Drug Monitor

A Dangerous Mix: Opioids, Sedatives, and Alcohol

As many as one-third of patients being treated with opioids are also using sedatives and engaging in "risky drinking," despite risks of oversedation and respiratory depression, according to a study by researchers from Kaiser Permanente of Northern California in Oakland, California; and the Group Health Research Institute, the University of Washington, and the Harborview Medical Center all in Seattle, Washington. Moreover, the problem is prevalent even among patients who have no history of substance abuse.

The researchers used data from the CONSORT study (CONsortium to Study Opioid Risks and Trends) and telephone surveys of 1,848 patients prescribed long- or short-acting opioids for chronic noncancer pain. Concurrent sedative use was defined as receiving sedatives for ≥ 45 days of the 90 days preceding the interview. Participants were classified as concurrent users of alcohol if they reported having had ≥ 2 drinks within 2 hours before or after taking opiates in the preceding 2 weeks. Substance abuse was defined as a diagnosis in the 3 years before the study, a self-report of an alcohol or drug problem, or a score of > 7 on the AUDIT-C alcohol screen (on a scale of 0-12). The researchers note that alcohol consumption has been shown to increase markedly with AUDIT-C scores > 7. Risky drinking was defined by an AUDIT-C score of 3 to 6 for women and 4 to 6 for men.

Of 2,163 survey respondents, 1,883 (87%) reported using opioids every day for the previous 2 weeks. Those included 1,848 patients who could be classified as to substance-abuse status. One-third of the respondents were found to have a history of substance abuse.

About 12% of participants concurrently used alcohol, 32% were taking sedatives, and 3% were using all 3 substances concurrently. About 60% of the participants were classified as depressed. Women were more at risk for combining sedatives and opioids, whereas men were more at risk for combining alcohol and opioids.

One in 8 patients had 2 or more drinks within 2 hours of taking an opioid, regardless of substance abuse history. In fact, rates of concurrent alcohol use were similar among respondents with a history of substance abuse (13%) and those with no such history (12%). By contrast, concurrent sedative use was higher among patients with a history of substance abuse compared with those without (39% vs 29%).

The researchers note that most patients reported very high levels of pain (average intensity of 5.8), although the majority said opioids were very or extremely helpful in managing the pain. Two-thirds were taking opioids for > 1 pain condition. The average daily opioid dose was 81 mg (morphine equivalent dose). The close timing between drinking and taking the opioids suggests that some patients may view alcohol as another way of controlling pain, the researchers say.

Across all substance abuse strata, concurrent sedative use was associated with women, younger age, depression, higher daily opioid doses, and taking opioids for > 1 pain condition. Patients taking the highest daily doses were twice as likely to use sedatives.

The researchers acknowledge that the prescribed sedatives were mostly those used to treat anxiety and sleep disorders, which are common with chronic pain. However, they advise that the "widespread practice" of prescribing opioids (particularly high dose) and sedatives concurrently deserves increased scrutiny. They also emphasize that it's important not to focus solely on the "high-risk" patients—even patients without a history of substance abuse can be at risk.

Source: Saunders KW, Von Korff M, Campbell CI, et al. *J Pain.* 2012;13(3):266-275. doi:10.1016/j.jpain.2011.11.004.

UI Drugs Benefit Fewer Than Thought

Drugs for urgency urinary incontinence (UI), unfortunately, aren't all that effective, and adverse effects (AEs) cause many women to drop the regimen after > 1 year, say researchers from the University of Minnesota in Minneapolis, Minnesota. In fact, they suggest that the sphere of influence is so small, and strong evidence about benefits is so sparse, that such drugs should be reserved for very specific groups and monitored closely.

The researchers analyzed data from 94 randomized trials of drug efficacy or comparative effectiveness that examined AEs and treatment discontinuations due to AEs. They focused on patient-centered outcomes, relying on self-reported AEs regardless of the authors' conclusions about causality, and analyzed all unusual, harmful symptoms the patients noticed.

