Effect of high-carbohydrate or high-*cis*-monounsaturated fat diets on blood pressure: a meta-analysis of intervention trials[1–3]

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ABSTRACT

Background: The Dietary Approaches to Stop Hypertension (DASH) diet is recommended to manage blood pressure. The DASH diet is low in saturated fat, but it is not clear whether saturated fat should be preferentially replaced with carbohydrate or unsaturated fat, especially *cis*-monounsaturated fat.

Objective: A meta-analysis of intervention studies comparing high-carbohydrate and high-*cis*-monounsaturated fat diets was conducted to increase understanding of the effect of carbohydrate and *cis*-monounsaturated fat on blood pressure.

Design: For study diets to be included in the analysis, they had to be isoenergetic, and the subjects' body weight had to remain stable. Ten studies (6 randomized crossover, 1 randomized parallel, and 3 nonrandomized) met the inclusion criteria.

Results: According to the random-effects model, which incorporates between-study variation to estimate the overall effect, diets rich in carbohydrate resulted in significantly higher systolic blood pressure [$\bar{x}$ difference: 2.6 (95% CI: 0.4, 4.7) mm Hg; $P = 0.02$] and diastolic blood pressure [1.8 (0.01, 3.6) mm Hg; $P = 0.05$] than did diets rich in *cis*-monounsaturated fat. When the meta-analysis was limited to randomized crossover studies, both systolic [1.3 (−0.3, 2.9) mm Hg; $P = 0.11$] and diastolic [0.9 (−0.2, 2.1) mm Hg; $P = 0.11$] blood pressure were higher with a high-carbohydrate than with a high *cis*-monounsaturated fat diet, but the differences were not significant.

Conclusions: Diets rich in carbohydrate may be associated with slightly higher blood pressure than diets rich in *cis*-monounsaturated fat. However, the magnitude of the difference may not justify making recommendations to alter the carbohydrate and *cis*-monounsaturated fat content of the diet to manage blood pressure. *Am J Clin Nutr* 2007;85:1251–6.

KEY WORDS High-carbohydrate diet, high-*cis*-monounsaturated fat diet, high-*cis*-MUFA diet, blood pressure, meta-analysis, hypertension

INTRODUCTION

According to the most recent National Health and Nutrition Examination Survey, which was conducted from 1999 to 2000, 27% of adult Americans have hypertension [systolic blood pressure (SBP) ≥ 140 mm Hg, diastolic blood pressure (DBP) ≥ 90 mm Hg, or the use of antihypertensive medications], and another 31% have prehypertension [SBP of 120 to 139 mm Hg or DBP of 80 to 89 mm Hg and no use of medication (1)]. Blood pressure is a continuous, consistent, and independent risk factor for cardiovascular disease (CVD) (2). A decrease in blood pressure can lead to a significant reduction in mortality from CVD. Stamler (3) evaluated the effect of populationwide shifts in SBP distributions on mortality and reported that a reduction of only 3 mm Hg in SBP can lead to an 8% reduction in mortality from stroke and a 5% reduction in mortality from coronary heart disease.

It is well established that lifestyle modifications such as weight loss (4), increased physical activity (5), moderation of alcohol consumption (6), reduction in sodium intake (7, 8), following the Dietary Approaches to Stop Hypertension (DASH) diet [a diet that is low in saturated fat, total fat, and dietary cholesterol and rich in low-fat dairy products, fruit, vegetables, calcium, potassium, and fiber (9)], or a combination of these modalities (8, 10, 11) lower blood pressure. The above modifications have been recommended by the seventh report of the Joint National Committee (JNC7) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (2) and the American Heart Association (12) as approaches to managing blood pressure. Although the DASH diet is low in saturated fat intake, it is not clear whether saturated fat should be preferentially replaced with carbohydrate or *cis*-monounsaturated fat. Compared with diets rich in carbohydrates, diets rich in *cis*-monounsaturated fats lower fasting triacylglycerol, VLDL cholesterol, and glucose concentrations and modestly raise HDL-cholesterol concentrations in subjects without diabetes and in those with type 2 diabetes mellitus (13, 14). However, because it is not clearly understood how varying these nutrients can affect blood pressure, the major guidelines for managing blood pressure have not made any specific recommendations regarding the proportions of carbohydrate and *cis*-monounsaturated fat in the diet. Intervention trials comparing these nutrients have reported either a higher blood pressure with the high-carbohydrate diet than with a high-*cis*-monounsaturated fat (high-*cis*-MUFA) diet (15–19) or no difference in blood

