Drug Monitor

Is There an Advantage to Omeprazole Prophylaxis?

Omeprazole is used widely to prevent upper gastrointestinal (GI) bleeding in patients with stress-related mucosal disease—although little is known about the incidence, cause, and outcome of such bleeding in patients outside of an intensive care unit setting, and there is no consensus about the treatment. And in fact, in a study of internal medicine patients, researchers from Curry Cabral Hospital in Lisbon, and Fernando Fonseca Hospital in Amadora, both in Portugal, found no real advantage to omeprazole prophylaxis.

They conducted a retrospective study to evaluate the incidence of upper GI bleeding possibly associated with stress-related mucosal disease in 535 patients admitted to an internal medicine ward. Of those patients, 140 were treated with omeprazole 40 mg IV, 193 were treated with 20 mg omeprazole PO, and 202 had no prophylaxis.

There was only 1 episode of clinically relevant bleeding, which occurred in a patient from the no-prophylaxis group.

The mean age of the patients was 70 years, and the mean length of hospitalization was 9.6 days. The researchers note that most of the patients had comorbidities and were being treated with more than 1 drug, including nonsteroidal anti-inflammatory drugs, antiplatelet or anticoagulant drugs, or steroids, all of which have a higher risk of stress-related mucosal disease bleeding. They add, however, that even if a significant risk exists, the short time of admission lowers the probability of relevant bleeding.

Source: *Eur J Intern Med.* 2010;21(5):386–388. doi:10.1016/j.ejim.2010.06.010.

Exenatide vs Insulin Glargine for Body Fat and Cardiac Biomarker Effects

Patients treated for 1 year with exenatide for diabetes mellitus have markedly reduced total fat mass, including visceral fat, while lean body mass is not significantly altered, compared with those treated with insulin glargine, according to researchers from VU University in Amsterdam, the Netherlands; Sahlgrenska University Hospital in Göteborg, Sweden; Helsinki University Central Hospital in Finland; and Eli Lilly and Company in Houten, the Netherlands. Moreover, in their study, circulating cardiac biomarkers, such as high-sensitive C-reactive protein (hs-CRP) improved.

In previously published research, the investigators had shown that exenatide improves glycemic control to the same extent as insulin glargine, although exenatide reduced body weight and insulin glargine raised it. In that study, 69 patients treated with metformin were randomly assigned to receive exenatide or insulin glargine. Additional data show that, at 1 year, exenatide treatment had reduced body weight by 6%, waist circumference by 5%, total body fat mass by 11%, and trunk fat mass by 13%. Total adiponectin levels rose by 12% and hs-CRP levels declined by 61%. Insulin glargine reduced endothelin-1 concentrations, while exenatide did not.

The researchers say the changes in biomarkers were particularly interesting, given that the changes appeared to be independent of the changes in body fat mass. They note that although results of animal studies have found similar beneficial effects of exenatide on visceral fat mass and circulating adiponectin, leptin, and C-reactive protein levels, to the best of their knowledge no controlled clinical studies have been done on the long-term effects of glucagon-like peptide-1 receptor agonists on body composition and biomarkers of cardiac risk.

Source: *Diabetes Care.* 2010;33(8):1734–1737.

Antipsychotics and Venous Thromboembolism: Who's at Greatest Risk?

Antipsychotic medications have been associated with a higher risk of venous thromboembolism (VTE), but studies have been small; restricted to certain populations, such as nursing home residents; or have not covered newer atypical antipsychotic drugs. In a large nested case-control study of patients identified from a primary care database, researchers from Hucknall Health Centre in Nottingham, United Kingdom, found a risk that increased dramatically in some patients.

The researchers identified 25,532 cases of VTE, of whom 15,975 had deep vein thrombosis and 9,557 had pulmonary embolism. The patients were each matched to 4 control patients (by age, calendar time, sex, and practice), for a total of 89,491 controls.

Patients prescribed antipsychotic drugs in the previous 24 months had a 32% greater risk of VTE than nonusers, despite adjustment for potential risk factors. Risk doubled for patients who had started a new drug in the previous 3 months. The risk was greater for patients prescribed atypical rather than conventional drugs, and

for those prescribed low- rather than high-potency drugs.

Patients with a diagnosis of dementia were at higher risk than those with schizophrenia or bipolar disorder. Patients with a higher risk of VTE were also more likely to have the usual risk factors for VTE, although for many conditions the difference was small. However, cancer more than tripled the risk, and recent surgery or fractures multiplied the risk by 13.

The researchers note, as well, that patients with VTE were more likely to have a high body mass index and were slightly more likely to live in an area of socioeconomic deprivation. Case patients were more likely to be using drugs that increase the risk of VTE, such as oral contraceptives.

If other studies replicate the findings, the researchers advise using antipsychotic drugs more cautiously for nausea and agitation, especially among patients at high risk for thromboembolism. They also suggest new algorithms designed to estimate a patient's absolute risk of thromboembolism that take account of such individual factors as age, sex, deprivation, smoking, comorbidities, and concurrent drugs.

Source: *BMJ.* 2010;341:c4245. doi:10.1136/bmj.c4245.

New Formulation Offers Help for Heavy Menstrual Bleeding

A new oral formulation of tranexamic acid (marketed as Lysteda, Ferring Pharmaceticals, Saint-Prex, Switzerland), recently approved by the FDA, may offer women with heavy periods relief with fewer gastrointestinal (GI) adverse effects than the older immediate-release form.

A competitive plasminogen inhibitor, tranexamic acid has been used outside the United States for several decades to treat heavy menstrual bleeding and is generally well tolerated, despite GI adverse effects. The new formulation provides a higher per-tablet dose and increased absorption to reduce the rate of drug delivered to the gastric mucosa, which maintains efficacy while minimizing adverse effects. A phase 3 trial to evaluate effectiveness was conducted by researchers from Carolina Women's Research and Wellness Center in Durham, North Carolina; the University of Kentucky in Lexington; Cleveland Clinic Fertility Center in Canfield, Ohio; Danderyds Hospital in Stockholm, Sweden; the University of Alabama at Birmingham; The Center for Women's Health & Wellness in Plainsboro, New Jersey; the University of Miami in Florida; and the University of Washington in Seattle.

Women with a mean blood loss of 80 mL or greater per cycle were randomly assigned to receive tranexamic acid 3.9 g/day or placebo for up to 5 days per menstrual cycle through 6 cycles.

Blood loss was significantly reduced in the 115 women who received tranexamic acid, compared with the 72 women who received placebo (–69.6 mL [40.4% reduction], compared with –12.6 mL [8.2% reduction]). The reduction in blood loss from baseline with tranexamic acid was reported by women after the first treatment cycle; the reduction was maintained in each measured treatment cycle. Tranexamic acid effectively reduced menstrual bleeding regardless of presence of leiomyomas or baseline menstrual blood loss. The blood loss on treatment declined to less than 80 mL in 43% of menstrual cycles in the treatment group, compared with 17% of cycles in women receiving placebo.

Women in the treatment group also reported better quality of life, with higher scores for being able to engage in social, leisure, and physical activities and work. The majority of adverse events were mild to moderate, and the incidence of GI adverse events was comparable to placebo.

Eye examinations were included in the evaluation of safety because focal areas of retinal degeneration have been observed in animal studies of intravenous tranexamic acid and visual abnormalities have been noted in postmarketing surveys. In this study, 1 woman in the treatment group missed a blue-yellow color vision plate and another reported a nonspecific visual disturbance; these conditions were not considered clinically significant.

Source: *Obstet Gynecol.* 2010;116(4):865–875.