Statin therapy and SAR-CoV-2: an available and potential therapy?

The epidemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) due to a novel coronavirus (COVID-19) has emerged as a worldwide threat. Like other coronaviruses, SARS-CoV-2 results in a cytokine storm upon viral entry which leads to acute respiratory distress syndrome and subsequent organ damage. The virus activates immune cells, inducing a proinflammatory state which leads to further clinical deterioration. Patients with cardiovascular risk factors and pre-existing cardiovascular disease tend to have worse outcomes.1 Additionally, studies have linked myocardial injury among COVID-19 patients with higher mortality.2 Importantly, none of the published experiences from China or Italy has commented on the proportion of patients on statin and the potential impact of statin therapy on outcomes.

The benefits of statins have been established for primary and secondary prevention of cardiovascular diseases. The role of statins in reducing cardiovascular risk is not limited to the cholesterol-lowering effect only, but is also due to several pleiotropic mechanisms. Statins attenuate myocardial injury and improve survival in viral myocarditis among experimental animals. Statins also reduce T-cell frequency and macrophages in myocardial infiltrates.3 Coronary atherosclerotic plaques are prone to rupture in response to an exacerbated inflammatory response as the case with severe COVID-19 infection.2 Atherosclerotic plaque stabilization and regression achieved by statins along with their anti-inflammatory effects could confer protection in these patients. Prevention of lung tissue damage has been suggested as a result of the inhibitory effect of statins on leucocyte–endothelial interaction and inflammatory gene transcription.4 In fact, some observational data suggest that moderate dose statin therapy was associated with lower mortality among patients with influenza pneumonia.5 Arrhythmias are another frequently encountered complication among hospitalized patients with COVID-19 in intensive care units,6 and statins have been shown to exhibit some antiarrhythmic activity.7

Lipid rafts with a high concentration of cholesterol provide a platform to concentrate angiotensin-converting enzyme 2 (ACE2) as clusters on host cell membranes to anchor with the coronaviral spike glycoprotein and facilitate cellular entry.8 Statins inhibit Ebola virus...
production and glycoprotein processing, so a similar pattern might be a target for SARS-CoV-2. Host ACE2 receptors utilized by SARS-CoV-2 might be potential targets for viral therapeutic intervention. Experimental studies suggest that statins might up-regulate ACE2 expression. Clinical studies are encouraged to investigate the effect of ACE2 expression in protection against respiratory distress and the role of statin therapy for this postulated hypothesis. Main protease (Mpro) is a key enzyme for coronavirus replication via post-translational processing of the RNA replicase machinery and is responsible for processing the polypeptide into functional proteins. Targeting Mpro could be an attractive therapeutic approach against SARS-CoV2. Ongoing experimental studies are investigating the role of statins in inhibiting this enzyme.

Collectively, these findings suggest that statins might represent an enforcement in the battle against the COVID-19 outbreak. The repurposing of statins as safe, available, and inexpensive therapy could be a promising therapeutic approach against SARS-CoV-2. Further clinical studies are warranted to evaluate the efficacy of statin therapy against COVID-19 and determine the effective therapeutic dose.

Conflict of interest: none declared.

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