Could Hepatitis C Drugs Help Treat PTSD?

Mavyret was associated with the most improvement in post-traumatic stress disorder symptoms.

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Certain direct-acting antiviral drugs appeared to reduce symptoms of post-traumatic stress disorder (PTSD) in veterans treated for hepatitis C, researchers reported recently in the American Journal of Epidemiology. Further studies are now underway to evaluate whether these medications could be used to treat PTSD.

More than 6% of Americans will develop PTSD in their lifetime, according to the U.S. Department of Veterans Affairs (VA). PTSD is a well-known after-effect of military combat, but it can also result from other traumatic life events, such as childhood sexual abuse, serious accidents, natural disasters and violence. An estimated 60% of men and 50% of women will experience at least one such trauma in their lives.

Although PTSD can lead to mental health problems and suicidal thoughts, treatment remains limited. The Food and Drug Administration (FDA) has approved only two medications—the antidepressants paroxetine (Paxil) and sertraline (Zoloft)—for this indication, and these have shown only limited effectiveness in reducing PTSD symptoms, according to a press release about the study.

“Many people have PTSD, but there few effective pharmacologic treatments and limited drug development for PTSD,” said senior study author Jaimie Gradus, MPH, of Boston University School of Public Health. “Existing effective treatments are mostly psychotherapy, and while they work well, there are also issues with them, including a lot of treatment drop-out and they’re time-intensive, so adding to the suite of treatment options for people is a high priority.”

Gradus and her team first conducted an exploratory analysis to look for existing drugs that might improve PTSD using VA electronic health records from 168,941 veterans over a 20-year period. They used a data-mining technique for all FDA-approved medications to identify those associated with greater-than-expected improvement in PTSD symptoms using a standard 20-item checklist.

As described in a 2021 report in Biological Psychiatry, they found that medications typically used to treat PTSD, including sertraline, were associated with some improvement, but the effects were small. However, they unexpectedly found that some direct acting antivirals (DAAs) used to treat

hepatitis C virus (HCV) were strongly associated with symptom improvement. First approved in 2013, second-generation DAAs can cure more than 90% of people with HCV in two or three months without the onerous side effects of interferon-based therapy.

These findings set the stage for a follow-up study limited to 254 veterans in the cohort who were diagnosed with PTSD and hepatitis C between October 1999 and September 2019. Using propensity score weighting, the researchers analyzed changes in PTSD symptoms over the eight- to 12-week course of HCV treatment using the same checklist. In this cohort, 54 people used Mavyret (glecaprevir/pibrentasvir), 54 used Epclusa (sofosbuvir/velpatasvir) and 145 used Harvoni (sofosbuvir/ledipasvir).

The study showed that Mavyret was associated with the greatest improvement in PTSD symptoms after adjusting for other factors that could influence the results, followed by Epclusa, while Harvoni was associated with the least improvement.

“While almost all patients were cured of HCV (92.5%) regardless of the agent received, PTSD outcomes were superior for those receiving [glecaprevir/pibrentasvir] compared with those receiving [sofosbuvir/ledipasvir], indicating that [glecaprevir/pibrentasvir] may merit further investigation as a potential PTSD treatment,” the study authors concluded.

“The level of improvement we see for [glecaprevir/pibrentasvir] is impressive and over twice what we have seen for paroxetine and sertraline,” Gradus said. “I think we have done the best we can with medical records data; an important next step in this line of work will be a prospective placebo-controlled study in patients without hepatitis C virus infection.”

The researchers recently received funding from the Department of Defense to conduct a prospective randomized placebo-controlled trial of Mavyret for PTSD treatment. A small open-label study of Mavyret for PTSD in veterans without hepatitis C is underway (NCT05446857).

“It will be several years until we see the results, but this is a very exciting case where we used VA patient data to identify a potential treatment for PTSD, which is a very important problem for veterans’ health,” said study investigator Brian Shiner, MD, of the White River Junction VA Medical Center in Vermont and Dartmouth University. “In this way, veterans have informed PTSD treatment development.”

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