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Effects of Lowering Glycemic Index of Dietary Carbohydrate on Plasma Uric Acid: The OmniCarb Randomized Clinical Trial

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Abstract

Objective—The effects of carbohydrates on plasma uric acid levels are controversial. We determined the individual and combined effects of carbohydrate quality (glycemic index, GI) and quantity (proportion of total daily energy, %carb) on uric acid.

Methods—We conducted a randomized, crossover feeding trial in overweight or obese adults without cardiovascular disease (N=163). Participants were fed each of four diets over 5-week periods separated by 2-week washout periods. Body weight was kept constant. The four diets were: high GI (GI ≥ 65) with high %carb (58% kcal), low GI (GI ≤ 45) with low %carb (40% kcal), low GI with high %carb; and high GI with low %carb. Plasma uric acid was measured at baseline and after each feeding period for comparison between the 4 diets.

Results—Study participants were 52% women and 50% non-Hispanic black with a mean age of 52.6 years and a mean uric acid of 4.7 (SD, 1.2) mg/dL. Reducing GI lowered uric acid when the %carb was low (-0.24 mg/dL; $P < 0.001$) or high (-0.17 mg/dL; $P < 0.001$). Reducing the %carb marginally increased uric acid only when GI was high ($P = 0.05$). The combined effect of lowering GI and increasing the %carb was -0.27 mg/dL ($P < 0.001$). This effect was observed even after adjustment for concurrent changes in kidney function, insulin sensitivity, and products of glycolysis.

Conclusions—Reducing GI lowers uric acid. Future studies should examine whether reducing GI can prevent gout onset or flares.

TRIAL REGISTRATION—clinicaltrials.gov, Identifier: NCT00608049

Keywords

carbohydrate; macronutrient; protein; fat; diet; glycemic index; uric acid; gout; trial

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This trial is registered at clinicaltrials.gov, number: NCT00608049.

Conflict of Interest

The authors have no conflicts of interest to report.

Gout is a debilitating form of inflammatory arthritis, caused by the precipitation of uric acid crystals in joints (1). The prevalence of gout is rising in the US, currently estimated to affect over 8 million people in 2007–2010 (2). Pharmacologic therapies to prevent recurrent flares have primarily focused on uric acid reduction (3). However, urate-lowering therapy is not without adverse effects (4). In contrast, dietary interventions may be an attractive alternative to prescription drug therapy, particularly among those with mild gout, a population representing over 3 million adults in the US (5).

Dietary approaches to reduce uric acid include lowering protein intake and consuming low purine foods (6). Evidence for dietary recommendations is largely derived from observational studies. However, these studies have not consistently demonstrated that lower dietary protein intake is associated with a reduction in uric acid (7–9). Furthermore, there are few trials examining the effects of increasing dietary protein on uric acid while minimizing the effects of weight loss (10). Whether replacing protein with carbohydrates or changing the type of carbohydrates in diet has an impact on uric acid concentration is unknown.

The Effect of Amount and Type of Dietary Carbohydrates on Risk for Cardiovascular Heart Disease and Diabetes Study (OmniCarb) trial is a clinical feeding study that examined the impact of modifying carbohydrate intake on cardiovascular risk factors among relatively healthy adults (11). The dietary interventions in this trial varied by glycemic index (≥ 65 versus ≤ 45) or by amount of carbohydrates (58% versus 40%). It was found that reducing the amount of carbohydrates (%carb) decreased triglyceride levels.

Further, reducing glycemic index increased low density lipoprotein cholesterol and increased insulin resistance in the setting of a high carbohydrate diet (11). As insulin resistance is strongly associated with hyperuricemia (12), we conducted an ancillary study of the OmniCarb trial, examining the effects of varying the type and amount of carbohydrate on plasma uric acid. We hypothesized that decreasing glycemic index would increase uric acid concentration, as higher insulin levels are known to lower renal uric acid excretion (12). Furthermore, since decreasing carbohydrate amount was achieved by increasing amount of dietary protein, we expected that decreasing carbohydrate amount would increase uric acid concentration as well.

