

Research and Professional Briefs

Comparative Effects of Three Popular Diets on Lipids, Endothelial Function, and C-Reactive Protein during Weight Maintenance

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ABSTRACT

Although popular diets focus on weight loss and their favorable biochemical and physiological effects, fewer investigations have evaluated the biological impact of these diets during weight maintenance. To study this issue, three popular diets—Atkins, South Beach, and Ornish—were tested in a randomized and counterbalanced cross-over study between January and December 2006. Participants completed each of the three 4-week isocaloric dietary intervention phases followed by a 4-week wash-out period. They were weighed weekly and caloric adjustments made if weight change exceeded 1 kg. At the completion of each dietary phase, 3-day food records were analyzed, fasting blood sampled, and brachial artery reactivity testing performed. Eighteen adults completed all three isocaloric dietary phases. During the South Beach and Ornish maintenance phase, there were significant reductions in low-density lipoprotein cholesterol (11.8%; $P=0.01$, 16.6%; $P=0.0006$, respectively) compared to prediet baseline. In addition, in contrast to the Atkins

maintenance phase, significant reductions in low-density lipoprotein cholesterol and apolipoprotein B levels were observed after the South Beach ($P=0.003$, $P=0.05$; repeated measures analyses of variance) and Ornish maintenance phases ($P=0.0004$, $P=0.006$, repeated measures analyses of variance). Brachial artery testing revealed an inverse correlation between flow-mediated vasodilatation and intake of saturated fat ($r=-0.33$; $P=0.016$). These data suggest that during weight maintenance, less favorable biological effects are observed during a simulated, high-fat Atkins diet when compared to the South Beach and Ornish diet. The findings support additional study in subjects with visceral obesity and the metabolic syndrome, in whom an increased risk of coronary disease at baseline may be accentuated with chronic consumption of a diet that exhibits unfavorable effects on lipids and endothelial function.

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Popular diets designed to induce acute weight reduction represent a multibillion dollar a year industry (1). While numerous studies have evaluated the effectiveness of weight reduction and the extent to which weight loss is associated with improvement in a variety of metabolic parameters (eg, glucose, lipids, blood pressure), considerably less information is available with regard to the effect of these parameters during weight maintenance. This is an important area to investigate because weight maintenance often represents the chronic phase prescribed after acute weight reduction has been achieved. Yet, surprisingly few data are available in the assessment of popular diets during weight maintenance. Because coronary heart disease (CHD) remains the leading cause of death in the United States and dietary factors contribute to development and acceleration of atherothrombosis (2), the present study was designed to evaluate the impact of biochemical and physiological parameters affecting CHD risk during weight maintenance. If saturated fat is associated with low-density lipoprotein (LDL) receptor downregulation (3) and endothelial dysfunction (4), two potential mechanisms accounting for elevated CHD risk (5), then popular diets that advocate high saturated fat intake (ie, Atkins) may exhibit unfavorable effects on lipids and endothelial function compared to lower saturated fat intake during the weight-maintenance phase.

METHODS

Subjects

A total of 26 adults responded to a posted advertisement seeking healthy adults aged 20 years and older. Because the study was not designed to investigate weight loss, inclusion criteria consisted of body mass index (calculated as kg/m^2) <30 and with no history of metabolic, hepatic, renal, or systemic disease. They were comprised predominantly of medical students, residents, and hospital employees. Participants were asked not to use herbal remedies, fish oils, or anti-inflammatory medications. Alcohol use was permitted provided that intake was regular and that no more than 1 ounce was consumed daily. None of the volunteers were taking lipid-lowering or antihypertensive agents. Patients taking vasoactive medications (eg, cetirizine) were asked not to take the medication the evening prior to brachial artery reactivity testing. Volunteers were asked to maintain the same level of physical activity throughout the study. All studies were performed after an overnight fast of at least 12 hours, which included restriction of caffeine and alcohol. The protocol was approved by the Institutional Review Board and all subjects provided written informed consent.

Study Methods

This was a randomized crossover study of three 4-week dietary interventions with a 4-week washout period after each dietary phase for a total study period of 6 months for each participant. At the end of each 4-week interval, subjects returned for fasting blood measurements and brachial artery reactivity testing. The study was undertaken between January and December 2006.

