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RE: High-polyphenol Chocolate Protects against Acute Hyperglycemia-induced Endothelial Dysfunction and Oxidative Stress


Type 2 diabetes mellitus is associated with increased cardiovascular risk, which may be in part due to the inflammatory effects of hyperglycemia. Such inflammation may lead to increased endothelial dysfunction and oxidative stress, both of which have been measured by biomarkers of nitric oxide and endothelial function in healthy populations or people with type 2 diabetes.¹ Cocoa (*Theobroma cacao*) polyphenols, such as monomeric flavan-3-ols (e.g., epicatechin) found in chocolate, have demonstrated beneficial cardiovascular effects in healthy and diabetic populations both in the fasting state and 2 hours after ingestion.²,³ Moreover, a meta-analysis suggests cocoa consumption improves endothelial function. However, it is unknown whether cocoa polyphenols can protect against the inflammatory effects of an oral glucose load. Therefore, the aim of this double-blind, randomized, controlled, crossover study was to investigate the effects of consuming high-polyphenol chocolate, prior to an oral glucose load, upon endothelial function and oxidative stress in people with type 2 diabetes during acute transient hyperglycemia.

A total of 10 patients with type 2 diabetes mellitus who were being treated with metformin or lifestyle behaviors alone (aged 40-75 years; median age=61 years; 9 males and 1 female) were recruited. Patients underwent a 2-week "wash-out" period where they abstained from foods with high polyphenol content, including cocoa and chocolate products. After a 12-hour fast, baseline parameters for endothelial function were obtained by both functional hyperaemia peripheral artery tonometry (PAT) and from blood samples of patients. Following these tests, patients were randomly assigned to consume either 13.5 g of high-polyphenol chocolate (3.5% polyphenols; Acticoa™; Barry Callebaut Belgium N.V.; Belgium) or 13.5 g of low-polyphenol chocolate (control; identical to high-polyphenol product except with 0.9% polyphenols) with 200 ml of water. A 75-g oral glucose load was given to patients 60 minutes after ingestion of the chocolate, and then again after 120 minutes; the same measurements taken at baseline were repeated. A 24-hour urine sample was obtained at baseline and after the test period to measure the oxidative stress marker 15-F2t-isoprostane. Dietary intake
was also recorded during the period of urine collection to assess dietary adherence. Following a 1-week washout period, patients were crossed over to the other treatment.

The 10 patients in the study were obese (body mass index [BMI]: 32.5 ± 6.0 kg/m²), had good metabolic control (hemoglobin A1c [HbA1c]: 48 ± 5 mmol/mol; 6.5 ± 0.7%), and total cholesterol (3.9 ± 1.4 mmol/L). Baseline results indicated no significant differences for glucose, insulin, endothelial function, or oxidative stress. There were also no differences in area under the curve for glucose during the 75-g glucose load (P=0.77). There were no significant differences between diet and physical activity among the groups.

A significant difference (P=0.03) was seen in 15-F2t-isoprostane between the high-polyphenol chocolate (110 ± 3.0 mg/mol) and control (207.1 ± 5.7 mg/mol) treatments. An improvement in endothelial function was also seen when the oral glucose load was preceded by high-polyphenol chocolate (P=0.01); this may have been in part a regression to the mean, as baseline measurements between the 2 groups differed by 0.3%, but this was not found to be significant (P=0.09). Furthermore, the control treatment indicated more oxidative stress (P=0.02) and intercellular adhesion molecule-1 (P=0.04) compared to baseline values.

Based on the percentage change from baseline, a significant improvement was found for endothelial function following high-polyphenol chocolate compared to the control. Furthermore, 3 of the 4 adhesion biomarkers (intercellular adhesion molecule-1, E-selectin, and P-selectin glycoprotein ligand-1) used to assess endothelial function decreased significantly with the high-polyphenol chocolate compared to both baseline and the control. High-polyphenol chocolate also reduced urinary 15-F2t-isoprostane and was significantly different than the control.

Although this pilot trial was small, it is the first to show that cocoa can protect against both acute hyperglycemia-induced endothelial dysfunction and oxidative stress in people with type 2 diabetes. A potential mechanism for these effects may involve a reduction in reactive oxygen species, which may prevent depletion of nitric oxide and thereby endothelial dysfunction, or an effect on angiotensin-converting enzyme (ACE). More trials are warranted to evaluate the mechanisms involved in the protective effects of cocoa consumption in relation to hyperglycemia-induced endothelial dysfunction and cardiovascular disease.

—Laura M. Bystrom, PhD

References