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pressure between the 2 diets (20–24). To better understand the effect of *cis*-MUFA and carbohydrate on blood pressure, we systematically reviewed all randomized and nonrandomized intervention trials reporting the effect of varied concentrations of these nutrients on blood pressure.

MATERIALS AND METHODS

Identification of relevant trials

We searched the MEDLINE database (National Library of Medicine, Bethesda, MD) for articles from the year of MEDLINE's inception through August 2006. The key phrases used to identify relevant articles included "monounsaturated fat, carbohydrate, and blood pressure"; "monounsaturated fat and blood pressure"; "nuts and blood pressure"; "olive oil and blood pressure"; and "high-carbohydrate diet and blood pressure." The search was not limited by study design or language. All relevant articles were identified by using the first 3 key phrases and by reviewing publications cited by some of the selected articles. No additional relevant articles were identified by using the last 2 key phrases, and, therefore, the search results from only the first 3 key phrases will be described in Results.

Inclusion criteria

Both randomized and nonrandomized intervention studies comparing the effect of high-carbohydrate diets with those of high-*cis*-MUFA diets on blood pressure were included in the meta-analysis. The randomized studies could be either crossover or parallel in design. To be included in the meta-analysis, the comparison diets of each study had to be isoenergic; in addition, the body weight of the subjects had to remain stable throughout the study.

From the list of articles identified by the key-word searches, one of us (MS) selected the abstracts that contained the potential inclusion criteria. The corresponding articles for the selected abstracts were then checked for the inclusion criteria by the other authors. All authors considered the selected articles to contain the necessary inclusion criteria.

Data extraction

One of the authors (MS) extracted data from the selected articles and tabulated them. This process was verified by another author (BAH). Any discrepancies were resolved by discussion among the authors. The following data were extracted: study design (randomized parallel, randomized crossover, or nonrandomized crossover intervention trial), sample size, composition of the study diets, study duration, health status, body weight, method of assessment of blood pressure, and SBP and DBP at the end of each diet phase (crossover studies) or change in SBP and DBP from baseline to the end of each diet (parallel design studies).

Statistical analysis

The outcome variable was the mean difference in blood pressure between the high-*cis*-MUFA diet and the high-carbohydrate diet. The variance used for each study was calculated in 1 of the 3 ways: *1*) calculated directly from the paired differences, *2*) imputed from the exact *P* value or the upper boundary of the *P* value where reported, or *3*) imputed by assuming a correlation coefficient of 0.5 between blood pressure values on the diets, because a correlation of $\geq$0.5 is expected for a 2-diet crossover or paired design (25). For studies with multiple comparisons or multiple timepoints, a composite effect size and variance were obtained for each study before the meta-analysis. The independent studies were then included in the meta-analysis to estimate the overall effect size and 95% CIs. The overall effect was estimated both with and without the nonrandomized studies. The overall effect was also estimated with the randomized crossover studies only. Results from both the fixed- and random-effects models were tabulated. The fixed-effects model assumes similar conditions and similar subjects with no between-study variation, whereas the random-effects model incorporates between-study variations to estimate the overall effect size. Results from the random-effects model were considered the main focus of the meta-analysis. Heterogeneity was assessed with Cochran's Q statistic and publication bias was assessed graphically with funnel plots and with Egger's regression test (26). Statistical analyses were performed with SAS software (version 9.1.3; SAS Institute, Cary, NC) and COMPREHENSIVE META-ANALYSIS software (version 2.2; Biostat, Inc, Englewood, NJ)

