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Therapeutic Approaches to the Neurologic Manifestations of COVID-19

As of May 2022, there were more than 527 million infections with severe acute respiratory disease coronavirus type 2 (SARS-CoV-2) and over 6.2 million deaths from Coronavirus Disease 2019 (COVID-19) worldwide. As many as “one-third of patients may experience persistent neurologic symptoms as part of a Post-Acute Sequelae of SARS-CoV-2 infection (Neuro-PASC) syndrome. This Neuro-PASC syndrome can affect patients who required hospitalization for COVID-19 or patients who did not require hospitalization and who may have had minor or no pulmonary symptoms. Given the large number of individuals affected and the ability of neurologic complications to impair quality of life and productivity, the neurologic manifestations of COVID-19 are likely to have major and long-lasting personal, public health, and economic consequences. While knowledge of disease mechanisms and therapies acquired prior to the pandemic can inform us on how to manage patients with the neurologic manifestations of COVID-19, there is a critical need for improved understanding of specific COVID-19 disease mechanisms and development of therapies that target the neurologic morbidities of COVID-19.” [1]

The mechanisms of neuropsychiatric complications of long COVID are multifactorial, including long-term tissue damages from direct CNS viral involvement, unresolved systemic inflammation and oxidative stress, maladaptation of the renin-angiotensin-aldosterone system and coagulation system, dysregulated immunity, the dysfunction of neurotransmitters and hypothalamus–pituitary adrenal (HPA) axis, and the psychosocial stress imposed by societal

changes in response to this pandemic. [2]

"The strength of safety, well-acceptance, and accumulating scientific evidence has now afforded nutritional medicine a place in the mainstream of neuropsychiatric intervention and prophylaxis." [2]

Long chain omega-3 polyunsaturated fatty acids (omega-3 or n-3 PUFAs) might have favorable effects on immunity, inflammation, oxidative stress and psychoneuroimmunity at different stages of SARS-CoV-2 infection. Omega-3 PUFAs, particularly EPA, have shown effects in treating mood and neurocognitive disorders by reducing proinflammatory cytokines, altering the HPA axis, and modulating neurotransmission via lipid rafts. In addition, omega-3 PUFAs and their metabolites accelerate the process of cleansing chronic inflammation and restoring tissue homeostasis, and therefore offer a promising strategy for Long COVID. [2]

Coenzyme Q10 (CoQ10) and selenium have effects on oxidative stress and inflammation in viral infection and show promise in the treatment of patients with COVID-19 disease. [3]

Vitamin D is considered an immunomodulatory agent that regulates both innate and adaptive immune systems. Vitamin D has pleiotropic effects against endothelial cell dysfunction and vascular thrombosis, which may mitigate vascular leakage secondary to systemic inflammatory response and prevent COVID-associated arterial and venous thrombosis. Vitamin D supplementation prior to or during COVID-19 has been associated with better 3-month survival in geriatric patients. Of 4,599 Veterans Administration patients with a positive SARS-CoV-2 test, vitamin D deficiency (< 20 ng/mL) was identified in 665 (14.5%); 964 (21.0%) were hospitalized; and 340 (7.4%) died. Continuous blood 25(OH)D concentrations were independently associated with COVID-19-related hospitalization and mortality in an inverse dose-response relationship in this large racially and ethnically diverse cohort. After adjusting for all covariates, including race/ethnicity and poverty, there was a significant independent inverse dose-response relationship between increasing continuous 25(OH)D concentrations (from 15 to 60 ng/mL) and decreasing probability of COVID-19-related hospitalization (from 24.1 to 18.7%, p=0.009) and mortality (from 10.4 to 5.7%, p=0.001). The greatest risk for hospitalization and death was observed at lower 25(OH)D concentrations. [4,5,6] Patients with low vitamin D levels present an increased risk of Acute Respiratory Distress Syndrome (ARDS) requiring admission to intensive care unit (ICU) or mortality due to SARS-CoV-2 infection and a higher susceptibility to SARS-CoV-2 infection and related hospitalization.[7]

A clinical study conducted in Singapore showed that older COVID-19 patients who were given combined oral treatment of combination magnesium (150 mg daily), vitamin D3 (1000 IU daily) and vitamin B12 (500 mcg daily) had reduced COVID-19 symptom severity. and supplements significantly reduced the need for oxygen and intensive care support. [8]

References:

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