Overall, they found rates of continence and clinically important improvement were definitely better with drug treatment compared with placebo. However, fewer than 200 cases of continence per 1,000 patients

treated were attributable to drug treatment. Patients with more frequent UI had slightly greater benefit from some drugs, such as tolterodine and fesoterodine, than from placebo. Fesoterodine was more effective in patients with > 2 urgency UI episodes per day. Trospium was better than placebo at resolving UI only in patients with < 5 UI episodes per day. (By the same token, patients with 2 to 4 episodes of urgency UI per day were more likely to stop because of AEs.)

Moreover, any benefits generally weren't long-term, because AEs forced women off the treatment. More than half of patients stop taking UI drugs after 1 year of treatment, the researchers say. The lowest rates of treatment discontinuations were with solifenacin 5 mg.

AEs ranged from "bothersome"—such as dry mouth and constipation—to downright dangerous. For example, tolterodine was strongly associated with a significant risk of hallucinations over the long-term. Older people using UI drugs in combination with antihistamine or cytochrome inhibitors were at high risk of ventricular arrhythmia or sudden death. Not surprisingly, AEs were more common in women taking 7 or more concomitant medications.

Given the poor risk-benefit ratios for most patients, and because all the drugs studied were similarly effective, the researchers advise making therapeutic choices based on the AE profile and informing all patients of the possible AEs. They also suggest tailoring the decisions by age and other criteria: For instance, oxybutynin, trospium, and darifenacin improved UI in older women. Trospium reduced the number of urgency UI episodes irrespective of concomitant medications and improved quality of life in older patients with overactive bladder. Women with urgency UI for whom previous treatments had failed might benefit from solifenacin; the 5-mg dose was associated with improved quality of life.

Interestingly, transdermal oxybutynin neither improved quality of life nor resulted in treatment satisfaction compared with placebo. Dry mouth occurred most often with oxybutynin, although 1 study found severe dry mouth and constipation were less common with transdermal than oral immediate-release (IR) oxybutynin. However, AEs were less common with the once-daily, controlled-release form vs the IR form.

In their analysis, the researchers focused on the people who were most affected by the drugs—the patients. However, they point out that few of the randomized controlled trials they looked at examined how patient characteristics might modify drug effects, and none provided strong evidence for individualized treatment decisions.

Source: Shamliyan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. *Ann Intern Med.* 2012 Apr 9. [Epub ahead of print.]

Time to Switch to Sublingual Immunotherapy?

Subcutaneous immunotherapy for allergies has a major drawback: Because it's an injection, it has very poor adherence, especially among children. Even among adults, adherence is very low—more than two-thirds drop out within a year of initiation. By contrast, sublingual immunotherapy (SLIT) is easy to use and economical, but why isn't it more common in the United States? In part because its efficacy is still debated, say researchers from the Allergy Association of La Crosse in La Crosse, Wisconsin; the Mayo Clinic Health System Franciscan Healthcare in La Crosse and Onalaska, Wisconsin; and the University of Wisconsin-La Crosse, also in La Crosse, Wisconsin. So they conducted a study to help evaluate quality-of-life outcomes in 51 adult patients with allergic rhinoconjunctivitis.

The patients were recruited from the Allergy Associates of La Crosse, which has been offering SLIT for 41 years. Most tested positive to > 1 allergen, including dust, grass, trees, and weeds. Dosing for each patient was tied to skin-test results and adjusted over the course of treatment.

New patients to the clinic were given the Rhinoconjunctivitis Quality-of-Life Questionnaire before treatment and at follow-up visits at 3 and 6 months. After 4 months of treatment, patients improved significantly in 6 domains: activity limitations, nonnose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional function. The patients also reported improved sleep, although this didn't reach statistical significance. Sneezing and irritability, which in a previous efficacy study were unaffected, in this study declined over the first 4 months.

Improvements were sustained and continuous and were demonstrated again after 10 to 12 months of treatment.

Source: Morris MS, Lowery A, Theodoropoulos DS, Duquette RD, Morris DL. *J Allergy (Cairo).* 2012:253879. doi:10.1155/2012/253879.