Drug Monitor

A Couple of "Cuppas" May Be a Good Thing for Coronary Artery Disease Patients

A 200-mg capsule of caffeine can improve brachial endothelial function in patients with coronary artery disease (CAD), say researchers from Sheba Medical Center in Tel Hashomer, Israel. In their double-blind, placebo-controlled study of 40 patients with documented, stable CAD and 40 volunteers without CAD, they found caffeine also lowered markers of inflammation. Increasing serum caffeine levels by almost 4 µg/mL reduced high-sensitivity C-reactive protein (hs-CRP) and increased serum adiponectin, a protein with antidiabetic and antiatherogenic properties.

Participants fasted overnight, and discontinued all medications for at least 12 hours and all caffeine for at least 48 hours. They were given 200-mg caffeine capsules (1 cup of coffee equals 80 mg caffeine) or placebo at 7:00 AM. One hour after taking caffeine, participants underwent brachial artery flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NTG) using high-resolution ultrasound.

Although acute caffeine ingestion significantly improved FMD in CAD patients (from 5.6% to 14.6%), improvement was more marked in those without CAD (from 8.4% to 18.6%). Acute caffeine ingestion did not significantly change NTG in the 2 groups. Heart rate at rest did not change in either group. Systolic and diastolic blood pressure did not change in the non-CAD participants, but it significantly increased in the CAD patients. In multivariate analysis, serum caffeine levels were independent predictors for percent FMD, after controlling for age, gender, CAD, baseline brachial artery diameter, and hyperlipidemia.

The study's findings differ from those of others. For example, another study found a cup of coffee decreased brachial FMD for as long as 1 hour or more after intake. The discrepancy, suggest the authors of the current study, could be explained by the fact that a cup of coffee contains other

ingredients, such as polyphenols and antioxidants, which may act differently on peripheral vasculature.

The researchers also note some weaknesses in their own study. For example, FMD was only measured twice: before the study began and 1 hour after caffeine ingestion. They suggest that 4 measurements (baseline, 30 minutes, 1 hour, 2 hours) would have better described the FMD changes. Further, few women participated in the study, and a relatively large dose of caffeine (equal to 2.5 cups of coffee) may not be generally accepted as typical consumption. Longer-term, larger studies are warranted, they suggest, to investigate the effect of long-term caffeine intake on the heart and on cardiovascular risks.

Source: *Am J Cardiol.* 2011;107(5):1255-1261. doi:10.1016/j.amjcard.2010.12.035.

Adding a Third Drug to Diabetes Treatment

When it comes to adding a third antihypoglycemic agent to metformin-plus-sulfonylurea therapy, let the patient be the guide. According to a meta-analysis by researchers from Universidade Federal do Rio Grande do Sul (Federal University of Rio Grande do Sul) in Porto Alegre, Brazil, all of the choices were pretty much the same; therefore, it comes down to individual patient needs.

The researchers looked at 18 trials that lasted at least 24 weeks and involved 4,535 patients. Study treatments added acarbose, thiazolidinediones, glucagon-like peptide-1 (GLP-1) agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, or insulins.

When added to metformin and a sulfonylurea, all of the drugs reduced hemoglobin A_{1c} levels about equally (–0.96%). Insulin was associated with more weight gain and doubled the frequency of severe hypoglycemic episodes. GLP-1 agonists led to more weight loss than did other agents and might be chosen as a third agent on that basis, the researchers say. But, they were also associated with more severe hypoglycemic reactions than any other drug class, except insulin. Thiazolidinediones seemed to cause more weight gain (4.25 kg) than insulins (2.84 kg), but the findings were not significantly different.

Thus, the researchers conclude, when choosing a third drug for diabetes therapy, individualization is the

key, taking into account the patient's clinical features, such as the importance of weight changes and incidence of hypoglycemia.

Source: *Ann Intern Med.* 2011;154(10):672-679.

Amino Acids Help Combat Infection in Elderly

Essential amino acids (EAAs) can help cut down on infections among geriatric patients, according to a study at the 220-bed Istituto Geriatrico Piero Redaelli in Milan, Italy.

In the 30-day study, 80 patients were given an oral nutritional mixture supplement that provided 8 g/day of EAAs or a similar isocaloric product containing maltodextrine.

Overall, 54 patients (67.5%) developed an infection. When the groups were analyzed separately, however, the infection rate was 30% lower in the EAA group: 21 patients (52.5%), compared with 33 (82.5%) in the placebo group.

Patients who developed infections were significantly older, more anemic, and had worse inflammation, reduced serum concentration of nonreactant proteins, increased blood urea nitrogen and serum creatine levels, and lower energy and protein intakes. C-reactive protein (CRP) and hemoglobin (Hb) levels were statistically associated with higher risk for future infection. Indeed, the researchers say, patients with a CRP $>$ 0.8 mg/dL had 4 times the risk of patients with CRP $\leq$ 0.8 mg/dL. Hb concentration $<$ 13 g/dL in men, and 12 g/dL in women, more than tripled the risk.

The researchers point to studies that have shown amino acids influence immune function in many ways, including boosting protein synthesis. Interestingly, they add, their formula did not contain glutamine, the most important amino acid for immune function. However, the principal amino acid in the formula they used, leucine, is a potent stimulator of glutamine formation, directly acts on immune cell function, and is the most important amino acid for protein synthesis. In other research, they have found that 8 g/day of EAAs increased baseline plasma glutamine levels in healthy older subjects by 10%, lasting for 3 hours, without impairing concentration of arginine, another amino acid essential in immune function.

Source: *Arch Gerontol. Geriatrics.* 2011;52(5-6): e123-e128. doi:10.1016/j.archger.2010.09.005.

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