Statin use is linked to lower death rate in hospitalized COVID-19 patients

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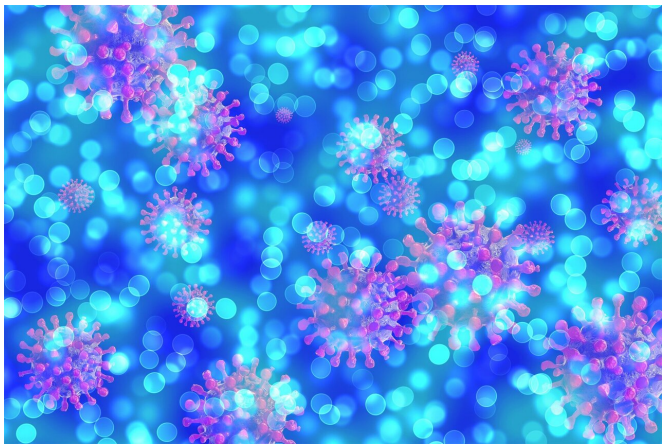

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The use of cholesterol-lowering drugs called statins is associated with a lower death rate and a lower incidence of mechanical ventilation in patients hospitalized with Coronavirus disease 2019 (COVID-19), researchers report June 24 in *Cell Metabolism*. The large-scale retrospective study also showed that mortality risk and other negative outcomes were not increased by combination therapy consisting of statins and blood pressure-lowering drugs called angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs).

"These results support the safety and potential benefits of statin therapy in hospitalized patients with COVID-19 and provide a rationale for prospective studies to determine whether statins confer protection against COVID-19-associated mortality," says senior study author Hongliang Li of Wuhan University. "Moreover, our findings represent an important contribution to the accumulating clinical evidence regarding the beneficial or detrimental effects of prescribing ACE inhibitors or ARBs to patients with COVID-19."

Currently, there is no vaccine or specific antiviral drug approved to prevent or treat severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which causes COVID-19. Because a vaccine or drugs for COVID-19 will likely not be available for months or even years, repurposing clinically approved therapies might be a more attractive option. Statins may serve such a purpose because these drugs slow the progression of lung injury in animals, improve immune cell responses, and strongly reduce inflammation, which is likely responsible for severe COVID-19 complications such as organ damage.

Although statins generally have an excellent safety profile in humans, animal studies have shown that they increase the expression of angiotensin-converting enzyme II (ACE2)—the receptor that SARS-CoV-2 binds to and uses to enter host cells. On the other hand, animal studies have also shown that ACE2 protects organs such as the lungs against virus-induced injury. As a result, it has not been clear how clinical outcomes in patients with COVID-19 are affected by the use of statins, either alone or in combination with ACE inhibitors and ARBs, which are commonly prescribed with statins and also increase ACE2 expression in animals.

To address this gap in knowledge, Li and his collaborators carried out a retrospective study of 13,981 COVID-19 patients admitted to 21 hospitals in Hubei Province, China. Among these patients, 1,219 used statins, primarily atorvastatin at an average dose of 20 mg/day. Among patients with hypertension (i.e., high blood pressure), 319 used statins combined with ACE inhibitors or ARBs, and 603 used statins combined with other antihypertensive drugs.

The researchers analyzed mortality rates and secondary outcomes, including the incidence of invasive mechanical ventilation, admission to intensive care units, acute respiratory distress syndrome, and liver, kidney, or heart injury.

Because patients on statins were older and had a higher incidence of lung lesions and chronic diseases, the researchers also performed analyses on subsets of patients that were matched for baseline characteristics such as age, disease severity, and pre-existing conditions.

Over a 28-day follow-up period, statin use was associated with a lower death rate and a lower incidence of mechanical ventilation. Statin use was associated with 5.5% mortality rate, compared to 6.8% without statin use, representing a 19% decrease. When the researchers examined the matched cohort of 861 patients in the statin group and 3,444 patients in the non-statin group, statin use was associated with a 45% decrease in the mortality rate, from 9.4% to 5.2%. In the matched cases, statin use was also associated with lower levels of three inflammation biomarkers, and a lower incidence of acute respiratory distress syndrome and admission to intensive care units.

In the unmatched sample, mortality and secondary outcomes over 28 days were not affected by the use of statins combined with ACE inhibitors or ARBs, compared to combination therapy consisting of statins and other antihypertensive drugs. But in the matched cohort with 204 patients in each group, the use of statins combined with ACE inhibitors or ARBs versus other antihypertensive drugs was associated with a 65% drop in the death rate (3.4% versus 9.8%) and a lower incidence of heart injury and acute respiratory distress syndrome.

"Although the use of an ACE inhibitor or ARB was once speculated to be potentially harmful in patients with COVID-19, several professional societies have recommended the continued use of these drugs in patients with COVID-19 and pre-existing hypertension," Li says. "To our knowledge, the results from this study are the first clinical evidence supporting the notion that the risk of COVID-19 mortality is not increased by using ACE inhibitors or ARBs in combination with statin treatment."

However, the study does not prove that the lower death rate of patients with COVID-19 is directly caused by the use of statins, either alone or in combination with ACE inhibitors or ARBs. For now, it is also unclear whether the findings apply to non-hospitalized patients with COVID-19. Moreover, the results of retrospective studies should be interpreted with caution, Li says. "Although these data do provide supportive evidence for the safety of statins or the combination of statins with ACE inhibitors or ARBs for treatment in patients with COVID-19, further randomized controlled trials to prospectively explore the efficacy of statins on COVID-19 outcomes appear justified."

More information: Xiao-Jing Zhang et al, In-hospital Use of Statins is Associated with a Reduced Risk of Mortality among Individuals with COVID-19, *Cell Metabolism* (2020). DOI: 10.1016/j.cmet.2020.06.015

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