Pharmacology Watch

Evidence-based updates in clinical pharmacology

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CDC: U.S. Must Intensify Efforts to Improve Safer Prescribing of Prescription Opioids

USPSTF Modifies Statin Treatment Guideline

The U.S. Preventive Services Task Force (USPSTF) has issued a draft recommendation statement on Statin Use for Primary Prevention of Cardiovascular Disease in Adults: Preventive Medication. The guideline builds on the "risk-based" statin treatment recommendations rather than the previous "treat-to-target" method of treating to a specific LDL cholesterol. The new draft recommends low- to moderate-dose statins for adults 40 to 75 years of age without a history of cardiovascular disease and who have at least one cardiovascular disease risk factor (dyslipidemia, diabetes, hypertension, or smoking), with a calculated 10-year risk of a cardiovascular event of ≥ 10%. For those individuals with one risk factor and a calculated risk of 7.5-10%, a low- to moderate-dose statin should be considered. There is insufficient evidence to assess the risk vs harm for adults ≥ 76 years of age without a history of myocardial infarction or stroke. Low-dose statins include lovastatin 20 mg, pravastatin 10-20 mg, and simvastatin 10 mg. Moderate-dose regimens include atorvastatin 10-20 mg, lovastatin 40 mg, rosuvastatin 5-10 mg, and simvastatin 20-40 mg (uspreventiveservicestaskforce.org).

Report: Opioid Overdose Deaths Up 200% Since 2000

The national opioid overdose epidemic is worsening, according to a report in the *Morbidity and Mortality Weekly Report* (MMWR). The rate of opioid overdose deaths has increased 200% since 2000, with a record high in 2014 of 9 per 100,000, a 14% increase over 2013. There were dramatic increases in both prescription-based overdoses and overdoses from heroin. Illicitly manufactured fentanyl contributed to the epidemic in 2014. Deaths from prescription drugs, such as morphine and oxycodone, accounted for 3.8 deaths per 100,000, a 9% increase. As the opioid overdose epidemic continues unabated, the CDC recommends that "efforts to improve safer prescribing of prescription opioids must [intensify]," noting that opioid pain reliever prescriptions have quadrupled since 1999. The CDC also recommend expanding access to and use of naloxone for those who are at risk of overdose (*MMWR* Dec. 18, 2015/64 [Early Release]; 1-5).

Comparing Type 2 Diabetes Drug Therapies

A new evidence review compares the weekly glucagon-like peptide-1 receptor agonists (GLP-1RAs) for the treatment of type 2 diabetes. Three of the drugs are marketed in the United States, including dulaglutide (Trulicity), once weekly exenatide (Bydureon), and albiglutide (Tanzeum). Other drugs in the review included semaglutide, which is in Phase III trials, and taspoglutide, which is no longer in development. Each drug reduced A1c levels, with dulaglutide and taspoglutide resulting in the greatest difference (-0.4%; 95% confidence interval, -0.7%

to -0.2%). Semaglutide and taspoglutide also resulted in the largest reduction in body weight, although once-weekly exenatide also reduced weight but to a lesser degree. Each drug had minimal to no effect on blood pressure, blood lipids, or C-reactive protein levels (*Ann Int Med* published online Dec. 8, 2015; doi:10.7326/M15-1432). Taspoglutide had a significant risk for nausea, a side effect that derailed the drug's development. Several once-a-day GLP-1RAs are also on the market, including liraglutide (Victoza) and exenatide (Byetta).

FDA Actions

The FDA may soon recommend against using codeine for pain and cough in children < 18 years of age based on the recommendations of a joint statement from two FDA advisory groups. The concern stems from deaths reported in children who are "ultra-rapid metabolizers" of codeine, a situation in which the liver converts codeine to morphine in high enough concentrations to cause respiratory depression. Many of the deaths have occurred after tonsillectomy or adenoidectomy surgery in which patients consumed codeine to manage postoperative pain. The FDA added a boxed warning against use for this indication last summer. Most advisors recommended restricting codeine for those < 18 years of age while others recommended restricting the drug for younger children. The FDA is expected to act on the recommendation later this year.

Forget about vitamin D supplementation as a strategy to help prevent falls in the elderly. Although previous research had suggested a benefit, new research reached the opposite conclusion. Researchers from Switzerland studied 200 elderly men and women with a history of a prior fall. They were randomized to 24,000 IU of vitamin D3 per month, 60,000 IU per month, or 24,000 IU plus 300 µg of calcifediol per month. Nearly 60% were vitamin D deficient at baseline. Vitamin D levels improved in all three groups, but there was no effect on lower extremity function, which did not differ among the three groups (P = 0.26). During 12 months of follow-up, the highest incidence of falls occurred in the 60,000 IU vitamin D group (66.9%) and the vitamin D plus calcifediol group (66.1%) compared to the 24,000 IU vitamin D group (47.9%, P = 0.048). The authors concluded that monthly doses of vitamin D3 effectively raise vitamin D levels, but there was no benefit in lower extremity function, and higher doses increased the risk of falls (*JAMA Intern Med* 2016. Published online Jan. 4. doi:10.1001/jamainternmed.2015.7148).

The FDA has approved insulin glargine for the treatment of type 1 and type 2 diabetes. The drug is similar to insulin glargine, marketed as Lantus by Eli Lilly. The drug is considered a "follow-on" product akin to biosimilar drugs and was similar enough to Lilly's product that it gained an accelerated review process. Lilly and Sanofi, the manufacturer of the new insulin glargine, were locked in a patent litigation battle until the two sides reached a resolution in September, clearing the way for the approval. Like Lantus, the new insulin glargine is dosed once a day. Under the terms of the litigation agreement, Sanofi has granted marketing approval to Eli Lilly, who will market the drug as Basaglar. It is expected to be priced at a discount to Lantus.

The FDA has approved mepolizumab for maintenance treatment of asthma when used with other asthma medications. The drug is approved for patients who have a history of severe asthma attacks despite their current regimen. Mepolizumab is a humanized monoclonal antibody to interleukin-5 that a healthcare professional injects subcutaneously every 4 weeks. The drug's primary effect is reducing blood eosinophils. In clinical trials, the drug resulted in fewer exacerbations requiring hospitalization and/or emergency visits, along with a longer time to first exacerbation. Treated patients also required lower doses of maintenance oral corticosteroids. Mepolizumab is marketed by GlaxoSmithKline as Nucala. One year of the drug is expected to cost more than $32,000.

The FDA has approved lesinurad to lower uric acid levels in patients with gout. The drug is the first approved selective uric reabsorption inhibitor, which works by blocking the action of a urate transporter and increasing renal excretion of uric acid. The drug is dosed at 200 mg orally once a day and should be taken with a xanthine oxidase inhibitor (XOI), such as allopurinol. The drug was approved on the strength of three studies of more than 1500 participants, which showed the drug lowered uric acid levels compared to placebo. Lesinurad has a boxed warning regarding the risk of acute renal failure, which is more common if the drug is used without a XOI. The drug is marketed by AstraZeneca as Zurampic. ■

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