Tips from Other Journals

Tips from Other Journals are written by the medical editors of *American Family Physician.*

The trade names of drugs listed in Tips from Other Journals are based on what is currently available and not necessarily the brand of drug that was used in the study being discussed.

Do Coffee and Tea Help Prevent Diabetes Mellitus?

Background: A meta-analysis published in 2005 reported that the risk of developing diabetes mellitus was approximately two-thirds lower among persons who consume high levels of coffee compared with those who consume less. Since then, additional studies have suggested that tea and decaffeinated coffee may also provide a similar benefit. This suggests that ingredients other than caffeine may have a protective effect (e.g., lignans or chlorogenic acid, which have antioxidant properties). Huxley and colleagues updated the previous meta-analysis, and conducted an overview of the evidence for decaffeinated coffee and tea consumption on subsequent risk of developing diabetes.

The Study: The authors systematically reviewed prospective studies from 1966 to July 2009, and examined the association between new-onset type 2 diabetes and the intake of coffee, decaffeinated coffee, or tea (i.e., green, black, and oolong). Cross-sectional studies and studies that did not specify the number of cups of beverages consumed per day were excluded.

Results: Twenty studies including 517,325 participants were reviewed, with a median follow-up of two to 20 years. Most participants were white; 21 percent were Asian. After controlling for multiple variables, each cup of coffee consumed daily was associated with an approximately 7 percent reduction in the risk of developing diabetes. Overall, consuming three to four cups of coffee per day was associated with a 25 percent risk reduction compared with persons drinking two or fewer cups per day; however, a greater effect was reported in the smaller studies. Estimates using the six largest studies found a 15 percent reduction in diabetes risk at this level of intake.

Persons who drank more than three to four cups of decaffeinated coffee per day were less likely to develop diabetes than those who did not consume decaffeinated coffee (relative risk = 0.64). Three to four cups of tea per day also showed some protective effect (relative risk = 0.82).

Conclusion: The authors conclude that high intake of coffee, decaffeinated coffee, or tea is associated with substantial reductions in the risk of new-onset diabetes. The authors believe that a causal effect is supported by the presence of an apparent dose-response relationship. However, they caution that it is unknown whether their findings are applicable to nonwhite populations because of the predominantly white study population.

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Source: Huxley R, et al. Coffee, decaffeinated coffee, and tea consumption in relation to incident type 2 diabetes mellitus: a systematic review with meta-analysis. *Arch Intern Med.* December 14, 2009;169(22):2053-2063.

What Is the Best Treatment for Childhood Absence Epilepsy?

Background: Childhood absence epilepsy is the most common form of epilepsy in children. Ethosuximide (Zarontin), lamotrigine (Lamictal), and valproic acid (Depakote) are options for initial monotherapy, but their relative effectiveness and tolerabilities have not been determined. Glauser and colleagues conducted a double-blind, randomized controlled trial to assess for these effects and determine the optimal therapy for childhood absence epilepsy.

The Study: The authors enrolled 453 children 2.5 to 13 years of age who were newly diagnosed with childhood absence epilepsy. Patients received ethosuximide (maximal dosage: 60 mg per kg or 2,000 mg per day), lamotrigine (maximal dosage: 12 mg per kg or 600 mg per day), or valproic acid (maximal dosage: 60 mg per kg or 3,000 mg per day). Medications could be titrated upward for persistent seizures, up to the maximal allowed dosages. The primary outcome was freedom from treatment failure after 16 to 20 weeks; treatment failure was defined as persistent absence seizures, generalized tonic-clonic seizures, or drug-related systemic toxicity. Attentional dysfunction was the secondary outcome, measured by neuropsychological testing at baseline and at the conclusion of the study.