RESULTS

A total of 158 articles were identified from the first 3 searches and from the reference list of the selected articles. Of these, 148 studies were excluded because they did not meet the inclusion criteria: one study did not provide data on DBP; data from one study was previously published in another of the 158 studies identified; 60 studies investigated the effect of other types of interventions on blood pressure, other CVD risk factors, or both; 25 studies were either cross-sectional or prospective observational studies; 49 articles were either reviews, guidelines, summaries, or newsletters, or they described only the study method; 10 studies were conducted in animals; one study was retracted; and one study was conducted in pregnant women. Ten articles (15–24), one of which was in Spanish (17), were selected for the meta-analysis and were considered by us to meet all the eligibility criteria. The characteristics of the 10 selected studies are listed in **Table 1**. Six of the 10 studies compared the high-carbohydrate and high-*cis*-MUFA diets by using a randomized crossover design (15, 18, 19, 22–24), 1 did so by using a randomized parallel design (20), and 3 did so by using a nonrandomized crossover design (16, 17, 21). The studies contained only adults, because no such intervention trials in children were found.

Heterogeneity was observed qualitatively between studies according to the study design, diet composition, and subject population and quantitatively according to a significant Q statistic ($P < 0.001$) for both SBP and DBP. Therefore, the final analysis is based on the random-effects model.

Meta-analysis of data from all 10 selected studies found that diets rich in carbohydrate resulted in significantly higher SBP and DBP than did diets rich in *cis*-MUFA [random-effects model: 2.6 mm Hg ($P = 0.02$); 1.8 mm Hg ($P = 0.05$), respectively] (**Table 2**). A significantly different blood pressure (systolic or diastolic or both) between the 2 diets was seen in 5 of the 10 studies (15–19) (**Figure 1**). All of those 5 studies showed a higher blood pressure on a high-carbohydrate diet than on a high-*cis*-MUFA diet.

When the 3 nonrandomized studies (16, 17, 21) were excluded from the meta-analysis, both SBP and DBP remained higher with a high-carbohydrate diet than with a high *cis*-MUFA diet, but the

TABLE 1
Characteristics of the 10 intervention studies included in the meta-analysis[1]

							Proportion of total energy intake				
Study	Study design	Subject status	BP measure	Type of diet	Subjects	Duration	Carb	Fat	MUFA	PUFA	SFA
					n	*wk*					
Mensink et al, 1988 (20)	Randomized parallel	Normotensive	CBP	High-carb	24	5	62	22	9	5	7
				High-*cis*-MUFA	23	5	46	41	24	5	10
Pagnan et al, 1989 (21)	Nonrandomized crossover	Normotensive	CBP	High-carb	11	3	56	28	13	4	12
				High-*cis*-MUFA	11	3	46	38	25	4	10
Rasmussen et al, 1993 (15)	Randomized crossover	T2DM	ABP (24-h)	High-carb	15	3	49	32	11	7	11
				High-*cis*-MUFA	15	3	36	50	30	7	10
Nielsen et al, 1995 (22)	Randomized crossover	T2DM	ABP (24-h)	High-carb	10	3	48	30	9	8	10
				High-*cis*-MUFA	10	3	34	50	30	7	10
Walker et al, 1995 (23)	Randomized crossover	T2DM	CBP	High-carb	24	12	50	23	10	4	9
				High-*cis*-MUFA	24	12	40	36	20	5	11
Espino-Montoro et al, 1996 (16)	Randomized crossover[2]	Healthy	CBP	High-carb	20	3	55	30	12	8	10
				High-*cis*-MUFA	20	4	45	40	22	8	10
				High-*cis*-MUFA	20	4	45	40	22	8	10
Salas et al, 1999 (17)	Nonrandomized crossover	Healthy	CBP	High-carb	41	4	57	28	12	6	10
				High-*cis*-MUFA	41	4	47	38	22	6	10
Jenkins et al, 2002 (24)	Randomized crossover	Hyperlipidemic	CBP	High-carb	27	4	55	26	9	8	7
				High-*cis*-MUFA	27	4	48	32	15	8	8
				High-*cis*-MUFA	27	4	45	36	19	8	7
Shah et al, 2005 (18)[3]	Randomized crossover	T2DM	CBP	High-carb	41	6	55	30	10	10	10
				High-*cis*-MUFA	41	6	40	45	25	10	10
				High-carb	13	14	55	30	10	10	10
				High-*cis*-MUFA	13	6	40	45	25	10	10
				High-carb	8	6	55	30	10	10	10
				High-*cis*-MUFA	8	14	40	45	25	10	10
Appel et al, 2005 (19)	Randomized crossover	Pre-HTN or stage I HTN	CBP	High-carb	164	6	58	27	13	8	6
				High-*cis*-MUFA	164	6	48	37	21	10	6

