SL Nutrition And Metabolism

Special Issue Article "Vitamin D"

Mini Review

Vitamin D and COVID-19

Uwe Gröber*

AMM-Academy for Micronutrient Medicine, Essen, Germeny

ARTICLE INFO

Received Date: June 02, 2022
Accepted Date: July 26, 2022
Published Date: July 28, 2022

KEYWORDS

Vitamin D insufficiency
Vitamin D
25(OH)D
ACE-2
1,25(OH)2D

Citation for this article: Uwe Gröber. Vitamin D and COVID-19. SL Nutrition And Metabolism. 2022; 2(1):124

Corresponding author:
Uwe Gröber,
AMM - Academy of micronutrient medicine, Zweigertstrasse 55, 45130, Essen, Germany, Tel: +49-201-8742984;
Email: uwegroeber@gmx.net

ABSTRACT

Worldwide the pandemic of Covid-19 spreads rapidly and has an enormous public health impact with substantial fatal outcomes especially in high-risk groups, such as older people and patients with comorbidities like diabetes, dementia or cancer. In the absence of a vaccine against Covid-19 there is an urgent need to find supportive therapies that can stabilize the immune system and can help to deal with the infection (Figure 1). It has been suggested that vitamin D has a protective effect against Covid-19. Vitamin D has complex anti-inflammatory and immunomodulatory activity – as 1,25(OH)2D it interacts with its receptor (VDR) in immune cells, modulates the innate and acquired immune systems in response to invasion of bacterial and viral pathogens. 1,25(OH)2D also acts as a modulator of renin-angiotensin pathway and down-regulates ACE-2. Therefore, vitamin D might help in treatment of Covid-19 by preventing the cytokine storm and subsequent ARDS which is commonly the cause of mortality.

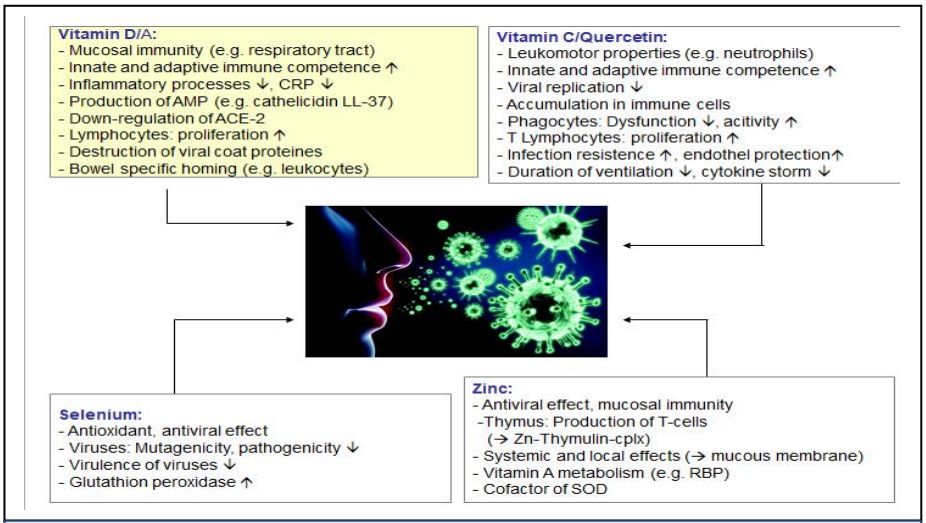

Figure 1: Immunrelevant micronutrients and Covid-19.

INTRODUCTION

Coronavirus (COVID-19)

A novel coronavirus (SARS-CoV-2) that causes the disease Coronavirus Disease 2019 (COVID-19) emerged in a seafood and poultry market in the Chinese city of Wuhan in 2019. Cases have been detected in most countries worldwide, and on March 11, 2020, the World Health Organization characterized the outbreak as a pandemic. COVID-19 can cause lung complications such as pneumonia and, in the most severe cases, acute respiratory distress syndrome (ARDS).

The coronavirus was first described in winter 2019 and affected predominantly elderly people. The virus infects enterocytes and pneumocytes as the primary target cells. Spike proteins of this virus facilitate viral entry into the target cells through binding with the angiotensin converting enzyme 2 (ACE-2) on the surface of the cells. ACE-2 is a regulator of the renin-angiotensin system and is distributed in many tissues in the body including lung, kidney, gastrointestinal (GI) tract, and cardiovascular system. This could explain multi-organ failure in susceptible patients.