MATERIALS and METHODS

OmniCarb was an investigator-initiated trial sponsored by the National Heart, Lung, and Blood Institute (11). In brief, OmniCarb was an isocaloric, crossover feeding study with 4-dietary intervention periods. Each participant was fed 4 distinct diets in random order. These 4 diets differed in composition by glycemic index (≥ 65 versus ≤ 45) and carbohydrate amount (58% vs. 40%). Glycemic index is a measure of carbohydrate quality, representing the amount of glucose released into circulation by foods containing carbohydrates (13). It is determined by comparing the area under the glucose curve between 50g of carbohydrates from a food of interest and 50g of glucose during a 2-hour period (13).

The four diets were as follows: high carbohydrate and high glycemic index (CG), high carbohydrate and low glycemic index (Cg), low carbohydrate and high glycemic index (cG), or low carbohydrate and low glycemic index (cg). A detailed description of the diets may be found in Table 1. Sodium, fiber, and calories were consistent across diets.

Participant recruitment

Adult men and women, aged 30 years and older, were recruited from areas around Boston, Massachusetts, and Baltimore, Maryland. All participants had a body mass index (BMI) ≥ 25 kg/m² with a systolic blood pressure (SBP) of 120–159 and a diastolic blood pressure (DBP) of <100 mm Hg. Persons with a prior diagnosis of diabetes, chronic kidney disease, or cardiovascular disease or persons taking medications for blood pressure (including diuretics), lipids, or diabetes were excluded (11). Participants were asked to refrain from taking non-steroidal anti-inflammatory agents two days prior to blood draws. Institutional Review Boards at Johns Hopkins University, Brigham & Women's Hospital, and the Harvard School of Public Health approved the study protocol.

Controlled feeding

The study was initiated in April 2008 and completed in December 2010. Participants were provided with 100% of their meals from the study centers and were fed each of the 4 diets in random order (11). Each of the diets was designed to be healthful like the DASH diet (14) using typical American foods that were low in saturated fat, cholesterol, and sodium while rich in fruits, vegetables, fiber, potassium, and other minerals. Dietary fiber, sodium, and potassium were constant across the 4 diets. Body size, sex, and physical activity level were used to determine calorie targets for each participant.

Study diets were consumed for 5 weeks followed by a 2-week washout period, during which participants could eat a self-selected diet. Diets were adjusted on an individual basis throughout the study to keep each participant's weight stable within 2% of baseline values. Participants were asked to minimize changes to their activity levels and alcohol use for the duration of the study. Each participant maintained a diary for every day on the controlled diets, listing protocol and non-protocol foods. Meal attendance was recorded. Participants had to consume the entire meal on-site and were observed while eating. Trays were cleared with staff present to prevent food from being discarded. Each day of the feeding period, the food diary contained questions about beverage and alcohol consumption on the previous day. Sugary beverages were prohibited, while no more than two diet beverages were allowed per day. Participants were also allowed to drink up to 5 ounces of wine per drink limited to 1 drink per day for women and 2 drinks per day for men.

Overall, participants reported eating only study foods on 96% of person-days. Any alcohol consumption was reported on 11% of person-days.

Uric acid

At baseline and at the completion of each 5-week feeding period, fasting plasma specimens were collected, centrifuged, aliquoted, and stored at -70°C . It was a study requirement that participants fast for at least 8 hours prior to laboratory specimen collection. Virtually all

blood collections occurred before noon at the completion of each feeding period. Uric acid was measured on a Siemens Dimension Vista 1500 chemical analyzer (Siemens, Erlangen Germany) via a uricase method that involves the conversion of uric acid to allantoin (15). Uric acid concentration was ultimately determined via spectrophotometry (16) with an inter-assay coefficient of variation of 1.3% (mean 5.275 mg/dL). Hyperuricemia was defined as a uric acid concentration >6 mg/dL in women and >7 mg/dL in men (2).