Dietary Phases

Outpatient dietary interventions were based on three popular diets, the high-fat, low-carbohydrate Atkins diet (6), the Mediterranean South Beach diet (7), and the high-carbohydrate, low-fat Ornish diet (8). Dietary assignment was randomized and counterbalanced. At baseline, each volunteer provided 72-hour food records for analysis by a registered dietitian (RD), which served as the template for teaching participants how to record food items and quantity consumed during the trial. Subjects were informed at the outset that the study was not aimed at weight reduction but rather weight maintenance (eg, within 1% to 2% of body weight) throughout the 6-month trial. Therefore, volunteers were weighed at weekly intervals and, if weight alterations exceeded 1 kg, the RD adjusted caloric and nutrient intake accordingly. A total of six volunteers had dietary adjustments made during their 4-week dietary phase in order to maintain their weight within the designated range. At the conclusion of each 4-week dietary phase and 4-week washout phase, subjects presented after a 12-hour fast for blood drawing and endothelial testing. In all, there were six different phases: first diet, washout, second diet, washout, third diet, and washout, for a total of 24 weeks from first diet to study completion.

Laboratory Methods

Lipoprotein and Biochemical Analysis. Following an overnight fast and signed consent, 30 mL blood was collected by venipuncture into two tubes containing ethylene diamine tetraacetic acid centrifuged within 30 minutes at 4°C to separate plasma. Total cholesterol and triglycerides were measured using a Hitachi 704 clinical chemistry analyzer (Boehringer Mannheim Diagnostics, Indianapolis, IN) and high-density lipoprotein (HDL) cholesterol was measured following precipitation of apolipoprotein B-containing lipoproteins as described previously (9). Apolipoproteins A-I and B were measured using a nephelometer (Behring Diagnostics, Inc, Westwood, MA) with reagents supplied by the manufacturer. Electrolytes, hepatic function, and high-sensitivity C-reactive protein were measured by Quest Diagnostics (Van Nuys, CA).

Brachial Artery Flow-Mediated Vasodilation. Brachial artery flow-mediated (endothelial-dependent) vasodilation (FMD) was measured using an 11-5 MHz broadband linear-array transducer and baseline images were acquired after a 15-minute supine equilibration period as described previously (10). Poststimulus images were acquired 1 minute \pm 15 seconds following release of a 5-minute upper-arm occlusion. Baseline measurements were performed prior to each 4-week dietary phase and represented the average of three measurements that were analyzed by an experienced investigator blinded to subject's identity and study phase.

Statistics

Sample-size calculations determined that 18 subjects would be required to detect a 15% reduction in total cholesterol between the high- and low-fat dietary phases, with a standard deviation of 27 mg/dL, power 90%, and $\alpha=0.05$. Following each dietary phase, 72-hour food records were analyzed by an RD (C.D.) using the Nutri Base V Personal Plus edition (version 5.19, 2005, CyberSoft, Inc, Phoenix, AZ). Participants were asked to record the amount of each item consumed; one RD reviewed the food records for completion and a second RD checked all entries to verify accuracy. Differences in energy intake, lipids (including log transformation for triglyceride analysis), lipoproteins, and other biochemical measurements before and after each dietary phase were analyzed using STATA Statistical Data Analysis software (version 8.2, January 2003, StataCorp, College Station, TX) and SAS (version 9.13, 2005, SAS Institute, Cary, NC). Repeated measures analyses of variance (SAS proc Mixed, with a repeated statement and compound symmetric covariance structure) was used to estimate the mean within-person (post-prevalue) change and standard error of the within-person changes in metabolic parameters. A two-tailed $P\leq 0.05$ was considered significant. For the brachial artery studies, FMD was quantified as the percent diameter change of the postocclusion arterial diameter measurement relative to baseline and end-diastolic frames. Pearson's correlation analysis was used to evaluate the association of change between saturated fat intake and FMD.

RESULTS AND DISCUSSION

Of 26 participants who enrolled in the study, 18 (nine men and nine women) completed the study; eight with-

Table. The effect of three popular diets on lipids, lipoproteins, apolipoproteins A-I and B (mg/dL), and C-reactive protein (mg/L) before and after completion of each 4-week dietary phase of the crossover study^{ab}

