Plasma levels of sICAM-1 rose after the high-fat meal (from 652 to 940 ng/mL). Subjects ate the following meals in random order and separated by a 1-week interval: (1) a high-fat meal (760 kcal; 50 g of fat, 20.4 g of saturated fat, 58 g of carbohydrates); (2) an isoenergetic high-carbohydrate meal (pizza) (758 kcal; 17 g of fat, 2.2 g of saturated fat, 58 g of carbohydrates); and (3) a high-fat meal with dietary antioxidants. The high-fat meal consisted of 2 sausages (80 g), 6 bread slices (90 g), 1 small egg (40 g), butter (15 g), and olive oil (5 g). The high-carbohydrate meal consisted of a pizza (300 g) with tomatoes (60 g). The third meal consisted of an isoenergetic high-fat meal plus vegetable foods: 100 g of tomatoes, 200 g of carrots, and 100 g of peppers (184 mg vitamin C, 19.65 mg vitamin E, 15 mg β-carotene, 9.2 g fiber). The meals were prepared in one batch in the same kitchen and consumed under supervision. Serum concentrations of sICAM-1 and sVCAM-1 were determined in the same kitchen and consumed under supervision. Serum samples were taken before breakfast and 95 to 940 minutes after the meal. Plasma levels of sICAM-1 and sVCAM-1 were determined using commercially available immunosorbent kits (R and D Systems).

Basal parameters were similar on each of the 3 study days. Plasma levels of sICAM-1 rose after the high-fat meal (from 210±41 to 284±48 μg/L; P<0.01), as did sVCAM-1 levels (from 652±95 to 940±109 μg/L; P<0.01). No significant increase of sICAM-1 and sVCAM-1 levels occurred after the pizza meal and the high-fat meal with antioxidants.

Unlike pizza, a single high-fat meal modifies the adhesive properties of the endothelium toward a more atherogenic profile. Nutrients may increase short-term levels of soluble CAMs, and humans are usually in a nonfasting state. Pizza and vegetables do not increase stickiness of endothelium, whereas a high-fat meal increases it. We studied 25 healthy non-obese volunteers (13 men and 12 women) aged 27±5.3 years (mean±SD). Subjects ate the following meals in random order and separated by a 1-week interval: (1) a high-fat meal (760 kcal; 50 g of fat, 20.4 g of saturated fat, 58 g of carbohydrates); (2) an isoenergetic high-carbohydrate meal (pizza) (758 kcal; 17 g of fat, 2.2 g of saturated fat, 58 g of carbohydrates); and (3) a high-fat meal with dietary antioxidants. The high-fat meal consisted of 2 sausages (80 g), 6 bread slices (90 g), 1 small egg (40 g), butter (15 g), and olive oil (5 g). The high-carbohydrate meal consisted of a pizza (300 g) with tomatoes (60 g). The third meal consisted of an isoenergetic high-fat meal plus vegetable foods: 100 g of tomatoes, 200 g of carrots, and 100 g of peppers (184 mg vitamin C, 19.65 mg vitamin E, 15 mg β-carotene, 9.2 g fiber). The meals were prepared in one batch in the same kitchen and consumed under supervision. Serum concentrations of sICAM-1 and sVCAM-1 were determined using commercially available immunosorbent kits (R and D Systems).

Response

Metabolic changes during postprandial phase may be important in the pathogenesis of atherosclerosis. As Professor Giugliano and colleagues state in their letter, short-term ingestion of high-fat meals in healthy subjects increases serum levels of the vascular cell adhesion molecule-1 (VCAM-1) and the intracellular adhesion molecule-1 (ICAM-1), two proteins involved in early atherogenesis. Various reports have also demonstrated that hypercholesterolemia increases cellular adhesion molecule (CAM) expression in rabbit atherosclerotic lesions, that LDL upregulates CAM expression in cultured human endothelial cells, and that hyperlipemic patients have increased VCAM-1 serum levels.

The expression of these adhesion molecules is regulated by nuclear factor (NF)-κB, an ubiquitous transcription factor involved in the inflammatory response. In our article, we demonstrated that a fat-enriched breakfast increased NF-κB in blood mononuclear cells of healthy individuals between 6 and 9 hours after the meal. This could explain the increment of soluble CAM (sCAM) after a high-fat meal observed by Giugliano et al. Unfortunately, they do not mention when the measurement of these proteins was performed. If they measured sCAM levels 9 hours after diet intake, one might assume that NF-κB could be implicated in the regulation of sCAM. By contrast, if they measured sCAM <9 hours after diet intake, the effect of high-fat diet would probably be independent of NF-κB activation. Only a sequential examination of both parameters (NF-κB and CAM levels) after the short-term fat ingestion could help to unravel this issue.

Giugliano et al also demonstrate that the simultaneous administration of some vegetables containing a relatively small amount of antioxidants, accompanying the high-fat meal, prevented VCAM-1 and ICAM-1 serum increment. In addition, other authors have demonstrated that gallates (gallic acid esters) and vitamin E, which are abundant in red wine, can inhibit cytokine-induced activation of NF-κB and thereby reduce the expression of VCAM-1 and ICAM-1 in cultured endothelial cells. We have also demonstrated that the antioxidants quercetin and α-tocopherol succinate inhibited NF-κB activation caused by VLDL. In conclusion, Seljeflot et al did not observe differences in sCAM in hyperlipemic patients treated with approximately the same amount of the antioxidants used by Giugliano et al.

In conclusion, both a short-term high-fat diet and hyperlipidemia may increase VCAM-1 and ICAM-1 serum levels, probably through the activation of NF-κB. However, the role of antioxidants in the prevention of sCAM levels increment in those settings deserves further investigation.

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