Drug Monitor

Ondansetron Mixes Safely With Tramadol

The aftermath of postoperative anesthesia often includes nausea and vomiting, for which, the commonly used analgesic tramadol tends to be blamed, especially if large doses are injected quickly. Some studies have suggested that ondansetron reduces the tramadol-associated adverse effects, but other reports raised concerns that the combination of ondansetron and tramadol increases emetic sequelae and ondansetron failure. The fact that both drugs act on the serotonin (5-hydroxytryptamine) pathway is one possible explanation.

However, researchers from University of Bonn in Germany and University Hospital of Bern in Switzerland, who explored the controversy in a randomized, double-blind study, found that administering the drugs together did not increase postoperative analgesia consumption or the frequency of emesis.

In their study, 179 patients who had had major surgery received intravenous ondansetron, metoclopramide, or placebo for emesis prophylaxis. The analgesic regimen consisted of tramadol intraoperative loading, and subsequent patient-controlled analgesia.

The researchers then compared tramadol consumption and the response to antiemetic treatment. They found no difference in the tramadol consumption during the first 8 postoperative hours. Also during that time, 85% of odansetron patients, 70% of metoclopramide, and 67% of placebo patients responded to the antiemetic prophylaxis without any nausea or vomiting.

Given that antagonistic actions between ondansetron and tramadol have been reported, the results were somewhat unexpected, the researchers say. However, they add, their findings do not exclude any possible opposing actions of these drugs within the serotonergic pathway.

Source: *J Pain.* 2010;11(12):1274–1281. doi:10.1016/j.jpain.2010.03.003.

Beta-Blockers and Bad Dreams

When a normally nonviolent man began behaving violently in his sleep, his clinical team at the Royal Infirmary of Edinburgh in the United Kingdom narrowed the cause down to propranolol, with a diagnosis of rapid eye movement (REM) sleep behavior disorder.

For 3 years, the patient had been experiencing violent dreams several times a month. He would act out by shouting, swearing, punching, and even trying to strangle his wife. He snored occasionally during sleep and had intermittent choking and gasping arousals, but reported no apnea or daytime sleepiness.

Three years earlier, he had a period of insomnia due to stress and was sleeping only 2 hours a night. After treatment with fluoxetine, for depression, the insomnia improved; whereupon, the fluoxetine was stopped. He had been taking gabapentin, ibuprofen, and atorvastatin for years for chronic back pain and hypercholesterolemia. When his sleep violence began, he had been diagnosed as hypertensive and was being treated with propranolol LA 160 mg/day.

His examination included overnight polysomnography, which revealed an apnea/hypnea index of 25 events per hour; consistent with moderate sleep apnea, but no behavioral events were recorded.

The physicians diagnosed REM sleep behavior disorder caused by propranolol. The propranolol was reduced by 20 mg every 3 days until it was stopped, and was replaced by lisinopril 2.5 mg. He also was given clonazepam at night during the tapering period.

By the 6-week follow-up, the violent behavior had stopped completely and he was no longer taking clonazepam. He also remained normotensive on lisinopril and declined treatment for his sleep-disordered breathing.

His physicians note that lipophilic beta-blockers have been associated with a number of sleep disturbances, including insomnia, hallucinations, and sleepwalking. Serotonin has been implicated, as has been a relationship between 5-hydroxytryptamine receptor occupancy and beta-blocker–induced sleep disorder. It's possible, the authors of the report say, that the beta-blockers bind to 5-hydroxytryptamine receptors and precipitate abnormal REM and non–REM sleep behavior. They add that beta-blockers have been shown to bind to central beta-adrenoreceptors and influence melatonin release; it may be that this increases arousal during sleep and leads to the abnormal behaviors.

Source: *Am J Med.* 2011;124(1):e11. doi:10.1016/j.jamjmed.2010.04.023.

Cancer Treatment-Related Urogenital Disorders Underestimated

Urogenital symptoms may be more frequent than previously estimated from clinical trials of breast cancer patients, say researchers from Örebro University and Uppsala University in

Sweden. They found more than half of women treated with aromatase inhibitors (AI) had at least 1 moderate-to-severe symptom of vaginal atrophy, as did one-third of women on tamoxifen—numbers "substantially higher" than those already published.