[1] BP, blood pressure; Carb, carbohydrate; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids; CBP, clinic BP; ABP, ambulatory BP; T2DM, type 2 diabetes mellitus; HTN, hypertension.

[2] All subjects consumed the high-carb, low-fat diet first and then the 2 high-*cis*-MUFA diets (one prepared using virgin olive oil and the other using high-oleic sunflower oil) in a randomized crossover design.

[3] Shah et al compared the effect of the 2 diets on 42 patients for 6 wk each in a crossover study, and 21 patients continued the diet that they received during the second phase for an additional 8 wk.

difference was not significant [random-effects model: 1.3 mm Hg ($P = 0.06$); 0.9 mm Hg ($P = 0.09$), respectively] (Table 2). Similar results were seen when the randomized parallel design study (20) and the nonrandomized studies (16, 17, 21) were excluded and the meta-analysis was restricted to the 6 randomized crossover studies. SBP and DBP were higher with a high-carbohydrate diet than with a high-*cis*-MUFA diet, but the difference was not significant [random-effects model: 1.3 mm Hg ($P = 0.11$); 0.9 mm Hg ($P = 0.11$), respectively] (Table 2).

The above analyses, using the fixed-effects model, resulted in a difference in blood pressure with the 2 diets similar to that seen with the random-effects model (Table 2), but the difference in both SBP and DBP with the 2 diets was highly significant ($P < 0.001$ to $P = 0.002$) in the fixed-effects model (Table 2). Funnel plots (not shown) did not reveal any significant publication bias for SBP ($P = 0.65$) or DBP ($P = 0.42$).

DISCUSSION

Meta-analysis of the data from all the selected studies showed that both the SBP and DBP were significantly higher with a high-carbohydrate diet than with a high-*cis*-MUFA diet. This was observed in both the random- and fixed-effects models. When the meta-analysis was limited to the randomized studies, both SBP and DBP remained higher with a high-carbohydrate diet than with a high-*cis*-MUFA diet, but the difference was not significant in the random-effects model. This may be due in part to the smaller effect size and smaller sample size following the exclusion of the nonrandomized studies.

Of the 10 studies, 5 (20–24) reported no difference in blood pressure between the 2 diets, whereas the other 5 (15–19) reported a higher SBP, DBP, or both with a high-carbohydrate diet than with a high-*cis*-MUFA diet. The sample size in the studies that reported no difference in blood pressure on the 2 diets ranged from 10 to 27, and this small sample size may have limited the power to detect significant differences. In contrast, the sample size of the studies that found a significant difference in blood pressure on the 2 diets ranged from 15 to 164. The conflicting results cannot be explained by body weight, the study duration, or the method of measuring blood pressure (ambulatory versus clinic). Body weight remained stable in all of the studies, which probably resulted from the facts that the meals were prepared for the subjects in metabolic kitchens and that food consumption was monitored in most of the studies. Study duration ranged from 3 to 14 wk in the studies that reported significant differences between the 2 diets and from 3 to 12 wk in the studies that did not. Of the

TABLE 2
Net change in systolic (SBP) and diastolic (DBP) blood pressure in subjects following a high-carbohydrate diet or a high-*cis*-monounsaturated fat diet[1]

