Researchers urge clinical trial of blood pressure drug to prevent complication of COVID-19

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Researchers in the Ludwig Center at the Johns Hopkins Kimmel Cancer Center report they have identified a drug treatment that could—if given early enough—potentially reduce the risk of death from the most serious

complication of Coronavirus disease 2019 (COVID-19), also known as SARS-CoV-2 infection.

Prazosin, a U.S. Food and Drug Administration-approved alpha blocker that relaxes blood vessels, may specifically target an extreme inflammatory process often referred to as cytokine storm syndrome (CSS) that disproportionately affects older adults with underlying health conditions, and is associated with disease severity and increased risk of death in COVID-19 infection. Using it pre-emptively to address COVID-19-associated hyperinflammation of the lungs and other organs has the potential to reduce deaths in the most vulnerable populations, they say.

In a report of their findings published April 30 in the *Journal of Clinical Investigation*, the researchers caution that although they believe if given early enough after viral exposure, the drug could prevent some deaths, it would not work in patients with advanced stages of the disease. They also emphasize that controlled clinical trials for this novel use of prazosin are needed before it can be safely recommended.

The investigators published the letter, they said, in hopes of stimulating rapid efforts to conduct such trials.

In the letter, the researchers described how they have been working in collaboration with researchers in the Johns Hopkins Divisions of Rheumatology and Infectious Diseases, and Departments of Neurology and Neurosurgery, to identify chemical ways of safely blocking the actions of catecholamines and cytokine responses. Together, catecholamines and cytokines enhance the inflammatory process that leads to severe COVID-19 symptoms, explains Chetan Bettegowda, M.D., Ph.D., Jennison and Novak Families Professor of Neurosurgery, who is senior author of the paper.

"The purpose of our article is to make the biomedical community aware of the potential of this approach and to stimulate additional basic and clinical research. Although, we are excited about this idea, we stress that a clinical trial is necessary to know if this intervention will help COVID patients, and that is where we are focusing all of our attention," says Bettegowda.

In mouse models of CSS, they found that prazosin—commonly used to treat blood pressure, prostate gland enlargement and other conditions—blocked catecholamines (hormones released by the adrenal glands when the body is under stress), reduced cytokine levels, and increased survival after exposure to agents that trigger cytokine storm responses similar to those observed in COVID-19.

Drugs that target CSS have been found to reduce the risk of death from other viral illnesses by up to 55%, according to preliminary results from a retrospective clinical study.

Prazosin is taken by mouth, costs less than $25 per month in the United States, and has been safely taken by millions of people over the last two decades. This should enable highly expedited clinical trials in people early after exposure to the SARS-CoV-2 virus, say the researchers.

"All drugs can have unanticipated side effects when used in new situations, so it is critical to evaluate the effectiveness and side effects of this drug in controlled clinical trials before it can be safely recommended for public use. This is particularly important for drugs like prazosin, which are already sold in pharmacies," says Bettegowda.

Maximilian Konig, M.D., research fellow and lead author of the report, says a vaccine remains the best long-term hope to prevent deaths from COVID-19 but notes, at present, there are hundreds of individuals throughout the world who are dying every day. "Prazosin is already

widely available, known to be safe and inexpensive, and the regulatory path for use in individuals exposed to the virus is straightforward," he says.

The CSS treatment was granted Food and Drug Administration approval to be studied in a clinical trial for individuals with COVID-19.

More information: Maximilian F. Konig et al, Preventing cytokine storm syndrome in COVID-19 using α-1 adrenergic receptor antagonists, *Journal of Clinical Investigation* (2020). DOI: 10.1172/JCI139642

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