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HYPOTHESIS PAPER

The latitude hypothesis, vitamin D, and SARS-Co-V2

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ABSTRACT

The Latitude Hypothesis may explain seasonal variation in occurrence of flu and influenza-like illness, including SARS-CoV-2. We focus on one variable, vitamin D adequacy in the general population, and consider statistics of two sub-populations to propose a possible treatment to improve outcomes.

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Introduction

It has long been proposed (Davidson, 1897; Martin et al., 1978) that latitude affects the occurrence and severity of respiratory disease. This hypothesis is especially explanatory for seasonal influenza-like illness (ILI) (Lipsitch & Viboud, 2009; Tamerius et al., 2011). Possible mechanisms to explain the autumnal increase in illness include lower temperature and humidity supporting the lipid capsids of viri (Lofgren et al., 2007; Pitzer et al., 2015), decreased outdoor activity and limited fresh air concomitant with staying indoors (Singh et al., 2020), and falling vitamin D levels due to the shorter days and less direct sun exposure (Lofgren et al., 2007; Pitzer et al., 2015; Singh et al., 2020).

A search of PubMed (Sayers et al., 2020) for vitamin D and latitude finds steady increase in research since 2004 (post SARS-1). That search yields publication counts in 2004 of 19, and in 2019 of 67.

The hypothesis

From 2004 to 2018 the Office of Dietary Supplements (ODS) at the National Institutes of Health (NIH) led and sponsored several efforts to advance scientific understanding of the importance of vitamin D to health (NIH) (NIH, 2018). The remainder of this section is extensively based on NIH (NIH, 2020) and National Institute on Aging (NIA) (NIA, 2019) publications.

Vitamin D is a fat-soluble vitamin that is naturally present in very few foods, added to others (e.g. milk), and available as a dietary supplement. It is also produced endogenously, when ultraviolet rays from sunlight strike the skin and trigger vitamin D synthesis. Vitamin D obtained from sun exposure, food and supplements is biologically inert and must undergo two hydroxylation events in the body for activation. The first occurs in the liver and converts vitamin D to 25-hydroxyvitamin D [25(OH)D], also known as calcidiol. The second occurs primarily in the kidney and forms the physiologically active 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], also known as calcitriol, both of which have a role in stimulating calcium absorption in the gut and promoting skeletal health.

Vitamin D has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation. Many genes encoding proteins that regulate cell proliferation, differentiation and apoptosis are modulated in part by vitamin D.

Evaluation of the hypothesis

People with dark skin

Greater amounts of the pigment melanin in the epidermal layer result in darker skin and reduce the skin's ability to produce vitamin D from sunlight. Reports consistently show lower serum 25(OH)D levels in persons identified as black compared with those identified as white. This constitutes the vitamin D paradox in people with dark skin.

The NIH led an expert panel on December 1, 2017, titled, 'A Systems-Based Approach to Investigating the vitamin D Paradox in Black American'. It was a forum to: (1) explore the paradox through various multidisciplinary lenses (genetics, epigenetics, molecular mechanisms, and behavior) to determine the factors affecting vitamin D requirements in Black Americans; (2) identify potential unintended consequences of current clinical practices and public health polices (e.g.

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vitamin D supplementation, food fortification) on minority health and health disparities.

Older adults

The older population is at increased risk of developing vitamin D insufficiency in part because, as they age, skin cannot synthesize vitamin D as efficiently as skin of young people, they are likely to spend more time indoors, and they may have inadequate intakes of the vitamin D. Therefore, the NIA published the following guidelines for vitamin D status and requirements for older adults: If you are age 51–70, you need at least 15 mcg (600 IU) each day, but not more than 100 mcg (4,000 IU). If you are over age 70, you need at least 20 mcg (800 IU), but not more than 100 mcg (4,000 IU) (NIA, 2019). Taking 60,000 international units (IU) a day of vitamin D for several months has been shown to cause toxicity (NIH, 2020).

SARS-CoV-2 mortality (selected groups)

CDC collected and published figures (Calgary, 2020) indicate that elderly and non-white persons are at greater risk of dying from SARS-CoV-2. Elderly (65+ y.o.) constituted 48,932 of 54,861 deaths or 89% reported through week 18 of COVID-19 pandemics (Calgary, 2020). Non-white, those identifying as black, represented 33% (328) of deaths reported during week 18, whereas those identifying as hispanic counted for 37% (351) of COVID-19-related deaths during same period (note that ethnicity is not consistently reported.)

Vitamin D

Vitamin D is indicated to suppress cytokine cascade, resulting in reduced mortality in SARS-CoV-2 (Daneshkhah et al., 2020) and has been shown in mouse models to have anti-inflammatory and anti-oxidant effects both peripherally and centrally (Almeida Moreira Leal et al., 2020). Interest in vitamin D research is reflected in nine articles in April and May of 2020 retrieved on PubMed (Sayers et al., 2020). Particularly, in those studies it was shown that 25(OH)D levels are lower in patients with positive PCR for SARS-CoV-2 (D'Avolio et al., 2020), that $1,25(OH)_2D$ can protects against age-related osteoporosis (Yang et al., 2020), and that the hypovitaminosis D contributes to the sex-specific SARS-CoV-2 mortality (La Vignera et al., 2020). It was also pointed out that the levels of vitamin D might impact mortality from the SARS-CoV-2 infection (Marik et al., 2020), and that therefore vitamin D might play a role in the prevention of COVID-19 infection and mortality (Carter et al., 2020; Ilie et al., 2020; Jakovac, 2020).

Consequences and possible intervention

Taken together, the latitude hypothesis and the statistically concomitant vitamin D deficit in the populations at greatest risk for SARS-CoV-2 mortality (Calgary, 2020) (elderly, non-white persons), and the action of vitamin D on immunity (Almeida Moreira Leal et al., 2020; Daneshkhah et al., 2020) suggest that vitamin D supplementation (400–4000 IU *pod*) is a safe intervention with great potential to reduce morbidity during flu season and in current COVID-9 pandemic.

Disclosure statement

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