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Mechanics Insights of Alpha-Lipoic Acid against Cardiovascular Diseases during COVID-19 Infection

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Abstract

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China, in late December 2019. Since then, COVID-19 has spread rapidly worldwide and was declared a global pandemic on 20 March 2020. Cardiovascular complications are rapidly emerging as a major peril in COVID-19 in addition to respiratory disease. The mechanisms underlying the excessive effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on patients with cardiovascular comorbidities remain only partly understood. SARS-CoV-2 infection is caused by binding of the viral surface spike (S) protein to the human angiotensin-converting enzyme 2 (ACE2), followed by the activation of the S protein by transmembrane protease serine 2 (TMPRSS2). ACE2 is expressed in the lung (mainly in type II alveolar cells), heart, blood vessels, small intestine, etc., and appears to be the predominant portal to the cellular entry of the virus. Based on current information, most people infected with SARS-CoV-2 virus have a good prognosis, while a few patients reach critical condition, especially the elderly and those with chronic underlying diseases. The "cytokine storm" observed in patients with severe COVID-19 contributes to the destruction of the endothelium, leading to "acute respiratory distress syndrome" (ARDS), multiorgan failure, and death. At the origin of the general proinflammatory state may be the SARS-CoV-2-mediated redox status in endothelial cells via the upregulation of ACE/Ang II/AT1 receptors pathway or the increased mitochondrial reactive oxygen species (mtROS) production. Furthermore, this vicious circle between oxidative stress (OS) and inflammation induces endothelial

dysfunction, endothelial senescence, high risk of thrombosis and coagulopathy. The microvascular dysfunction and the formation of microthrombi in a way differentiate the SARS-CoV-2 infection from the other respiratory diseases and bring it closer to cardiovascular diseases like myocardial infarction and stroke. Due the role played by OS in the evolution of viral infection and in the development of COVID-19 complications, the use of antioxidants as adjuvant therapy seems appropriate in this new pathology. Alpha-lipoic acid (ALA) could be a promising candidate that, through its wide tissue distribution and versatile antioxidant properties, interferes with several signaling pathways. Thus, ALA improves endothelial function by restoring the endothelial nitric oxide synthase activity and presents an anti-inflammatory effect dependent or independent of its antioxidant properties. By improving mitochondrial function, it can sustain the tissues' homeostasis in critical situation and by enhancing the reduced glutathione it could indirectly strengthen the immune system. This complex analysis could open a new therapeutic perspective for ALA in COVID-19 infection.

Keywords: COVID-19; SARS-CoV-2; alpha-lipoic acid; cardiovascular disease; inflammation; oxidative stress.

Conflict of interest statement

The authors declare no conflict of interest.