Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letters to the Editor

What Is the Role of Angiotensin-Converting Enzyme 2 (ACE2) in COVID-19 Infection in Hypertensive Patients With Diabetes?

To the Editor:

The recent publication by Bombardini et al. suggests an important role of the renin angiotensin aldosterone system (RAAS) in the development of acute respiratory distress syndrome (ARDS) in patients with underlying infection with the novel coronavirus, SARS-CoV-2.[1]

The complex interplay between the angiotensin-converting enzyme (ACE)/ACE2 pathways in the development of ARDS is supported by extensive literature. This is further highlighted by Bombardini et al. in their article describing the translational mechanisms behind lung injury in patients with SARS-CoV-2.[1]

We, however, contest the suggestion made by the authors regarding the presence of increased levels of ACE2 expression in patients with underlying hypertension, diabetes, and cardiovascular disease. Previous work on both animal and human models have, in fact, suggested otherwise.[2,3] There is still, however, an imbalance, as suggested by the authors in favour of the vasoconstrictive, proinflammatory, and profibrotic ACE/angiotensin II (ATII)/angiotensin type 1 receptor (AT1R) pathway in comparison with the counterregulatory ACEII/angiotensin 1-7/angiotensin type 2 receptor pathway. This may explain the development of severe acute lung injury in these groups of high-risk patients when infected with SARS-CoV-2.

Hypertensive patients with diabetes who are treated with ACE inhibitors and angiotensin receptor blockers (ARBs) may, however, express increased levels of ACE2 on cell-surface membranes. Whether this necessarily translates into increased coronavirus viral load or severity of disease is still not known.[4] It has rather been suggested that despite increasing ACE2 levels, ACE inhibitors and ARBs may rather play a protective role. ACE-I, by reducing the conversion of ATI to ATII and ARBs, by reducing the binding of ATII to AT1R (and preferably binding AT2R), may tilt the scale suggested by Bombardini et al. in favour of a protective ACE2-signalling pathway.

This, however, does not take away from recognizing the subtle balance between the ACE/ACE2 pathways and how it may contribute to the development of lung injury in SARS-CoV-2. It is thus suggested that modulators of the RAAS system may be therapeutic targets against SARS-CoV-2. The findings of current trials using ARBs, as well as early-phase 2B trials using intravenous recombinant human ACE2, may provide further evidence to support the suggestions of Bombardini et al.[4]

Thadathilankal-Jess John, MBChB, DipHIV Man (SA), MMed (Int Med), MRCP (UK), FCP (SA)
jessjohnt@gmail.com

Kiran John, MBChB, DipHIV Man (SA), MMed (Int Med), FCP (SA)

Disclosures

The authors have no conflicts of interest to disclose.

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