Drug Monitor

Breaking the Crohn Cycle

Many patients with ileal or ileocolonic Crohn disease need resection of the diseased bowel because of complications or intractable disease. New lesions, however, are common after resection—and these lead to recurring symptoms and, eventually, to new complications and reoperation. But ornidazole, a nitroimidazole antibiotic, can help break the cycle and give the gut a chance to recover, according to findings from a study by researchers from University Hospital Gasthuisberg, Leuven, Belgium.

In this study, 80 patients were assigned randomly to one year of treatment with ornidazole 1 g/day or placebo, which was started within one week of resection. At 54 weeks, only three (8%) of the 38 patients taking ornidazole had clinical recurrence of lesions, compared to 15 (38%) of the 40 patients in the placebo group.

Unfortunately, the effect was seen only during the active treatment phase. Two years after the drug was stopped (three years after study initiation), 17 (46%) of the 37 patients remaining from the original ornidazole group had lesions, as did 19 (48%) of the 40 placebo patients.

Significantly more ornidazole patients than placebo patients reported adverse effects (26 versus 12, respectively) and significantly more dropped out due to adverse effects (12 versus five, respectively). Among the most commonly reported adverse effects were abnormal liver tests, paresthesias, and gastrointestinal intolerance. The researchers suggest that a lower dose, such as 500 mg/day, might be better tolerated over the long term, but it isn't clear whether that dose would be as effective.

The only other clinical parameter predicting clinical recurrence was the discontinuation of immunosuppressants, the researchers say. Patients whose immunosuppressants were stopped at the time of resection had approximately five times the chance of having a clinical recurrence at one year, compared with patients who were not taking these drugs.

Source: *Gastroenterology*. 2005;128:856–861.

Preop NSAID Withdrawal: How Close Can You Cut It?

It's common practice to advise healthy patients to stop taking nonsteroidal anti-inflammatory drugs (NSAIDs) seven to 10 days before surgery. But researchers from the Mountain States Regional Hemophilia and Thrombosis Center at the University of Colorado Health Sciences Center, Aurora say it's probably all right to cut that down to just 24 hours.

They recruited 11 healthy volunteers to take ibuprofen every eight hours for seven days, and tested the volunteers' platelet function at baseline and at 40 minutes, eight hours, and 24 hours after the last ibuprofen dose. In seven patients, platelet function was still abnormal at the 40-minute mark. But by 24 hours, it had normalized in all patients.

The researchers point out that few studies have evaluated the duration of platelet dysfunction after stopping therapy with ibuprofen or other NSAIDs, and only two published studies evaluated participants taking long-term NSAIDs. As a result, they say, there is little consensus as to the safe withdrawal of conventional NSAIDs before surgery. They also point to a "limited understanding" of how long NSAIDs must be suspended before diagnostic testing for bleeding disorders can be performed reliably—a concern given that one in 100 Americans has von Willebrand disease.

The researchers were intrigued by their finding that systemic contraceptive use had a mitigating effect on ibuprofen-induced platelet dysfunction. Platelet function remained normal at all time points in four of the 11 participants, including all three who were taking contraceptives, perhaps due to estrogen's prothrombotic effects.

Source: *Ann Intern Med*. 2005;142:506–509.

Does Bariatric Surgery Reduce Medication Use?

Gastric bypass surgery can be an effective, last-resort intervention for achieving weight loss, but how does it affect patients' need for

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medications taken for obesity-related conditions? To answer that question, researchers from Albany College of Pharmacy and Albany Medical College, Albany, NY conducted a chart review of 114 patients who had undergone bariatric surgery and had completed two years of postoperative follow-up. One year after surgery, drug therapy for diabetes, hypertension, and osteoarthritis was significantly reduced, but little had changed in patients' use of drugs for other obesity-related conditions.

At 12-month follow-up, of the patients who, prior to surgery, had been taking angiotensin converting enzyme inhibitors or receptor blockers, nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors for osteoarthritis, or diabetes medications, only 45%, 44%, and 35%, repectively, were still taking them. By contrast, of the patients who had been taking beta-blockers or selective serotonin reuptake inhibitors before surgery, 86% and 92%, respectively, were still taking them.

Following surgery, more patients were taking nutritional supplements because the surgery can lead to deficiencies in vitamin B_{12}, folate, zinc, iron, and calcium. And since 5% to 15% of patients develop marginal ulcers after the surgery, it's customary to prescribe a prophylactic histamine$_2$ receptor antagonist or a proton pump inhibitor for the first three to six months. In this study, some patients continued to take acid suppressants for more than six months. The researchers suggest several possible reasons for this, including persistent acid reflux, inadequate counseling about the duration of therapy, and poor adherence to appropriate counseling.

Source: *Ann Pharmacother*. 2005;39:637–642.

Coxibs and Hypertension: Weighing the Risks

Selective cyclooxygenase-2 inhibitors (coxibs) raise both systolic and diastolic blood pressure (BP) more than either placebo or nonselective nonsteroidal anti-inflammatory drugs (NSAIDs), say researchers from Monash University and Alfred Hospital, Melbourne, Australia who analyzed data on 45,451 patients in 19 clinical trials. In addition, they found that, with coxib use, the rise in systolic BP tended to be disproportionate to the rise in diastolic BP. Such a widened pulse pressure, they say, could have significant implications for cardiovascular risk, as has been shown in the Framingham study. Although, in this study, the incremental

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change in BP was small, they suggest widespread use of the drugs makes it an important consideration.

In trials comparing rofecoxib to celecoxib, the relative risk of developing a clinically important elevation was 1.5 for systolic BP and 1.55 for diastolic BP. The researchers say the differential effects on BP by seemingly similar agents may relate to differences in pharmacokinetic and pharmacodynamic properties, such as celecoxib's shorter half-life.

Most of the patients in these trials had arthritis. The researchers acknowledge that coxibs have been a welcome addition to the armamentarium used for this condition. Nevertheless, any drug that raises BP should be administered with caution, especially to elderly patients in whom both arthritis and hypertension are prevalent.

Source: *Arch Intern Med*. 2005;165:490–496.

Rethinking Asthma Therapy

"Take as needed" could be the new corticosteroid regimen for some adults with mild, persistent asthma if prescribing clinicians heed results from the one-year, multicenter Improving Asthma Control Trial (IMPACT), conducted by the National Heart, Lung, and Blood Institute's Asthma Clinical Research Network.

IMPACT researchers compared changes in lung function, frequency and severity of asthma symptoms, and quality-of-life scores in 255 patients. Two groups of patients were assigned to twice-daily doses of either an inhaled steroid (budesonide) or a leukotriene modifier (zafirlukast) in pill form. The third group received placebo. All patients were given medications for asthma symptoms: inhaled bronchodilator (albuterol), inhaled corticosteroid (budesonide), and oral corticosteroid (prednisone), as well as instructions on how to tailor these treatments to the severity and duration of symptoms.

After one year, changes in lung function and number of severe attacks did not differ significantly among the three study groups. The patients using an inhaled steroid daily reported significantly more symptom-free days (roughly equivalent to an additional 26 days per year) than those in the other two study groups, but these differences were not reflected in quality-of-life scores.

Source: NIH News Release. April 13, 2005.