Pharmacology Watch

Evidence-based updates in clinical pharmacology

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American Medical Association Calls for Ban on Direct-to-Consumer Advertising for Drugs, Medical Devices

Group Calls for Generic Drug Use

The American College of Physicians recommends the use of generic medications when possible in a new clinical guideline published in the *Annals of Internal Medicine*. In the guideline, the authors sought to answer five questions: 1) How commonly are brand-name medications used when a generic version is available? 2) How does the use of generic medications influence adherence? 3) What is the evidence that brand name and generic medications have similar clinical effects? 4) What are the barriers to increasing use of generic medications? 5) What strategies can be used to promote cost savings through greater generic medication use? In the guideline, they systematically answer these questions and find brand-name medications show no superiority in effectiveness compared with molecularly identical generic medications. Using generic medication reduces out-of-pocket costs for patients and encourages better adherence to therapy, especially chronic diseases. A major barrier is physician perception about the safety and efficacy of generic medications, along with patient expectations and preferences. The authors recommended using electronic health records to notify prescribers about formulary status and medication costs, including out-of-pocket costs. Further, they recommended tiered formulary copayment systems and perhaps even a prior authorization for brand-name drugs when a generic drug is available. Additionally, they recommended patient and physician education, along with physician performance measurements. (*Ann Intern Med* 2015 Nov 24. doi: 10.7326/M14-2427. [Epub ahead of print].)

Sildenafil Improves Insulin Sensitivity

Chronic use of sildenafil (Revatio, Viagra) improves insulin sensitivity in prediabetics, according to a new study. In a randomized, double-blind, placebo-controlled study, subjects were randomized to treatment with sildenafil 25 mg three times a day or matching placebo for 3 months. Twenty-one subjects completed each treatment arm. After 3 months, the insulin sensitivity index was significantly greater in the sildenafil group compared to the placebo group (P = 0.049). Sildenafil also decreased the urine albumin to creatinine ratio, an effect that persisted 3 months after discontinuation. Further study is needed to see if sildenafil can prevent diabetes in high-risk individuals, but these early results are promising (*J Clin Endocrinol Metab* doi: 10.1210/jc.2015-3415).

AMA: Ban Direct-to-Consumer Ads

The American Medical Association (AMA) is calling for a ban on direct-to-consumer (DTC) advertising for drugs and medical devices. The recommendation is based on concerns that the billions of dollars spent on drug and device ads is "driving demand for expensive treatments despite the clinical effectiveness of less costly alternatives" and is "fueling escalating drug prices." The United States and New Zealand are the only two countries in the world that allow DTC advertising for prescription drugs. Manufacturers spend $4.5 billion a year on such ads. The AMA is calling for a physician task force and advocacy campaign to promote prescription drug affordability, which would focus on choice and competition in

the pharmaceutical industry and greater transparency in pricing. Drug company consolidation and anticompetitive behavior is also increasing costs, according to the AMA. More information is available at ama-assn.org.

Breakthrough in Hepatitis C Treatment?

There may be new options available soon for the treatment of hepatitis C (HCV). In a company-sponsored study, patients with HCV genotype 1, 2, 4, or 6 were randomized to sofosbuvir plus a new NS5A inhibitor velpatasvir or matching placebo. Nearly half of the 700 treated patients had genotype 1a or 1b, while 17% had genotype 2, 19% genotype 4, 6% genotype 5, and 7% genotype 6. An additional group of 35 patients with genotype 5 were not randomized because of the very low prevalence of this type of HCV. One-third of all patients had been previously treated and 19% had cirrhosis. The overall sustained virologic response (SVR) at 12 weeks after end of therapy was 99% (95% confidence interval [CI], 98 to > 99). Serious adverse events were reported in 2% of the treatment group. The authors concluded that once-daily sofosbuvir-velpatasvir for 12 weeks provided high rates of SVR in both previously treated and treatment-naïve patients with HCV genotypes 1, 2, 4, 5, or 6, including patients with cirrhosis. (*N Engl J Med* 2015 Nov 16. doi:1056/NEJMoa1512610.)

A second trial used the same combination with and without ribavirin in 267 patients with decompensated cirrhosis across the same genotypes (78% genotype 1). In this trial, patients were assigned in a 1:1:1 ratio to sofosbuvir-velpatasvir once daily for 12 weeks or 24 weeks, or 12 weeks of sofosbuvir-velpatasvir plus ribavirin. Overall, SVR was 83% (95% CI, 74-90) for 12 weeks of sofosbuvir-velpatasvir, 94% (95% CI, 87-98) for sofosbuvir-velpatasvir plus ribavirin, and 86% (95% CI, 77-92) for 24 weeks of sofosbuvir-velpatasvir. A post-hoc analysis did not detect a significant difference in SVR among the three groups. Adverse events were similar for the three groups, although there was a higher frequency of anemia with ribavirin. The authors concluded that sofosbuvir-velpatasvir with or without ribavirin for 12 weeks or sofosbuvir-velpatasvir alone for 24 weeks resulted in high rates of SVR in patients with HCV and decompensated cirrhosis (*N Engl J Med* 2015 Nov 16. doi:10.1056/NEJMoa1512614). Both trials were sponsored by Gilead, the manufacturer of sofosbuvir/ledipasvir (Harvoni), which is approved for treatment of HCV genotype 1.

FDA Actions

The FDA has approved a naloxone nasal spray to stop or reverse opioid overdose. Previous versions of naloxone were only approved in injectable forms, most commonly delivered via syringe or autoinjector. Many feel the nasal spray is easier to deliver by first responders and primary caregivers, and eliminates the risk of a contaminated needle sticks. Some pharmacies have previously compounded naloxone as a nasal spray for the same indication. In clinical trials, naloxone nasal spray administered in one nostril delivered approximately the same level or higher of naloxone compared to a single dose of naloxone intramuscular injection, and achieved blood levels over the same time frame. Naloxone nasal spray is marketed as Narcan and distributed by Adapt Pharma Inc. The nasal spray is priced at $37.50 per dose for large group purchasers such as government, community, and education organizations, including law-enforcement, fire departments, and schools. This is less expensive than the injectable version.

An FDA panel recommends stronger warning labels on fluoroquinolones (ciprofloxacin, levofloxacin, and others) regarding the risk of cardiac arrhythmia, peripheral neuropathy, tendinopathy, and cognitive problems. The drugs are commonly used to treat sinus infections, urinary tract infections, and bronchitis complicating chronic obstructive pulmonary disease. The FDA's Drug Safety and Risk Management Advisory Community and Antimicrobial Drugs Advisory Community made the recommendations. The FDA usually endorses its committee's recommendations.

The FDA has approved a new once-daily, fixed-dose combination pill for treating HIV-1 infection. The pill combines elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide (a new formulation of tenofovir) as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients ≥ 12 years of age. The new formulation of tenofovir is thought to reduce toxicity of the drug while maintaining efficacy. The combination's safety and efficacy were evaluated in 3171 patients enrolled in four clinical trials and showed comparability to other treatments in reducing viral loads. The new combination is marketed by Gilead as Genvoya. ■

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