Cave: vitamin d insufficiency

Vitamin D insufficiency and deficiency are common in COVID-19 patients and correlates with disease progression. 25(OH)D is the vitamin D metabolite that is measured to assess a patient's vitamin D status. Vitamin D deficiency is diagnosed when 25(OH)D < 20 ng/mL, vitamin D insufficiency is defined as 25(OH)D of 21–29 ng/mL, and 25(OH)D >30 ng/mL is considered sufficient, with 40–60 ng/mL being the preferred range. Vitamin D intoxication usually doesn't occur until 25(OH)D > 150 ng/mL. Vitamin D intoxication is only to be expected at levels of 25(OH)D > 150 ng/mL.

Based on different guidelines, the threshold for serum 25(OH)D has been set at 20-30 ng/mL for bone health. With respect to vitamin D's non-skeletal effects, including the immuno-preventative effects, it has been suggested that a higher blood level of 25(OH)D of at least 30 ng/mL is required with the preferred range being 40-60 ng/mL. For improvement of the vitamin D status children and adults have to supplement approximately 50 I.E. Vitamin D per kg bodyweight per day [1-3].

The vitamin D hormone 1,25(OH)2D

The vitamin D hormone $1,25(OH)_2D$ influences cell metabolism via genomic and non-genomic metabolic processes. $1,25(OH)_2D$ binds mainly to the vitamin D receptor (VDR) and, after forming a heterodimer with the retinoic acid receptor (RXR), translocates this into the cell nucleus. Once there, it binds to the vitamin D responsive element (VDRE) in the DNA and regulates the transcription of numerous genes. The endogenous production of AMPs such as denfensins and Cathelicidin (e.g. LL-37) has an antiviral effect and lowers the infectivity of cold viruses such as influenza and corona. The response to a vaccination can also be increased by vitamin D. Besides, vitamin D supplementation increases the biodiversity of the gut microbiome, which means their resistance against stressors and intestinal inflammation [1,4].

Table 1: Effects of 1,25(OH)2D in Covid-19 infections

- Innate and acquired immune system ↑
- Synthesis of antimicrobial peptides (AMPs) that have an antiviral effect ↑
- Down regulation of ACE-2
- Regulation of $Th_{17}/Th_1\text{-}T_{reg}/Th_2$ balance
- Lymphocyte percentage ↑
- Anti-inflammatory effects (e.g. CRP ↓, TNFα ↓)
- Gut microbiome: biodiversity ↑

Vitamin D strengthens both innate and acquired immune system and increases the synthesis of antimicrobial peptides (AMPs), such as cathelicidin LL-37, that have an antiviral effect. $1,25(OH)_2D$ acts as a modulator of renin-angiotensin pathway and down-regulates ACE-2. The anti-inflammatory role of $1,25(OH)_2D$ could explain the protective role of vitamin D against immune hyper reaction and cytokine storm in patients with severe COVID-19. Vitamin D may help in treatment of COVID-19 by preventing the cytokine storm and subsequent ARDS which is commonly the cause of mortality. The reduction in serum CRP, an inflammatory marker, along with increased lymphocytes percentage suggest that vitamin D also may help modulate the immune response possibly by reducing risk for cytokine storm in response to this viral infection [1,5].

Vitamin D and COVID-19

Several studies suggest an association between vitamin D deficiency and risk of viral upper respiratory tract infections and mortality from coronavirus disease-2019 (COVID-19). In a recent study that used a retrospective, observational analysis of deidentified tests performed at a national clinical laboratory to determine if circulating 25(OH)D levels are associated with severe acute respiratory disease coronavirus 2 (SARS-CoV-2) positivity rates. A total of 191,779 patients from all 50 states with SARS-CoV-2 were analyzed (median age, 54 years) and the results performed mid-March through mid-June, 2020 and matching 25(OH)D results from the preceding 12 months were included.