Patients were excluded if they had a history of other types of seizures, severe rashes with any medication, a

Table. Relative Effectiveness and Safety of Agents for Childhood Absence Epilepsy Seizures

Agent	*Odds ratio of controlling seizures without drug toxicity*	*Odds ratio of having persistent seizures*	*Odds ratio of attentional dysfunction*
Ethosuximide (Zarontin; versus lamotrigine [Lamictal])	2.66	0.19	1.56 (NS)
Valproic acid (Depakote; versus lamotrigine)	3.34	0.16	3.04
Valproic acid (versus ethosuximide)	1.26 (NS)	0.84 (NS)	1.95

NOTE: *All odds ratios are significant unless otherwise noted.*

NS = not significant.

major psychiatric disease, an autism spectrum disorder, abnormal liver enzymes or complete blood count, or any other clinically significant medical conditions.

Results: Baseline characteristics were similar among the groups, with a median age of seven years, five months. Overall, 47 percent of the patients were free from treatment failure at the end of the study. Patients taking ethosuximide or valproic acid were less likely to experience treatment failure (47 and 42 percent, respectively) compared with those taking lamotrigine (71 percent). More patients were seizure-free with ethosuximide and valproic acid than with lamotrigine *(see accompanying table)*. However, valproic acid was associated with more attentional dysfunction than ethosuximide or lamotrigine.

Conclusion: The authors conclude that ethosuximide and valproic acid are more effective than lamotrigine in controlling seizures associated with childhood absence epilepsy. However, valproic acid is associated with greater attentional dysfunction, indicating that ethosuximide is the more appropriate initial therapy for this seizure disorder.

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Source: Glauser TA, et al. Ethosuximide, valproic acid, and lamotrigine in childhood absence epilepsy. *N Engl J Med.* March 4, 2010;362(9):790-799.

Is BNP-Guided Treatment for Heart Failure Effective?

Background: B-type natriuretic peptide (BNP) and N-terminal pro-BNP levels are useful in diagnosing acute decompensated heart failure, and can also predict clinical outcomes in patients with chronic heart failure. It has been proposed that adjusting heart failure therapy to reduce BNP plasma levels may improve clinical outcomes. However, the benefit of this approach remains uncertain because many trials have been underpowered to detect the effect on major cardiovascular events. Porapakkham and colleagues performed a meta-analysis of prospective randomized controlled trials that examined BNP-guided therapy versus clinically guided treatment in the outpatient management of heart failure.

The Study: Trials had to have more than 20 patients and have clinically relevant end points (e.g., all-cause mortality, hospitalization) to be included in the meta-analysis. The likelihood of these end points was assessed when standard heart failure treatments (e.g., angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists, beta blockers) were titrated to improve clinical status (e.g., New York Heart Association [NYHA] functional class) versus adjusting treatment to acheive specified BNP or pro-BNP levels, with or without clinical status improvement (e.g., the Systolic Heart Failure Treatment Supported by BNP study had a target BNP level of less than 100 pg per mL [100 ng per L], whereas the Trial of Intensified versus Standard Medical Therapy in Elderly Patients with Congestive Heart Failure used a target N-terminal pro-BNP level of less than 400 pg per mL [400 ng per L] in addition to NYHA functional class II or lower in adults younger than 75 years).

Results: Eight trials with 1,726 patients were analyzed. All participants were 18 to 85 years of age and had NYHA functional class II or greater heart failure with left ventricular ejection fraction less than 50 percent. The mean follow-up duration was 17 months (range: three to 24 months). All-cause mortality was significantly lower among patients in the BNP-guided therapy group compared with those in the standard therapy group (relative risk = 0.76). Subgroup analysis found this effect was even more significant in patients younger than 75 years (relative risk = 0.52), but BNP-guided therapy did not reduce mortality in patients 75 years and older. No significant differences were noted between groups with regard to all-cause hospitalization or hospitalization-free survival.

Conclusion: The authors conclude that BNP-guided therapy can significantly lower all-cause mortality in patients younger than 75 years with chronic heart failure compared with standard therapy. However, all-cause hospitalization and hospitalization-free survival rates remain unaffected.

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Source: Porapakkham P, et al. B-type natriuretic peptide–guided heart failure therapy: a meta-analysis. *Arch Intern Med.* March 22, 2010;170(6):507-514. ■