Could vitamin D reduce the risk of COVID-19?

Turashvili N.1,2 Javashvili L.3

Abstract

In December, 2019, several cases of pneumonia of unknown cause were identified in Wuhan City, Hubei Province of China. Further analysis revealed the reason of an outbreak—a novel β coronavirus which was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that causes coronavirus disease 2019 - COVID-19. The outbreak of novel coronavirus has spread rapidly worldwide. At the same time, scientists started working hard to create a medicine and a vaccine. However, there is still no specific drug for COVID-19 now. In this situation, before creating specific treatment and vaccine, it is especially important to find some therapeutic option that may have a positive effect in the prevention or treatment of the disease. We have reviewed the literature on the possible link between vitamin D and COVID-19. (TCM-GMJ April 2020; 5(1):P4-P6)

Keywords: COVID-19; Vitamin D; SARS-CoV-2.

Introduction

Coronavirus disease of 2019 (COVID-19) was first identified in Wuhan, Hubei, China in December 2019 and was declared a pandemic by the World Health Organization (WHO) on 11th March 2020. As of 12th April 2020, 04:00 GMT+4, the WHO database confirms 1 654 247 cases of coronavirus disease and 102193 confirmed death (1). However, this number is subjected to change every second. International Committee on Taxonomy of Viruses named the virus „severe acute respiratory syndrome coronavirus 2“ (SARS-CoV-2). This virus belongs to β – coronavirus and is RNA virus. SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a receptor. Coronavirus mainly recognizes the corresponding receptor on the target cell through the S protein on its surface and enters into the cell, then causing the occurrence of infection. The disease primarily involves the respiratory tract but it may deteriorate to multi-organ failure (2). ACE2 is found in the lower respiratory tract of humans on epithelial cells lining the lung alveoli and bronchioles as well as the endothelial cells and myocytes of pulmonary blood vessels, partly explaining the severe respiratory syndrome associated with these viruses. ACE2 is also found on the enterocytes in the small intestines, which may further explain the gastrointestinal symptoms associated with the viral infection (3). Elderly people and individuals with a history of chronic illness are at higher risk of corona attack and mortality. COVID-19 has a broad clinical spectrum with patients showing only mild and subclinical illness at the early phase of the disease, but some of them develop severe acute respiratory disease which requires intensive care and oxygen supplementation (4,5).

WHO released a series of recommendations for the prevention and control the spreading of the disease (6). Unfortunately, there is still no specific medicine and vaccine for COVID-19.

In the absence of a specific treatment and vaccine for this novel virus, it is especially important to find some therapeutic options that may have a positive effect in the prevention or treatment of the disease. We have reviewed the current literature on the role of vitamin D in relation to the new coronavirus.

The effect of vitamin D on the immune system and its antiviral action

Nowadays data has been collected that vitamin D is not only a nutrient but also a hormone. Vitamin D exists in several forms including 25-hydroxyvitamin D [25(OH)D]-the major circulating form and 1,25-dihydroxyvitamin D [1,25(OH)2D]-the active form. Vitamin D is mainly produced in the skin upon ultraviolet B radiation exposure, a few amounts is obtained from foods. The effects of 1,25(OH)2D are mediated by its binding to the vitamin D receptor (VDR), which is found in almost all cells. Vitamin D has long been recognized as essential to the skeletal system, but newer studies indicate that it influences various organ cells and systems, including the immune system (7). Active vitamin D is a modulator of the innate and adaptive immune system. Active vitamin D regulates T cells: It inhibits the proliferation of T helper 1 (Th1) and decreases the production of cytokines such as interleukin 2, interferon γ, tumor necrosis factor. Vitamin D shifts the polarization of T cells from Th1 toward Th2 and promotes apoptosis of dendritic cells (8). Lower levels of circulating cytokines lead to less antigen presentation by dendritic cells and less T lymphocyte recruitment.
and proliferation.

1α -hydroxylase is the key in the synthesis of active vitamin D. This enzyme was first found in the kidneys where it has the highest expression. Since that extrarenal 1α -hydroxylation was described in other tissues, including cells of the immune system (monocytes, macrophages, dendritic cells) and epithelial cells. Recent studies indicate that scientists found the expression of this enzyme in normal lung epithelial cells. Thus during viral infection more circulating vitamin D can be converted to active vitamin D by the respiratory epithelium (9). This local conversion from inactive to active vitamin D induces the production of antimicrobial peptides, including human cathelicidin (in the form of LL-37), human beta-defensin 2. Cathelicidin has direct antimicrobial activities against Gram-positive and Gram-negative bacteria, some viruses, and fungi. Those peptides kill the pathogens by perturbing their cell membranes and can neutralize the biological activities of endotoxins (7,10,11).

