Antihypertensive drugs and risk of COVID-19?

Lei Fang and colleagues[1] postulate that because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) binds to the angiotensin-converting enzyme 2 (ACE2) receptor to facilitate host cell entry,[2,3] disease severity and mortality of coronavirus disease 2019 (COVID-19) might be increased in patients taking angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) during the COVID-19 pandemic, because the ACE2 receptor might be upregulated with use of ACEIs and ARBs.

Although it is true that many patients with severe COVID-19 have hypertension and diabetes, as reported by Guan and colleagues in a study of more than 1000 patients,[4] in that study other factors were also notably unevenly distributed among groups, including age, sex, smoking status (eg, current smoker), and chronic pulmonary disease. Even though patients with diabetes and hypertension frequently use ACEIs and ARBs, many confounders must be accounted for when interpreting findings of observational studies.[5] In another study looking at risk factors for mortality among patients with COVID-19,[6] despite hypertension and diabetes being identified as the most frequently associated comorbidities, after multivariate regression the association between these disorders and COVID-19 mortality was no longer significant.

In theory, use of ACEIs and ARBs over time would result in an upregulation of ACE2 receptors. In children and young adults, ACE2 receptors are present at a much higher density in lung tissue than in older individuals. Thus, the condition in people taking ACEIs and ARBs emulates that in young people. It is possible that having more ACE2 receptors provides a reserve against target-mediated destruction by SARS-CoV-2.[7] ACE2 functions to produce the heptapeptide angiotensin (1-7), which has favourable effects on the pulmonary endothelium and might provide resilience from development of pulmonary failure in COVID-19.[7]

We caution against indiscriminate discontinuation of ACEIs and ARBs in patients who rely on these drugs for treatment of heart failure and who, additionally, might benefit from the postulated positive effects during overwhelming infection with SARS-CoV-2. Discontinuation of ACEIs or ARBs is associated with readmission to hospital and mortality among patients with heart failure.[8] A surge of admissions to hospital for heart failure because of indiscriminate cessation of these important agents could overload already burdened health-care systems with vulnerable patients and cause diagnostic problems in view of the range of symptoms shared between acute heart failure and COVID-19, such as cough and shortness of breath.

The quick developing nature of the COVID-19 pandemic, and uncertainty around best practice, calls for caution when putting forward hypotheses that suggest a change in drugs. More evidence is needed before any clinical decisions are made.

We declare no competing interests.

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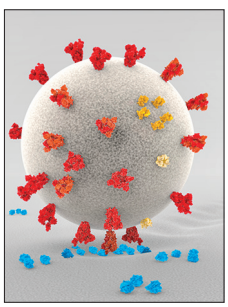

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Lancet Respir Med 2020

Published **Online**
March 26, 2020
https://doi.org/10.1016/S2213-2600(20)30156-9