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File: ■ Cocoa
■ Cardiovascular Disease

HC 120391-391

Date: December 31, 2009

RE: Anti-inflammatory Effects of Cocoa Consumption May Help Prevent Atherosclerosis

Monagas M, Khan N, Andres-Lacueva C, et al. Effect of cocoa powder on the modulation of inflammatory biomarkers in patients at high risk of cardiovascular disease. *Am J Clin Nutr*. 2009;90:1144-1150.

Studies have indicated that dietary flavonoids may help prevent coronary heart disease (CHD). Cocoa and its products are a rich source of dietary flavonoids. The health benefits of cocoa are related to the capacity to improve lipid profiles and insulin sensitivity, lower blood pressure, reduce platelet activity and function, and diminish endothelial dysfunction.[1-3] Recent evidence has linked inflammation with the initiation and progression of atherosclerosis. According to the authors, few human trials have studied the anti-inflammatory effects of cocoa, and those studies have reported contradictory results—either neutral effects or single inflammatory biomarker changes, including endothelial-derived adhesion molecules, proinflammatory cytokines, and high-sensitivity C-reactive protein (hs-CRP). The authors conducted a randomized, crossover, controlled clinical trial to assess chronic cocoa consumption in subjects at high-risk for CHD on the expression of soluble adhesion molecules and proinflammatory cytokines associated with early atherosclerosis stages.

The authors recruited 47 high-risk subjects who were patients in the outpatient clinic of the Internal Medicine Department of the Institut d'Investigació Biomèdica August Pi i Sunyer at the University of Barcelona, Spain. Of those 47 recruits, 5 declined, leaving 42 (19 men and 23 women) participating subjects. Their mean age ± standard deviation was 69.7 ± 11.5 years. The subjects had diabetes mellitus or at least 3 or more of the following risk factors: tobacco smoking, hypertension, plasma low-density lipoprotein (LDL) cholesterol ≥160 mg/dL, plasma high-density lipoprotein (HDL) cholesterol ≤35 mg/dL, obesity (body mass index ≥30), and/or family history of premature CHD.

The study was a randomized, crossover, controlled clinical trial of two 4-week periods. After a 2-week lead-in diet, half of the subjects (who made up the C+M group) received two 20-g sachets of soluble cocoa powder (Nutrexpa S.A.; Barcelona, Spain) per day (1 for breakfast and another for the afternoon snack or after dinner) (total, 40 g per day) with 250 mL skim milk each (total, 500 mL per day). The other half of the subjects was placed in the M intervention group and consumed 500 mL skim milk per day with no cocoa. After 4 weeks, the interventions were switched between the 2 groups, for another 4-week period, with no washout period.

All subjects followed an isocaloric Mediterranean diet and were asked to exclude all other cocoa-containing foods and to limit intake of high polyphenol content foods like tea, red wine, vegetables, and fruit. At the beginning of the study and after each intervention period, the subjects completed a 3-day food record questionnaire. At baseline and after each intervention, anthropometric and blood pressure measurements were recorded, and fasting blood samples and a 24-hour urine specimen were collected. Immunophenotyping of peripheral blood mononuclear cells was performed.

The authors report the following results:

- Body weight was slightly higher after the C+M intervention than after the M intervention, with a mean increase of 0.50 kg (P=0.013).
- No significant changes were observed in systolic and diastolic blood pressure or in heart rate between the 2 interventions.
- Of the biochemical variables, serum concentrations of fasting glucose, total cholesterol, LDL cholesterol, and triglycerides did not change significantly after the 2 interventions. However, the HDL cholesterol concentration was modestly higher after C+M intake (mean increase: 2.2 mg/dL, P=0.033) than after M intake.
- The expression of the adhesion molecules on the surface of monocytes, but not on T lymphocytes, was significantly lower for very late activation antigen-4 (VLA-4) (P=0.005), CD40 (P=0.028), and CD36 (P=0.001) after C+M intake than after M intake.
- For the remaining molecules (lymphocyte function-associated antigen-1 [LFA-1], Mac-1, and Sialil-Lewis X [SLe^x]), no significant differences were observed on the monocyte or T lymphocyte surfaces.
- Regarding changes in circulating inflammatory markers, statistically significant lower concentrations of P-selectin (-10.8%, P=0.007) and intercellular adhesion molecule-1 (ICAM-1) (-9.7%, P=0.007) occurred with the C+M intervention than with the M intervention. Vascular cell adhesion molecule-1 (VCAM-1) and monocyte chemoattractant protein-1 (MCP-1) concentration changes were lower but were not statistically significant. E-selectin, interleukin-6 (IL-6), and hs-CRP concentrations remained almost constant after C+M intake in comparison with M intake.

The authors cite other studies on consumption of various cocoa products in which the outcomes are mixed and contradictory. They conclude that the results of their study suggest that the common form of intake of cocoa and its polyphenols in milk may modulate inflammatory mediators in patients at high risk for cardiovascular disease. "These anti-inflammatory effects, together with other previously reported effects, including those of antioxidant, antiplatelet, and positive vascular effects, may contribute to the overall benefits of cocoa consumption against atherosclerosis." The issue of weight gain with cocoa use needs more in-depth study; those who use cocoa products daily should incorporate an equivalent caloric reduction in their normal diet.

—Shari Henson

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