	Pre ^c (SD ^d)	Changes	SE ^e	95% CI ^f		P Value		
						Between Diets ^g		
						AS	AO	SO
TC^h						0.007	<0.0001	0.06
Atkins	183.8 (44.0)	9.2	4.7	0.0 to 18.3	0.06			
South Beach	182.6 (47.6)	-9.8	4.7	-19.0 to 0.7	0.04			
Ornish	191.7 (51.2)	-22.7	4.7	-31.8 to -13.5	<0.001			
TGⁱ						0.95	0.08	0.07
Atkins	83.3 (29.7)	-3.7	7.9	-19.1 to 11.8	0.65			
South Beach	94.9 (47.6)	-4.3	7.9	-19.8 to 11.1	0.59			
Ornish	86.1 (41.3)	16.2	7.9	0.7 to 31.6	0.048			
TG^j						0.56	0.03	0.10
Atkins	4.37 (0.34)	-0.08	0.08	-0.23 to 0.08	0.35			
South Beach	4.44 (0.50)	-0.01	0.08	-0.16 to 0.15	0.91			
Ornish	4.35 (0.47)	0.18	0.08	0.02 to 0.33	0.03			
HDL^k						0.98	0.01	0.01
Atkins	62.9 (18.0)	1.2	2.6	-3.9 to 6.4	0.64			
South Beach	62.0 (15.3)	1.1	2.6	-4.0 to 6.3	0.67			
Ornish	64.3 (14.7)	-8.7	2.6	-3.6 to 13.9	0.002			
LDL^l						0.003	0.0004	0.44
Atkins	96.1 (24.8)	8.1	4.4	-0.4 to 16.7	0.07			
South Beach	93.1 (48.4)	-11.8	4.4	-20.4 to -3.3	0.01			
Ornish	102.2 (37.1)	-16.6	4.4	-25.2 to -8.1	0.0006			
ApoA-I^m						0.83	0.0007	0.001
Atkins	168.4 (35.7)	3.0	4.0	-4.7 to 10.7	0.45			
South Beach	170.2 (29.3)	1.8	4.0	-6.1 to 9.6	0.67			
Ornish	171.9 (29.8)	-17.8	4.0	-10.1 to -25.6	0.0001			
ApoBⁿ						0.05	0.006	0.37
Atkins	81.7 (28.9)	4.8	2.7	-0.45 to 10.0	0.08			
South Beach	77.9 (26.8)	-2.9	2.7	-8.3 to 2.4	0.29			
Ornish	83.4 (31.0)	-6.4	2.7	-1.2 to -11.6	0.02			
CRP^o						0.13	0.04	0.63
Atkins	0.39 (0.31)	0.18	0.11	-0.04 to 0.41	0.12			
South Beach	0.64 (0.65)	-0.09	0.13	-0.33 to 0.16	0.50			
Ornish	0.60 (0.51)	-0.17	0.12	-0.4 to 0.06	0.16			

^an=18.

^bRepeated measures of analysis of variance using general linear modeling for each variable.

^cPre=prediatory phase baseline.

^dSD=standard deviation.

^eSE=standard error.

^fCI=confidence interval.

^gDifferences between Atkins and South Beach (AS), Atkins and Ornish (AO), and South Beach and Ornish diets (SO).

^hTC=total cholesterol.

ⁱTG=triglyceride.

^jLog-transformed analysis.

^kHDL=high-density lipoprotein.

^lLDL=low-density lipoprotein.

^mApoA-I=apolipoprotein A-I.

ⁿApoB=apolipoprotein B.

^oCRP=C-reactive protein.

drew due to logistical reasons or inability to continue with a specified dietary phase. Mean age was 30.6±9.6 years, and mean body mass index was 22.6±3. Mean fasting lipids and lipoproteins included total cholesterol of 184.9±48.3 mg/dL, triglycerides of 78.1±32.7 mg/dL, low-density lipoprotein (LDL) cholesterol of 107.2±48.3 mg/dL, and HDL cholesterol of 62.2±17.0 mg/dL.

Baseline dietary composition was most consistent with a Mediterranean-like diet with mean total fat intake of 30%±10%. Dietary intake estimates of 72-hour food records demonstrated no appreciable change in energy intake between the Atkins (7,216±1,844 kJ/day), South Beach (6,732±1,338 kJ/day), and Ornish (6,869±1,380 kJ/day) phases consistent with the absence of weight loss.

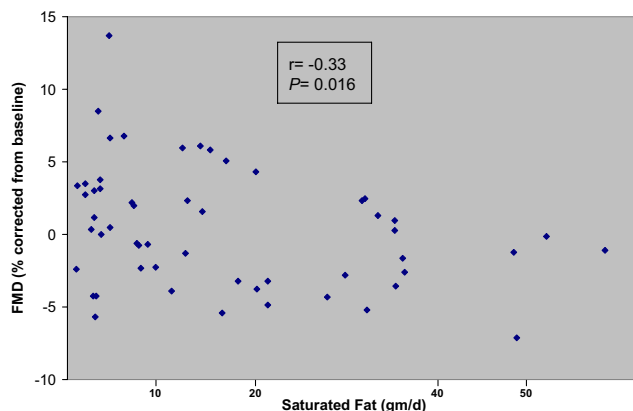


Figure. Inverse correlation between saturated fat intake (g/day) and flow-mediated vasodilation (FMD) after correcting for baseline values.

