Indian Heart Journal 72 (2020) 212–213

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Letter to the Editor

Continue ACE inhibitors / ARB'S till further evidence in coronavirus disease 2019 (COVID-19)

Keywords:
ACE inhibitors
ARB'S
ACE2
COVID-19

The Coronavirus disease 2019 (COVID-19) has been declared as a pandemic by world health organization (WHO). In the pandemic of Coronavirus, the consequences of hypertension, heart failure and coronary artery disease have been overlooked. One in every three Indian adults has high blood pressure.[1] We wish to highlight the apprehension of cardiologists and physicians on the use of ACE inhibitors/ARB's in the Indian population who are at risk of COVID-19.

Association of coronavirus with angiotensin converting enzyme 2 (ACE2) has been simplified in Fig. 1. The SARS-Cov-2 virus enters the cell through ACE 2 receptor on the lung membrane. ACE 2 predominantly catalyzes the conversion of angiotensin II to angiotensin 1-7, and its lesser action is on conversion of angiotensin 1 to angiotensin 1-9. ACE 2 is present at lung alveolar epithelial cells, heart and kidneys. It is having protective effects on the cardiovascular system by degrading angiotensin II, and acts as a vasodilator. After entry inside the cell, SARS-Cov-2 replicates inside the cell, and cause down regulation of ACE2. The protective role of ACE 2 vanishes and high

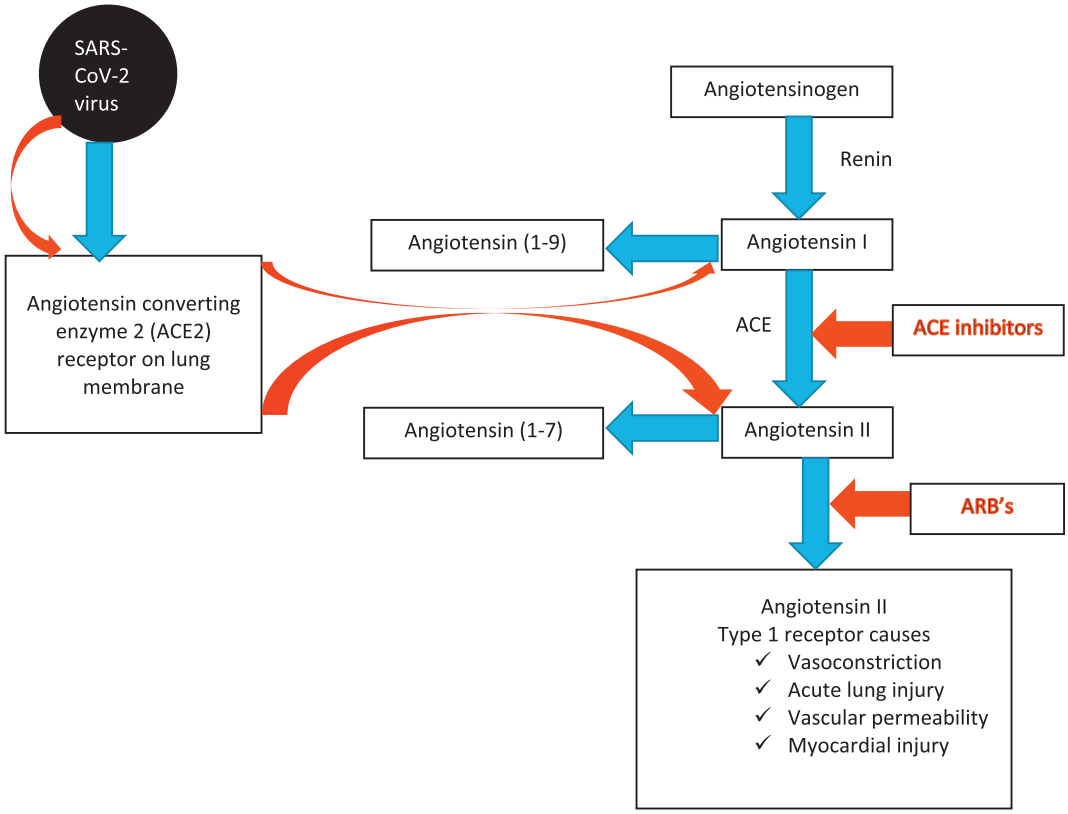

Fig. 1. SARS-Cov-2 virus enters into cell through angiotensin converting enzyme 2 (ACE 2) receptor on lung membrane, replicates and further downregulates ACE 2. The physiological function of ACE 2 is to degrade angiotensin II. Downregulation of ACE 2 by virus leads to increase in Angiotensin II, which causes systemic injury. Angiotensin converting enzyme inhibitors (ACEi) block ACE and aldosterone receptors blockers (ARB's) block angiotensin II blockers. Red arrow depicts negative regulation and blue arrow depicts positive regulation. SARS-Cov-2 (Severe acute respiratory syndrome- Coronavirus 2).

https://doi.org/10.1016/j.ihj.2020.04.007

levels of angiotensin II in the vascular system causes vasoconstriction, acute lung injury and myocardial injury.[2]

Effects of ACEi/ARB's on ACE2 level

Angiotensin-converting enzyme inhibitors (ACEi) inhibits angiotensin-converting enzyme (ACE). ACE catalyzes Angiotensin I to angiotensin II. Few animal (rat) studies showed the beneficial effects of ACEi by upregulating ACE 2 mRNA level. A similar effect had been seen by ARB's by upregulating messenger RNA (mRNA) of ACE2 and increasing ACE 2 level.[3–5]

Contrary to previous studies, recent animal studies showed no effect of ACEi/ARBs on ACE2 gene expression.[6] Likewise, human studies of ACEi/ARB's showed conflicting results.[7–9]

In SARS-Cov-2, ACE2 acts as a receptor for the entry of viruses inside the cell. Theoretically, upregulation of ACE2 by ACE i/ARB's helps the entry of virus inside cell; however, no study showed the deleterious effect of ACEi/ARB's in Covid-19 patients or causal relationship among ACEi/ARB's with COVID-19.[10]

There is robust evidence of the mortality-lowering effects of ACEi/ARB's in heart failure and postmyocardial infarction. Sudden discontinuation of heart failure therapy leads to precipitation of heart failure. Similarly, ACEi/ARB's, are part of the standard therapy in hypertension, and sudden withdrawal will cause rebound hypertension. Recent literature firmly emphasizes on the continuation of these drugs.[2,11]

Current evidence doesn't support withdrawal of ACEi/ARB's in the population already on these drugs. We should continue using these drugs to prevent mortality due to heart failure and myocardial infarction, until further research on SARS-Cov-2 interaction with ACEi/ARB's shows a strong reason to stop these drugs.

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Sandeep Bansal, Sourabh Agstam*, Anunay Gupta, Preeti Gupta, H.S. Isser

Department of Cardiology, VMMC and Safdarjung Hospital, New Delhi, India

* Corresponding author. Department of Cardiology, Room no. 720, Superspeciality Block, VMMC and Safdarjung Hospital, New Delhi, India

E-mail address: sourabhagstam@gmail.com (S. Agstam).

10 April 2020

Available online 7 May 2020