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COVID-19: Oxidative Preconditioning as a Potential Therapeutic Approach

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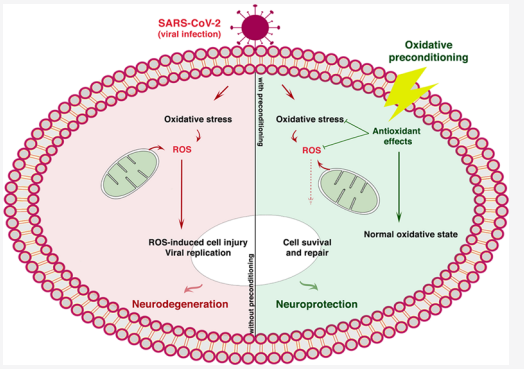
ABSTRACT: This Article summarizes the likely benefits of central nervous system oxidative preconditioning in the reduction of COVID-19 based on its putative pathogenesis. The current COVID-19 outbreak caused a pandemic with millions of infected patients and death cases worldwide. The clinical features of severe acute respiratory syndrome coronavirus (SARS-CoV) was initially linked with respiratory disorders, but recent studies have reported alterations of neurological and cerebrovascular functions in COVID-19 patients. The main viral infection features are related to cell death, inflammation, and cytokine generation, which can be associated with the dysregulation of redox systems or oxidative stress. However, until now, there is no available and effective therapeutic approach. Thus, it is necessary to search for care and adequate protection against the disease, especially for susceptible and vulnerable groups. Preconditioning, a well-known antioxidative stress and anti-inflammatory approach, is protective against many neurological age-related disorders. COVID-19 severity and morbidity have been observed in elderly patients. The aim of the present study is to elucidate the possible protective role of oxidative preconditioning in aged patients at high risk of developing severe COVID-19 complications.



KEYWORDS: *Preconditioning, SARS-CoV-2, COVID-19, antiviral, oxidative stress, CNS*

1. INTRODUCTION

COVID-19 has been described for the first time as a pneumonia of unknown cause by Zhu et al.[1] who reported the results of a study of three cases who were admitted to the hospital in Wuhan and diagnosed with severe pneumonia at an early stage of the outbreak. Patient clusters were diagnosed with acute respiratory syndrome.[2] Typical clinical symptoms at onset of illness are fever, dry cough, breathing difficulties (dyspnoea), and pneumonia; fewer common symptoms were sputum production, headache, hemoptysis, myalgia or fatigue, and diarrhea,[1−3] but respiratory distress worsened a few days later and required mechanical ventilation. This respiratory failure has been linked to alveolar damage,[2] and the novel coronavirus, named 2019-nCoV, was reported as the likely etiological agent of the viral pneumonia[1] and may result in death.[3]

However, epidemiological studies confirmed that the disease can be transmitted by human-to-human contact[4] and reported the potential of global spread.[5,6] By October 13, 2020, SARS-CoV-2 had infected more than 38 028 000 people around the world and killed more than 1 085 000.

The complete genome sequences obtained at an early stage of the outbreak are similar to those of SARS-CoV, the virus that caused the SARS epidemic in 2003, and use the same receptors, angiotensin converting enzyme II (ACE2), to enter into the human cell.[2] In addition to the airway epithelia, ACE2 is widely expressed throughout the human body in the kidneys, intestine, lungs, vascular endothelia, and central nervous system (CNS).[7] This widespread expression and distribution of ACE2 receptors in the human brain, on the surface membrane and in the cytoplasm of neurons, but also in glial cells determines the neurotropism of SARS-CoV-2[7] and indicates that this virus may cause some neurologic manifestations through direct or indirect mechanisms.

In the CNS, SARS-CoV-2 triggers neuroinflammatory events, which may be a potential cause of the nervous system abnormalities observed in COVID-19 patients. Published data attributes those events initiated by viral infections mainly to ROS production and oxidative stress.[8−11] Herein, we provide evidence indicating that oxidative preconditioning will have supportive utility in alleviating the impact of COVID-19 induced alteration of tissue homeostasis and integrity that

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