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High-fat, energy-dense, fast-food–style breakfast results in an increase in oxidative stress in metabolic syndrome

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Abstract

The metabolic syndrome (MetS) is associated with an increased incidence of diabetes and coronary heart disease. Postprandial lipemia is a prominent feature of dyslipidemia in both type 2 diabetes mellitus and MetS and is also associated with coronary heart disease. Oxidative stress and inflammation are pivotal in all stages of atherosclerosis; however, there is a paucity of data on postprandial oxidative stress and inflammation in subjects with MetS. Thus, the primary aim of this study was to compare the postprandial effects of an energy-dense, high-fat, fast-food–style (FFS) meal with an American Heart Association (AHA)–recommended heart-healthy meal on biomarkers of oxidative stress and inflammation in subjects with MetS. A total of 11 subjects with MetS completed the study. Glucose levels were significantly increased 2 hours after both FFS and AHA diets ($P < .0001$), and high-density lipoprotein cholesterol levels significantly decreased in FFS diet but not in the AHA diet (P for interaction $< .05$). Total triglyceride levels significantly increased postprandially only in the FFS meal but not in the AHA meal (P for interaction $= .03$). Plasma thiobarbituric acid reactive substances and malondialdehyde + hydroxynonenal increased significantly with time in both dietary groups, and the postprandial increase was greater in the FFS diet compared to the AHA diet ($P < .0005$). Serum high-sensitivity C-reactive protein, interleukin 6, and tumor necrosis factor levels did not change with time or dietary treatment. The postprandial increase in interleukin 1b was significantly higher with the FFS meal, thus resulting in significant differences between both treatments (P for interaction $= .03$). Thus, in subjects with MetS, consumption of an energy-dense, fatty meal (FFS breakfast) results in increased postprandial oxidative stress compared to a heart-healthy meal (AHA).

1. Introduction

The metabolic syndrome (MetS) affects 1 in 4 individuals in the United States and is associated with increased incidence of diabetes and heart disease [1,2]. Humans spend most of the day in the postprandial state [3]. The magnitude of postprandial lipemia is an independent risk factor for CVD and has been suggested to be predictive of risk for myocardial infarction. Postprandial lipemia is an independent risk factor for CVD, and a prominent feature in diabetes and MetS [4,5]. Epidemiologic studies suggest that postprandial perturbations are involved in the pathogenesis of diabetic vasculopathies [4,5]. Oxidative stress may be an important mechanism by which postprandial lipemia alters vascular function [4-6]. High-fat meals seem to be particularly damaging to the vasculature. The typical Western diet with 3 meals per day causes postprandial lipemia for 18 hours. Consumption of a fatty meal results in impaired vascular function and increased concentrations of proinflammatory cytokines [7]. Oxidative stress and inflammation are pivotal in atherosclerosis; however, there is a paucity of data on postprandial oxidative stress and inflammation in MetS. While several Americans consume fast-food–style (FFS), high-energy, high-fat breakfasts rather than a heart-healthy breakfast, the effects of such a meal have not been studied previously. Thus, the primary aim of this study was to compare the postprandial effects of a FFS meal (breakfast) with an American Heart Association (AHA)–recommended meal on biomarkers of oxidative

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Table 1
Composition of the FFS and AHA breakfast

	AHA	FFS
kJ (kcal)	3175.6 (759)	3827.1 (914.7)
% Protein	13.5	14.1
% Carbohydrate	77.9	35.8
% Fat	8.6	50.1
Protein (g)	26.7	32.2
Carbohydrate (g)	154	81.9
Fat (g)	7.6	51
Saturated fat (g)	3.3	15.5
MUFA (g)	1.5	0
PUFA (g)	0.6	0
Cholesterol (mg)	16.6	280
Sodium (mg)	507	2194
Fiber (g)	13.8	4

MUFA indicates monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

stress and inflammation in subjects with MetS because this captures the real life situation of the American population.

