

Differential effects of two different isoenergetic meals one rich in saturated and one rich in monounsaturated fat on endothelial function in subjects with type 2 diabetes mellitus

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Objective- This cross-over study examined the acute effects of consumption of monounsaturated (MUFA) and saturated fatty acids (SAFA) on endothelial function in subjects with type 2 diabetes (T2DM).

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 ($+5.2 \pm 2.5$ %) and decreased after the SAFA-rich meal (-16.7 ± 6.0 %) ($\Delta = -11.5 \pm 6.4$ %, $P=0.008$).

Conclusions- Consumption of a SAFA-rich meal is harmful for the endothelium while a MUFA-rich meal does not impair endothelial function in subjects with T2DM.

Endothelial dysfunction occurs early in the course of type 2 diabetes mellitus (T2DM) and contributes to the development of macrovascular complications of the disease (1,2). Consumption of saturated fatty acids (SAFA) impairs endothelial function for up to 6 hours postmeal (3) while data on the effect of monounsaturated fatty acids (MUFA) on endothelial function in subjects with T2DM are limited. According to the 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 T2DM is not known. The research hypothesis we tested herein was that consumption of MUFA in the form of olive oil exerts a better effect on endothelial function in subjects with T2DM than consumption of butter. Because endothelial function is affected by high blood glucose, lipid and insulin concentrations as well as increased oxidative stress (2) we measured these parameters during the study.

RESEARCH DESIGN AND METHODS

We studied 21 men and 12 women with T2DM attending the outpatient diabetes clinic of our hospital. Current smokers, subjects older than 70 years and those with clinically apparent macrovascular disease, renal impairment or microalbuminuria, GHbA1c (A1c) >8.5% and fasting triglycerides >300 mg/dl were excluded.

We designed a cross-over study. Each subject consumed a standard test meal in the morning of the study; a meal rich in SAFA in the form of 4 pieces of white toast bread and 40 g of butter (total energy content 557.6 Kcal, carbohydrates 50.1 g, protein 9.2 g, fat 35.6 g: SAFA 62.9%, polyunsaturated fatty acids [PUFA] 0.3%, MUFA 31.9%) and a

meal rich in MUFA in the form of 4 pieces of white toast bread and 33 g of extra virgin olive oil (total energy content 559.4 Kcal, carbohydrates 50.1 g, protein 9.2 g, fat 35.8 g: SAFA 14.6%, PUFA 7.9%, MUFA 77.0%). The test meals were given in random order with an interval of about 1 week in between.

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 suggested previously (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 h, 4 h, and 6 h postprandially.

Two-way analysis of variance (ANOVA) for repeated measurements was performed to examine the effect of time (within-subject factor), the test meal (between-subject 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 0.05 level was >90% for the aforementioned effects.

RESULTS

The mean \pm SD value of age was 58.1 \pm 9.2 years, duration of diabetes 3.8 \pm 3.2 years, BMI 29.6 \pm 4.3 Kg/m², waist circumference 102.8 \pm 10.9 cm, and A1c 7.0 \pm 1.3%.

After consumption of the MUFA-rich meal FMD did not change during the experiment, while after consumption of the SAFA-rich meal a significant reduction in FMD was observed (Table 1). The FMD values during the experiment, expressed as incremental area under the curve, was +5.2 \pm 2.5% after the MUFA-rich meal and -16.7 \pm 6.0% after the SAFA-rich meal (Δ = -

11.5±6.4% between the test meals, $P=0.008$). Baseline brachial artery diameter, baseline and peak blood flow as well as % 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 triglycerides 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 T2DM. On the contrary, consumption of a SAFA-rich meal exerts a noxious effect on endothelial function which starts 2 h and is maintained up to 6 h postprandially. Noteworthy, 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 in reactive hyperemia.

Concerning the effect of MUFA on endothelial function in subjects with T2DM, one previous study showed that consumption 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 the diet for two 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 which 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 can be due to either 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 T2DM, a population vulnerable to macrovascular complications. We studied uncomplicated subjects with T2DM and with short duration of diabetes; therefore, our findings cannot be extrapolated to all patients with T2DM. 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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Table 1-Fasting and postprandial profiles of the hemodynamic parameters in the study subjects

	Fasting	2 h	4 h	6 h	<i>P</i>	<i>P*</i>	<i>P**</i>
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 shown as mean ± SD. *P* values indicate the results of two-way ANOVA for repeated measurements for the effect of time (within-subjects factor) after consumption of the meal rich in monounsaturated fatty acids (MUFA) and the meal rich saturated fatty acids (SAFA). **P* values indicate the results of two-way ANOVA for the effect of the meal (between-subjects factor). ***P* values indicate the result of two-way ANOVA for repeated measurements for the time by meal interaction. Baseline values are the values before occlusion of the forearm artery and maximum values are the values observed within 15 s post-occlusion.