Other covariate measurements and definitions

Additional covariates were ascertained via questionnaire, laboratory specimens, and physical examination. BMI was calculated using baseline height and weight measurements and categorized as overweight (25–29.9 kg/m²) or obese (≥30 kg/m²). Fasting glucose and insulin were measured in serum and used to determine the homeostasis model assessment index (HOMA), a measure of insulin resistance (17). HOMA was determined via the following equation: $HOMA = [(fasting\ serum\ insulin\ concentration\ in\ \mu U/mL) \times (fasting\ serum\ glucose\ concentration\ in\ mg/dL)] / 405$ (17). HOMA was also dichotomized using the baseline median value of ≥1.48 units. Insulin sensitivity was determined using the Matsuda Index, derived from glucose and insulin levels measured during oral glucose tolerance testing (11,18).

We also used standard laboratory assays to measure total cholesterol, triglycerides, and high density lipoprotein (HDL) cholesterol in serum. Total cholesterol was dichotomized using a cut point of 240 mg/dL and HDL cholesterol was dichotomized using gender-specific cutpoints (<40 mg/dL for men; <50 mg/dL for women). Lactate was measured in plasma via a lactate-pyruvate conversion reaction. Glomerular filtration rate (GFR) was estimated using the Chronic Kidney Disease Epidemiology Collaboration cystatin C equation (19) and dichotomized based on the baseline median value of 106.5 mL/min/1.73 m². Cystatin C was used to estimate GFR rather than creatinine due to the influence of dietary protein on creatinine (20). Hypertensive status (yes or no) was determined by an average of 3 baseline blood pressure measurements in which SBP was >140 mmHg or DBP was >90 mmHg. Alcohol use (g/d) was ascertained with an abbreviated food frequency questionnaire administered at baseline and dichotomized using the median baseline consumption (1.045 g/d, i.e. ~0.5 drink per week).

Statistical Analysis

Study population characteristics were evaluated using means (SD) and proportions. We also performed a baseline cross-sectional analysis of uric acid and factors traditionally associated with uric acid using Pearson's correlation coefficient and linear regression with adjustment for age, sex, and race.

We examined change in uric acid from baseline (end-of-period minus baseline) during consumption of each of the 4 diets. We then compared uric acid levels at the end of each feeding period within person, specifically examining the effects of reducing glycemic index (cg vs. cG or Cg vs. CG), reducing proportion of carbohydrate (cg vs. Cg or cG vs. CG), or changing both factors simultaneously (Cg vs. cG or cg vs. CG), using forest plots for visual presentation. These analyses were repeated after adjustment for factors thought to represent

pathways influenced by glycemic index or proportion of carbohydrates that could affect uric acid concentrations, including kidney function (GFR) (21–23), glucose homeostasis (glucose, insulin, and Matsuda index) (12,18,24,25), and products in equilibrium with the glycolytic pathway (lactate and triglycerides) (26–28). These adjustments were based on measurements at baseline and the end of each feeding period, representing changes in eGFR, glucose, insulin, Matsuda index, lactate, and triglycerides during the 4 feeding periods that were concurrent with the changes in uric acid.

We also performed a stratified analysis to assess for effect modification of baseline covariates known to influence uric acid concentrations. Strata were based on race, hypertension status, total cholesterol, HDL cholesterol, HOMA, eGFR, BMI, baseline uric acid concentration (<4, 4–<5, 5–<6, ≥6 mg/dL), and alcohol use. Finally, we performed a sensitivity analysis in which we restricted the analysis to period 1 only as if it were a parallel design. This served a dual purpose of removing potential carryover effects as well as estimating the magnitude of changes achieved when replacing the participants' baseline American diet with the OmniCarb diets.