2. Research design and methods

This study was approved by the institutional review board at University of California Davis Medical Center. All subjects provided informed consent. Subjects with MetS were recruited as per National Cholesterol Education Panel Adult Treatment Panel-III guidelines as reported previously [8]. Briefly, they had to present with 3 of the following 5 features: waist of more than 35 inches in women or more than 40 inches in men; fasting glucose of more than 100 mg/dL and less than 126 mg/dL; blood pressure of more than 130/85mm Hg or on antihypertensive medication; high-density lipoprotein cholesterol of less than 40 mg/dL in men or less than 50 mg/dL in women; and fasting triglycerides of more than 150 mg/dL. All subjects had a baseline C-reactive protein (CRP) of less than 10 mg/L and normal white blood cell count. Exclusion criteria were smoking, pregnancy or lactation, renal, liver or thyroid dysfunction; consumption of other antioxidants/supplements; chronic exercise; or chronic medical conditions.

This is a randomized crossover trial. A total of 11 subjects with MetS (7 females and 4 males) were recruited to participate in two 1-day studies, separated by at least 1 week (when they followed their usual diet and exercise). After a 12-hour fast, subjects reported for each 8-hour study day. A catheter was placed in a vein in the forearm for the 5 blood draws (baseline and at 2, 4, 6, and 8 hours postprandial). After the baseline blood draw, subjects consumed 1 of 2 meals, an AHA breakfast that had 759 energy, 13.5% protein, 78% carbohydrate, and 8.6% fat (consisting of bagel, cheese, fruit, and milk) or an energy-dense, high-fat, FFS breakfast that had 914 energy, 14.1% protein, 36% carbohydrate, and 50% fat (consisting of burger, fries, and drink, obtained from McDonalds) (Table 1). No other foods or beverages were consumed during the 8 hours, except water. The long duration of the study (8 hours) was to ensure that changes in biomarkers of inflammation could be captured given their long half-lives.

The analyses performed included baseline and postprandial plasma glucose, and lipid profile using standard clinical chemistry laboratory techniques. Biomarkers of oxidative stress included plasma oxygen radical absorbance capacity (ORAC), plasma thiobarbituric acid reactive substances (TBARS), plasma malondialdehyde and hydroxyalkenals (MDA and HNE), and plasma lipid peroxide concentrations as described previously [9,10]. Biomarkers of inflammation included CRP by a high-sensitivity method (Beckman Coulter, Fullerton, CA), interleukin (IL)–6, IL-1β, and tumor necrosis factor, using high-sensitivity immunoassays [8,11]. Inter- and intra-assay coefficients of variation of these assays were less than 10%.

Statistical analyses were performed using GraphPad Prizm software (Graph Pad, San Diego, CA). Repeated-measures analysis of variance was performed followed by *t* tests for parametric and Mann-Whitney for nonparametric data.

3. Results

A total of 11 subjects completed the study. The average age of the subjects was 49 ± 18 years, and average body mass index was 35 ± 5 kg/m^2. Glucose levels were significantly

Table 2
Postprandial changes in lipid profile in subjects with MetS after FFS vs AHA breakfast

		0 h	2 h	4 h	6 h	8 h
Triglyceride (mg/dL)*	FFS	186 ± 95	256 ± 112†	276 ± 130†	259 ± 134†	230 ± 154†
	AHA	197 ± 95	200 ± 105	228 ± 123	216 ± 111	191 ± 83
Total cholesterol (mg/dL)	FFS	220 ± 23	210 ± 20	212 ± 23	220 ± 21	221 ± 22
	AHA	226 ± 29	219 ± 24	219 ± 26	226 ± 30	228 ± 27
LDL cholesterol (mg/dL)	FFS	149 ± 27	118 ± 34	116 ± 39	127 ± 35	132 ± 40
	AHA	143 ± 38	137 ± 37	132 ± 41	140 ± 41	147 ± 35
HDL cholesterol (mg/dL)*	FFS	44 ± 9	40 ± 10†	41 ± 8†	41 ± 8†	44 ± 8
	AHA	43 ± 8	42 ± 9	42 ± 8	43 ± 9	43 ± 9
Glucose (mg/dL)*	FFS	102 ± 40	133 ± 70†	103 ± 49	95 ± 31	93 ± 19
	AHA	99 ± 29	138 ± 66†	106 ± 41	88 ± 23	87 ± 15

Data are presented as mean ± SD. LDL indicates low-density lipoprotein; HDL, high-density lipoprotein.
* $P < .03$ (time × diet interaction).
† $P < .05$ compared to baseline.

