Drug Monitor

Minimizing Muscle-Related Adverse Effects of Statins

About 5% to 10% of patients taking statins develop muscle-related adverse effects, which sometimes lead to treatment cessation. For those patients, extended-release fluvastatin (fluvastatin XL) may offer a way to continue statin therapy, say researchers from the Metabolic and Atherosclerosis Research Center, Cincinnati, OH; Methodist DeBakey Heart Center and Baylor College of Medicine, Houston, TX; University Hospital, Hamburg, Germany; Feiring Heart Clinic, Feiring, Norway; Institute of Clinical Cardiology, Moscow, Russia; Haseki Hospital, Istanbul, Turkey; and Novartis Pharma AG, Basel, Switzerland.

They assessed the efficacy and tolerability of fluvastatin XL, alone and in combination with ezetimibe, a nonstatin lipid lowering drug with a "placebo-like" adverse event profile. In their double-blind trial, the researchers randomly assigned 199 dyslipidemic patients to receive fluvastatin XL 80 mg/day, ezetimibe 10 mg/day, or both for 12 weeks. All study participants previously had reported muscle-related adverse effects during statin therapy that led them to switch to another statin or discontinue statin therapy.

Fluvastatin XL alone reduced low-density lipoprotein (LDL) cholesterol levels by 33%, compared with 16% for ezetimibe alone. Combination therapy lowered LDL by 46%—an additive effect similar to that reported for other statin-ezetimibe combinations.

Overall, 37 study participants (19%) reported muscle-related adverse effects, most of which were mild or moderate. Frequencies of these adverse effects were 24% among patients taking ezetimibe alone, 17% among those taking fluvastatin XL alone, and 14% among those taking combination treatment. Five patients taking ezetimibe alone, three taking fluvastatin XL alone, and two taking combination treatment stopped the study due to muscle-related problems. There were no instances of rhabdomyolysis or creatine kinase increases of more than 10 times the upper limit of normal.

The researchers say the slow release of fluvastatin XL from the gastrointestinal tract increases first-pass hepatic uptake, avoiding hepatic saturation and "markedly" reducing peripheral blood concentrations of the drug. They also point out that fluvastatin's relatively low lipophilicity may contribute to a slower and lower rate of passage into muscle cells.

Source: *Am J Cardiol.* 2008;101(4):490–496. doi:10.1016/j.amjcard.2007.09.099.

Can Acetyl L-Carnitine Fight Fatigue in Elders?

Fatigue is a problem for many elders, but it can be challenging to diagnose and treat. Suggestions that abnormalities in muscle mitochondrial energy production may underlie fatigue in older adults have led to interest in acetyl L-carnitine (ALC), an amino acid that plays an important role in intermediary metabolism, as a possible treatment.

To test ALC's efficacy in elders with fatigue, researchers from Università degli Studi di Catania, Catania, Italy conducted a double-blind, randomized, placebo-controlled trial involving 96 patients older than 70 years who met established fatigue criteria. Half of the patients received twice daily supplementation with ALC 2 g and half received placebo for 180 days.

The ALC group showed significant improvement from baseline in: daily activity reduction of greater than 50% (–25%), muscle discomfort (–27%), prolonged fatigue after exercise (–51%), sleep disorders (–28%), physical fatigue (–7 points), and mental fatigue (–3.3 points). The researchers also saw a significant drop of 22.5 points on the fatigue severity scale and significant increases in functional status (7.1 points) and mental status (3.4 points) in this group. By contrast, the placebo group had no significant changes from baseline. No adverse events or laboratory abnormalities were reported in either group.

Source: *Arch Gerontol Geriatr.* 2008;46(2):181–190. doi:10.1016/j.archger.2007.03.012.

New Option for Treating Hemophilia A

A newly approved, genetically engineered version of factor VIII offers patients with hemophilia A a treatment option that may carry less infection risk. Xyntha Antihemophilic Factor (Recombinant) Plasma/Albumin Free (Wyeth Pharmaceuticals, Philadelphia, PA), is made using genes from Chinese hamster ovary cells, which are free from known infectious agents. The lack of human or animal additives also minimizes the risk of infection.

In clinical trials, Xyntha was effective at preventing and controlling bleeding, including surgical bleeding, for patients with hemophilia A. The most frequently reported adverse reactions were headache in nonsurgical patients and fever in surgical patients. Additionally, two of 89 patients who received Xyntha for 50 days developed factor VIII inhibitors. ●

Source: FDA news release. February 21, 2008.