All analyses were performed with STATA version 14.0 (Stata Corporation, College Station, TX, USA) using generalized estimating equation (GEE) regression models with a Huber and White robust variance estimator (29), which assumed an exchangeable working correlation matrix. *P*-values for each stratum of the stratified analysis were generated using interaction terms. Statistical significance was defined as $P \leq 0.05$. Missing data were rare ($N=4$) and evenly distributed between feeding periods and diets.

RESULTS

Baseline characteristics & cross-sectional analysis

Characteristics of the study population at randomization ($N=163$) are reported in Table 2. The mean age of participants was 52.6 ± 11.4 years; 52% were women and 50% were non-Hispanic black race. Furthermore, 56% of the study participants were obese and 26% were hypertensive (but not on medications for hypertension). The mean (SD) uric acid was 4.7 (1.2) mg/dL. Notably, only 8 (5%) of the participants met criteria for hyperuricemia at baseline. Cross-sectional associations of uric acid with study covariates ($N=159$) may be found in the Supplemental Material, Table S1. After adjustment for age, sex, and race, the following were significantly associated with higher uric acid concentrations: lower eGFR (-0.02 mg/dL; $P < 0.001$) and higher values of BMI (0.06 mg/dL; $P < 0.001$), triglycerides (0.004 mg/dL; $P = 0.003$), fasting glucose (0.02 mg/dL; $P = 0.003$), fasting insulin (0.04 mg/dL; $P = 0.004$), HOMA (0.15 mg/dL; $P = 0.002$), and Matsuda index (-0.03 mg/dL; $P = 0.04$).

Change in uric acid from baseline

A comparison of end-of-period uric acid measurements with baseline measurements is shown in Supplemental Material, S2. Uric acid was not significantly different from baseline during either CG or cg diets. In contrast, there was a significant decrease in uric acid during the Cg diet (-0.11 mg/dL; $P = 0.03$) and a significant increase in uric acid during the cG diet

(0.16 mg/dL; $P = 0.01$). Moreover, adjustment for concurrent changes in eGFR, glucose, insulin, Matsuda index, lactate, and triglycerides did not significantly alter changes in uric acid from baseline measurements.

Between diet comparison of change in uric acid

The effects of reducing glycemic index, proportion of carbohydrates, or both factors on uric acid are shown in Figure 1. Replacing high-glycemic index foods with low-glycemic index foods reduced uric acid whether the diet was low (-0.24 mg/dL; $P < 0.001$) or high in carbohydrate content (-0.17 mg/dL; $P < 0.001$). In contrast, replacing high-proportion carbohydrate foods with low-proportion carbohydrate foods did not affect uric acid when glycemic index was low (0.03 mg/dL; $P = 0.51$), but increased uric acid when glycemic index was high (0.10 mg/dL; $P = 0.05$). Changing both factors simultaneously, i.e. reducing glycemic index while increasing the proportion of carbohydrates, had the largest effect on uric acid (-0.27 mg/dL; $P < 0.001$).

The effects of the controlled diets on uric acid, adjusted for changes in eGFR, glucose, insulin, Matsuda index, lactate, and triglycerides at each feeding period, were compared between diets in Table 3. Adjustment did not meaningfully alter the relationship between glycemic index reduction and uric acid. In contrast, reducing the proportion of carbohydrates was more strongly associated with an increase in uric acid after accounting for eGFR, lactate, and triglycerides. In the fully adjusted model, decreasing carbohydrate proportion increased uric acid by 0.11 mg/dL ($P = 0.006$) when glycemic index was low and by 0.19 mg/dL when glycemic index was high ($P < 0.001$).