Table 3
Postprandial changes in biomarkers of oxidative stress in subjects with MetS after FFS vs AHA breakfast

		0 h	2 h	4 h	6 h	8 h
Plasma ORAC (mmol/L Trolox equivalents)	FFS	4.0 ± 1.4	4.4 ± 1.0	4.4 ± 1.3	4.1 ± 1.3	4.0 ± 1.6
	AHA	4.1 ± 0.8	4.4 ± 1.1	4.5 ± 0.9	4.4 ± 0.9	4.0 ± 1.1
Plasma TBARS (nmol/L)*	FFS	5.6 ± 0.8	7.1 ± 1.3†	8.1 ± 1.5†	8.8 ± 1.1†	8.1 ± 1.0†
	AHA	5.3 ± 1.2	5.9 ± 1.0	6.3 ± 1.5	6.3 ± 0.8†	5.7 ± 0.9
Plasma MDA and HNE (μmol/L)*	FFS	1.3 ± 0.5	2.1 ± 0.2†	1.8 ± 0.3†	2.1 ± 0.4†	2.0 ± 0.3†
	AHA	0.8 ± 0.2	0.9 ± 0.4	0.8 ± 0.3	0.9 ± 0.3	0.8 ± 0.2
Plasma lipid peroxides (μmol/L)*	FFS	1.5 ± 0.8	4.3 ± 1.9†	6.6 ± 1.8†	10.6 ± 3.5†	9.0 ± 2.6†
	AHA	1.8 ± 1.0	2.1 ± 1.5	2.0 ± 1.0	2.2 ± 1.4	2.4 ± 1.9

Data are presented as mean ± SD.
* $P < .005$ (time × diet interaction).
† $P < .05$ compared to baseline.

increased 2 hours after both FFS and AHA breakfast ($P < .0001$); however, there was no significant change between the 2 meals. No appreciable change was observed in total and low-density lipoprotein cholesterol concentrations. High-density lipoprotein cholesterol levels were significantly decreased after FFS meal but not after the AHA meal (time vs treatment-diet effect, $P < .05$; time effect, $P < .0001$). Total triglyceride levels significantly increased postprandially only with the FFS meal but not with the AHA meal (P for interaction, ie, differences vs baseline and between diets = .03 and for time effect = $P < .0001$) (Table 2).

Plasma TBARS increased significantly with time in both dietary groups, and the postprandial increase was greater in the FFS meal compared to the AHA meal, ($P < .0005$, Table 3). After the FFS meal, there was a significant postprandial increase in MDA + HNE levels; however, there was no significant change in the AHA group with time ($P = .05$ for interaction, ie, differences vs baseline and between diets). Similarly, plasma lipid peroxides increased significantly only in the FFS group postprandially ($P < .0001$). Neither meal affected ORAC values.

Serum high-sensitivity CRP and tumor necrosis factor levels did not change with time or dietary treatment (P for interaction, ie, differences vs baseline and between diets = .84 and .9, respectively). Plasma IL-6 levels increased at 8 hours after both AHA and FFS meals, with no significant differences between the 2 meals. There was a significant increase in IL-1β levels only in the FFS group compared to baseline, thus resulting in significant differences between both dietary treatments (P for interaction, ie, differences vs baseline and between diets = .03) (Table 4).

Table 4
Postprandial changes in biomarkers of inflammation in subjects with MetS after FFS vs AHA breakfast

		0 h	2 h	4 h	6 h	8 h
CRP (mg/L)	FFS	2.2 ± 1.1	2.3 ± 1.0	2.3 ± 1.1	2.2 ± 1.5	2.3 ± 1.1
	AHA	1.8 ± 1.0	2.1 ± 1.5	2.0 ± 1.0	2.2 ± 1.4	2.4 ± 1.9
IL-1β (ng/mL)*	FFS	1.1 ± 0.8	1.3 ± 0.8	1.5 ± 1.1	1.8 ± 1.6†	2.1 ± 1.2†
	AHA	1.4 ± 1.2	1.4 ± 1.1	1.3 ± 1.2	1.3 ± 1.6	1.6 ± 1.1
IL-6 (ng/mL)	FFS	1.2 ± 0.8	1.2 ± 0.6	1.9 ± 1.0	2.9 ± 2.4	3.8 ± 2.9
	AHA	0.7 ± 0.4	1.1 ± 0.8	1.8 ± 1.2	2.4 ± 1.6	3.9 ± 2.7
Tumor necrosis factor α (ng/mL)	FFS	2.9 ± 2.3	3.4 ± 2.3	3.6 ± 2.2	3.7 ± 2.1	4.1 ± 2.5
	AHA	3.5 ± 2.4	3.6 ± 2.3	3.9 ± 2.7	4.6 ± 3.1	4.7 ± 3.1

Data are presented as mean ± SD.
* $P < .05$ (time × diet interaction).
† $P < .05$ compared to baseline.

