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LETTER TO THE EDITOR

The other possible mechanism of the benefits of RAAS inhibition in the athogenesis of COVID-19

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Letter to the Editor,

We read with interest the meta-analysis of association of angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs) with the risk and severity of COVID-19.[1] Another possible explanation of the beneficial effect of renin- angiotensin-aldosterone system (RAAS) inhibition on the severity of COVID-19 is via increasing tissue kallikrein and upregulating ACE-2 receptors.

It is proven that tissue kallikrein prevents apoptosis and ventricular remodeling after myocardial infarction.[2] Since organ injury determines mortality in hypertensive patients infected with SARS-CoV-2, increased bradykinin levels induced by ACE inhibition may provide more protection than harm in cardiovascular disease (CVD)-comorbid COVID-19 patients.

Animal models of infection with SARS-CoV showed that ACE-2 downregulation resulted in pro-inflammatory responses, including lung injury and impairment of cardiac contractility.[3] If SARS-CoV-2 infections progress like SARS-CoV, the virus may deteriorate a patient's condition by lowering ACE-2 expression and by decreasing the degradation of angiotensin II (Ang-II). Overabundance of Ang-II has multiple deleterious cardiovascular consequences including elevating blood pressure, cardiomyocyte apoptosis, cardiac infiltration by macrophages, and secretion of pro-inflammatory cytokines. Secondly, less ACE-2 reduces the formation of angiotensin (1-7) (Ang 1-7) and its CVD-protective vasodilatory, anti-inflammatory, antifibrillatory, and antiproliferatory effects.[4] In particular, Ang 1-7 can diminish Interleukin-6 (IL-6), Tumor necrosis factor-alpha (TNF-α), macrophage infiltration, vascular cell adhesion protein.

Ferrario and co-workers have showed that ACEI caused a 1.8-fold rise of plasma Ang 1-7 concentrations and an approximately 25% increase of ACE-2 expression in the left ventricle.[5] Thus, the usage of ACE inhibitors and ARBs may have a potential benefit in preventing COVID-19-triggered organ damage via its upregulation of Ang 1-7, depletion of Ang-II, and upregulating ACE-2 receptors.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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