Pizza and Vegetables Don't Stick to the Endothelium

To the Editor:

Blanco-Colio et al[1] showed that a fat-enriched breakfast increased the activation of the transcription factor nuclear factor-κB in peripheral blood mononuclear cells of normal subjects, an effect prevented by antioxidants present in red wine. We compared the effects of a high-fat meal and a high-carbohydrate meal (pizza), with or without dietary antioxidants, on the levels of soluble intercellular adhesion molecule-1 (sICAM-1) and vascular adhesion molecule-1 (sVCAM-1) in normal subjects. The genes of adhesion molecules are regulated by nuclear factor-κB,[2] and circulating adhesion molecules are considered a molecular marker of early atherosclerosis.[3]

We studied 25 healthy non-obese volunteers (13 men and 12 women) aged 27 ± 5.3 years (mean$\pm$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 (pizza) meal (758 kcal; 17 g of fat, 2.2 g of saturated fat, 144 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).

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,[4] and humans are usually in a nonfasting state. Pizza and vegetables do not increase stickiness of endothelium, which may contribute to the healthier cardiovascular outlook of people consuming a Mediterranean diet.[5]

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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,[1] that LDL upregulates CAM expression in cultured human endothelial cells,[2] and that hyperlipemic patients have increased VCAM-1 serum levels.[3]

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)[4] and vitamin E,[5] 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 contrast, Seljeflot et al[3] 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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