Effect of Black Tea on Aortic Stiffness

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Background: We have shown that caffeine increases acutely arterial stiffness. Tea is a widely consumed beverage, however, its effect on arterial stiffness has not been defined.

Aortic stiffness is an important prognosticator of cardiovascular risk.

Methods: We studied 12 healthy volunteers (33±5 years) in a randomized, single-blind, crossover fashion. The subjects were studied on 3 separate occasions: a) 6 g of black tea, b) 175 mg of caffeine alone (the amount contained in 6 g of tea) and c) placebo. Cardiot-ferom-oral pulse wave velocity ( PWV ) was measured as an index of aortic stiffness using a validated automated, non-invasive device (Complior®).

Results:茶 had a biphasic effect on aortic stiffness. Initially it led to a marginal (P=0.07) increase in PWV, which, however, rapidly disappeared. In contrast, caffeine alone led to a sustained increase in PWV (P<0.05, figure). The reversal of aortic stiffness increase with tea after the initial 30 minutes can be attributed to a beneficial effect of tea flavonoids that peak later than caffeine. Pressures were increased in a similar manner both with tea and caffeine (ystolic: by 8.8 and 7.8 mmHg respectively, P<0.001 for both).

Conclusions: Tea shows a tendency to increase initial aortic stiffness due to the caffeine that it contains. However, this effect is promptly counterbalanced by a beneficial effect of tea flavonoids. This finding provides valuable insights for the effects of tea consumption on the cardiovascular system.

Preservation of Brachial Artery Endothelial Function in Otherwise Healthy Patients With Obstructive Sleep Apnea

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Background: Obstructive sleep apnea (OSA) has been implicated in several cardiovascular disease conditions including hypertension, heart failure and cerebrovascular disease. Impaired endothelial function is thought to be involved in risk for future cardiovascular disease in OSA. We tested the hypothesis that otherwise healthy OSA patients, in the absence of any confounding factors, have impaired brachial artery endothelial function.

Methods: We studied 16 newly diagnosed, never treated OSA patients (age: 44.7±3.7 years; apnea-hypopnea index: 45±10 events/hour) and 16 matched normal controls (age: 43±2.7 years; apnea-hypopnea index: 2±4 events/hour). All subjects were on no medications and free of any other diseases. None of the subjects smoked and both patients and controls had similar body mass index, blood pressure, fasting glucose and plasma lipids. Control subjects underwent complete polysomnography to exclude occult OSA. Conduit-vessel endothelial function was evaluated by high-resolution ultrasound of the brachial artery. Brachial artery diameter was measured at baseline and after five minutes of ischemia induced by cuff inflation as a measure of endothelium-dependent vasodilation, and after sublingual administration of nitroglycerin, endothelin-independent vasodilation.

Results: Data are presented as mean ± standard error. Baseline brachial artery diameters were similar in OSA and control subjects (4.34 ± 0.1 mm in OSA and 4.04 ± 0.1 mm in controls; p= 0.12). Percent changes of brachial artery diameter in response to ischemia were similar in both groups (7.8 ± 0.8% in OSA vs 6.5 ± 1.3 in controls; p=0.73). Percent changes of brachial artery diameter to nitroglycerin were also similar in both groups (15.0 ± 1.8% in OSA vs 15.3 ± 1.3% in controls; p=0.91), thus confirming the absence of structural abnormalities of conduit-vessels in OSA patients.

Conclusions: We conclude that in otherwise healthy patients with OSA, in the absence of potential confounding factors that would affect measurements of brachial artery endothelial function, there is no evidence of impaired endothelial function in conduit-vessels.

Influence of Coenzyme Q10 and Cerivastatin on the Flow-Mediated Vasodilation of the Brachial Artery: Results of the ENDOTACT Study

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Aim: Endothelial dysfunction (ED) is the functional prepulse in atherosclerosis. Different studies could show a positive effect of statins on ED. Coenzyme Q10 (CoQ10) is known as a potent natural antioxidant which is part of mammalian mitochondria. Since the production of CoQ10 under physiological conditions is HMG-CoA-Reductase dependent, an effect of statin therapy on CoQ10 levels is discussed. Aim of the present study was to evaluate the effects of CoQ10 on ED of the brachial artery, and the influence of statin therapy on plasma CoQ10 levels.

