A small, double-blind study has found that the anti-emetic ondansetron can reduce withdrawal symptoms in chronic pain patients weaning off opioid therapy.

The results, presented at the 2010 annual scientific meeting of the American Pain Society, suggest that ondansetron, a 5-HT3 receptor antagonist, may become a useful addition to the armamentarium of opioid withdrawal medications, according to investigators (abstract 310).

Indeed, any tool that helps decrease the distress associated with opioid withdrawal increases the likelihood of a successful detoxification, said Ashok Mallya, MD, medical director of the Opiate Addiction Treatment Program at the VA Medical Center, in St. Louis.

"Current detoxification regimens are inadequate and do not address all of the symptoms of opioid withdrawal. Many patients consequently continue the use just to avoid withdrawal-related distress," Dr. Mallya told Anesthesiology News. "These impressive preliminary findings suggest [that] ondansetron is an effective non-narcotic agent that may be used as an alternative to the traditional opiate-tapering drugs such as methadone, buprenorphine or naloxone, which require special training or a special setting."

According to primary investigator Sean Mackey, MD, PhD, chief of pain management, and associate professor at Stanford University School of Medicine, in Stanford, Calif., studies in mice have shown that 5-HT3 receptors are triggered by opioid withdrawal (Hum Psychopharmacol Clin 2008;28:189-194). To examine whether ondansetron also can help relieve opioid withdrawal symptoms, Dr. Mackey and his team enrolled nine chronic pain inpatients at Stanford’s Comprehensive Pain Interdisciplinary Pain Program. Subjects had a diverse set of diagnoses and used a variety of opioids, including methadone, oxycodone and hydrocodone. Morphine-equivalent daily doses at the time of admission ranged from 0 to 1.178 g, and between 0 and 40 mg on the day of opioid withdrawal. The study included three women and six men (average age, 44 years).

All participants were weaned off their opioid medications during a one- to two-week period and were concurrently administered a combination of methadone, clonidine, baclofen and cherry syrup during this weaning period. In addition, in a double-blind fashion, patients were given a placebo immediately after a baseline assessment and then 8 mg of ondansetron one hour later. Following each administration, patient pain and withdrawal symptoms were assessed using the 60-point Subjective Opioid
Withdrawal Scale (SOWS), the 13-point Objective Opioid Withdrawal Scale (OOWS) and the visual analog scale (VAS).

Dr. Mackey and his team found that OOWS scores dropped from a mean of 4.1 at baseline to 3.2 after placebo and then decreased further to 2.5 after ondansetron administration (placebo vs. baseline, \( P < 0.05 \); ondansetron vs. baseline, \( P < 0.001 \); ondansetron vs. placebo, \( P = \text{NS} \)). Similarly, mean scores on the SOWS fell from 26.3 at baseline to 20.7 after placebo administration and 16.4 after subjects received ondansetron (baseline compared with both placebo and ondansetron, \( P < 0.001 \)). VAS scores dropped from 6.65 at baseline to 6.27 post-placebo and 5.50 one hour after administration of ondansetron (\( P = \text{NS} \)).

In the presentation of his group’s findings, Dr. Mackey admitted that the effects of ondansetron on withdrawal symptoms may have been masked by the concurrent administration of a pain cocktail that included clonidine, methadone and diclofenac. Furthermore, he noted that the small study population represented a subset of patients with mild withdrawal symptoms that do not represent the severity of withdrawal symptoms exhibited by many opioid-dependent chronic pain patients.

“Our preliminary results suggest patients undergoing withdrawal subjectively improve once they receive ondansetron,” Dr. Mackey said. “However, further studies are needed to explore the relationship between ondansetron and opioid withdrawal symptoms and to identify responders and nonresponders.”
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