However, the Atkins diet was associated with a greater intake of dietary cholesterol compared to South Beach or Ornish (567 ± 267 vs 202 ± 186 and 114 ± 89 mg/day; $P < 0.05$) as well as higher total fat (58 ± 9 vs 31 ± 11 and 9 ± 3 ; $P < 0.001$) and saturated fat content (30 ± 8 vs 14 ± 7 and 3 ± 1 ; $P < 0.001$) compared to the other two dietary phases. The Table outlines predietary phase baseline after the 4-week washout phase and the respective post-dietary changes following each assigned 4-week phase. There were no appreciable differences between baseline levels of lipids, lipoproteins, or apolipoproteins in the three predietary phases. However, total cholesterol and LDL cholesterol were reduced after the South Beach and Ornish phases, whereas apolipoprotein B and apolipoprotein A-I were only reduced after Ornish. When comparing the three dietary phases, the Atkins diet evidenced greater increases in total cholesterol and LDL cholesterol compared to either South Beach ($P = 0.007$, $P = 0.003$) or Ornish ($P < 0.0001$, $P = 0.0004$). In contrast, the Ornish diet was associated with reduced HDL cholesterol and apolipoprotein A-I compared to either Atkins ($P = 0.01$, $P = 0.0007$) or South Beach ($P = 0.01$, $P = 0.001$), and lower levels of C-reactive protein ($P = 0.04$) compared to Atkins dietary phase.

Baseline measurements of brachial artery FMD were similar in the Atkins (3.18 ± 0.59 mm), South Beach (3.16 ± 0.58 mm), and Ornish (3.18 ± 0.64 mm) diets. However, after the assigned dietary period, the Ornish diet was associated with higher FMD compared to Atkins and a nonsignificant increased FMD was also observed after the South Beach diet compared to Atkins. An inverse correlation between on-treatment FMD and saturated fat intake is illustrated in the Figure and an inverse trend was observed between FMD and total fat intake ($r = -0.22$; $P = 0.12$).

The most noteworthy finding in the present study was that during weight maintenance, the Atkins diet was associated with higher total cholesterol and LDL cholesterol compared to the South Beach and Ornish dietary phases and reduced endothelial vasoreactivity compared to the Ornish phase. Moreover, saturated fat intake correlated inversely with endothelial function as assessed by brachial artery reactivity testing. Previous isocaloric

studies have demonstrated that a low-fat, high-carbohydrate diet is associated with elevation in triglycerides and reductions in LDL cholesterol and HDL cholesterol compared to higher total and saturated fat intake (11,12). Surprisingly, however, there have been minimal isocaloric comparative evaluations of lipids and endothelial function. One study compared a diet high in carbohydrates (18% fat) to high saturated fat (37% fat), monounsaturated fat (37% fat), and polyunsaturated fat (36% fat) each for a 3-week intervention period. Substantial reductions in brachial FMD were observed during the high saturated fat diet phase (4), although the short testing interval without a washout and lack of adjustment for covariates (13-15) may have impacted the modest effects observed. Because most dietary studies are relatively short term (ie, less than 1 year) and focus on weight reduction efficacy, considerably less information is available regarding the potential clinical impact of popular diets after weight has been stabilized (ie, long-term maintenance). Results of the present study suggest that a diet that exhibits unfavorable effects on lipids and endothelial function during the maintenance phase may be less advantageous compared with diets associated with improvement in these parameters. This is particularly noteworthy in subjects at increased risk of CHD (eg, metabolic syndrome) (16), for whom long-term dietary recommendations are often required.

There are several limitations associated with the present study. First, the study was not designed to compare the weight-loss effects of popular diets, but rather to evaluate the biological effects that occur during weight maintenance in apparently metabolically healthy nonobese men and women. Therefore, the study results are neither generalizable to obese subjects nor to those enrolled in the weight-loss induction phase of these diets. Secondly, although lipid- and endothelial-related differences between the dietary phases were discernible despite a relatively small size, C-reactive protein measurements displayed greater variability, suggesting that a larger sample size would be required to better delineate differences between the groups during the maintenance phase. A third limitation relates to verification of adherence to dietary therapy. Specifically, it is recognized that weight monitoring and dietary food records, the primary tools used in the present study, are less sensitive when compared with more reliable methods, such as having assigned dietary meals prepared in a metabolic kitchen.

CONCLUSIONS

High saturated fat intake may adversely impact lipids and endothelial function during weight maintenance. As such, popular diets such as Atkins may be less advantageous for CHD risk reduction when compared to the Ornish and South Beach diets once weight loss has been achieved. The findings support additional study, especially in subjects with or at increased risk of CHD, in order to further explore the potential clinical implications of popular diets during long-term maintenance.

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