NEW DRUG

Serotonin-4 Receptor Agonist for IBS with Constipation

People with irritable bowel syndrome (IBS) have a lower gastrointestinal (GI) tract that might be more sensitive and work more slowly than it should, causing abdominal pain and discomfort, bloating, and altered bowel function (constipation and/or diarrhea). Tegaserod maleate (Zelnorm, Novartis) activates serotonin-4 receptors, which stimulates peristaltic reflex and normalizes the impaired motility in the GI tract.

DRUG NEWS

Patients and Doctors Disagree about Benzodiazepine

In a survey of 93 patients and 25 physicians, University of Toronto researchers found a major disconnect: patients perceived higher benefits and lower risks with benzodiazepines than physicians did.

According to the investigators, the evidence on benzodiazepine use in older patients with insomnia is “either inconclusive, conflicting, or anecdotal.” They say, for instance, that no prospective studies have looked at the efficacy of benzodiazepine use for insomnia for longer than one month, even though many older patients might be taking these drugs for a year or more. Nor have long-term studies validated concerns about addiction and dose escalation, they add. Risks and adverse effects have mostly been associated with long-acting benzodiazepines or higher doses. Short-acting benzodiazepines are generally viewed as safe in small doses. Although the drugs aren’t without risks in older patients, “the fear engendered in using [them]...is not substantiated by the current evidence,” the researchers say.

To their knowledge, the researchers say, this is the first study to directly compare patients’ and physicians’ perceptions of the benefits and risks of benzodiazepine use for insomnia. They believe the discordance is clinically important in part because it can lead to nonadherence (source: BMC Family Practice 2002, 3:9).

Eyedrops Could Delay Onset of Glaucoma

Using eyedrops to reduce pressure in the eye can help keep glaucoma at bay, according to the Ocular Hypertension Treatment Study, cosponsored by the National Eye Institute. Researchers found that eyedrops reduced open-eye glaucoma, the most common form of glaucoma, by more than 50%.

Of 1,636 patients between 40 and 80 years old who had elevated eye pressure but no glaucoma, half were given commercially available eyedrops daily (either singly or in combination) and the other half received no medication. The eyedrops reduced eye pressure by approximately 20%—a relatively modest reduction with an apparently protective effect. Of patients who received eyedrops, 4.4% developed glaucoma within five years, compared with 9.5% of those who did not receive the eyedrops. The researchers also found several significant risk factors associated with glaucoma: older age, African descent, higher eye pressure, certain characteristics in the anatomy of the optic nerve, and thinness of the cornea.

Despite the benefits, the researchers say, eye care professionals should not prescribe eyedrops for all people who have elevated eye pressure but no sign of glaucoma. In fact, 90% of participants in the observation group did not develop glaucoma within five years. The research team advises factoring in individual risk, health status, and life expectancy, as well as the cost, inconvenience, and possible side effects of daily treatment. Their study took into account the fact that African Americans are three to four times more likely to develop glaucoma than Caucasians, so 25% of the study participants were African American.

In the study, patients given eyedrops did not show increased evidence of health problems compared with the observation group.

The study was published in the July 2002 issue of Archives of Ophthalmology (source: www.nei.nih.gov/glaucomaeyedrops).

Testing Visual Compatibility of Drugs

Compatibility data on commonly used drug combinations ensure safe and efficacious administration. The data can also improve patient care and decrease costs by eliminating the need for additional venous access. However, compatibility information is only available from pharmaceutical companies for admixtures in various solutions.

Researchers from the University of Utah Hospital tested the visual compatibility of drugs with azithromycin in a simulated Y-site delivery. Azithromycin proved visually incompatible with 20 of 24 commonly used drugs. The drugs were considered incompatible if color changes or precipitate were visible to the unaided eye during infusion, or if the number of particles on the filter exceeded the number stated in the USP guidelines. The only visually compatible drugs were diphenhydramine, dolasetron, droperidol, and ondansetron.

The researchers emphasize that the study was of visual compatibility, and results cannot be extrapolated to admixture compatibility (source: www.medscape.com).

COX-2 Inhibitor for NSCLC

The overexpression of cyclooxygenase-2 (COX-2) in a variety of human tumors, including non-small cell lung cancer (NSCLC) might contribute to carcinogenesis by reducing immune surveillance, inhibiting apoptosis and/or stimulating angiogenesis. Celecoxib (Celebrex, Pfizer/Pharmacia), a COX-2 inhibitor, might enhance response to preoperative chemotherapy in patients with resectable NSCLC, say researchers from Weill Medical College of Cornell University who reported their findings at the 38th annual meeting of the American Society of Clinical Oncology.

The researchers administered 400 mg of celecoxib twice daily and between two cycles of preoperative chemotherapy with paclitaxel and carboplatin, up to the day of surgery. Of 16 patients with stage IB to stage IIIA cancer who completed the study, 12 responded to treatment either partially (8) or completely (4). In the remaining four patients, the disease was stable (sources: www.medscape.com; www.asco.org).

Turning Up the Heat On Breast Cancer Chemotherapy

A new breast cancer treatment uses an unusual method of administering chemotherapy—patients soak their breasts in hot water, which forces the chemotherapy drugs that are encapsulated in liposomes to release most of their contents into the breast tissue. The liposomal packaging melts above the usual body temperature (in this study, 104°F).

The encapsulation allows delivery of 30 times more of the drug to the breast tissue, without poisoning the rest of the body, according to researchers who reported on their study at the annual meeting of the American Society of Clinical Oncology. The 12-week, phase I trial of doxorubicin encased in liposomes (Myocet, The Liposome Company Inc.) and paclitaxel (Taxol, Bristol-Myers Squibb Company) is the only clinical trial of its kind in the U.S.

