Drug Monitor

Rifaximin for IBS

Although the cause of irritable bowel syndrome (IBS) remains unclear, studies suggest that bacterial overgrowth in the small intestine may play a role. Accordingly, several antibiotics have been tested as IBS treatments—but each has fallen short. Neomycin improves symptoms but eliminates bacterial overgrowth in only about 25% of patients, and treatment is stymied by adverse effects. Other agents, such as doxycycline, have shown low efficacy.

Researchers from Cedars-Sinai Medical Center, Los Angeles, CA and the University of Chicago, Chicago, IL have higher hopes for rifaximin. This antibiotic, recently FDA approved for treating travelers' diarrhea, is "gut selective," with negligible systemic absorption, which should minimize adverse effects. Furthermore, a previous study demonstrated bacterial overgrowth eradication rates as high as 70%.

The researchers randomly assigned 87 patients with IBS to receive 10 days of rifaximin 400 mg three times daily or placebo. Over the 10 weeks following therapy, rifaxamin treatment significantly improved global IBS symptoms and bloating scores, compared with placebo. Adverse effects in both groups were similar and occurred rarely.

The researchers acknowledge that their study's small sample size limited assessment of adverse effects and its duration was not long enough to "recognize any meaningful recurrence" of bacterial overgrowth. They also note that recent data support using a higher rifaximin dosage. They call for larger, longer-term, multicenter studies to clarify these issues—and to compare antibiotic therapy with other IBS treatment strategies.

Source: *Ann Intern Med.* 2006;145:557–563.

Inhaled Corticosteroids and Fracture

Research has strongly suggested a link between inhaled corticosteroid use and fracture risk, due to effects on bone mineral density. But the studies have been limited by short follow-up (less than four years) and lack of information on potential confounders (such as physical activity), say researchers from the University of Nottingham and the London School of Hygiene and Tropical Medicine, both in the United Kingdom. To better quantify the relationship between inhaled corticosteroids and facture, they conducted a study with over nine years of prescribing and diagnostic data.

Of 1,671 patients aged 75 or older, 982 had been prescribed an inhaled corticosteroid, and 187 had an incident fracture. After adjusting for age and gender, the researchers found a dose-response relationship between inhaled corticosteroid use and fracture risk. This proved independent of incident and historical exposure to oral corticosteroids, type of airflow obstruction, use of bronchodilators, self-reported activities of daily living, physical activity, and socioeconomic status.

Source: *Chest.* 2006;130:1082–1088.

Risks and Benefits of Atypical Antipsychotics in AD

Considered to be safer and at least as effective as conventional antipsychotic drugs, atypical antipsychotics have become common choices for treating delusions, hallucinations, aggression, and agitation in patients with Alzheimer disease (AD). According to the members of the multicenter Clinical Antipsychotic Trials of Intervention Effectiveness–Alzheimer's Disease (CATIE-AD) Study Group, however, data about such treatment are relatively sparse and inconsistent. Their own findings challenge the conventional wisdom.

They randomly assigned 421 outpatients with AD and psychosis, aggression, or agitation to receive olanzapine, quetiapine, risperidone, or placebo. Study physicians adjusted dosages as clinically indicated, and treatment continued for up to 36 weeks. At 12 weeks, the researchers found similar response rates between the groups: 32%, 29%, 26%, and 21% in the olanzapine, risperidone, quetiapine, and placebo groups, respectively.

Overall, 82% of patients discontinued their study medication, with no significant differences between groups in the time to discontinuation for any reason. In terms of time to discontinuation due to lack of efficacy, however, the researchers found an advantage for both olanzapine and risperidone over placebo and for olanzapine over quetiapine. Discontinuation due to intolerance of the study drug, adverse effects, or death was significantly less likely with placebo compared to all three atypical antipsychotics.

Sedation occurred more commonly with all the antipsychotics compared with placebo, and increased confusion or mental status changes were more likely with olanzapine and risperidone. These two drugs also were associated with more extrapyramidal signs. All three antipsychotics caused weight gain, compared to an overall weight loss in the placebo group. Accordingly, the researchers advise further investigation into the possible link between antipsychotic drugs and metabolic syndrome in elders. ●

Source: *N Engl J Med.* 2006;355:1525–1538.