ORLANDO, Florida — A novel approach to opioid detoxification that does not involve the use of opioids may be superior to a protocol that includes buprenorphine.

The results of a new study show that the combination of tizanidine (Zanaflex, Acorda Therapeutics), hydroxyzine, and gabapentin is superior to a buprenorphine/naltrexone protocol for treatment retention and discharge to further treatment in opioid-dependent patients.

In addition, this 3-drug combination was just as effective for symptom control and length of hospital stay.

The findings were presented here at the American Society of Addiction Medicine (ASAM) 45th Annual Medical-Scientific Conference.

"We were trying to find a way of dealing with opiate withdrawal and facilitate people to the next stage of addiction treatment," lead author Gregory Rudolf, MD, from the Swedish Addiction Recovery Service, in Seattle, Washington, told Medscape Medical News.

"Opiate withdrawal is always the first hurdle to overcome when a person is ready to quit using, so having an effective withdrawal management tool is very important. Even if people are going to substitution therapy with buprenorphine and naloxone, they still need to have a couple of days without opiates before they can make that transition," Dr. Rudolf said.

The investigators conducted a retrospective chart review of patients diagnosed as having opioid dependence on the basis of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria who were admitted for inpatient detoxification between January 1, 2011, and November 30, 2012.

The review included 84 nonopioid protocol patients and 40 buprenorphine/naloxone protocol patients.

The nonopioid protocol, which was followed for 4 days, consisted of the muscle relaxant tizanidine, 8 mg orally every 6 hours, the antihistamine hydroxyzine, 100 mg orally every 4 hours, and the anticonvulsant gabapentin, 300 mg orally 3 times daily and 600 mg orally each night at bedtime.

The buprenorphine/naloxone protocol consisted of the following:

- Day 1: 2 mg SL q 2 h x 3, 8 mg SL BID
- Days 2-3: 8 mg SL
- Day 4: 4 mg SL

In addition, both protocol groups received ancillary medications as needed, as well as standard counseling.

"The nonopioid medications have sedating properties that are welcome to people in withdrawal, and the tizanidine in
particular is a strong muscle relaxant, which is useful," Dr. Rudolf said.

The results of the review showed that the nonopioid protocol was just as good as or better than buprenorphine/naltrexone.

"We found that the new protocol was as effective in getting them through the detox, getting to the next phase of treatment, and they subjectively reported that their withdrawal symptoms were equal or better, and we didn't have any worse adverse effects," he said.

Nonopioid patients had a greater treatment retention ($P = .026$) and discharge to further chemical dependency treatment ($P = .006$) than buprenorphine/naltrexone patients.

The Clinical Opiate Withdrawal Scale (COWS) scores were similar in both groups.

The incidence of bradycardia was greater in the buprenorphine/naloxone patients (65%) compared with the nonopioid group (44%; $P = .029$).

Finally, 28.6% (95% confidence interval, 19% to 40%) of the nonopioid patients were successfully transitioned to treatment with injectable, extended-release naltrexone (Vivitrol, Alkermes, Inc).

The results also showed that there were no significant differences in asymptomatic hypotension between the nonopioid and buprenorphine/naltrexone groups (26.2% vs 35%), nor in symptomatic hypotension (8.3% vs 10.0%), ancillary medication use (11.6 vs 11.8 doses), and length of stay (3.6 vs 3.4 days).

"We were worried that we might have more blood pressure or other cardiac issues with tizanidine, but we actually had less bradycardia and equivalent scores on hypotension with the nonopioid protocol than with the buprenorphine protocol," Dr. Rudolf said.

He also added that with a nonopioid protocol, there is no spike in withdrawal symptoms when it finishes.

"You can tell patients at the completion of their detox that they are done with the worst of it and that things are going to be okay from here. We can say that we are done with controlled substances and that our protocol works."

**Interesting Approach**

Richard Ries, MD, professor of psychiatry and director, Division of Addictions, at the University of Washington and Harborview Medical Center, Seattle, who was not part of the study, called the nonopioid approach an interesting one for people who want to go completely off of all opioids, rather than transition to buprenorphine/naltrexone or methadone.

"People who have been dealing with the opioid epidemic are increasingly interested in using nonopioid approaches. Most people are leery about going to pure abstinence right off the bat because the danger of relapse is high," Dr. Ries said.

"The nonopioids modulate the withdrawal process. Even the COWS scores were as good or, in some cases, better with the nonopioids than with buprenorphine/naloxone.

"So by the end of the 4 or 5 days of serious withdrawal, you will still have some opioid around when you transition to a blocker, and you will go into more withdrawal, but with the nonopioid approach, you can transition more quickly to a blocker. This is where I see the biggest impact of such an approach," he said.
The nonopioid approach is better for people who want to become fully abstinent as quickly as possible, he added.

*Dr. Rudolf and Dr. Ries reported no relevant financial relationships.*


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