Existing heart failure drug may treat potential COVID-19 long-hauler symptom

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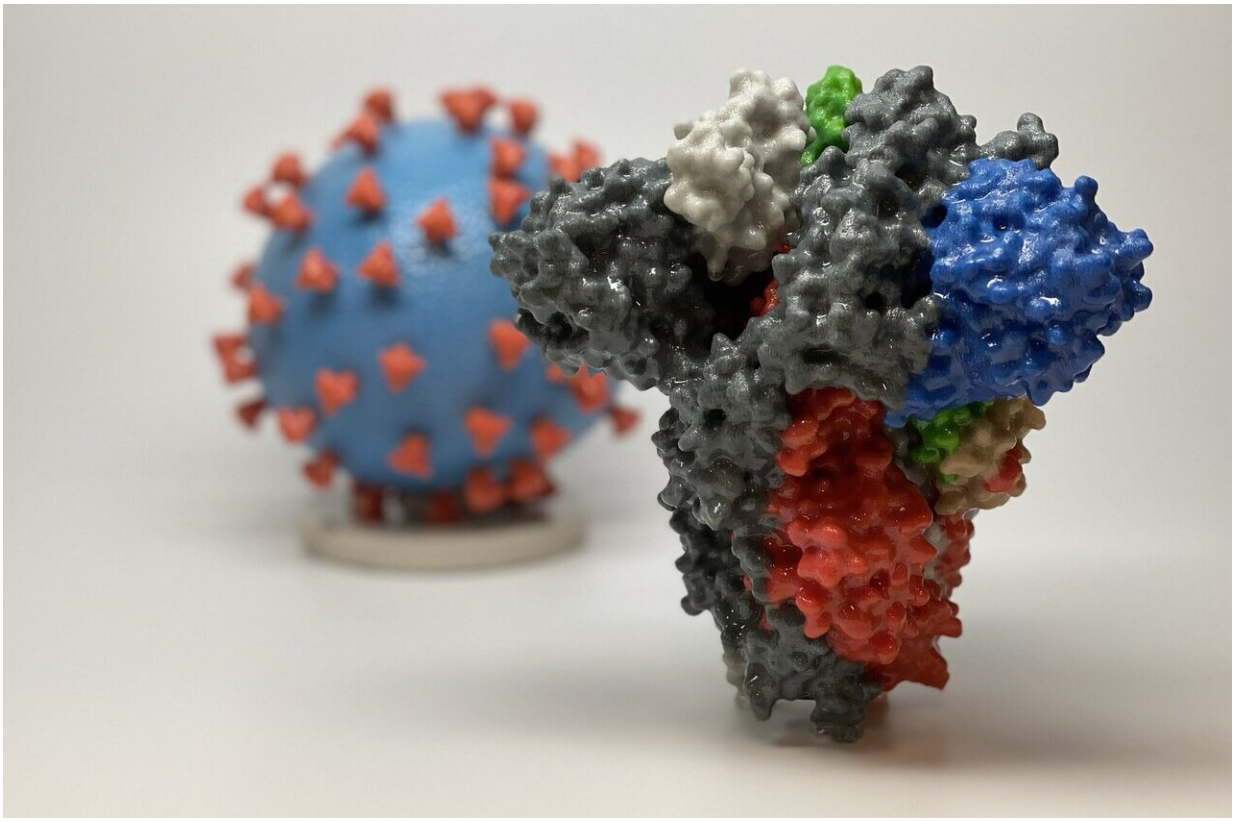

3D print of a spike protein of SARS-CoV-2, the virus that causes COVID-19—in front of a 3D print of a SARS-CoV-2 virus particle. The spike protein (foreground) enables the virus to enter and infect human cells. On the virus model, the virus surface (blue) is covered with spike proteins (red) that enable the virus to enter and infect human cells. Credit: NIH

In a new study out of University of California San Diego School of Medicine, researchers found a drug used for heart failure improves symptoms associated with postural orthostatic tachycardia syndrome, otherwise known as POTS. This complex, debilitating disorder affects the body's autonomic nervous system, causing a high heart rate, usually when standing.

Writing in the February 15, 2021 online issue of the *Journal of the American College of Cardiology*, study authors investigated the drug ivabradine and its effects on heart rate, quality of life and plasma norepinephrine levels in persons living with POTS. Norepinephrine is a stress hormone and neurotransmitter. In blood plasma, it is used as a measure of sympathetic nervous system activity. Trial participants experienced a reduction in heart rate, improvement in their symptoms and overall quality of life one month after taking the drug.

"Ivabradine is a novel agent that's FDA-approved for heart failure, but based on its mechanism we thought it could be helpful for patients with POTS as it reduces heart rate without impacting blood pressure," said Pam Taub, MD, cardiologist at the Cardiovascular Institute at UC San Diego Health and associate professor of medicine at UC San Diego School of Medicine. "When we can lower the heart rate, we're providing these patients with the ability to stand up, something they couldn't do without difficulty before due to their POTS diagnosis."

The study involved 22 individuals whose average age was 32 years. Each participant had been screened and recruited from cardiology clinics at UC San Diego Health from 2018 to 2020.

The study utilized a randomized, double-blinded, placebo-controlled crossover design in which patients started on either ivabradine or a placebo for one month. At the end of the month, all participants underwent a washout period where neither drug nor placebo was taken

for one week. After the washout period, the participants who had previously received ivabradine switched to placebo and vice versa for one month.

Over the course of the two months, patients also met with researchers for seven different clinic visits in which plasma norepinephrine levels were measured and head-up tilt testing conducted to observe the patient's heart rate when sitting, lying down or standing up.

"Before the study, these patients would be living with elevated heart rates ranging between 100 to 115 beats per minute when standing," said Taub. "After taking ivabradine twice a day for one month, the standing heart rate decreased significantly to around 77 beats per minute compared to the placebo group. Participants also reported improvement in quality of life measures when on the drug."

The researchers also noted ivabradine was well-tolerated with no significant side effects while other drugs used to lower heart rate, such as beta blockers, can cause fatigue and decreased blood pressure.

Taub said the study was the first randomized clinical trial using ivabradine to treat POTS.

POTS is typically caused by a viral infection, trauma, surgery or enforced bedrest, and most commonly affects young women who are either athletes or highly active. Currently, there is no FDA-approved treatment for POTS and the condition can severely impact quality of life. Other symptoms of POTS include "brain fog," lightheadedness, palpitations, tremors, weakness, blurry vision and fatigue.

Recently, POTS has been identified as a potential "long-hauler" symptom of COVID-19.

"In our contemporary practice, we are seeing patients who have previously been infected with COVID-19 present with symptoms consistent with POTS," said Jonathan Hsu, MD, cardiologist at UC San Diego Health. "Given the similarities, this study leads to the question whether therapy with ivabradine may help patients who experience similar symptoms after a COVID-19 infection, and provide an important area for future study as well."

The authors said they hope ivabradine will be considered as a possible treatment option for those with a confirmed diagnosed of POTS. Currently, the drug is not FDA-approved for the disease and when used clinically it would be "off-label" use.

"Similar to patients with COVID-19, patients with POTS need to be followed carefully," said Taub. "Treatment for POTS needs to be personalized for each individual and with this drug, paired with lifestyle therapy, including exercises specific for POTS, we hope we will see more individuals overcome this unfortunate condition."

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