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ROLE OF ANGIOTENSIN-CONVERTING ENZYME RECEPTOR IN THE PATHOGENESIS OF COVID-19

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At the end of 2019, a group of pneumonia patients of unknown cause emerged in Wuhan China. Subsequently, the World Health Organization (WHO) announced a standard format of Coronavirus Disease-2019 (COVID-19), according to its terminology, for this novel coronavirus pneumonia on February 11, 2020.

Asymptomatic patients in the incubation period continuously shed the virus, so they are a potential source of infection.[1,2] Moreover, samples taken from recovered patients continue to show positive RT-PCR test that makes them a source of infection.[3] Respiratory droplets and contact transmission are considered the only ways of transmission until now.

Pathophysiology of COVID-19

The virus enters the cell by using the action of Angiotensin converting enzyme (ACE-2) on the cell membrane. ACE-2 mainly spread in the alveolar cells of the lung.[4] The spike (S) proteins bind to ACE-2, then endosome formation occurs to complete cell entry.[5] A single-stranded positive-sense RNA virus causes COVID-19, so when the viral genome released into the cell, transcription occurs by the RNA-dependent RNA polymerase (RdRp).[6]

Organ protective effect of ACE-2 receptor

ACE-2 is a carboxypeptidase homology to ACE. Although ACE-2 and ACE are similar, its function is various.[7] ACE-2 plays an important role in the body as it is present in different sites in the body. The most important sites are lung, heart, kidney, alveolar epithelial cells, and vascular endothelial cells. Angiotensin II is the substrate to the ACE-2 receptor, so it plays an important role in RAS, and it is considered the single entry for COVID-19 to invade the body.[8]

There are a lot of hypotheses that ACE Inhibitors have a role in the treatment or prevention of invasion of COVID-19 as they can reduce the activity of ACE-2 receptors. This could reduce the penetration of the virus to the cells. However, ACE Inhibitors increase the amount of Angiotensin I, which leads to the up-regulating of ACE-2 receptors. Therefore, there is no strong evidence that ACE Inhibitors are effective in the treatment of COVID-19.[9]

Nowadays, some studies report that ACE Inhibitors could have a bad effect on patients with COVID-19 as they up regulate the ACE-2 receptor and increase the chance of viral invasion. From another view, there is evidence that ACE Inhibitors antagonize the effect of Angiotensin II, so they have a role in protection from lung injury and ARDS.[10] Another therapeutic approach in COVID-19 is to block the surface of the ACE-2 receptor by using anti-ACE-2 antibodies or peptides, which block the interaction site between protein and receptor so prevent the entry of virus.[11]

Recombinant human ACE

RAS has a role in the mechanism of ARDS & part of it is ACE-2 that has a negative effect on the axis, so any injury of alveolar epithelial & Clara cells decreases ACE-2 during ARDS. The receptor blocker of Angiotensin II or ACE-1 can protect the lungs from any injury caused by ARDS, but the problem is the systemic hypotension. Therefore, it is a good idea to use recombinant ACE-2 protein in protection. However, it is a soluble form that has a short half-life, so it is given by continuous infusion.[12] It acts by preventing the fusion of COVID-19 with its receptor on the cells as it neutralizes spike protein on the viral surface and prevents its invasion.[13] This is like a snare for the virus.

Conflict of interest

The authors state that there are no conflicts of interest.

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