Stratified analysis and other sensitivity analyses

Stratified analyses may be found in Supplemental Material, Table 3. Ultimately, there was little evidence of effect modification with a few notable exceptions. Compared to participants with a total cholesterol < 240 mg/dL, uric acid reduction was significantly greater in participants with a total cholesterol ≥ 240 mg/dL in the cg vs. CG (-0.25 vs. -0.07 mg/dL; $P = 0.02$) and cg vs. cG (-0.37 vs. -0.16 mg/dL; $P = 0.02$) diet comparisons. Similarly, compared to participants drinking more than the median baseline alcohol consumption (> 1.045 g/d), participants drinking less than the median baseline alcohol consumption (≤ 1.045 g/d) experienced greater reductions in uric acid in the Cg vs. CG (-0.28 vs. -0.05 mg/dL; $P = 0.002$) and cg vs. CG (-0.23 vs. -0.05 mg/dL; $P = 0.02$) diet comparisons. Notably, the effect of reducing glycemic index or proportion of carbohydrate did not differ significantly by strata of baseline uric acid (< 4 , 4 to < 5 , 5 to < 6 , and ≥ 6). Lastly, in a sensitivity analysis, restricting the analysis to feeding period 1 alone increased the magnitude of the effect of simultaneously reducing glycemic index and increasing carbohydrates (-0.39 mg/dL; $P = 0.001$) (Supplemental Material, Table 4).

DISCUSSION

In this trial, reducing dietary glycemic index decreased uric acid concentrations, while reducing the proportion of dietary carbohydrate increased uric acid concentrations. The combined effect of reducing glycemic index and increasing the proportion of carbohydrate

was a uric acid reduction of 0.27 mg/dL. These effects were independent of changes in eGFR, glucose, insulin, Matsuda index, lactate, and triglycerides. The greatest difference in uric acid was observed when glycemic index was reduced and the amount of carbohydrates was increased simultaneously, suggesting that adopting a diet rich in low glycemic index carbohydrates may result in the greatest reduction in uric acid. However, changing glycemic index seemed to be more important than changing carbohydrate proportion with regards to uric acid reduction. While these effects did not vary by strata of baseline uric acid, they did vary by strata of baseline alcohol consumption, such that reducing glycemic index did not affect uric acid in participants with regular alcohol consumption at baseline.

In this study, contrary to our hypothesis reducing glycemic index lowered uric acid concentrations. Glycemic index is a measure of post-prandial glucose, based on the amount the carbohydrates in a food increase blood glucose over a 2-hour period. Examples of low glycemic index foods include: legumes, dairy products, and some fruits (13). While a few studies have reported associations between glycemic index and factors related to uric acid, such as triglycerides (30) and glycemia (31), there is relatively little evidence relating glycemic index to uric acid. One physiology study of 13 participants found that replacing refined carbohydrates with “complex carbohydrates” reduced uric acid; although, this effect was confounded by weight loss (32). Similarly, a small controlled feeding study (N=12) found that type of carbohydrate (dietary sucrose compared with starch) was associated with significant increases in uric acid. However, this observation was complicated by fructose, a low glycemic index type of carbohydrate (13), known to increase uric acid (33). By design, the OmniCarb diets minimized the presence of dietary fructose, which may be an important consideration in practice when applying glycemic index target ranges used in this trial.

The relationship between glycemic index and uric acid was independent of the pathways explored in this study – namely, kidney function, glucose homeostasis (including insulin sensitivity), and products associated with glycolysis. This suggests that the effects of glycemic index on uric acid are not primarily mediated through changes in kidney function and glucose homeostasis (or insulin sensitivity), nor products of glycolysis (34). This was unexpected given the strong association between insulin resistance and hyperuricemia (12,24,25). It is also possible that the high versus low glycemic index diet comparison represents a contrast of an unanticipated micronutrient. Further analysis of the micronutrient content of the diets is needed to evaluate this hypothesis, however.

The low carbohydrate diet in the OmniCarb study is also a higher protein diet. Early observational studies have reported an association between dietary protein intake and gout (7), while subsequent observational studies have been inconsistent (8,9,35,36). However, human physiologic studies report that higher consumption of dietary protein increases uric acid excretion, thereby decreasing blood concentrations of uric acid (21,23,37). In contrast to our findings, one feeding study of 20 participants without weight loss showed a 0.6 mg/dL reduction in uric acid after 1 month on a lower carbohydrate, higher protein diet (10). This may be due to the opposing effect of glycemic index on uric acid, which was not reported for the diets in this study and could confound the macronutrient comparison.

