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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.

Valsartan May Decrease the Incidence of Diabetes Mellitus

Background: Several trials have reported that inhibiting the renin-angiotensin system (i.e., with angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs]) may prevent patients with hypertension or other cardiovascular disease from developing diabetes mellitus. However, this effect was not a primary outcome of most trials, and results were not confirmed by systematic glucose measurements. McMurray and colleagues used the NAVIGATOR (Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research) trial to study the effectiveness of ACE inhibitors and ARBs at reducing the risk of diabetes and cardiovascular events in patients with impaired glucose tolerance.

The Study: Investigators randomized 9,306 patients to receive valsartan (Diovan) in dosages of 80 to 160 mg daily or placebo. All patients participated in a lifestyle intervention program designed to reduce the risk of diabetes. In addition to having impaired glucose tolerance, all eligible participants had preexisting cardiovascular disease or at least one risk factor for cardiovascular disease. Exclusion criteria included the use of antidiabetic medications within the previous five years, or the use of an ACE inhibitor or ARB for hypertension.

Three coprimary outcomes were evaluated: the incidence of diabetes; a composite cardiovascular outcome including development of heart failure, nonfatal myocardial infarction or stroke, unstable angina, arterial revascularization, or cardiovascular-associated death; and a similar composite cardiovascular outcome that excluded unstable angina and the need for revascularization.

Results: Diabetes was less likely to develop in the valsartan group than in the placebo group (33.1 versus 36.8 percent, respectively; hazard ratio = 0.86). Fasting and two-hour postload glucose levels were also lower in the valsartan group (–0.59 mg per dL [0.03 mmol per L] versus –3.15 mg per dL [0.17 mmol per L] in the placebo group). However, cardiovascular outcomes remained similar between the groups (14.5 versus 14.8 percent for placebo).

Conclusion: The authors conclude that valsartan therapy (in a dosage up to 160 mg daily) reduces the likelihood that patients with impaired glucose tolerance will develop diabetes (relative risk reduction = 14 percent). This translates into roughly 26 patients needing to be treated for five years to prevent one new case of diabetes. However, valsartan does not reduce the risk of cardiovascular events.

KENNETH T. MOON, MD

Source: The NAVIGATOR Study Group, McMurray JJ, et al. Effect of valsartan on the incidence of diabetes and cardiovascular events [published correction appears in *N Engl J Med.* 2010;362(18):1748]. *N Engl J Med.* April 22, 2010;362(16):1477-1490.

Probiotics vs. Antibiotics to Treat Lactation-Associated Mastitis

Background: Mastitis affects up to 33 percent of lactating mothers and is a common reason why women stop breastfeeding. It can also be difficult to treat because of its polymicrobial nature. Several strains of lactobacilli have shown promise as probiotic agents that might be useful in treating mastitis. Arroyo and colleagues compared the effectiveness of probiotic and antibiotic therapies in women with lactation-associated mastitis.

The Study: A total of 352 women with mastitis symptoms were randomized to receive one of three treatments: a daily capsule with 200 mg of a freeze-dried probiotic containing 9 $\log_{10}$ colony-forming units (CFUs) per mL of *Lactobacillus fermentum* (CECT5716), a similar amount of *Lactobacillus salivarius* (CECT5713), or an antibiotic prescribed by their physician. Patients were followed for 21 days, with pain scores and breast milk samples obtained at the beginning and end of the study. All patients had breast inflammation, painful breastfeeding, and initial milk bacterial counts of more than 4 $\log_{10}$ CFU per mL. Women with mammary abscesses, Raynaud syndrome, or any other breast-related pathology were excluded.

Results: Initial pain scores and bacterial counts were similar among the three groups. The three most ▶

Table. Risk of Adverse Events with High- vs. Low-Dose Colchicine for Gout Flare-ups

	Treatment group			*Odds ratio*		
Adverse event	*High-dose colchicine (%)*	*Low-dose colchicine (%)*	*Placebo (%)*	*High- vs. low-dose colchicine*	*Low-dose colchicine vs. placebo*	*High-dose colchicine vs. placebo*
Diarrhea	76.9	23.0	13.6	11.2	1.9*	21.3
Nausea	17.3	4.1	5.1	5.0	0.8*	3.9*
Vomiting	17.3	0	0	†	†	†
Serious adverse events‡	0	0	0	†	†	†

**—Not significant.*

†—Not calculable.

