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Original Contribution

Effects of black tea consumption on plasma catechins and markers of oxidative stress and inflammation in patients with coronary artery disease

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Abstract

We previously demonstrated that black tea consumption reverses endothelial dysfunction in patients with coronary artery disease. To investigate potential mechanisms of this effect, we examined plasma catechins and systemic markers of oxidation, inflammation, and antioxidant protection from 66 subjects enrolled in that study. We collected samples at baseline, 2 h after 450 ml of black tea (acute), after 4 weeks of 900 ml of black tea per day (chronic), and after acute and chronic consumption of water. Total catechins increased 33% after acute tea ($P < 0.05$) and 29% after chronic tea ($P < 0.05$). Of individual catechins, plasma epicatechin gallate (ECG) concentration significantly increased with acute tea consumption, and plasma epicatechin (EC) increased with chronic tea consumption. Tea consumption did not improve plasma antioxidant capacity and did not reduce urinary 8-hydroxy-2′-deoxyguanosine, or urinary 8-isoprostane levels. Changes in catechin levels did not correlate with changes in endothelial function, plasma markers of oxidative stress, or C-reactive protein. In contrast, endothelial function at baseline correlated with dietary flavonoid intake ($\beta = 0.32$, $P = 0.02$) and with baseline plasma EC concentration after adjusting for confounding variables ($\beta = 0.39$, $P = 0.03$). These findings suggest that the benefits of black tea consumption on endothelial function may not be attributable to tea catechins or a systemic antioxidant or anti-inflammatory effect. Chronic dietary flavonoid status appears to relate to endothelial function, possibly suggesting that other flavonoids or polyphenolic components of tea favorably influence vascular health and risk for cardiovascular disease.

Keywords: Endothelium; Catechins; Tea; Antioxidants; Flavonoids; Free radicals

Introduction

Numerous epidemiological studies have reported inverse associations between tea consumption and cardiovascular events [1]. Although several studies failed to observe such a relation [2,3], those findings may have been confounded by high baseline tea consumption or the socioeconomic status of the participants [1]. Additional studies indicate that polyphenolic flavonoids in tea may mediate the observed cardiovascular benefits [4–6]. Among the many mono- and polymeric polyphenolic compounds found in green and black tea, investigators have recently focused on the catechins, in part because they are more readily measurable, but also because catechin intake correlates inversely with cardiovascular risk [7]. In addition, recent experimental studies have demonstrated protective effects of individual catechins on the vasculature [8–10].

Abbreviations: EC, epicatechin; ECG, epicatechin gallate; EGC, epigallocatechin; EGCG, epigallocatechin gallate; ORAC, oxygen radical absorbance capacity; FRAP, ferric-reducing ability of plasma; CRP, C-reactive protein; ANOVA, analysis of variance.

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The mechanisms that account for the benefits of catechins and other flavonoids remain incompletely understood. Several prior studies focused on the antioxidant properties of these compounds that might prevent lipid peroxidation and oxidative modification of DNA and proteins that may contribute to atherogenesis [11]. Flavonoids also have anti-inflammatory and antithrombotic properties that might reduce the development and/or clinical expression of cardiovascular disease [10,12,13]. In addition, recent studies suggest that these compounds may act by improving the function of the vascular endothelium [1]. In particular, flavonoids increase the production and bioavailability of endothelium-derived nitric oxide, a potent vasodilator and inhibitor of platelet activity and inflammation in the vascular wall [8,9,14–16]. In support of those findings, clinical studies have shown that consumption of tea and other flavonoid-containing beverages improves endothelium-dependent vasodilation in patients with cardiovascular disease and/or risk factors [17–20].

We recently reported that chronic black tea consumption improves endothelial function and increases total plasma catechins in patients with coronary artery disease [17]. The present study utilized samples from that study to investigate the possible contribution of individual catechins to the observed improvement in endothelial function. In addition, we measured systemic markers of oxidative stress and inflammation to gain further insight into the potential mechanisms of benefit.

Methods

Subjects

The details of patient eligibility and recruitment for this study have been previously reported [17]. Briefly, we enrolled consecutive subjects with angiographically proven, clinically stable coronary artery disease. Patients taking antioxidant supplements (vitamin C >60 mg per day or vitamin E >30 IU per day) were excluded. The Institutional Review Board of Boston University Medical Center approved the protocol. We obtained written informed consent from all participating subjects.

Study design

We previously described the details of subject preparation and tea consumption [17]. Briefly, subjects made three visits to our clinical research unit and consumed black tea or water (900 ml per day) for 4 weeks between visits. The black tea for this chronic phase was supplied to subjects as a freeze dried powder, reconstituted in hot or cold water, and consumed with additives such as milk or sugar according to the subject's preference. Subjects completed chronic tea consumption the evening before the follow-up visit (approximately 14 h before sample collection and assessment of vascular function). During each visit, we also examined the acute response to each beverage by measuring endothelial function before and 2 h after subjects drank 450 ml of freshly brewed black tea or an equivalent volume of water. Analysis of the tea preparations was previously reported [17], and total catechin content was 12.9 and 13.3 mg/dl and the total polyphenol content was 150 and 163 mg/dl for the freeze-dried and freshly brewed tea, respectively.

Subjects continued their usual diet until entry into the study, and average flavonoid consumption (flavonols, quercetin, kaempferol, myricetin, and catechins) was estimated by a 1-week food frequency questionnaire and food flavonoid content charts [21]. Thereafter, patients refrained from drinking tea or red wine until completion of the study. In preparation for study of vascular function, subjects did not take vasoactive medications for 24 h prior to each visit. Smokers also refrained from tobacco use for at least 12 h prior to each visit. At each visit, we examined brachial artery vasodilator function by ultrasound and collected blood and urine samples.

Measurement of brachial artery vasodilator function

Flow-mediated dilation and nitroglycerin-mediated dilation (0.4 mg sublingual) were measured as previously reported [17]. Briefly, ultrasound images of the brachial artery were digitized and stored at baseline and 1 min after induction of reactive hyperemia, which was induced by 5-min cuff occlusion of the upper arm. Image analysis was performed in a blinded manner with commercially available software (Brachial Analyzer, Medical Imaging Applications, Iowa City, IA).

Biochemical analyses

The Boston Medical Center Clinical Chemistry Laboratory measured fasting serum total cholesterol, HDL cholesterol, triglycerides, and glucose using an automated analyzer (Hitachi 917). LDL cholesterol was calculated using the Friedewald formula [22]. We measured plasma concentrations of epicatechin (EC),[1] epicatechin gallate (ECG), epigallocatechin (EGC), and epigallocatechin gallate (EGCG) using high-performance liquid chromatography as previously described [23].

Total plasma antioxidant capacity was assessed using Trolox, an aqueous analog of α-tocopherol, as reference antioxidant. Whole and protein-free plasma antioxidant capacity was assessed via the oxygen radical absorbance capacity (ORAC) assay using the method described by Cao and colleagues [24]. The ferric-reducing ability of plasma (FRAP), which measures the ability to donate electrons, was assessed with the method of Benzie and Strain [25]. Units for both ORAC and FRAP are in micromole Trolox activity per liter plasma.

Serum C-reactive protein (CRP) was measured using a high-sensitivity nephelometric method by the Brigham and