4. Discussion

According to the National Cholesterol Education Panel ATP-III guidelines, the primary management of subjects with MetS involves therapeutic lifestyle changes including decreasing intake of saturated fat, cholesterol, trans fat, and increasing physical activity and addition of sterols and fiber in the diet [12]. Postprandial lipemia is an independent risk factor for heart disease [4,5]. Oxidative stress and inflammation play a pivotal role in atherogenesis. High-fat meals seem to be particularly damaging to the vasculature. Because many Americans consume an energy-dense, high-fat breakfast and not the AHA-recommended heart-healthy breakfast, we wished to test the acute effects of these 2 meals on biomarkers of oxidative stress and inflammation. In this study, we provide novel data in subjects with MetS that, in comparison to an AHA meal, a high-fat, high-energy, high-salt meal (the FFS meal), results in significant augmentation in biomarkers of oxidative stress in the postprandial state. This could be due to the increase in fat or increase in energy or the combination of the two.

Previous studies have shown that a carbohydrate-restricted diet results in increased weight loss, and improvement in insulin sensitivity and triglycerides in patients with MetS or diabetes that are severely obese when compared to an energy- and fat-restricted diet [13]. They did not assess effects of these diets on biomarkers of oxidative stress and inflammation. However, in this study, we have examined the acute effects of a high-fat, energy-dense breakfast compared to a heart-healthy

breakfast on biomarkers of oxidative stress and inflammation, and chronic effects will be examined in future studies comparing high-fat vs low-fat isocaloric diets on biomarkers of oxidative stress and inflammation.

With regard to postprandial oxidative stress, Ursini et al [14] previously demonstrated that a test meal (English breakfast providing 11% protein, 34% carbohydrate, and 55% fat, approximately 5021 kJ [1200 kcal]) in 9 healthy males resulted in significant 123% postprandial increases in plasma lipid peroxides at 2 hours after the meal. In the present study, there was a similar significant increase in postprandial lipid peroxides, which was accentuated with the FFS meal compared to the AHA meal. Furthermore, in the Ursini study, they only examined one point postprandially in normal healthy subjects. Here, we have compared 2 different meals on postprandial oxidative stress over an 8 hour period in subjects with MetS.

Oxidative stress appears to be an important mechanism by which postprandial lipemia alters vascular function. However, only one study has investigated directly the effect of an oral prooxidant lipid challenge on vascular function. Consumption of a meal containing 65 g fat used repeatedly in deep fat frying, and rich in lipid hydroperoxides, produced a sevenfold decrease in endothelium-dependent flow-mediated dilation, whereas no effect was found with the same amount of unused cooking fat [15].

With regard to cytokines, Esposito et al [16] showed that the consumption of a high-fat meal was associated with increased IL-18 and decreased adiponectin concentration, whereas there was no effect on plasma IL-8 in healthy subjects. However, both postprandial oxidative stress and inflammatory cytokines were not examined, and subjects with MetS were not studied. Lundman et al [17] recently studied the effect of a high fat meal on IL-6 levels. While IL-6 levels increased, they also failed to find any significant differences postprandially between CAD subjects and controls. Similarly, Motton et al [18] investigated the effect of a high-glycemic vs low-glycemic index meal on postprandial monocyte cytokines and also failed to observe any significant differences. In the present study, among the cytokines, only the increase in IL-1β release was significantly increased postprandially after the FFS meal vs the AHA meal.

In summary, we demonstrate for the first time in subjects with MetS that consumption of an energy-dense, high-fat, FFS breakfast results in increased postprandial oxidative stress. We have not speculated if this increased postprandial oxidative stress is due to the increased energy content or due to the high fat content of the diet or both, and this will be examined in future studies. Future studies will examine mechanisms for this increased postprandial oxidative stress and test the effect of therapeutic lifestyle changes and nutritional interventions, especially in the postprandial state.

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