Of the 21 patients with newly diagnosed, large invasive breast tumors, 33% had complete remission; 17% were able to have lumpectomy instead of mastectomy, and 11% had complete pathologic responses. Tumor growth
Anastrozole–Heir to Tamoxifen

Anastrozole could be the most significant treatment for breast cancer since the introduction of tamoxifen in the 1970s, according to initial findings from the Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial of anastrozole for early breast cancer. The efficacy and safety of anastrozole (Arimidex, AstraZeneca) was compared to tamoxifen, the standard treatment for breast cancer, because tamoxifen has often been associated with serious adverse events, including endometrial cancer and thromboembolic events.

Anastrozole, which became available in 1995, is an aromatase inhibitor, one of a class of compounds that inhibit the synthesis of estrogen from androgens in postmenopausal women. In the largest adjuvant therapy trial ever completed, 9,241 women were studied for a median of 33.3 months. In patients with estrogen-receptor-positive tumors, anastrozole performed significantly better than tamoxifen in reducing the risk of recurrence by a relative 22% and reducing the risk of developing a second primary cancer by a relative 58%. These findings translate into 91% disease-free survival at three years, compared with 89% in the tamoxifen patients and those in the combination group.

Anastrozole was less likely than tamoxifen to be associated with hot flashes, vaginal bleeding, ischemic cerebrovascular events, venous thromboembolic events, and endometrial cancer. However, anastrozole deeply suppresses estrogen and lacks tamoxifen’s osteoprotective benefits; musculoskeletal disorders and fractures were significantly more common with anastrozole, prominently polyarthritis. (An increase in rheumatic symptoms seems to argue for a hormonal component in rheumatic diseases, the researchers say.)

The findings are applicable only to newly diagnosed patients with early, operable breast cancer after initial treatment with surgery, radiotherapy, and/or chemotherapy. The data should not be used, the researchers say, to recommend switching patients to anastrozole if they are already on tamoxifen (source: www.thelancet.com; Lancet 2002;359:2131-2139).

Dopamine Agonists and Sleep Attacks

In a review of 20 articles covering adverse sleep events in 124 patients, researchers from Karl Franzens University in Graz, Austria classified 96 as “sleep attacks”—sleep that is sudden and irresistible. They found that the sleep attacks were a class effect, caused by dopamine agonists such as levodopa and bromocriptine. In 17 cases, the sleep event happened during driving, leading to road crashes in 10 cases. In 12 cases, non-driving attacks occurred during standing, walking, talking, and other activities. Twenty patients had recurrent attacks. In 11 cases, somnolence preceded a driving attack. Ten patients had non-driving attacks before a driving attack. Three patients had both.

The researchers identified two distinct clinical courses from the available data: sleep attacks and sleep episodes. Patients who suffered sleep attacks fell asleep suddenly with no warning signs. One patient described it as feeling “like a short circuit.” After two to five minutes, they woke abruptly. Patients with sleep episodes reported prodromal signs of tiredness, such as waves of sleepiness, followed by a slow and irresistible nodding off, with sleep lasting about an hour. They could be awakened during the sleep but couldn’t stay awake.

The researchers note that up to 30% of patients taking dopamine agonists for Parkinson’s disease have sleep attacks. They acknowledge that the idea of sleep attacks has been disputed by some authors, who speculate that such episodes are only exaggerated daytime drowsiness.

Risk factors are hard to isolate, the researchers add. Some preliminary findings suggest the risk of a sleep event is higher in men and in patients with dysautonomia. However, anastrozole deeply suppresses estrogen and lacks tamoxifen’s osteoprotective benefits; musculoskeletal disorders and fractures were significantly more common with anastrozole, prominently polyarthritis. (An increase in rheumatic symptoms seems to argue for a hormonal component in rheumatic diseases, the researchers say.)

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Etoricoxib and Arthritis

Etoricoxib, a highly selective COX-2 inhibitor, was evaluated in two recent trials: one for patients with rheumatoid arthritis, the other for patients with acute gouty arthritis.

In the first study, conducted for the Etoricoxib Rheumatoid Arthritis Study Group, 687 patients completed 12 weeks of treatment with placebo, etoricoxib 90 mg/day, or naproxen 500 mg BID. The study was conducted at 67 sites in 28 countries. Compared with patients on placebo, patients in both drug groups showed significant improvements in all endpoints. Similar percentages (58% and 59%) of naproxen and etoricoxib patients, respectively, responded according to American College of Rheumatology criteria: tender joint and swollen joint counts, patient and investigator assessment of disease activity. Etoricoxib’s treatment effects were rapid, the investigators say, occurring at the earliest time measured (week two) and were maintained over the entire study period. Both drugs were similarly well-tolerated. Only three serious clinical adverse events were judged to be drug-related: two patients on etoricoxib (duodenal ulcer and hip pain), and one on naproxen (hypertension).

In the second trial, of 150 patients in 11 countries with acute gouty arthritis, a once-daily dose of etoricoxib 120 mg worked as well for symptoms as did indometacin 50 mg three times daily for eight days. There were also controls for each drug. Both etoricoxib and indometacin groups experienced comparable pain relief, starting four hours after the initial dose. The two drugs were well-tolerated. Four patients in the indometacin group reported serious adverse events (vomiting and headache). Etoricoxib was associated with a lower incidence of drug-related adverse events ($p=0.003$) than indometacin (sources: www.bmj.com; BMC Family Practice 2002, 3:10).