinant of gout [2]. Several observational studies and randomized control trials have demonstrated associations between dietary patterns and SUA levels [3–7], supporting a potential role for dietary recommendations in adults with gout. A recent report from the Dietary Approaches to Stop Hypertension (DASH)–Sodium randomized trial demonstrated that consuming the DASH diet significantly reduced SUA compared to a typical American diet [8]. However, the duration of adherence to the DASH diet necessary to achieve a lower SUA and whether its effects are maintained over time remain unknown.

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Conflicts of interest

The authors have no conflicts of interest to report.

Using the repeat SUA measures recorded in the DASH-Sodium trial, we examined the effects of the DASH dietary intervention at 30-day intervals over a 90-day period. We hypothesized that the effects of the DASH diet on SUA levels (1) would increase over time and (2) would differ by baseline SUA levels.

Methods

Study Design

In the original DASH-Sodium trial (NCT00000608), adults with pre- or stage 1 hypertension, who were not on hypertensive medications, were recruited to 4 clinical research centers between September 1997 and November 1999. Participants underwent a two-week run-in period where they consumed an isocaloric diet typical of the American diet (control diet), designed to minimize weight gain or loss. They were then randomized using a parallel design to either continue the control diet or start the DASH diet, which is rich in fruits, vegetables, and low-fat dairy foods with reduced intake of saturated and total fat (Supplement Table S1) [9]. Randomization assignment was computer-generated and stratified by site. While consuming either of the two diets, participants were crossed over in random order to each of three different sodium levels: low (60 mmol/d), medium (120 mmol/d), and high (180 mmol/d), each for 4-week periods separated by 5-day breaks. All foods were provided for both diets as prepared and packaged isocaloric meals to maximize compliance. Participants and dietary staff were blinded to the outcomes data, while measurement staff were blinded to the diet assignments. Over 98% of participants completed each of the intervention periods. The primary outcome of the original trial was systolic blood pressure (BP). Additional details regarding the study design have been published [10].

Participants

DASH-Sodium recruited men and women over 22 years of age with a systolic BP between 120 and 159 mmHg and a diastolic BP between 80 and 95 mmHg via targeted and mass mailings, mass media, and community screenings. Exclusions included: prior heart disease, renal insufficiency, poorly controlled dyslipidemia, or diabetes mellitus. Furthermore, participants could not be taking antihypertensive, diabetes, or lipid-lowering medications, nor drinking over 14 alcoholic drinks a week [10, 11]. While medication use was generally rare, participant use of urate-lowering pharmacotherapies was not ascertained.

The ancillary analysis presented here was limited to participants at the Johns Hopkins University clinical center in Baltimore, Maryland. The protocol was approved by the Institutional Review Board at Johns Hopkins University (IRB number:NA_00047061). Written informed consent was provided by all participants.

Serum Uric Acid Measurement

Fasting blood was collected from participants following each feeding period and analyzed by Quest Diagnostics (Madison, New Jersey). SUA levels were measured using spectrophotometry [10]. Non-physiologic SUA levels (defined as a SUA < 1.0 mg/dL) and missing values were excluded from the analyses (2 values excluded).

Statistical Analysis

Analyses were conducted on an intention-to-treat basis. The study population was characterized with means (SD) and proportions. Mean SUA was determined at each visit by dietary assignment, independent of sodium level assignment. Differences in means were assessed via unpaired Student's t-tests. Trends across the 4 study visits were assessed using linear and quadratic regression terms, which were compared via F-statistics. We performed a subgroup analysis stratified by baseline SUA (≥ 6 mg/dL versus <6 mg/dL); ≥ 6 mg/dL was chosen based on the distribution of baseline SUA levels and for consistency with the American College of Rheumatology (ACR) management guidelines for urate lowering therapy [12]. All analyses were performed using Stata v14.0.

Results

The mean age of participants was 51.5 ± 9.7 years, 55% were women, 75% were black, 42% were obese, and 34% had hypertension (Supplement Table S2). Participants, on average, consumed 1.3 g of alcohol per day. The mean SUA level at baseline was 5.0 ± 1.3 mg/dL. Notably, 24 of the 103 (23.3%) participants had a baseline SUA ≥ 6 mg/dL. Participants with high SUA levels were more likely to be male (79.2% vs 34.2%), had a lower average baseline estimated glomerular filtration rate (eGFR) (85.5 mL/min/ 1.73 m² vs 96.1 mL/min/ 1.73 m²), and were proportionately less hypertensive compared to those with a baseline SUA <6 mg/dL, but were comparable on other baseline characteristics (Supplement Table S3).

Overall, compared to control, the difference in SUA from the DASH diet observed at 30 days (-0.5 mg/dL; 95% CI: $-0.9, 0.0$; $P=0.07$) was similar to the difference observed at 90 days (-0.5 mg/dL; 95% CI: $-1.0, 0.0$; $P=0.06$) (Figure 1, Supplement Table S4). There was no trend in the differences observed between dietary assignment over time after the initial reduction in the first 30 days ($P_{trend} = 0.2$). In participants with a baseline SUA ≥ 6 mg/dL, the DASH diet lowered SUA by 0.8 mg/dL (95% CI: $-1.7, 0.2$; $P=0.10$) at 30 days and by 1.02 mg/dL (95% CI: $-2.0, -0.1$; $P=0.03$) at 90 days (Figure 2A, Table 1). This effect was non-linear, with a plateau observed at 60 days (P -value comparing models' fit was 0.05 , suggesting that a quadratic model was better suited to fit the data). By contrast, in participants with a baseline SUA <6 mg/dL, the effect of the DASH diet was minimal and did not change over time after accounting for the initial reduction ($P_{trend} = 0.4$) (Figure 2B, Table 1).