Because no comparative studies had been done, the researchers say, it wasn't known whether urogenital symptoms are more common in women with breast cancer than in those without. To their knowledge, the researchers say, theirs is the first study to evaluate urogenital symptoms and vaginal atrophy in breast cancer patients on adjuvant endocrine treatment, compared with control groups.

The researchers assessed vaginal atrophy in 97 breast cancer patients and 105 women without breast cancer. The women also answered questionnaires about atrophy-related signs and symptoms and urinary incontinence.

Of 33 women treated with an AI, 19 (58%) reported at least 1 symptom of vaginal atrophy, as did 11 (32%) of 34 tamoxifen users. By contrast, only 1 woman of 55 who were not taking estrogen treatment, and 11 (22%) of 49 who were taking estrogen treatment had any sign or symptom.

Vaginal dryness, and pain or discomfort with intercourse, were far more common in AI users than in both control groups and tamoxifen users. The only vaginal atrophy symptom that was more common among tamoxifen users was moderate to severe vaginal discharge.

AI users had moderate and severe atrophy more often than both control groups and the tamoxifen group. They had higher vaginal pH than all the other groups, and showed a higher grade of atrophy than women on tamoxifen or estrogen.

Both drug-treated groups reported moderate or severe vasomotor symptoms, such as hot flashes, cold sweats, and night sweats, more often than the control groups. There was no difference in frequency or intensity of incontinence symptoms among the groups. Between 49% and 73% of women in all groups reported frequent urination, urgency incontinence, and stress incontinence.

In previous studies, 2% to 26% of women had symptoms of vaginal atrophy. Similarly, studies have reported that 15% to 25% of AI-treated women have dyspareunia; in this study, that number was 65%. One reason the numbers were higher, the researchers theorize, is that women may be more inclined to reveal symptoms to a gynecologist than to an oncologist. In this study, experienced gynecologists performed all examinations.

Many women with breast cancer can now expect to be cured or to live a long time with the disease, the researchers say. As more and more women receive adjuvant endocrine therapy after primary therapy, treating the adverse effects becomes more of an issue. The impact of treatment-related symptoms on quality of life is important, and should be studied "more intensively to optimize breast cancer therapy."

Source: *Am J Obstet Gynecol.* 2011;204(1):26.e1–26.e7. doi:10.1016/j.ajog.2010.08.035

Ginger Can Help Shorten ICU Stays

Ginger extract may be a simple way of making the ICU stay more comfortable for patients receiving enteral nutrition. To find out if they could ameliorate the problem of delayed gastric emptying (DGE), researchers from Shahid Beheshti University in Tehran, Iran, gave 32 patients with adult respiratory distress syndrome either 1 g of coconut oil as placebo, or 120 mg of ginger extract.

The patients in the ginger extract group tolerated a significantly higher amount of feeding during the first 48 hours of therapy. The 2 groups didn't differ in the amount of feeding tolerated beyond the 48 hours, perhaps because those for whom therapy failed at 48 hours were switched to erythromycin.

The number of ICU-free days (7 days in the ginger-extract group vs 4 days in the control group) and ventilator-free days (11 days in the ginger-extract group vs 7 days in the control group) were significantly different between the 2 groups. The ginger extract group also showed a trend toward lower incidence of nosocomial pneumonia. This may be due to a reduction in DGE and subsequent reflux, the researchers say. They cite research that increased gastric volume results in gram-negative bacterial overgrowth in the stomach; subsequent reflux may lead to tracheal colonization.

The active components of ginger are shogaols (believed to be antiemetic) and gingerols (stimulating gastric secretion and peristalsis). They note that gastric feeding has advantages over transpyloric feeding, including being easier and more convenient. They suggest that gastric feeding, with ginger extract, might not only reduce DGE and help prevent nosocomial pneumonia, but also eliminate the use of transpyloric feeding.

Source: *J Crit Care.* 2010;25(4):647–650. doi:10.1016/j.jcrc.2009.12.008.