Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Vitamin D supplementation: An alternative to enhance the effectiveness of vaccines against SARS-CoV-2?

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Letter to editor

The unprecedented worldwide dissemination of SARS-CoV-2 infection, has challenged scientists, governments and pharmaceutical industry in halting this pandemic in a context of profound uncertainty. Multiple prophylactic and therapeutic strategies have been evaluated in a short time, driven by the urgent need of preventing COVID-19 spread and worldwide mortality.

Fortunately, the impressive and massive international effort of scientists, organizations, governments and pharmaceutical industry concluded in the development of several effective vaccines, with unprecedented speed and scale, which undoubtedly are an invaluable tool for preventing COVID-19, although duration of vaccine protections is not yet clearly defined.

COVID-19 vaccines can elicit not only neutralizing antibodies (with detectable antibodies ranges from 50 to 94%), but also SARS-CoV-2-specific CD4+ and CD8+ T-cell responses. Nevertheless, the relevant measures of vaccine performance are vaccine efficacy (reduced risk of infection or disease among vaccinated individuals under controlled circumstances estimated from clinical trials), vaccine effectiveness (reduced risk of infection, symptomatic and severe disease among vaccinated individuals in real-world conditions estimated from observational studies) and vaccine impact (reduction in incidence of infection or disease in a population where some members are vaccinated) [1]. The latter depends on vaccine coverage and results from direct effects of vaccination, as well as herd protection. In a complex landscape of COVID-19 vaccine access inequities, some low-income countries are deferring second doses, delaying the achievement of vaccine impact. In this context, optimizing vaccines effectiveness (performance in real world) is of paramount importance.

The use of adjuvant strategies to improve responses to viral vaccines seems a helpful approach, particularly in immunosuppressed and immunosenescent persons [2]. Of interest, nutritional interventions are one of the possible approaches to improve vaccination response [3].

Multiple previous studies conclude that the supplementation of micronutrients such as vitamin D has a protective effect against some viral infections such as the common cold, influenza and dengue [4]. The approach of optimizing COVID-19 vaccines efficacy through vitamin D supplementation is currently being evaluated in numerous clinical trials [5]. In the meanwhile, due to its excellent toxic-therapeutic margin, the critical epidemiological situation, and the biological plausibility of its positive effect, especially in a context in which restrictive measures may have negatively impacted its serum levels, it seems appropriate to consider vitamin D supplementation to prevent and/or attenuate COVID-19 [6]. It has been observed an inverse correlation between vitamin D serum levels and the risk of SARS-CoV-2 infection and disease severity [7,8].

Insufficient vitamin D status, as defined by a low circulating level of 25-OH-D is associated with a reduced immune response to influenza vaccination, and to highlight, Ming-Dar et al. observed lower seroprotection rates of influenza A virus subtype H3N2 (A/H3N2) and B strain in vitamin D deficiency patients than patients with normal vitamin D levels [9].

The effect of vitamin D on immune system has been recognized [10–12]. Specifically, at a cellular and molecular level, vitamin D

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preferentially targets helper T cell activity (Th1) by inhibiting the secretion of both IL-2 and IFN-gamma by Th1 and by suppressing the secretion pro-Th1 cytokine IL-12 by antigen- presenting cells [13].

COVID-19 patients with low serum vitamin D levels have a reduction in CD8+ T lymphocytes with a low CD4 / CD8 ratio [14]. Furthermore, it has long been recognized that a large percentage of the worldwide population has low levels of vitamin D [15–17], which could currently be exacerbated by restrictive measures and their impact on sun exposure.

Vitamin D supplementation could optimize the ability of the immune system to respond appropriately to COVID-19 vaccination.

Routine dosing of vitamin D serum levels is neither usual nor inexpensive practice, and in knowledge of the significant percentage of the population that has shown to present vitamin D deficiency. Thus, awaiting the results of ongoing prospective studies, we encourage the scientific community considering vitamin D supplementation as a cost-effective, risk-free and inexpensive strategy that could have a great impact on optimizing the immune response to COVID-19 vaccines.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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