The results demonstrate an inverse relationship between circulating 25(OH)D levels and SARS-CoV-2 positivity. SARS-CoV-2 positivity was strongly and inversely associated with circulating 25(OH)D levels, a relationship that persists across latitudes, races/ethnicities, both sexes, and age ranges (Figure 2).

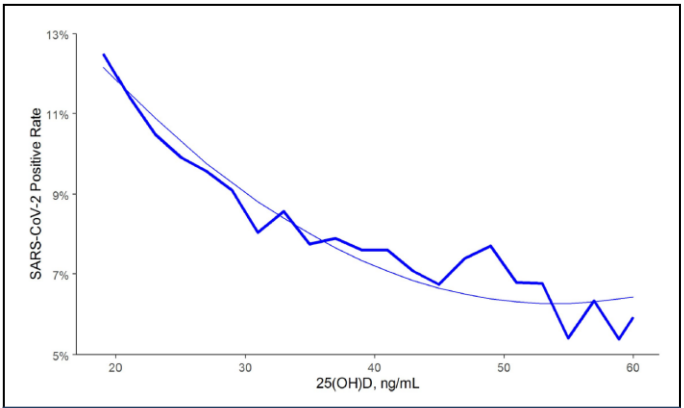

Figure 2: SARS-CoV-2 positive rate correlates inversely with 25(OH)D [5].

For the entire population those who had a circulating level of 25(OH) D <20 ng/mL had a 54% higher positivity rate compared to those who had a blood level of 30–34 ng/mL. The risk of SARS-CoV-2 positivity continued to decline until the serum levels reached 55 ng/mL. This finding is not surprising, given the established inverse relationship between risk of respiratory viral pathogens, including influenza, and 25(OH)D levels. Vitamin D supplementation may reduce acute respiratory infections, especially in people with vitamin D deficiency. A previous study found that each 4 ng/mL increase in circulating 25(OH)D levels was associated with a 7% decreased risk of seasonal infection, a decrement of approximately 1.75% per ng/mL. This is remarkably similar to the 1.6% lower risk of SARS-CoV-2 positivity per ng/mL found in this adjusted multivariable model [5].

In another recent trial of Holick et al. the hospital data of 235 patients infected with COVID-19 were analyzed (mean age: 58·7 years). Based on CDC criteria, among this study patients, 74% had severe COVID-19 infection and 32·8% were vitamin D sufficient [25(OH)D ≥ 30 ng/mL]. After adjusting for confounding factors, there was a significant association between vitamin D sufficiency and reduction in clinical severity, inpatient mortality, serum levels of C-reactive protein (CRP)and an increase in lymphocyte percentage. Therefore, it is recommended that improving vitamin D status in the general population and in particular hospitalized patients has a potential benefit in reducing the severity of morbidities and mortality associated with acquiring COVID-19 [6].

VITAMIN D

Dosage for prevention

To prevent a viral infection of the respiratory tract, elderly people, adolescents, and adults should take a vitamin D supplement of 50 IU/kg body weight/day.

Supportive treatment: hospital admission, severe course

a) Initially (day 1, bolus): 200,000 IU vitamin D by mouth.

b) Then: 1st week: 20,000 IU vitamin D daily; 2nd week: 10,000 vitamin D daily; 3rd week: 5000 IU vitamin D daily by mouth.

REFERENCES

Reference

1. Gröber U, Holick MF. (2020). Vitamin D: The healing power of the sun vitamin. 4th, updated, expanded edition, 490 pages. Scientific publishing company, Stuttgart. 2020.
2. Holick MF. (2007). Vitamin D deficiency. N Eng J Med. 357: 266-281.
3. Gröber U, Reichrath J, Holick MF. (2015). Live longer with vitamin D? Nutrients. 7: 1871-1880.
4. Charoenngam N, Shirvani A, Tyler A, Song A, Holick MF. (2020). The Effect of Various Doses of Oral Vitamin D Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study. Anticancer Res. 40: 551-556.
5. Kaufman HW, Niles JK, Kroll MH, Bi C, Holick MF. (2020). SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. PlosOne. 15: e0239252.
6. Maghbooli Z, Ebrahimi M, Shirvani A, Nasiri M, Pazoki M, et al. (2020). Vitamin D Sufficiency Reduced Risk for Morbidity and Mortality in COVID-19 Patients. D-20-12067.