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Viewpoint

COMBAT COVID-19 WITH EXERCISE AND VITAMIN D SUPPLEMENTATION

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INTRODUCTION

COVID-19 is a raging pandemic with cases, hospitalizations and deaths surging. Prevention has focused to date on mask wearing, social distancing, and the development of vaccines. Novel mitigation strategies, however, are needed to combat the pandemic optimally.

There was an epidemic of inactivity in 2020 partially because of government recommendations to stay indoors and the mandated closure of gyms. Vitamin D deficiency is also a common worldwide problem, especially for persons of color. These two issues are contributing to the severity of the pandemic and should be addressed.

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We suggest consideration of the following recommendations based on peer-reviewed published data.

1. Initiate "MOVE NOW to Mitigate COVID-19", an international campaign focused on exercise. Walk, hike, bike, participate in yoga or online exercise classes. Just get moving!
2. Supplement vitamin D in at risk-populations such as nursing home patients and any person of color using appropriate testing when needed.
3. Initiate basic science and clinical studies to evaluate the hypothesis that exercise and vitamin D supplementation can help mitigate COVID-19.

Winter in the Northern Hemisphere is the time to initiate an international exercise and vitamin D supplementation program to augment our prevention efforts. Significant data support using these strategies in combination to fight COVID-19 optimally. We will briefly review this data below to spark a more in-depth discussion about how exercise programs and vitamin D supplementation could help us navigate a horrific pandemic.

Several factors are known to increase the risk for contracting COVID-19 or dying from the disease, including age, sex, ethnicity, obesity, diabetes, hypertension, cardiovascular disease, chronic renal and lung disease. Many of these risk factors are exacerbated by inactivity. Physical inactivity also adversely affects both the innate and adaptive immune systems. It results in higher systemic inflammation levels as measured by TNF-alpha, c-reactive protein, and other markers.

The mechanisms underlying how exercise could help are related to the release of myokines in response to contracting skeletal muscle. Myokines are cytokines and proteins that have powerful immunoregulatory functions.[1] They can improve glucose metabolism and promote the release of anti-inflammatory cytokines such as IL-1ra and IL-10.[2] Specifically, exercise also helps mobilize various infection-fighting cells such as natural killer cells and neutrophils. After flu vaccination, immune responses have further been shown to be more robust with "better immunologic outcomes" in people who consistently exercise.[3]

Exercise can further help treat anxiety and depression, according to a recent review of ways to improve mental wellness during the pandemic. Exercise enhances explicitly one's sense of vigor and self-esteem, leading to sustainable improvements in overall wellbeing.[4]

Exercise also directly impacts epigenetic activation and genetic expression via the AMPK/ AAK-2 pathways that inhibit catabolic processes (mTOR, NF-kB, and CRTC-1).[5] When left unchecked, this results in metabolic dysfunction, loss of proteostasis, and finally, genomic instability.[6-8]

Therefore, it makes perfect sense when human beings do not exercise, the normal processes of function and energy creation are significantly impaired. This leads to a cascade of dysfunction, including compromise of the immune system, thus making individuals susceptible to viral infections.

Vitamin D deficiency is another known pandemic risk factor. Emerging evidence suggests supplementing vitamin D could decrease the risk of contracting COVID-19 and or reduce intensive care admissions. This data also suggests it could reduce the mortality rate. Importantly, vitamin D deficiency can be easily and inexpensively corrected. Vitamin D supplementation could further have a massive impact because published data suggests there are over one billion people worldwide with vitamin D deficiency.[9]

According to a recently published study, the rate of COVID-19 positivity also drops as vitamin D levels increase up to a level of 55 ng / mL.[10] This is especially true for Black and Hispanic populations where the infection rates are significantly higher than in Caucasian populations. This paper is a game-changer. It provides specific, actionable evidence supporting vitamin D supplementation to decrease COVID-19 infection rates and suggests a dose-response rate to increased vitamin D supplementation levels.

Other papers outline the specific odds ratios associated with vitamin D deficiency. "Low plasma 25(OH)D level appears to be an independent risk factor for COVID-19 infection and hospitalization. In multivariate analyses that controlled for demographic variables and psychiatric and somatic disorders, the adjusted OR of COVID-19 infection (1.45 [95% CI 1.08-1.95, $p<0.001$]), and of hospitalization due to the SARS-CoV-2 virus (1.95 [95% CI 0.98-4.845, $p=0.061$]) were preserved."[11]

Another prospective observational study found RT-PCR COVID positive patients requiring intensive care admission had significantly lower vitamin D levels (14.35 ng / mL vs 27.89 ng / mL, $p = 0.0001$) than those who were asymptomatic. Serum inflammatory markers (IL-6, Ferritin and TNF-alpha) were higher in the vitamin D deficient group.[12] Proinflammatory phenotypic changes in monocytes and increased monocyte-platelet aggregation is associated with vitamin D deficiency.[13] Vitamin D has further shown to have an immunomodulatory role on the innate and adaptive immune systems.[14]

Recently published data confirms, "Vitamin D is a hormone that modulates many of the same inflammatory and oxidative signaling pathways triggered during COVID-19. For example, vitamin D suppresses the actions of the renin-angiotensin system, which has a determining role in the pathophysiology of the inflammatory response related to COVID-19."[15,16]

VIEWPOINT

To be clear, there is no prospective, randomized trial confirming exercise or vitamin D supplementation reduces COVID-19 infection rates and or severity. However, powerful published data suggests both may significantly reduce the impact of COVID-19 by enhancing the immune system's infection-fighting ability while reducing systemic inflammation.

Exercising and Vitamin D supplementation should be explored in addition to vaccines, social distancing, and the use of masks. Both could function as powerful immunomodulatory tools against COVID-19 and the cytokine storms associated with significant morbidity and mortality. Both could also enhance the immunologic response to vaccination. The time is now to act to help save precious resources and lives.

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