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Covid-19 and the angiotensin-converting enzyme (ACE2): Areas for research

To the Editor,

The influence of the angiotensin-converting enzyme 2 (ACE2) receptor, as a port of host cell entry for the severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2), is a current epicenter for healthy debate in coronavirus disease 2019 (Covid-19). Highlighted below are issues regarding particular drugs that deserve special attention by researchers.

Logically, the effect of ACE-inhibitors and angiotensin receptor blockers (ARB's) on ACE2 are being examined. There are controversial data regarding ARB's causing an initial upregulation then downregulation of ACE2 expression during Covid-19 and whether this may result in net harmful or beneficial outcomes.[1] Out of the spotlight, statins have also been implicated in increasing ACE2 expression in animal models.[2,3] Whilst statins carry an anti-inflammatory repute, they have also been associated with increased interleukin levels and mortality in acute respiratory distress syndrome (ARDS); though not specifically Covid-19 related ARDS.

The issue with these omnipresent medications, is that scientific and clinical data are currently very limited, thus yielding contentious interpretations and accordingly, equipoise recommendations from authorities on the use of these drugs during Covid-19. Retrospective data associate baseline comorbidities with a severe course of Covid-19 but details of medications chronically used to treat those comorbidities and the fate of those drugs during the disease course, are not always reported. Scrupulous reporting of such data may also shed light on the concept of cessation of these medications in a prophylactic attempt against contracting SARS-CoV-2. Stopping ARB therapy can precipitate cardiovascular decompensation but cessation for primary preventative indications, as with statins, is a plausible strategy to reduce available receptors for SAR-CoV-2. Although these theories are tempting, especially to the lay-person and media, there are no high quality data upon which to base generalized practice. In an era of evidence-based and heavily litigious medicine, physicians are left in management dilemmas until higher quality research catches up to the pandemic.

A final noteworthy drug, propofol, has been previously associated with increased ACE2 expression in human endothelial cells. By increasing ACE2 mediated conversion of angiotensin II to angiotensin (1−7), propofol may exhibit a lung protective effect via reduced angiotensin II-induced endothelial dysfunction.[4,5] This is another area that deserves exploration since to date there are no studies specifically assessing its influence, if any, in Covid-19 related ARDS.

Authorship statement

Michael Omar: writing and revising the manuscript.

Declaration of Competing Interest

I, Michael Brandon Omar, certify that this manuscript, nor any part of it, is under consideration for publication elsewhere. There are no special issues or conflicts of interest to disclose.

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