We can only speculate as to the exact mechanism by which a low carbohydrate (higher protein) diet might increase uric acid. It is possible that animal protein is the main factor contributing to the difference either via exogenous purine consumption (6,9) or via the effects of amino acids on purine synthesis (22). It has also been shown that carbohydrates prevent ketosis, which contributes to uric acid production (38–40). We are unable to substantiate these hypotheses in this trial, however.

Among participants with a mild amount of alcohol consumption at baseline (>1.045 g/d or >0.5 drink a week), glycemic index had no impact on uric acid levels. This is likely due to the strong, positive association between alcohol consumption and uric acid levels (41). It may also be related to the observation that mild-to-moderate alcohol consumption improves insulin sensitivity (42); however, this is unlikely to be the case in our study given the minimal alcohol consumption reported by study participants.

The urate reduction achieved by reducing glycemic index and increasing the proportion of carbohydrate was 0.27 mg/dL, independent of change in weight, an important risk factor for hyperuricemia (2). This effect was even higher when restricted to the first feeding period alone and was greater or comparable to other trials of supplements or dietary interventions, such as, a lower salt diet (uric acid increase of about 1 mg/dL) (43), a lower fructose diet (no effect) (44), or vitamin C supplementation (-0.35 mg/dL) (45). By comparison, pharmacologic interventions such as allopurinol have been associated with an average reduction of 2–3 mg/dL (46). However, given their risk of adverse effects, it is recommended that pharmacologic interventions be reserved for patients with severe gout (47). There are an estimated 3 million persons in the US with mild gout and hyperuricemia (5), that could potentially benefit from a dietary intervention such as described in this study. Although, it should be noted that in this relatively healthy study population, uric acid levels were low at baseline (mean ~ 4.7 mg/dL). Whether greater reductions in uric acid could be achieved in persons with hyperuricemia or gout could not be tested because of the small number of participants ($N = 8$) with baseline hyperuricemia and the lack of ascertainment regarding gout status in the trial protocol.

This study has several limitations. First, there were few participants with hyperuricemia, making it difficult to assess the effects of diet on participants with an elevated uric acid. Similarly, gout status was not ascertained at baseline, and the study excluded people with chronic kidney disease or people being treated for diabetes, hyperlipidemia, or hypertension, limiting generalizability. In addition, the diets were healthier than most typical diets, which could possibly attenuate the effects of glycemic index on uric acid observed in this study. Furthermore, the feeding periods were too short to assess for clinical events such as the development of gout or gout exacerbations. Thus, it is difficult to infer how effective the dietary intervention in this trial would be in clinical practice. Finally, the low carbohydrate diet was compared to a diet with simultaneous increases in both protein and fat. Early physiology studies suggest conflicting roles for these macronutrients with some types of dietary proteins lowering (21,23,37,38) and dietary fat increasing (38–40) uric acid. It is possible that replacing protein with carbohydrates in absence of a change in fat (or similarly replacing fat with carbohydrates alone), would result in different effects on uric acid than what we report in this study.

This study also has several strengths. It was a randomized trial, designed to eliminate the effects of weight loss on outcome measures. The study population was diverse with few participants lost during follow-up. Diets were highly regulated, and the trial achieved excellent compliance with the interventions throughout the study. Furthermore, it is the first trial examining the effects of glycemic index on uric acid.

In conclusion, we found that reducing glycemic index lowered uric acid concentrations, while lower carbohydrate (or higher protein/fat) diets increased uric acid concentrations. Further, glycemic index was a more important determinant of uric acid than proportion of carbohydrates in this study. Future studies should examine these dietary effects in persons with clinically elevated uric acid concentrations and gout to determine whether reducing glycemic index can prevent gout or gout exacerbations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The authors' responsibilities were as follows—LJA and FMS: oversaw the data collection; SPJ and ERM: analyzed data and had primary responsibility for the final content of the manuscript; and all authors: contributed to the design of the study and the writing of the manuscript.