Methods and Results: 25 male patients with manifest ED (flow-mediated vasodilation (FMD%) < 4.5%) were included in this prospective, randomized, cross-over study. ED of the brachial artery was assessed by the use of high-resolution ultrasound. Each patient had to pass through three treatment phases in a randomized order (1: single therapy with cerivastatin (C), 2: single therapy with CoQ10, 3: combination therapy). FMD% significantly improved throughout all treatment phases (1: 3.50 ± 4.05% vs 8.60 ± 6.39%, p=0.009; 2: -0.25 ± 4.0% vs 7.06 ± 4.39%, p=0.004; 3: 3.14 ± 3.54% vs 8.82 ± 5.78%, p=0.011). C led to a significant decrease of CoQ10 plasma levels (1.23 ± 0.34 vs 0.87 ± 0.39 μg/ml, p=0.004).

Conclusion: Our results indicate a positive influence of CoQ10 supplementation on human ED, which appears to be independent of lipid-lowering and comparable to statin therapy. In addition, statin therapy lowered CoQ10 plasma levels. The pathophysiological relevance of this finding remains, however, unclear. Although large-scale studies evaluating other antioxidants failed to demonstrate a positive prognostic effect, CoQ10 has never been evaluated in larger trials. Experimental as well as our clinical results indicate that OSA warrants further attention in atherosclerosis research.

Cardiovascular Pharmacology

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m., Morial Convention Center, Hall G

Presentation Hour: 3:00 p.m.-4:00 p.m.

Pharmacokinetics of Clopidogrel and Its Active Metabolite in Human Plasma

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Background: Clopidogrel an ADP receptor antagonist is an inactive prodrug that is converted into both an active metabolite (2-1-(1H-82-chlorophenyl)-(2-oxetanyl)-4-sulfanyl-3- piperidnlydine)acetic acid) and an inactive carboxy metabolite (S2H26334) in the liver. So far, there are only data available regarding the pharmacokinetics of the inactive metabolite. The plasma kinetics of clopidogrel have not yet been elucidated and the active metabolite has not been measured in vivo so far. We developed a method to determine the plasma concentrations of clopidogrel and its active metabolite after a loading dose of 600 mg clopidogrel.

Methods: Ten healthy volunteers (9 men, 1 woman, age 25 – 48) received a single oral dose of 600 mg clopidogrel. Plasma was collected predose and at 0.5; 1; 1.5; 2; 3; 6 and 9 hours postdose. After protein precipitation with acetonitrile the concentrations of clopidogrel, the carboxy metabolite, and the active metabolite were measured by LC-ESI/MS/MS (TSQ Quantum Thermo Finnigan).

Results: Cmax, tmax and t1/2 (mean ± SEM) plasma concentrations of clopidogrel were 42.55 μg/ml ± 11.24; 1.45 h ± 0.27 and 1.6 h ± 0.13. Tmax and t1/2 were 1.65 h ± 0.23 and 3.23 h ± 0.17 for the carboxy metabolite. The plasma concentrations of the active metabolite of clopidogrel were correlated with clopidogrel plasma concentrations (r = 0.575; p < 0.001; n = 87). Dilatuzem (1 μg/ml) was used as internal standard.

Conclusions: This is the first report of the pharmacokinetics of clopidogrel and its active metabolite in man plasma. Measurement of clopidogrel and metabolite plasma concentrations may lead to a deeper understanding of clopidogrel resistance.

Negative Inotropic Effect of Selective AT2 Receptor Stimulation and Its Modulation by Endocar dial Endothelium, Nitric Oxide and Prostaglandins

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Introduction: Angiotensin II (ATII) is an endogenous peptide whose effects are mediated by two types of receptors, AT1 and AT2. AT2 receptors are responsible for the vasoconstrictor, positive inotropic and growth promoting properties of AT-II, while AT2 receptors have been linked to vasodilatation and anti-mitogenic properties. In this study we investigated the effects of selective AT2 receptor stimulation on myocardial contractility, which are not yet known. Methods: Effects of selective AT2 receptor activation were evaluated in rabbit right papillary muscles (n=35) by adding, to the superfusing solution ( Krebs-Ringer; 1.8 mmCaCl2; 35°C), increasing doses of AT-II (10-7, 10-6, 10-5 M) in the presence of a selective AT1 receptor antagonist (ZD7155, 10-5 M). Effects of select-