Drug Monitor

Pioglitazone: Beyond Glycemic Control

Pioglitazone, a thiazolidinedione (TZD) used to treat diabetes, may have cardiovascular benefits even beyond its effects on blood glucose. In a study of 136 patients with type 2 diabetes, researchers from Kyoto National Hospital, Kyoto University Graduate School of Medicine, and Saiseikai Noe Hospital in Japan found that pioglitazone significantly reduced high sensitivity C-reactive protein (CRP), a marker of inflammation, and pulse wave velocity (PWV), a direct parameter of arterial distensibility, even in patients who didn't experience significant improvements in glucose metabolism.

Although this study was observational and nonrandomized, it's the first to address the relationship between the antiatherogenic and antidiabetic effects of TZDs in humans. The researchers say the results support the usefulness of pioglitazone as a multibenefit drug, protecting the patient from several risk factors while helping to control hyperglycemia.

Source: *Diabetes Care*. 2003; 26:2493–2499.

New Antibiotic Approved for Skin Infection

This past fall, the FDA approved the first in a new class of antibiotics called cyclic lipopeptide antibacterial agents. Marketed as Cubicin (Cubist Pharmaceuticals Inc., Lexington, MA), daptomycin for injection is indicated for treating complicated infections of the skin and skin structure, specifically those caused by susceptible strains of such gram-positive microorganisms as *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Enterococcus faecalis*.

According to the FDA, the drug's action is distinct from other antibiotics in that it reversibly binds to human plasma proteins. Clinical studies in 1,400 patients have shown daptomycin's safety and efficacy to be equivalent to such standard treatments as vancomycin and the semisynthetic penicillins oxacillin and nafcillin.

The most commonly reported adverse effects were gastrointestinal disorders, injection site reactions, fever, headache, insomnia, dizziness, and rash. In addition, some patients taking daptomycin developed elevated creatine phosphokinase (CPK) levels, but these levels returned to normal after therapy. Patients receiving the drug should be watched for signs of muscle pain or weakness and should have their CPK levels monitored weekly. Rising CPK values should prompt more frequent monitoring or, in some cases, drug discontinuation.

Sources: FDA Talk Paper T03-66. September 12, 2003.

Cubicin package insert. Cubist Pharmaceuticals, Inc. September 2003.

New Hope for Advanced AD

The N-methyl-D-asparate (NMDA) receptor antagonist memantine, marketed as Namenda (Forest Labs, Jersey City, NJ), was approved by the FDA in mid October for the treatment of moderate to severe Alzheimer's disease (AD). Memantine, the first in this new class of drugs, is the only therapy approved for treating late-stage AD.

The drug's efficacy was studied in two double-blind trials involving about 650 patients. In both, memantine showed a significant advantage over placebo, reducing symptoms and deterioration of daily functioning with a low occurrence of adverse effects—the most common of which were dizziness, headache, constipation, and confusion. The drug's mechanism of action seems unlike that of other available AD drugs. Researchers believe that memantine works by blocking the action of glutamate, which is thought to play a part in AD by overexciting the NMDA receptors. The drug should be available by prescription in January.

Sources: FDA Talk Paper P03-82. October 17, 2003.

Doctor's Guide News Release. October 17, 2003.

Rofecoxib: An ADVANTAGE over Naproxen?

Can the selective cyclooxygenase (COX)-2 inhibitor rofecoxib control symp-

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toms of osteoarthritis as effectively as the nonselective COX inhibitor naproxen at a lower dose and with fewer adverse gastrointestinal (GI) effects? It can, according to researchers from the ADVANTAGE Study Group, who evaluated the use of rofecoxib 25 mg once daily versus naproxen 500 mg twice daily in 5,557 patients with osteoarthritis and a mean age of 63 years. The authors believe that, to date, this study is the largest prospective, randomized, controlled trial to compare osteoarthritis pain medications in terms of adverse GI effects that prompt patients to discontinue treatment.

After three months of treatment, significantly fewer patients stopped taking rofecoxib than naproxen because of such adverse GI effects as abdominal pain, diarrhea, heartburn, or nausea (5.9% versus 8.1%, respectively). The researchers found a similar tendency to stop treatment among subgroups of patients using concomitant low dose aspirin (5.2% versus 9.4%) and those who previously had stopped using their arthritis medication due to GI symptoms (7.6% versus 14.4%). The better GI tolerability was confirmed by less use of gastroprotective medications (9.1% versus 11.2%, respectively) and reduced incidence of serious GI events, such as perforations, ulcers, and bleeding (two versus nine events, respectively).

Source: *Ann Intern Med*. 2003; 139:539–546.

The Right Time for Simvastatin

When is the optimal time to take a statin? Study findings differ, but since most cholesterol is synthesized when dietary intake is low, statin manufacturers tend to recommend nighttime dosing. To find out if that's really best, researchers from the University of Sunderland and Grangewood Surgery, both in Tyne and Wear, United Kingdom, randomly assigned 60 patients (mean age, 66 years) who already were taking simvastatin at night to either continue this dosing schedule or switch to morning administration for eight weeks. Patients who switched had significantly higher total and low-density lipoprotein (LDL) cholesterol levels. And from baseline to the eighth week, total cholesterol rose a mean of 0.38 mmol/L and LDL rose a mean of 0.25 mmol/L. ●

Source: *BMJ*. 2003;327:788.