PHARMACOLOGY WATCH

Evidence-based updates in clinical pharmacology

NSAIDS for MI — Exercise Caution

In this issue: Treatment of Pharyngitis; and FDA Actions.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed after myocardial infarction (MI), but that practice may be putting patients at risk, according to a new study from Denmark. The records of nearly 62,000 patients with first-time MI were evaluated to examine the risk of bleeding and cardiovascular events while taking antithrombotic drugs along with NSAID therapy. All patients were on aspirin, clopidogrel, oral anticoagulants, or a combination of the three. Of those 62,000 patients, 34% filled at least one NSAID prescription.

Patients were followed for a median of 3.5 years. The rate of bleeding events was doubled with NSAID use (4.2 events per 100 person-years with NSAIDs vs 2.2 without NSAIDs (hazard ratio [HR], 2.02; 95% confidence interval [CI], 1.81-2.26), and the rate of cardiovascular events was also higher with NSAIDs (11.2 vs 8.3, HR, 1.40; 95% CI, 1.30-1.49). The increased risk of bleeding and cardiovascular risk was seen regardless of the antithrombotic treatment, type of NSAID, or duration of use. The authors state, "Among patients receiving antithrombotic therapy after MI, the use of NSAIDs was associated with increased risk of bleeding and excess thrombotic events, even after short-term treatment," and that physicians should exercise caution when prescribing NSAIDs for patients who have had a recent MI (*JAMA* 2015;313:805-814).

Treatment of Pharyngitis

Avoid azithromycin in the empiric treatment of pharyngitis, especially in young adults. That is the message from a study from the University of Alabama that looked at 312 students presenting to a student health clinic with acute sore throat and 180 asymptomatic controls. Students were swabbed to detect four species of bacteria, and signs/symptoms were used to calculate the Centor score, which predicts the likelihood of group A strep. *Fusobacterium necrophorum* was detected in 20.5% of patients and 9.4% of asymptomatic subjects. ββ-hemolytic strep was detected in 10.3% of patients and 1.1% of asymptomatic students. Other species found in symptomatic patients included group G/C ββ-hemolytic strep (9%) and *Mycoplasm pneumonia* (1.9%). Infection rates with *Fusobacterium necrophorum*, group A streptococcus, and group C/G streptococcus increased with higher Centor scores ($P < 0.001$). The authors conclude that *F. necrophorum* occurs more frequently than group A ββ-hemolytic strep in a student population, and the clinical presentation is similar (*Ann Intern Med* 2015;162:241-247). This may be important because current pharyngitis guidelines focus solely on group A strep. Fusobacterium infections are a common cause of peritonsillar abscess and are a primary cause of the Lemierre syndrome, a potentially fatal complication. Recent studies have suggested that *F. necropho-*

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rum infections caused more morbidity and mortality then strep pharyngitis. Fusobacterium is not treated by macrolides such as azithromycin but generally is sensitive to penicillin and first-generation cephalosporins. Clindamycin is also active against Fusobacterium. In an accompanying editorial, Dr. Jeffery Linder argues that most pharyngitis is viral and does not need treatment, but when treatment is indicated, "use penicillin" (*Ann Intern Med* 2015;162:311-312). ■

FDA Actions

The FDA has approved ranibizumab (Lucentis) to treat diabetic retinopathy in patients with diabetic macular edema. Ranibizumab is administered as an injection into the eye once a month. Safety and efficacy were established in two clinical studies of 759 patients who were followed for 3 years, in which the improvement of the severity of diabetic retinopathy was significant compared to patients who did not receive the injection. The drug was previously approved to treat diabetic macular edema and macular edema secondary to retinal vein occlusion, as well as wet age-related macular degeneration. Lucentis is marketed by Genentech.

The FDA has approved a new antibiotic combination, ceftazidime/avibactam, to treat adults with complicated intra-abdominal infections (in combination with metronidazole), and complicated urinary tract infections. Ceftazidime is a previously approved antibacterial, and avibactam is a new β-lactamase inhibitor. This is the fifth approved antibacterial under the Qualified Infectious Disease Product designation, which allows for priority review and an additional 5 years of patent protection. The drug is active against *Enterobacteriaceae* and *Pseudomonas aeruginosa*. It should be reserved for patients who have limited or no alternative treatment options. Ceftazidime/avibactam is marketed by Forest Pharmaceuticals as Avycaz.

Pfizer has received approval to market palbociclib for women with advanced breast cancer. The drug inhibits cyclin-dependent kinases (CDK) 4 and 6. It is indicated for treatment of postmenopausal women with ER-positive, HER2 negative, metastatic breast cancer who have not received and endocrine-based therapy. It should be used in combination with letrozole. The drug received "breakthrough therapy" status, allowing for accelerated review. Approval was based on a study of 165 postmenopausal women with ER-positive, HER2-negative advanced breast cancer treated in combination with letrozole or with letrozole alone. The combination resulted in about 20.2 months of progression-free survival, compared to 10.2 months with letrozole alone. Pfizer is marketing palbociclib as Ibrance.

The FDA has approved lisdexafetamine dimestlate (Vyvanse) to treat binge-eating disorder in adults — the first drug approved for this indication. The drug was previously approved to treat attention deficit hyperactivity disorder. Binge-eating disorder is characterized by recurrent episodes of compulsive overeating. Efficacy was shown in two studies of 724 patients with moderate-to-severe binge-eating disorder in which the drug reduced the number of binge eating days per week, with fewer obsessive-compulsive binge eating behaviors compared to placebo. The drug is a stimulant that can cause insomnia as well as psychiatric and cardiovascular complications. Vyvanse is marketed by Shire Pharmaceuticals.

The FDA has approved a new combination pill for the treatment of adults with type 2 diabetes. The new once-daily pill combines empagliflozin (Jardiance), a SGLT-2 inhibitor, along with linagliptin (Tradjenta), a DPP-4 inhibitor. It is approved as an adjunct to diet and exercise. The combination is marketed by Boehringer Ingelheim as GLYXAMBI.

The FDA has approved a new cyanoacrylate vein closure sealant for the treatment of varicose veins. The closure system is indicated for patients with varicosities that cause symptoms such as blood clots, mild-to-moderate pain, and skin ulcers. The compound is injected into a varicosity under ultrasound guidance, where it seals the vein. Approval was based on data from 108 treated patients vs 114 patients treated with radiofrequency ablation, which showed the device to be safe and effective. The new vein closure system is marketed by Covidien LLC as VenaSeal. ■