Abbreviations used

OmniCarb	The Effect of Amount and Type of Dietary Carbohydrates on Risk for Cardiovascular Heart Disease and Diabetes Study
CG	the high carbohydrate, high glycemic index diet
cG	the low carbohydrate, high glycemic index diet
Cg	the high carbohydrate, low glycemic index diet
cg	the low carbohydrate, low glycemic index diet
BMI	body mass index
LDL	low density lipoprotein
HDL	high density lipoprotein

HOMA	homeostatic model assessment
DASH	Dietary Approaches to Stop Hypertension
GEE	generalized estimating equation
CI	confidence interval

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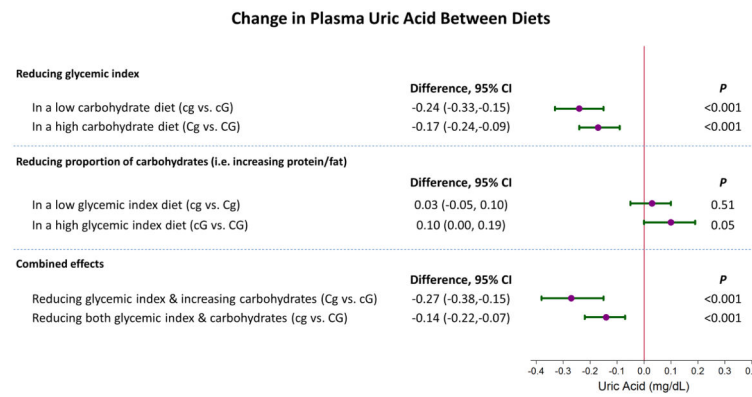


Figure 1. Change in plasma uric acid (mg/dL, 95% confidence intervals) between diets (N = 159). Comparisons are organized by dietary factor: glycemic index, proportion carbohydrate, or both factors. CG represents the high carbohydrate/high glycemic index diet. Cg represents the high carbohydrate/low glycemic index diet, cG represents the low carbohydrate/high glycemic index diet, and cg represents the low carbohydrate/low glycemic index diet.

Table 1Nutrient composition of the four diets used in the OmniCarb^{*}

Dietary Pattern	High Carbohydrate/High Glycemic Index (CG)	High Carbohydrate/Low Glycemic Index (CG)	Low Carbohydrate/High Glycemic Index (CG)	Low Carbohydrate/Low Glycemic Index (cg)
Energy, kcal	2011	1998	2011	1993
Glycemic Index	66	41	65	40
Carbohydrates, %kcal	58	57	41	40
Protein, %kcal	16	16	23	23
Fat, % kcal	27	27	37	37
Saturated, % kcal	6	6	7	7
Monounsaturated, % kcal	12	13	18	19
Polysaturated, % kcal	7	8	10	10
Animal Protein, g	42	46	78	81
Vegetable Protein, g	39	38	39	39
Fiber, g	32	37	29	33
Fructose, g	48	40	26	28
Cholesterol, mg	90	89	170	163
Calcium, mg	1032	1051	993	995
Potassium, mg	3963	4103	3949	4026
Sodium, mg	2245	2211	2305	2199
Magnesium, mg	462	429	468	440

^{*} Estimated from food analysis software (ESHA Food Processor SQL, version 10.2, ESHA Research)

Table 2Baseline characteristics of OmniCarb trial participants (N=163^{*}), mean (SD) or No. (%)