			Fixed-effects model		Random-effects model	
	Number and type of studies	Subjects	Change (95% CI)	*P*	Change (95% CI)	*P*
		n				
SBP (mm Hg)	7 randomized, 3 nonrandomized	400	2.0 (1.3, 2.8)	<0.001	2.6 (0.4, 4.7)	0.02
DBP (mm Hg)	7 randomized, 3 nonrandomized	400	1.3 (0.7, 1.8)	<0.001	1.8 (0.01, 3.6)	0.05
SBP (mm Hg)	6 randomized crossover, 1 randomized parallel	328	1.3 (0.5, 2.1)	0.001	1.3 (−0.1, 2.6)	0.06
DBP (mm Hg)	6 randomized crossover, 1 randomized parallel	328	0.9 (0.3, 1.5)	0.002	0.9 (−0.1, 1.9)	0.09
SBP (mm Hg)	6 randomized crossover	281	1.3 (0.6, 2.1)	0.001	1.3 (−0.3, 2.9)	0.11
DBP (mm Hg)	6 randomized crossover	281	0.9 (0.3, 1.5)	0.002	0.9 (−0.2, 2.1)	0.11

[1] Net change is expressed as the difference in blood pressure between a high-carbohydrate diet and a high-*cis*-monounsaturated fat diet.

2 studies that measured 24-h ambulatory blood pressure (15, 22), 1 reported a significant difference in blood pressure between the 2 diets (15), but the other (22) did not. Conflicting data also were reported by the remaining studies that assessed clinic blood pressure (16–21, 23, 24).

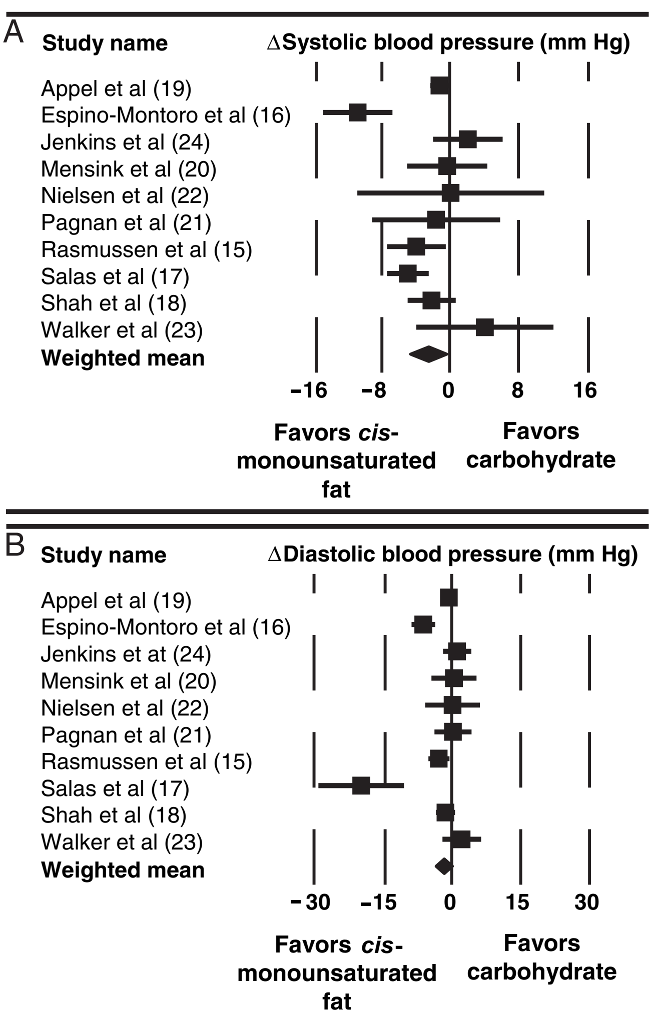

FIGURE 1. Net change (Δ) (95% CIs) in systolic (A) and diastolic (B) blood pressure with consumption of a high-carbohydrate diet and a high-*cis*-monounsaturated fat diet in 10 studies. The values shown are from the random-effects model.

