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EDITORIAL

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ACE inhibitors and COVID-19: We don't know yet

Dear Editor,

The SARS-CoV-2, the causative agent of COVID-19, has been established to gain access to human cells via the ACE2 receptor, similar to the related coronavirus SARS-CoV which led to an outbreak in 2003. A concern with the newer 2019 coronavirus is its 10 to 20-fold higher affinity to the ACE2 receptor that of SARS-CoV-2, aiding its effective human-to-human transmission. ACE2 receptor expression is thought to be upregulated in ACE inhibitors (ACEI) users. As ACEI are used extensively in the treatment of hypertension, there has been concern regarding the risk of using these medications in patients with COVID-19, and whether the use of such ACEI predisposes to COVID-19. ACEI are also used in the treatment regime of other common conditions including diabetes. Consequently, the increased expression of ACE2 would facilitate infection with COVID-19. Therefore, it may be hypothesized that diabetes and hypertension treatment with ACE2-stimulating drugs would increase the risk of developing severe and fatal COVID-19. The recent Chinese clinical studies detailing the clinical characteristics of patients infected by the novel coronavirus disease-19 (COVID-19) infection have confirmed many of these concerns.[1] A study included 1099 patient's laboratory-confirmed COVID-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China through 29 January 2020, of which 261 had associated comorbidity.[2] Hypertension yet again was the most common comorbidity with 165 patients, followed by 81 patients with diabetes. A meta-analysis[3] evaluating the comorbidities associated with COVID-19 found similar results. These statistics raise the question of whether hypertension itself is a high-risk comorbidity or is the use of angiotensin-converting-enzyme inhibitor (ACEI) specifically as treatment responsible for these statistics.

Despite coronary heart disease (CHD) being the most common chronic condition worldwide, a small percentage of COVID-19 patients suffered from the condition. The lower rates of CHD could be due to the lower ACE2 receptor expression in patients with CAD and heart failure,[4] there by reducing the likelihood of contracting COVID-19. Large cohort studies factoring in ACE2 expression as a variable while comparing the progression of COVID-19 infection in patients would indicate the relevance of ACE2 receptor in COVID-19 mortality and fatality.

According to data from the above study, 23.7% of patients with hypertension had a severe COVID-19 infection, followed by diabetes mellitus (16.2%), CHDs (5.8%), and cerebrovascular disease (2.3%). A high percentage (35.9%) of those who had hypertension died or required mechanical ventilation at the intensive care unit, while the same occured in 26.9% of diabetic patients. As ACEIs are predominantly used in hypertension this could potentially explain the high percentage of COVID-19 positive patients who develop a severe infection. Diabetic patients could also be on ACEIs to slow down the progression of vascular complications associated with diabetes, hence the high percentage of diabetic patients developing a severe infection. Still, the proportion of diabetic patients with severe infections were much less than hypertensive patients, which could be due to the less common use of ACEIs in diabetes in comparison.

On the other hand, studies[5] have suggested the use of ACEI might be protective against respiratory complications. The binding of SARS-CoV-2 to ACE2 exhausts ACE2, leading to an imbalance of the renin-angiotensin-aldosterone system which spirals into acute severe pneumonia. Blocking the renin-angiotensin-aldosterone system by ACEI might, therefore, reduce inflammation in COVID-19 pneumonia, potentially reducing mortality. A recent study[5] compared inflammatory marker found in COVID-19 positive patients on ACEIs versus non-ACEIs, revealing that interleukin-6 levels were reduced in the ACEI group. Large studies are needed to delineate the role of ACEI in treating COVID-19, ideally both in patients naïve to ACEI and chronic users of ACEI. Since small centers may have difficulty amassing enough cases, interinstitutional collaborations should be strongly encouraged. These would show whether the use of ACEIs in COVID-19 positive causes more harm than good or vice versa.

In short, both the concerns regarding ACEI use predisposing to infection by SARS-CoV-2 and the idea that ACEI may help treat COVID-19 have valid theoretical bases. At this point, there is insufficient clinical evidence pointing to either being true; thus, further studies are urgently required. Given the known, significant cardiovascular benefits of ACEI, patients should not stop taking them over the above theoretical concerns. Medical workers and researchers worldwide are strongly encouraged to report any available data regarding the relationship between ACEI and COVID-19.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

KEYWORDS

ACEI, coronavirus, COVID-19

ORCID

Taqua R. Khashkhusha http://orcid.org/0000-0002-0682-5615
Jeffrey Shi Kai Chan http://orcid.org/0000-0003-0231-2393
Amer Harky http://orcid.org/0000-0001-5507-5841

Taqua R. Khashkhusha[1]
Jeffrey Shi Kai Chan MBChB[2,3]
Amer Harky MBChB, MRCS, MSc[4]

[1]*School of Medicine, University of Liverpool, Liverpool, United Kingdom*
[2]*Faculty of Medicine, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong*
[3]*Division of Cardiology, Department of Medicine and Therapeutics, Prince of Wales Hospital, Shatin, New Territories, Hong Kong*
[4]*Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital, Liverpool, United Kingdom*

Correspondence
Amer Harky, MBChB, MRCS, MSc, Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital, Thomas Drive, Liverpool, L14 3PE, UK.
Email: aaharky@gmail.com

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