Differential Effects of Two Isoenergetic Meals Rich in Saturated or Monounsaturated Fat on Endothelial Function in Subjects With Type 2 Diabetes

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OBJECTIVE — To examine the acute effects of consumption of monounsaturated (MUFAs) and saturated fatty acids (SAFAs) on endothelial function in subjects with type 2 diabetes.

RESEARCH DESIGN AND METHODS — A total of 33 participants were examined after consumption of two different isocaloric meals: one rich in MUFA and one rich in SAFA, in the form of extra-virgin olive oil and butter, respectively. Endothelial function was assessed by determination of flow-mediated dilatation (FMD).

RESULTS — FMD did not change significantly after the MUFA-rich meal but declined after the SAFA-rich meal. The FMD during the experiment, expressed as incremental area under the curve, increased after the MUFA-rich meal by 5.2 ± 2.5% and decreased after the SAFA-rich meal by 16.7 ± 6.0% ($\Delta = -11.5 \pm 6.4\%$; $P = 0.008$).

CONCLUSIONS — Consumption of an SAFA-rich meal is harmful for the endothelium, while a MUFA-rich meal does not impair endothelial function in subjects with type 2 diabetes.

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Endothelial dysfunction occurs early in the course of type 2 diabetes and contributes to the development of macrovascular complications of the disease (1,2). Consumption of saturated fatty acids (SAFAs) impairs endothelial function for up to 6 h postmeal (3), whereas data on the effect of monounsaturated fatty acids (MUFAs) on endothelial function in subjects with type 2 diabetes are limited. According to recent nutritional recommendations, individuals with diabetes should substitute SAFA for MUFA in their diet (4), and the predominant source of MUFA in many countries is oleic acid contained in olive oil. However, the effect of consumption of olive oil on endothelial function in subjects with type 2 diabetes is not known. We tested the hypothesis that consumption of MUFA in the form of olive oil exerts a better effect on endothelial function in subjects with type 2 diabetes than that associated with consumption of butter. Because endothelial function is affected by high blood glucose, lipid and insulin concentrations, and increased oxidative stress (2), we measured these parameters during the study.

RESEARCH DESIGN AND METHODS

— We studied 21 men and 12 women with type 2 diabetes attending the outpatient diabetes clinic of Laiko General Hospital. Current smokers, subjects aged >70 years, and those with clinically apparent macrovascular disease, renal impairment or microalbuminuria, A1C >8.5%, and fasting triglycerides >300 mg/dl were excluded.

We designed a crossover study. Subjects consumed two different standard test meals on two separate mornings. The test meals were given in random order with an interval of ~1 week in between. The SAFA-rich meal consisted of four pieces of toasted white bread and 40 g butter (total energy content 557.6 kcal, 50.1 g carbohydrates, 9.2 g protein, and 35.6 g fat; 62.9% SAFA, 0.3% polyunsaturated fatty acids [PUFAs], and 31.9% MUFA). The MUFA-rich meal consisted of four pieces of toasted white bread and 33 g extra-virgin olive oil (total energy content 559.4 kcal, 50.1 g carbohydrates, 9.2 g protein, and 35.8 g fat; 14.6% SAFA, 7.9% PUFA, and 77.0% MUFA).

Endothelial function was assessed by determination of the change of the brachial artery diameter after removal of ischemic occlusion on the forearm (flow-mediated dilatation [FMD]), as previously described (5). Blood flow was measured at rest and within 15 s after the cuff release. Blood was collected after an overnight fast of 10–12 h for determination of A1C, glucose, lipids, insulin, and total plasma antioxidant capacity (TPAC). FMD, blood flow, and biochemical parameters were determined in the fasting state and 2, 4, and 6 h postprandially.

Two-way ANOVA for repeated measurements was performed to examine the effect of time (within-subject factor), the test meal (between-subjects factor), and their interaction on the studied parameters in the two phases of the study. The observed power of two-way ANOVA for the FMD at a 0.05 level was >90% for the aforementioned effects.

