Another old drug is being tried against COVID-19, and might actually help

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In the first few weeks of the pandemic, when physicians were grappling with the unknown like everyone else, psychiatrist Angela Reiersen recalled that an old drug in her field, called fluvoxamine, affected the body in ways that went beyond improving mental health.

In addition to easing symptoms of obsessive-compulsive disorder and depression, the drug also reduced inflammation, which was emerging as a key culprit in severe cases of COVID-19. She emailed Eric Lenze. a colleague at Washington University School of Medicine in St. Louis, and proposed testing the drug to see if it might help.

Others were trying to repurpose old drugs, too—such as hydroxychloroquine, the one touted by President Donald Trump, and ivermectin, a drug for treating parasites—and there were valid reasons to study them in each case. But most of the old medications, including those two, did not pan out.

Yet fluvoxamine, a 40-year-old drug that costs a fraction of the pricey new treatments for COVID, now looks as if might actually help.

The initial study by the St. Louis pair, conducted on a shoestring budget with no celebrity buzz, suggested that the drug might reduce the risk of severe symptoms. Then in a larger, follow-up study in Brazil, patients who took the drug were less likely to need emergency care and hospitalization, compared to those who were given a placebo.

For now, a National Institutes of Health panel says the evidence for treating COVID with fluvoxamine is inconclusive, but the FDA is weighing a request to authorize it for emergency use. At Johns Hopkins Medicine, treatment guidance recently was updated to state that the drug "may be considered" if other options are not immediately available. And in Canada, a group of scientists advising the province of Ontario recently gave fluvoxamine a conditional thumbs-up.

The appeal is the same as for all drugs already on the shelf. Having gone through the FDA approval process, their safety profile is well understood. And for those drugs available in generic form, the cost is minimal.

A cheap drug

That's the case with fluvoxamine, which costs just $4 wholesale for a 10-day treatment of COVID, said Lenze, a professor of psychiatry at the St. Louis medical school. (In contrast, the federal government is paying about $530 for a course of Paxlovid and $700 for molnupiravir, the new antiviral pills from Pfizer and Merck. And another type of COVID treatment, called monoclonal antibodies, costs more than $2,000.)

But the low cost of fluvoxamine comes with a catch. Because the patent expired on the original formulation of the drug long ago, there is little profit in it. No drug companies would throw their muscle behind such an effort, Lenze said.

"The very thing that makes it so ideal for repurposing—it's a generic, it's widely available, it's cheap—is also what's in our way," he said.

Pfizer and Merck antivirals may help vs. COVID, but they can be hard to get.

So Lenze cobbled together a small study with a $20,000 grant from the chair of his department, and he, Reiersen, and others donated their time.

"We were putting study supplies in brown paper bags and driving them out to patients' houses, because that's all we could afford," he said.

The evidence vs. covid

The team enrolled 152 COVID patients who were not hospitalized, and in their first week of symptoms, randomly selecting 80 volunteers to receive fluvoxamine and 72 to get a placebo. After 15 days, six people on the placebo had experienced "clinical deterioration"—defined as

developing shortness of breath or hospitalization with pneumonia, along with needing supplemental oxygen. But no one who took the real drug went downhill.

Published November 2020 in the *Journal of the American Medical Association*, the study was promising, but too small to draw definitive conclusions.

The Brazil study was 10 times that size, with close to 1,500 participants followed for 28 days. Among those who were given a placebo, 16% needed hospitalization or emergency care for at least 6 hours, compared with just 11% of participants who took the real drug.

It was by no means a magic bullet, but statisticians calculated that the difference between the two groups was likely not due to chance. That is, the drug seemed to reduce the need for emergency treatment by about one-third, the authors reported online in October in *The Lancet Global Health*. Reiersen and Lenze were among the coauthors, joined by researchers from Brazil and McMaster University in Hamilton, Ontario.

Some experts remain unconvinced. Among them is Andrea Druga, a research analyst at ECRI, a Plymouth Meeting-based nonprofit that evaluates the safety and quality of health care. Asked to review the Brazil study, she noted that the drug did not appear to have a significant effect on survival or on the need for mechanical ventilation.

The limitations

What's more, just 6% of study participants had been vaccinated against COVID. She said it was unclear whether the findings in that population would translate to the U.S., where most people have received at least one dose of a vaccine—a measure that most definitely does reduce the risk of death.

Paul Auwaerter, clinical director in the division of infectious diseases at Johns Hopkins University School of Medicine, agreed that more evidence was needed for fluvoxamine. But because some of the pricier treatments are in short supply, he and colleagues have updated in-house treatment guidelines to say fluvoxamine should be considered for outpatients when other options are unavailable.

"There doesn't seem to be a lot of downside," he said, noting that its potential side effects, chiefly nausea, are fairly benign. "But it's hard to feel convinced that there's an upside."

Another study of the drug is underway at the University of Minnesota. And David Boulware, an infectious diseases specialist at that university's medical school, has petitioned the FDA to authorize the drug for emergency use in treating COVID.

Even without that seal of approval, physicians are allowed to prescribe the drug for indications beyond those for which it is approved—a practice called off-label use.

Data from IQVIA, a health technology analytics company, suggest that many are doing so. In the latter part of 2021, pharmacies were filling nearly 130,000 prescriptions for the drug each month, an increase of 25,000 over the corresponding months in 2019, before the pandemic.

Why some doctors prescribe it

Among those who've prescribed it is Owen Muir, a psychiatrist at Brooklyn Minds, a mental-health practice in Brooklyn, N.Y., who recently diagnosed a patient with obsessive-compulsive disorder.

The following week, as Muir was deciding which medicine to prescribe, the person came down with COVID. The psychiatrist went with

fluvoxamine, reasoning that it might help with both conditions.

"In the context of having OCD and then coming down with COVID," he said, "it seemed like that then became the front-runner."

The patient recovered from COVID, but then again, so do most people. Like Druga and Auwaerter, Muir said he would like more data on fluvoxamine. Before prescribing it, a physician must ensure that patients realize the evidence is "not ironclad" and that it can interact negatively with certain other drugs, he said.

But that is true of many drugs, including Paxlovid, the Pfizer antiviral pill. Always remind your physician what other medications you're taking.

Lenze, the Washington University psychiatrist behind the initial study of fluvoxamine, acknowledges that the evidence for the antiviral drugs is "more solid." But he said that's no reason to write off fluvoxamine.

"It doesn't have to be an either-or thing," he said. "I'd hate for somebody to give up a perfectly good course of fluvoxamine hoping to get Paxlovid, only to not get it and then get really sick."

Also unclear is exactly how fluvoxamine might be protecting against severe COVID. In addition to its anti-inflammatory effect, it also may reduce the risk of abnormal blood clots.

Neither of these properties comes to mind for a typical mental-health professional, as they are unrelated to how the drug is thought to help patients with OCD or depression, Muir said. But they did for Reiersen. Muir was so impressed that he invited his fellow psychiatrist on his podcast.

"She was brilliant enough to recognize this might be something that

could help," he said. "And also brilliant enough to be willing to be proved wrong."