‡—For example, a life-threatening adverse event, need for hospitalization, or death.

common bacterial species identified were *Staphylococcus epidermidis, Staphylococcus aureus,* and *Streptococcus mitis* in statistically similar proportions among groups. By day 21, a greater bacterial reduction occurred in women receiving probiotics compared with antibiotics, with the greatest reduction in the *L. salivarius* group. Breast pain scores were also significantly lower in the probiotic groups, with complete recovery in 88 percent of the *L. fermentum* and 85 percent of the *L. salivarius* group by day 21, compared with 28.7 percent of the antibiotic group. Recurrence of mastitis was also significantly more common in the antibiotic group than in the *L. fermentum* or *L. salivarius* group (30.7, 10.5, and 7.1 percent, respectively).

Conclusion: The authors conclude that *L. fermentum* or *L. salivarius* is an effective alternative to antibiotics for the treatment of infectious mastitis during lactation.

KENNETH T. MOON, MD

Source: Arroyo R, et al. Treatment of infectious mastitis during lactation: antibiotics versus oral administration of lactobacilli isolated from breast milk. *Clin Infect Dis.* June 15, 2010;50(12):1551-1558.

Low-Dose Colchicine Effective for Acute Gout Flare-ups

Background: Although colchicine is commonly used to treat gout, dosing regimens have not been well studied. One randomized placebo-controlled trial reported that a mean dose of 6.7 mg (initially 1 mg orally, followed by 0.5 mg every two hours until relief or an adverse event occurred) improved pain within 48 hours, with diarrhea affecting all participants. Severe adverse events and death have occurred when colchicine is combined with P-glycoprotein and cytochrome P450 3A4 inhibitors (e.g., clarithromycin [Biaxin], erythromycin, cyclosporine [Sandimmune]). Low-dose colchicine regimens have never been fully evaluated. Terkeltaub and colleagues compared low- and high-dose colchicine with placebo in the treatment of gout flare-ups.

The Study: The AGREE (Acute Gout Flare Receiving Colchicine Evaluation) trial randomized 575 men and postmenopausal women to receive one of three treatments: low-dose colchicine (1.2 mg, followed by 0.6 mg one hour later [1.8 mg total]), high-dose colchicine (1.2 mg, followed by 0.6 mg every hour for six hours [4.8 mg total]), or placebo. Patients started the study medication within 12 hours of an acute gout flare-up and were monitored for adverse events (e.g., diarrhea). Simultaneous urate-lowering therapy was permitted. The primary end point was at least a 50 percent reduction in pain within 24 hours of the first dose without the need for a rescue medication.

Results: Overall, 185 patients had a gout flare-up during the study: 52 in the high-dose group, 74 in the low-dose group, and 59 in the placebo group. Less than one-third of patients were receiving concurrent urate-lowering therapy. Both high- and low-dose colchicine regimens were significantly more effective than placebo at relieving pain (32.7, 37.8, and 15.5 percent, respectively). Diarrhea was the most common adverse event, and was significantly more common in persons in the high-dose group compared with the other groups *(see accompanying table)*. Adverse event rates were similar between the low-dose colchicine and placebo groups.

Conclusion: Low-dose colchicine is as effective as the more traditional high-dose regimen in alleviating acute gout flare-ups, with an adverse event profile similar to placebo. The authors recommend an immediate change in clinical practice to use the low-dose regimen, which is consistent with recent expert opinion–based recommendations by the European League Against Rheumatism.

KENNETH T. MOON, MD

Source: Terkeltaub RA, et al. High versus low dosing of oral colchicine for early acute gout flare: twenty-four–hour outcome of the first multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-comparison colchicine study. *Arthritis Rheum.* April 2010;62(4):1060-1068. ■