RESULTS

— Mean ± SD age was 58.1 ± 9.2 years, duration of diabetes 3.8 ± 3.2 years, BMI 29.6 ± 4.3 kg/m^2, waist circumference 102.8 ± 10.9 cm, and A1C 7.0 ± 1.3%. After consumption of the MUFA-rich meal, FMD did not change, whereas after consumption of the SAFA-rich meal, a significant reduction in FMD was observed (Table 1). The FMD

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Table 1—*Fasting and postprandial profiles of the hemodynamic parameters in the study subjects*

	Fasting	2 h	4 h	6 h	*P*	*P**	*P*†
Baseline brachial artery diameter (mm)							
MUFA	4.1 ± 0.4	4.2 ± 0.5	4.2 ± 0.5	4.2 ± 0.5	0.56		
SAFA	4.2 ± 0.5	4.2 ± 0.5	4.3 ± 0.6	4.2 ± 0.6	0.25	0.84	0.66
Flow-mediated dilatation (%)							
MUFA	6.9 ± 3.7	5.8 ± 4.1	6.8 ± 4.5	5.8 ± 6.4	0.56		
SAFA	6.9 ± 5.9	5.1 ± 5.9	1.1 ± 3.3	3.9 ± 4.5	<0.001	0.01	0.001
Baseline blood flow (ml/min)							
MUFA	132.6 ± 64.1	111.6 ± 87.6	111.9 ± 53.1	103.9 ± 56.2	0.15		
SAFA	138.5 ± 91.5	130.7 ± 82.7	136.6 ± 86.5	109.9 ± 54.4	0.14	0.43	0.35
Maximum blood flow (ml/min)							
MUFA	524.7 ± 225.4	468.9 ± 203.1	491.9 ± 240.1	530.6 ± 203.9	0.42		
SAFA	548.6 ± 264.6	496.5 ± 248.2	532.8 ± 246.6	525.2 ± 268.4	0.68	0.74	0.64
Difference in flow (%)							
MUFA	323.8 ± 170.7	380.9 ± 224.3	395.6 ± 307.8	491.9 ± 244.7	0.39		
SAFA	367.9 ± 227.9	339.2 ± 238.2	350.6 ± 167.1	457.7 ± 312.5	0.10	0.72	0.61

Data are means ± SD unless otherwise indicated. *P* values indicate results of two-way ANOVA for repeated measurements for the effect of time (within-subject factor) after consumption of the MUFA-rich meal and the SAFA-rich meal. *Results of two-way ANOVA for the effect of the meal (between-subject factor). †Result of two-way ANOVA for repeated measurements for the time-by-meal interaction. Baseline values before occlusion of the forearm artery, and maximum values measured within 15 s after occlusion.

values, expressed as incremental area under the curve, were increased by 5.2 ± 2.5% after the MUFA-rich meal and decreased by 16.7 ± 6.0% after the SAFA-rich meal ($\Delta = -11.5 \pm 6.4\%$ between the test meals, $P = 0.008$). Baseline brachial artery diameter, baseline and peak blood flow, and percent increase in blood flow in the brachial artery did not change during the study after consumption of either test meal. Additionally, no significant differences in these parameters were observed between the test meals (Table 1).

After consumption of either test meal, plasma glucose, insulin, and triglyceride levels increased during the study, while the concentrations of total and HDL cholesterol and TPAC did not change. No significant differences were found in these parameters between the two meals, and the time-by-meal interaction was not significant (data not shown).

CONCLUSIONS — The main finding of this study is that consumption of a single MUFA-rich meal in the form of extra-virgin olive oil does not impair endothelial function in subjects with type 2 diabetes. On the contrary, consumption of a SAFA-rich meal exerts a noxious effect on endothelial function that starts at 2 h and is maintained up to 6 h postprandially. Notably, the differential effects of MUFA- and SAFA-rich diets on endothelial function were observed for similar changes in plasma glucose, insulin, and lipid concentrations in TPAC and reactive hyperemia.

Concerning the effect of MUFA on endothelial function in subjects with type 2 diabetes, one previous study showed that consumption of safflower and canola oil did not impair endothelial function 4 h postmeal (6), while another study demonstrated that substitution of PUFA for olive oil in a diet for 2 months resulted in improvement in FMD (7). Thus, our finding for a protective effect of MUFA on endothelium corroborates these reports. Consumption of olive oil attenuates endothelial cell activation in humans (8,9), and in vitro studies demonstrated that endothelial cells exposed to oleic acid reduce the expression of adhesion molecules (10). Furthermore, extra-virgin olive oil is rich in polyphenols that enhance the formation of nitric oxide by endothelial cells and protect endogenous antioxidant defenses postprandially (11–13). These data suggest that the protective effects of extra-virgin olive oil on endothelium could be due to the oleic acid per se, to the natural antioxidants contained in it, or to both.

Studies examining the effect of diet on endothelial function are of clinical relevance for prevention strategies in subjects with type 2 diabetes, a population vulnerable to macrovascular complications. We studied type 2 diabetic subjects without complications and with short diabetes duration; therefore, our findings cannot be extrapolated to all patients with type 2 diabetes. Moreover, we examined the effect of a single meal on endothelial function; prospective studies are needed to clarify the long-term effects of olive oil consumption on endothelial function.

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