Research is piling up to suggest antidepressants could treat COVID-19

By Ana Mulero

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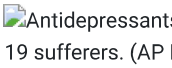

Antidepressants might have an unexpected benefit for COVID-19 sufferers. (AP Photo/Darron Cummings)

Antidepressants might have an unexpected benefit for COVID-19 sufferers. (AP Photo/Darron Cummings)

A study published in *Molecular Psychiatry* this month found a significant association between antidepressant use and a lower risk of intubation or death in hospitalized COVID-19 patients, adding to a body of converging evidence highlighting the potential of certain antidepressants to treat severe cases of the disease.

The report documents the results of a French observational study conducted early last year, and adds additional context from subsequent studies, which gauged the potential for certain antidepressants to treat COVID-19 and helped to frame the results more clearly as the virus became more prominent. The findings suggest that antidepressants could decrease the risk of death or intubation by up to 72% in COVID-19 patients.

Converging evidence from preclinical, clinical and observational research showed similar results. Another study published in *Open Forum Infectious Diseases* earlier this month reports on a

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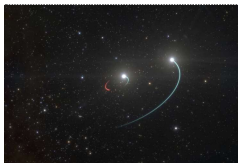

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real-world experience using the commonly prescribed fluvoxamine in patients with COVID-19.

The study in France dates to when Nicolas Hoertel, an associate professor of medicine at Paris University and a psychiatrist at Corentin Celton Hospital, had noticed fewer hospitalized COVID-19 patients with psychiatric disorders than without while working in the emergency room when France had its first three cases confirmed on Jan. 24, 2020.

Hoertel noticed there were "very few people" with COVID-19 with psychiatric disorders in the emergency room and psychiatry department, a 90-bed center specialized in old-age psychiatry that has only had four people hospitalized with severe cases of the disease.

Many more caregivers who worked with these patients were symptomatic, though few were hospitalized.

With most patients in the psychiatry center hospitalized for severe depression or anxiety disorders, the observations begged the question of whether antidepressant use was associated with a lower risk of death or intubation. This question also stemmed from research showing several inflammatory markers' association with severe COVID-19, includi[illegible] ukin-10, tumor [illegible]

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monocyte chemoattractant protein-1. Certain antidepressants have effects on such markers, also.

“These four inflammatory markers are associated with severe COVID-19 and several studies showed that antidepressant use among people with depressive disorders decreases these four specific inflammatory markers,” Hoertel explained. “We have evidence that antidepressants could extinguish this low-grade inflammation."

Before Hoertel’s team conducted the study in France, there were no studies that had examined whether antidepressants would also be able to reduce inflammation in severe COVID-19 infection where there are high levels of the four inflammatory markers. His team collaborated with engineers to build large databases that included all patients hospitalized for COVID-19 in 36 hospitals in Paris and its suburbs.

Results showed a potential decrease in the risk of death or intubation that could be up to 72% in COVID-19 patients on antidepressants, though not all had this effect. Those that did include fluoxetine, paroxetine, escitalopram, venlafaxine and mirtazapine. There was no clear explanation as to why some antidepressants had this effect while others did not when the results of the observational study were first made availabl

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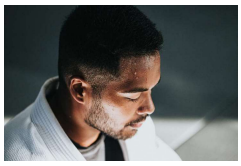

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Other evidence is bringing clarity to the phenomenon: To stop the virus in its tracks, antidepressants inhibit the acid sphingomyelinase enzyme. A 2013 study discussed this effect in detail. An October 2020 study suggested functional inhibitors of this enzyme activity may prevent epithelial cells from being infected with SARS-CoV-2.

More research is needed before the research community can set forth a worldwide approach for prescribing antidepressants for COVID-19, similar to other treatments for the disease. Researchers are working to collect additional data in Germany and the U.S.

Additional evidence will be published in the upcoming weeks. There are at least five ongoing clinical trials already underway in the U.S. and France, as well as several countries in Africa, with the goal of replicating results. A clinical trial led by Washington University is currently underway and expected to set the stage for the next phase of research, too.

Hoertel argues that researchers are "all fighting to get this data not only finalized but also reviewed and published as soon as possible," as the data "changes everything for the next step" in treatment efforts.

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also differ in other ways from the several categories of treatment attempts that have already entered the clinical setting. One is antiviral treatments such as remdesivir and hydroxychloroquine that decrease the replication of the virus inside the cells, while anti-inflammatory treatments represent a second category.

The treatment of COVID-19 using antidepressants could add a third mechanism of action to reduce infectivity, or reduce the ability of the virus to enter the cells. This treatment would be for preventing aggravation, but it could also potentially be curative, researchers have suggested.

Using antidepressants to treat severe COVID-19 patients holds other promising elements, as well. They are associated with fewer side effects than other treatments, such as remdesivir, and could potentially be more affordable. After asking local pharmacies, Hoertel found that a 15-day treatment of a fluoxetine-equivalent dose of 20 milligrams would cost $2 per treatment.

"It will be impossible to ignore that we may have the treatment, and potentially the curative treatment, of COVID-19," Hoertel argues. A large clinical trial like Washington University's needs to show similar results, which will then have to be positioned "within the context of whether antidepressants can be authorized" for the studied indication, he said.

The study, "Association between antidepressant use and reduced risk of intubation or death in hospitalized patients with COVID-19: results from an observational study" was published in Molecular Psychiatry on Feb. 4. The authors of the study were Nicolas Hoertel, Marina Sánchez-Rico, Raphaël Vernet, Nathanaël Beeker, Anne-Sophie Jannot, Antoine Neuraz, Elisa Salamanca, Nicolas Paris, Christel Daniel, Alexandre Gramfort, Guillaume Lemaitre, Mélodie Bernaux, Ali Bellamine, Cédric Lemogne, Guillaume Airagnes, Anita Burgun, and Frédéric Limosin, AP-HP / Universities / INSERM COVID-19 Research Collaboration and AP-HP COVID CDR Initiative.