Buprenorphine: Long-term Efficacy for Opioid Dependence

Pauline Anderson | May 25, 2016

ATLANTA — As prescription opioid use disorder reaches epidemic proportions in the United States, finding successful treatments for the condition has become hugely important.

Now, research shows that treating opioid-dependent patients with buprenorphine, a partial μ-opioid agonist and κ-opioid antagonist, appears to reduce the need for opioids.

Presented here at the American Psychiatric Association (APA) 2016 Annual Meeting, results of an extension trial showed that fewer than 10% of patents originally dependent on prescription opioids who were initially treated with buprenorphine were opioid dependent after 42 months.

However, some of these patients started taking heroin.

"Long-term outcomes are encouraging in this population, but of course there are dangers of people switching from prescription opioids to heroin." said Roger D. Weiss, MD, professor, psychiatry, Harvard Medical School, Boston, Massachusetts, and chief, Division of Alcohol and Drug Abuse, McLean Hospital, Belmont, Massachusetts.

Dr Weiss discussed the Prescription Opioid Addiction Treatment Study (POATS) at the APA meeting. This was the first large-scale trial to focus on treating prescription opioid dependence and had the first long-term follow-up in this population.

The typical treatment with buprenorphine involves patients initially taking the drug alone and then in a coformulation with naloxone (an opioid antagonist). The combination is meant to prevent misuse of the medication. If the medication is taken properly, the naloxone is not absorbed.

The treatment was originally available only in pill form but now comes in a "film" taken under the tongue (sublingually) or on the cheek (buccally).

To date, most studies of buprenorphine have been short term.

POATS originally included 653 patients at various centers across the United States who were seeking treatment for prescription opioid dependence. About half had been opioid dependent for 4 or more years and the rest for less than 4 years.

The study excluded those with more than "minimal heroin" use, so it didn't accept injection heroin users, according to Dr Weiss.

Opioid dependence was defined according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Participants had to meet at least three of the seven documented criteria.

These patients were randomly assigned to receive buprenorphine/naloxone treatment and standard medical management or to receive this treatment approach plus individual drug counseling.

The study used different intensities of counseling and lengths of buprenorphine use. Researchers assessed patients after a 4-week treatment with taper and a 12-week stabilization treatment for those who did not respond successfully to the initial treatment.

This main trial found that after a follow-up of up to 9 months, patients did much better when stabilized on buprenorphine than when they were tapered off the drug. Adding drug counseling to the buprenorphine treatment plus weekly medical management visits did not improve outcome.

Extension Trial

Researchers managed to contact 375 of the original group for the follow-up study. Although those who had been in the first study most recently were easier to contact and therefore more likely to be included in the extension part, clinical status did not differ between those who were and were not included in the extension phase, said Dr Weiss.

During the follow-up period, patients were free to pursue any treatment. Because this was a "naturalistic" follow-up study, "part of the goal was to see what kind of treatment they got," explained Dr Weiss.

Long-term follow-up assessments took place at 1.5 years, 2.5 years, and 3.5 years (42 months) after treatment.

Almost a third of participants (29.4%) were receiving opioid agonist therapy at 42 months but met no symptom criteria for dependence. About a third (31.7%) were abstinent from opioids and were not receiving agonist therapy. Another 31.4% were using opioids without agonist therapy, and the remaining 7.5% were using illicit opioids while receiving agonist therapy.

The finding that fewer than 10% of participants were opioid dependent at 42 months "is an encouraging outcome," commented Dr Weiss.

Taking opioid agonist treatment was associated with a greater likelihood of opioid abstinence at 42 months.

Heroin Use

The drawback to buprenorphine, however, appears to be heroin use. Study participants with a history of heroin use were more likely to be opioid dependent at 42 months (odds ratio, 4.56; 95% confidence interval, 1.29 - 16.04; $P < .05$). About 8% used heroin for the first time during follow-up, and 10% reported first-time injection of heroin.

Although this is a negative outcome, Dr Weiss stressed that the positive result was stronger. "A lot more people got better than got worse."

Buprenorphine is "an excellent treatment for opioid dependence," said Dr Weiss. "The main concern is that if you are on it and decide that you want to get off of it, it can be difficult to do that."

It may also still pose a problem in terms of diversion, he said.

Patients with opioid dependence disorder have been successfully treated for decades with methadone. Most data suggest that buprenorphine and methadone have "pretty equal" rates of decreased relapse to opioid use among patients who are "retained in care," according to Jeanette Tetrault, MD, assistant professor, medicine, Yale University, New Haven, Connecticut, who has a research interest in substance abuse.

However, the less than 10% opioid dependence rate in this POATS extension trial is "probably better than you would see for methadone among patients coming off treatment," she said.

"This is great research," said Dr Tetrault when asked to comment on the extension study results.

"It hits on the point of what we are seeing clinically, that this medication stabilizes people; it allows them to get back to their lives, to function appropriately, and just do well."

She stressed that opioid dependence is a relapsing condition. "It's a chronic disorder like diabetes, like hypertension; people don't choose it; it happens."

That engagement in agonist treatment was associated with a greater likelihood of abstinence "was not a huge surprise," commented Dr Tetrault.

The fact that there were "a fair number" of patients who "did okay" after coming off treatment and didn't continue on opioid agonist therapy suggests that many "were engaging in some other form of care whether it's counseling, whether it's family support, or whether it's AA/NA [Alcoholics Anonymous/Narcotics Anonymous]."

Dr Weiss has consulted to Reckitt-Benckiser. Dr Tetrault has disclosed no relevant financial relationships.

American Psychiatric Association (APA) 2016 Annual Meeting: Scientific and Clinical Reports (Marijuana and Opiates) 3. Presented May 17, 2016.