The contradictory results cannot generally be accounted for by differences in macronutrient content across the 2 diets. Nutrient content of the diets was assessed by chemically analyzing duplicate food portions (16, 17, 20), analyzing food records or experimental diets by using nutrition software programs (15, 17–24), or both. The difference in the percentage of energy from carbohydrate across the 2 diets ranged from 10% to 16% in the studies that reported no difference in blood pressure (20–24) and from 10% to 15% in the studies that reported a significant difference (15–19) in blood pressure between the high-carbohydrate and high-*cis*-MUFA diets. The corresponding ranges for the percentage of energy from *cis*-MUFA are 10–21% and 8–19%, respectively. The percentage of energy from polyunsaturated fat and saturated fat also did not differ significantly between the 2 diets in any of the studies. Dietary cholesterol intake either was not reported (22, 23) or did not differ significantly between the 2 diets (15–21, 24). The difference in percent energy intake from alcohol on the 2 diets was too small (0–2%) to influence blood pressure. The quality of the carbohydrate source, both the fiber content and glycemic index, may affect blood pressure. Several studies, including cross-sectional, prospective observational, and randomized trials, showed that dietary fiber intake is inversely related to blood pressure (27–30), and several intervention studies showed that lowering the glycemic index lowers blood pressure (31–33). In the present meta-analysis, dietary fiber was ≈8–17 g/d higher with the high-carbohydrate diet than with the high-*cis*-MUFA diet in the studies by Mensink et al (20), Walker et al (23), and Shah et al (18). The higher fiber content of the high-carbohydrate diet may have reduced a possible blood pressure–raising effect of carbohydrate in these studies. The remaining studies either did not report intake of dietary fiber (21) or reported the maintenance of a constant or similar fiber intake (15–17, 19, 22, 24) across the different diets. Information on glycemic index was reported by only one of the studies included in the meta-analysis (19). This study reported a moderate level of glycemic index across the different diets. Thus, future studies comparing high-carbohydrate and high-*cis*-MUFA diets need to take glycemic index as well as dietary fiber into consideration in the design of the diets.

Examining the information on intake and excretion of micronutrients such as sodium, potassium, calcium, and magnesium in these studies is also important, because a reduction in sodium (7, 8) and increases in potassium (34), magnesium (35), and calcium (36) intakes have been reported to lower blood pressure (although weakly in the case of magnesium and inconsistently in the case of calcium). Six of the 10 studies in this review (15, 16, 18, 19, 20, 22) provided some or all of this information. Mensink et al (20) and Shah et al (18) reported a slightly higher intake of sodium, potassium, calcium, and magnesium, which they derived by analyzing duplicate food portions (20) or calculated from menus (18), with the high-carbohydrate diet than with the high-*cis*-MUFA diet. It is unlikely that the higher sodium content of the high-carbohydrate diet would have affected the results, because any blood pressure–raising effect of sodium would probably have been balanced out by the blood pressure–lowering effect of potassium. The difference in magnesium and calcium content between the 2 diets in both the studies was too low to result in any clinically relevant difference in blood pressure. Appel et al (19) and Espino-Monotoro et al (16) reported similar intakes of sodium, potassium, magnesium, and calcium with the 2 diets. No difference in 24-h urinary excretion rates of sodium (15, 19, 21, 22), potassium (15, 19, 21, 22) or calcium (15) was found between the 2 diets.

The slightly higher blood pressure of subjects following the high-carbohydrate diet may be due to accentuation of hyperinsulinemia. Hyperinsulinemia is suggested to enhance sympathetic nervous system activity, which increases heart rate, cardiac output, vascular resistance, and sodium retention and thus blood pressure (37, 38).

In conclusion, diets high in carbohydrate are associated with slightly higher blood pressure than are diets high in *cis*-MUFA. The magnitude of the difference observed, however, may not justify making dietary recommendations to alter the carbohydrate and *cis*-MUFA content of the diet to manage blood pressure. Additional well-designed studies with a larger sample size would help to better assess the effect of high-carbohydrate and high-*cis*-MUFA diets on blood pressure. It is important that future studies carefully control the glycemic index and several nutrients, including the dietary fiber content of the intervention diets, given their possible confounding effects on blood pressure.

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The authors' responsibilities were as follows—MS: conducted the literature search, interpreted the data, and wrote the manuscript; BA-H: reviewed the selected articles, selected the statistical models, analyzed and interpreted the data, and edited the manuscript; and AG: reviewed the selected articles and edited the manuscript. None of the authors had a personal or financial conflict of interest.

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