PHARMACOLOGY WATCH

Evidence-based updates in clinical pharmacology

Are Vitamin and Mineral Supplements Really Beneficial?

In this issue: Vitamin and mineral supplements; antiplatelet therapy and drug-eluting stents; vitamin B12 deficiency and acid suppression; JNC8 releases new hypertension guidelines; and FDA actions.

Do supplements work for adults?

"Enough Is Enough: Stop Wasting Money on Vitamin and Mineral Supplements," is the title of an editorial in the December 17 issue of *Annals of Internal Medicine*. The strongly worded opinion piece is based on three studies in the same issue which suggest that vitamins and minerals are of no value for the healthy adult. The first study looked at use of high-dose oral multivitamins and minerals in more than 1700 patients who had a recent myocardial infarction and normal renal function. After an average follow-up of about 2.5 years, the supplements did not statistically reduce cardiovascular events. In the second study, nearly 6000 male physicians were given multivitamins or placebo over 12 years as part of the Physician's Health Study II to see if vitamins affect cognitive health in later life. Over the course of the study, the participants were given four tests of verbal memory, a strong predictor of Alzheimer's disease. Multivitamins had no effect on cognition and did not prevent cognitive decline. Finally, the U.S. Preventive Services Task Force did a systematic evidence review of vitamins and mineral supplements for the primary prevention of cardiovascular disease and cancer. They concluded that limited evidence supports any benefit from supplements, with two trials showing borderline-significant benefit for multivitamins on cancer in men only and no effect on cardiovascular disease (*Ann Intern Med* 2013;159:797-805, 806-814, 824-834, editorial 850-851). ■

Antiplatelet therapy and drug-eluting stents

Is 3 months of dual antiplatelet therapy enough after a drug-eluting stent? Researchers attempted to find out in a trial of more than 3100 patients with stable coronary artery disease (CAD) who underwent percutaneous coronary intervention (PCI) with a zotarolimus-eluting stent. Patients were then prescribed aspirin (100-200 mg daily) with clopidogrel (Plavix, 75 mg daily) for 3 months or 12 months with roughly the same number of patients in each group. The primary endpoint was net adverse clinical and cerebral events, including all-cause death, myocardial infarction, stroke, or major bleeding, with the secondary endpoint of major cardiac events. The primary outcome rate was the same in each group (P = 0.002 for noninferiority). Cardiac event rate was 8.3% in the short-term group and 7.4% in the long-term group (hazard ratio, 1.12; 95% confidence interval, 0.87-1.45). More importantly between 91 and 360 days (after stopping clopidogrel in the short-term group), the primary outcome was identical between the two groups at 2.6%. The authors conclude that in patients with stable CAD who were treated with zotarolimus-eluting stents, 3 months of dual antiplatelet therapy was noninferior to 12 months with regard to major clinical events and without a significantly higher risk of stent thrombosis (*JAMA* 2013;310:2510-2522). Larger studies

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are needed to definitively change the duration of therapy; however, this study offers some comfort for those PCI patients who need to stop clopidogrel early due to bleeding or surgery. ■

B12 deficiency and acid suppression

If your patient is on long-term acid-suppression therapy with a proton pump inhibitor (PPI) or histamine 2 (H2) blocker, be concerned about vitamin B12 deficiency. That is the message from a new study by Kaiser Permanente. Chronic use of acid-suppressing medications is common with hundreds of millions of prescriptions written every year as well as widespread over-the-counter use. The researchers found that among patients diagnosed with B12 deficiency, 12% were dispensed ≥ 2 year's supply of a PPI, and 4.2% were dispensed ≥ 1 year's supply or more of an H2 antagonist, which was significantly higher than the rate of patients without B12 deficiency (odds ratio [OR] of B12 deficiency with PPI 1.65 95% confidence interval (CI), 1.58-1.73); OR of B12 deficiency with H2 blocker 1.25 (95% CI, 1.17-1.34). The authors conclude that previous and current gastric acid suppression was significantly associated with the presence of B12 deficiency (*JAMA* 2013;310:2435-2442). Vitamin B12 deficiency is probably more common than we think and the long-term effects can be devastating. It is good to keep this in mind for patients on chronic acid-suppressing medications. ■

JNC8 releases new hypertension guidelines

The Eighth Joint National Committee (JNC8) has finally published updated hypertension guidelines more than 10 years since the JNC7. The guidelines raise the blood pressure (BP) treatment threshold for otherwise healthy adults aged 60 or older from a systolic BP of 140 mmHg to 150 mmHg. Treatment thresholds for diabetics or those with chronic kidney disease (CKD) remain at 140 mmHg, and the threshold of treatment of diastolic BP remains at 90 mmHg for all patients. The JNC7 recommended initial therapy with thiazide-type diuretics for most patients while the JNC8 recommends initial therapy with thiazides, calcium channel blockers (CCBs), angiotensin-converting enzyme (ACE) inhibitors, or angiotensin-receptor blockers (ARBs) for nonblack patients. For black patients, initial therapy should be a thiazide or a CCB. For all patients with CKD, initial therapy should include an ACE inhibitor or an ARB (*JAMA* published online December 18, 2013. Doi:10.1001/jama.2013.284427). ■

FDA actions

The FDA has approved a new combination, once-daily inhaler for the treatment of chronic obstructive pulmonary disease (COPD). The new agent combines two long-acting agents, the anticholinergic umeclidinium and the beta-agonist vilanterol. The safety and efficacy were evaluated in more than 2400 patients with COPD in which treated patients showed improved lung function compared to placebo. Like other drugs containing long-acting beta-agonists, the drug carries a boxed warning regarding the increased risk of asthma-related death. The drug is not approved for asthma. Umeclidinium and vilanterol inhalation powder will be marketed by GlaxoSmithKline as Anoro Ellipta.

The FDA has approved the first generic version of duloxetine (Cymbalta). The drug is approved for depression, neuropathic pain, generalized anxiety disorder, and fibromyalgia. Multiple generic manufacturers have been approved to market duloxetine.

The FDA has issued a warning regarding the attention deficit hyperactivity disorder (ADHD) drug methylphenidate and priapism (painful and prolonged erections). Methylphenidate is the active ingredient in many commonly used ADHD medications, including Ritalin, Concerta, Daytrana, Focalin, and Metadate. Although rare, priapism can lead to permanent penile damage, so patients should be warned about this potential side effect. Another ADHD drug atomoxetine (Strattera) has also been associated with priapism, perhaps at an even higher rate, but reports are limited so far.

The FDA is concerned about the safety of consumer antibacterial soaps that contain the ingredients triclosan (liquid soaps) and triclocarban (bar soaps). There is currently no evidence that these agents are any more effective than washing with plain soap and water and there is concern that they may pose a health risk such as bacterial resistance or even hormonal effects. They FDA is requiring the manufacturers of these products to demonstrate long-term safety and efficacy if they are to remain on the market. Both triclosan and triclocarban are found in a wide variety of consumer soaps, including Dial liquid and bar soap, Clearasil, and many generic house brand soaps such as CVS antibacterial soap. ■