A consensus statement on the use of angiotensin receptor blockers and angiotensin converting enzyme inhibitors in relation to COVID-19 (corona virus disease 2019)

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ABSTRACT

There has been a lot of speculation that patients with coronavirus disease 2019 (COVID-19) who are receiving angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) may be at increased risk for adverse outcomes. We reviewed the available evidence, and have *not* found this to be the case. We recommend that patients on such medications should continue on them unless there is a clinical indication to stop their use.

There has been an unprecedented interest generated in the medical community and on social media around the interaction of coronavirus (SARS-CoV2) and ACE inhibitors (ACEi) and angiotensin receptor blockers (ARB), and whether these medications increase the risk of COVID-19.

This was triggered by correspondences published in high-impact medical journals, Lancet Respiratory Medicine and BMJ.[1,2] They observed that the COVID-19 patients with comorbidities such as hypertension and diabetes, had more severe symptoms. The authors hypothesised that diabetes and hypertension treatment with ACE2-stimulating drugs increases the risk of developing severe and fatal COVID-19. They suggest that ACEi and ARB can increase ACE2, which is an enzyme used by the virus to gain entry into host cells. Therefore, these drugs could potentially increase the risk of severe infection.

We reviewed the evidence supporting this hypothesis, and would like to make the following observations:

1. The studies from China report higher prevalence of hypertension in those who developed severe COVID-19 disease.[3,4] However, a conclusion cannot be drawn that hypertension results in severe infection as these analyses were unadjusted for confounders such as age, and there was no reported data on ACEi and ARB use in these studies. Another recently published study evaluating cardiovascular implications of COVID-19 did not find any association between use of ACEi/ARB and mortality.[5]
2. Previous animal studies[6] showed that ACEi and ARB increase ACE2 activity. Based on this, Fang et al proposed that this would enhance infectivity of

the SARS CoV2 virus.[1] However, other studies did not find any change in ACE2 mRNA expression in rat heart cells treated with an ACEi[7] and no change in plasma ACE2 activity in the presence of either ACEi or ARBs in humans.[8] Therefore, it is questionable whether these drugs increase either the expression or enzymatic activity of ACE2 in tissues to cause severe viral infection.

3. To the contrary, there is evidence that ACEi might confer protection in some viral pneumonias.[9] Based on this, there are ongoing trials studying the effect of Losartan (an ARB) in patients with COVID-19 in outpatient and inpatient settings.[10,11]

Therefore, given the available evidence, we DO NOT advise patients on ACEi or ARB to change therapy. These commonly used medications confer benefits in patients with cardiovascular disease, kidney disease and diabetes, and should not be changed unless clinically indicated. The current evidence on COVID-19 and hypertension, and ACEi or ARB medication is inadequately adjusted and prone to bias, and therefore remains inconclusive.

Our recommendation to prescribed use of ACEi and ARBs is consistent with the viewpoint of numerous societies from around the world including the American College of Cardiology, American Heart Association, and Heart Failure Society of America, European Society of Cardiology, the International Society for Hypertension, European Renal Association and European Dialysis and Transplant Association.

Competing interests:
Nil.

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