Studies report an association between vitamin D deficiency and susceptibility to acute respiratory tract infections. Several recent meta-analyses have concluded that vitamin D supplementation can reduce the risk of respiratory tract infections in both children and adults (12).

Vitamin D is mostly obtained from sun exposure ("Sunshine vitamin"); Thus, serum vitamin D concentration is affected by season. Low vitamin D concentration has been shown in winter, the season when influenza occurs, and vitamin D3 supplementation during the winter may reduce the incidence of influenza A (13).

Vitamin D and the renin-angiotensin system (RAS)

The renin-angiotensin system (RAS) has long been recognized as an important regulator of blood pressure and electrolyte balance. The RAS exerts its effects through the production and action of angiotensin II (Ang II), which has potent vasoconstrictor, antinatriuretic, and diuretic properties. Ang II is generated by the serial cleavage of angiotensinogen, first by the aspartyl protease renin and then by the carboxydipeptidase angiotensin-converting enzyme (ACE). Scientist noted the inverse relationship between plasma vitamin D3 levels and blood pressure, hypothesized that vitamin D-Receptor (VDR) 3 may be a primary negative regulator of renin expression (14,15).

Xu J. et al. demonstrated that vitamin D inhibited renin, ACE, and Ang II expression (16). Hypothetically, if vitamin D reduces ACE2, which is the binding site of SARS-CoV2 on cells than vitamin D might decrease coronavirus infections.

COVID-19 and vitamin D

As mentioned, according to the studies there are several data that vitamin D can reduce the risk of infections by inducing cathelicidins and defensins that can lower viral replication rates and reducing concentrations of pro-inflammatory cytokines, vitamin D also regulates the concentrations of anti-inflammatory cytokines.

There are some opinions that vitamin D could reduce the risk of COVID-19 infection and its complications. According to scientists, this opinion is supported by several facts: First of all, the outbreak of COVID-19 has started in winter, when vitamin D level in blood is generally lowest. The number of coronavirus cases and death are significantly lower and show lower growth rates at higher temperatures and especially at higher irradiances. It has been claimed that 90% of the initial 2019-nCoV transmissions occurred within a certain range of temperature (3-17 C) and absolute humidity (4 to 9g/m3 ). UV radiation in natural sunlight stimulates vitamin D production. Backer A. obtained a similar negative correlation between temperature and COVID-19 death count growth. According to this data, "regarding irradiance, the sun’s UV radiation could reduce the virus’ half-life and could improve resistance to infection via stimulation of vitamin D production (17). The effect of temperature upon transmission of COVID-19 was studied according to Australia and Egypt Case. One degree Celsius increase in temperature and one percent increase in relative humidity lower R0 by 0.0383 and 0.0224, respectively. Their study also confirmed the relationship between temperature and coronavirus activity and spread (18).

Secondly, COVID-19 case-fatality rates increase with age and with chronic disease comorbidity, both of which are associated with lower vitamin D concentration.

In addition to the above facts, one way that CoVs injure the lung epithelial cells and facilitate pneumonia must be through increased production of Th1-type cytokines as part of the innate immune response to viral infections, giving rise to the cytokine storm. Cytokines are vital in regulating immunological and inflammatory responses. Higher levels of IL-6 and IL-10 and lower levels of CD4+T and CD8+T are observed in COVID-19 patients parallel with the severity of the disease (2). Among them, IL-6 has a major influence because of its pleiotropic effects. Circulating IL-6 levels are closely linked to the severity of COVID-19 infection due to possible shared mechanisms of cytokine-mediated lung damage caused by COVID-19 infection. Furthermore, it seems that the highly pathogenic SARS-CoV-2 is associated with rapid virus replication and a tendency to infect the lower respiratory tract, resulting in an elevated response of IL-6-induced severe respiratory distress (19). As is well known, vitamin D also enhances cellular immunity and reduces the cytokine storm induced by the innate immune system. Vitamin D can reduce the production of pro-inflammatory Th1 cytokines, such as tumor necrosis factor α and interferon γ (10). Studies indicate that vitamin D also inhibits IL-6 (20).

The influence of vitamin D on the renin-angiotensin system also might influence the invasion of the SARS-CoV -2 into cells.

Based on these studies, some authors suggest that
proper supplementation of vitamin D may improve patients' resistance to SARS-CoV-2 (2,21,22).

Conclusion

COVID-19 is a serious infectious disease caused by the novel coronavirus-SARS-CoV-2.

At present, no specific antiviral treatment or vaccine is available for COVID-19. Before creating specific treatment, there are various studies where scientists point to the possible positive effects of various nutrients in the fight against coronavirus. There are some data that vitamin D could reduce the risk of COVID-19 infection and its complications, but further studies are needed to evaluate the role of vitamin D in relation to COVID-19.

Conflict of interest disclosure

Authors declare no potential conflicting interests related to this paper.

References