Among trial participants with a baseline SUA ≥ 6 mg/dL, the DASH diet lowered SUA to <6 mg/dL in 7 out of 13 participants (54%) at 30 days, 9 out of 13 participants (69%) at 60 days, and 8 of the 12 (75%) participants at 90 days, suggesting that the majority assigned to the DASH dietary intervention achieved the ACR target at each time interval.

Discussion

This analysis of the DASH-Sodium trial demonstrated that compared to a typical American diet, the DASH diet lowered SUA within 30 days of its initiation; these effects were maintained at 90 days, the trial's conclusion. Furthermore, the reduction in SUA from the DASH diet was greater among participants with a baseline SUA ≥ 6 mg/dL; over half the

participants achieved a SUA <6 mg/dL by 30 days. These findings provide a meaningful timeline for health professionals and patients initiating the DASH diet to lower SUA.

The time course of change in uric acid with dietary interventions has not previously been reported. Prior clinical trials of the effects of diet or supplements on uric acid, namely glycemic index [13], sodium [14], dairy extract [15], or vitamin C [5] have varied in duration from 1 week to 3 months, but do not report interval time points between initiation and conclusion of the intervention. For the first time, we show that most of the SUA lowering effects of the DASH diet in participants with pre- or stage 1 hypertension, overall and within the stratum with baseline SUA $\geq$ 6 mg/dL, occurs within the first 30 days after initiating the dietary intervention and then plateaus at 60 days. This implies that SUA may be reassessed after 30 days of starting the DASH diet.

While the DASH diet lowered SUA by over 1 mg/dL in participants with baseline SUA $\geq$ 6 mg/dL, SUA levels never reached a nadir equivalent to those with a SUA <6mg/dL at baseline (5.6 versus 4.3 mg/dL). This suggests that diet alone, over a 3-month period, does not completely remove baseline differences in SUA. It is possible that other factors (e.g. lower eGFR, higher proportion male) present in this subgroup, may account for elevated SUA levels that cannot be entirely overcome by dietary change. Furthermore, there was minimal impact of the DASH diet on SUA levels in those with SUA <6 mg/dL at baseline, after accounting for the initial reduction.

Our study has limitations. First, there was limited power in this analysis as uric acid was available for only 1 of the 4 original research sites, which contributed to underpowered comparisons between the DASH and control diet at individual time points. Notably, despite the comparable reduction in SUA between measurements conducted at 30 days, 60 days and 90 days, the reduction only achieved statistical significance at the 90-day follow up. Second, our post-hoc subgroup analysis introduces imbalances that undermine the randomized design of the trial, either as disproportionate allocation of specific baseline characteristics or sodium assignment at 30, 60, or 90 days. Third, this was a controlled feeding study where participants were provided with all of their meals throughout the feeding periods, thus ensuring higher adherence to the dietary plan. In a clinical setting where adherence may not be so regulated, the effects may be less pronounced and may take longer to manifest. Lastly, the eligibility criteria excluded a number of comorbidities, such as renal insufficiency, which may also impact generalizability of the DASH diet to populations with chronic kidney disease. Similarly, participants were not characterized in terms of gout status at trial entry.

Despite these limitations, this analysis showed that the DASH diet reduced SUA within 30 days and that this effect was sustained over time. These findings may have important implications for the design of future dietary studies in patients with hyperuricemia or gout as well as for physicians and patients planning to implement dietary approaches for the management of these conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used

SUA	serum uric acid
DASH	Dietary Approaches to Stop Hypertension
CI	confidence interval

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Figure 1. Effect of DASH diet on Uric Acid

(A) Mean serum uric acid levels at baseline, 30 days, 60 days, and 90 days according to assignment to the DASH diet (red) or control diet (black). (B) Differences in mean serum uric acid levels at baseline, 30 days, 60 days, and 90 days. Vertical lines represent 95% confidence intervals. The P -value reflects linear regression of differences (control minus DASH) over visit modeled as a categorical variable.

Figure 2. Effect of DASH diet on uric acid, stratified by baseline uric acid levels

Mean serum uric acid levels at baseline, 30 days, 60 days, and 90 days according to assignment to the DASH diet (red) or control diet (black), stratified by baseline serum uric acid. Results are presented for: (A) participants with a baseline serum uric acid ≥ 6 mg/dL (N=24), or (B) participants with a baseline serum uric acid < 6 mg/dL (N=79). Vertical lines represent 95% confidence intervals.

Mean (95% CI) uric acid levels (mg/dL) and differences in mean uric acid levels (95% CI) by visit according to diet and baseline serum uric acid

Table 1

	Baseline uric acid < 6 mg/dL				Baseline uric acid ≥ 6 mg/dL			
	DASH	Control	Difference	P	DASH	Control	Difference	P
Baseline	6.6 (6.3, 6.9)	6.7 (6.3, 7.1)	-0.1 (-0.5, 0.4)	0.71	4.3 (4.0, 4.6)	4.6 (4.2, 4.9)	-0.3 (-0.7, 0.2)	0.24
30 days	5.9 (5.3, 6.5)	6.7 (5.8, 7.5)	-0.8 (-1.7, 0.2)	0.10	4.4 (4.1, 4.7)	4.9 (4.5, 5.2)	-0.4 (-0.9, 0.0)	0.07
60 days	5.6 (4.8, 6.4)	6.3 (5.5, 7.1)	-0.7 (-1.8, 0.4)	0.17	4.4 (4.1, 4.7)	4.8 (4.5, 5.1)	-0.4 (-0.9, 0.1)	0.09
90 days	5.6 (4.9, 6.3)	6.6 (5.9, 7.3)	-1.0 (-2.0, -0.1)	0.03	4.3 (4.0, 4.6)	4.7 (4.3, 5.0)	-0.4 (-0.9, 0.1)	0.12