Plasma uric acid, mg/dL	4.7 (1.2)
Age, y	52.6 (11.4)
Women	85 (52)
Race	
Non-Hispanic White	66 (40)
Non-Hispanic African American	82 (50)
Hispanic	11 (7)
Asian	4 (2)
Body mass index, kg/m ²	32.3 (5.5)
Body mass index	
25–29.9	71 (44)
≥ 30	92 (56)
HDL cholesterol, mg/dL	58.3 (16.0)
Total cholesterol, mg/dL	227.1 (45.0)
Triglycerides, mg/dL	104.6 (67.1)
eGFR _{cys} , mL/min/1.73 m ²	104.2 (16.0)
Fasting glucose, mg/dL	97.3 (13.6)
Fasting insulin, µU/mL	7.7 (5.8)
Homeostasis model assessment (HOMA), units	1.9 (1.6)
Matsuda index, units	7.3 (5.8) ****
Systolic blood pressure, mm Hg	132.0 (9.1)
Diastolic blood pressure, mm Hg	80.0 (7.5)
Hypertensive status **	
Non-hypertensive	120 (74)
Hypertensive	43 (26)
Hyperuricemia, %	8 (5)
Alcohol use, grams/day ****	1.045 (0.03 to 4.93)

* Maximum number present at baseline. For some variables the N was smaller due to missing laboratory data.

** Defined as baseline SBP≥140 or DBP≥90 mmHg

*** Median (interquartile range); 162 persons provided information for this food frequency questionnaire item. Fourteen people reported no alcohol consumption. One drink contains about 14 grams of alcohol.

**** Matsuda index was determined in 162 participants.

Table 3

Between diet comparison of uric acid adjusted for estimated glomerular filtration rate, glucose, insulin, Matsuda index, lactate, and triglycerides, N=159

	Mean (95% Confidence Interval), P	
	In a low carbohydrate diet (cg vs. cG)	In a high carbohydrate diet (Cg vs. CG)
Reducing glycaemic index		
Plasma uric acid, mg/dL	-0.24 (-0.33, -0.15)	-0.17 (-0.25, -0.10)
Adjusted for eGFR	-0.21 (-0.29, -0.13)	-0.13 (-0.21, -0.06)
Adjusted for fasting glucose, insulin, and Matsuda index	-0.24 (-0.33, -0.16)	-0.18 (-0.26, -0.10)
Adjusted for lactate and triglycerides	-0.23 (-0.32, -0.14)	-0.16 (-0.23, -0.08)
Adjusted for eGFR, glucose, insulin, Matsuda index, lactate, and triglycerides	-0.24 (-0.33, -0.16)	-0.18 (-0.26, -0.10)
Reducing carbohydrate proportion		
Plasma uric acid, mg/dL	0.03 (-0.05, 0.10)	0.10 (0.00, 0.19)
Adjusted for eGFR	0.07 (-0.00, 0.15)	0.15 (0.06, 0.25)
Adjusted for fasting glucose, insulin, and Matsuda index	0.03 (-0.05, 0.11)	0.09 (0.00, 0.19)
Adjusted for lactate and triglycerides	0.08 (-0.01, 0.16)	0.15 (0.05, 0.24)
Adjusted for eGFR, glucose, insulin, Matsuda index, lactate, and triglycerides	0.11 (0.03, 0.20)	0.19 (0.09, 0.28)
Changing both factors		
Plasma uric acid, mg/dL	-0.27 (-0.38, -0.15)	-0.14 (-0.22, -0.07)
Adjusted for eGFR	-0.29 (-0.39, -0.18)	-0.06 (-0.14, 0.02)
Adjusted for fasting glucose, insulin, and Matsuda index	-0.27 (-0.38, -0.16)	-0.15 (-0.23, -0.07)
Adjusted for lactate and triglycerides	-0.31 (-0.42, -0.19)	-0.08 (-0.16, -0.01)
Adjusted for eGFR, glucose, insulin, Matsuda index, lactate, and triglycerides	-0.32 (-0.43, -0.21)	-0.02 (-0.11, 0.06)

Note: CG represents the high carbohydrate, high glycaemic index diet; Cg represents the high carbohydrate, low glycaemic index diet; cG represents the low carbohydrate, high glycaemic index diet; cg represents the low carbohydrate, low glycaemic index diet; eGFR, represents estimated glomerular filtration rate derived from cystatin C.