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EC MICROBIOLOGY
Review Article

A Review of Major Role of Vitamin D3 in Human Immune System and its Possible Use for Novel Corona Virus Treatment

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Received: March 21, 2020; **Published:** May 06, 2020

Abstract

Considering growing concerns of the world's authorities on the spreading of novel corona virus (Covid-19), in this paper we review the evidences showing major role of Vitamin D3 in human immune system and its potential use for novel corona virus treatment. Our argument is based on research finding that corona virus has viral envelope glycoproteins. In this regard, Vitamin D3 proves to offer various beneficial effects, including immunomodulatory effect, in order to break the glycoproteins envelope of the virus. One of the greatest benefit of vitamin D3 is the fact that it is easy to get 10,000 - 20,000 IU of daily intake requirement, by sunbathing for more or less twenty minutes. Such a method is likely applicable in many tropical countries. Therefore, we submit a view which can be rephrased as follows: "Twenty minutes sunbathing a day may likely keep Covid-19 away".

"*It is better to light a candle than curse the darkness*" - a Chinese proverb[1].

Keywords: *Vitamin D3; Human Immune System; Corona Virus*

Introduction

The present paper reflects a growing concern on the spreading Covid-19 virus over more than 60 countries to date. The SARS-like coronavirus that appears to have originated in Wuhan, China has now infected thousands of people.

According to Worldometers, as of March 4, 2020, there have been 93,191 confirmed cases around the world, 3,203 death cases, and 50,984 recovered. The COVID-19 is affecting 80 countries and territories around the world and 1 international conveyance (the Diamond Princess cruise ship harbored in Yokohama, Japan)[2].

The virus was initially named novel coronavirus of 2019 (nCoV-2019 or 2019-nCoV) as of now. This has now been renamed as COVID-19. Sequencing of the virus has determined it to be 75 to 80 percent match to SARS-CoV and more than 85 percent similar to multiple coronaviruses found in bats. SARS stands for severe acute respiratory syndrome. It is also a coronavirus or CoV [2].

[1]Note: some authors attributed this quote to William Watkinson, 1907.

[2]Source: https://www.worldometers.info/coronavirus/

Despite this gloomy picture, there is also news reporting that all corona patients in 3 countries, including Vietnam and Nepal have recovered[3]. Therefore, there is ground to be hopeful that cure does exist.

Inspired by a recent video lecture by virus expert, Prof. Luc Montagnier [1], in this paper we will review some evidences suggesting immunomodulatory effect and other benefits of Vitamin D/D3 as potential way to Covid-19 treatment.

A short review of the basics of respiratory medicine

Covid-19 belongs to respiratory diseases related to viral pneumonia. Studies show that there are glycoprotein shells covering the corona viruses, which make it difficult to break the virus.

First of all, let us review some basic facts from textbooks of respiratory medicine:

- Oxford Handbook of Respiratory Medicine wrote regarding viral pneumonia, which can be rephrased as follows: Viral URTIs are normal, yet commonly self-restricting, and are typically overseen in the network. Viral pneumonia is less normal yet is progressively genuine and typically requires hospitalization. Viral pneumonia in the immunocompetent is uncommon and regularly influences kids or the old; flu strains are the commonest cause in grown-ups. Studies recommend that infections are perceivable in 15 - 30% of patients hospitalized with pneumonia. Infections may cause genuine respiratory disease in the immunocompromised (especially patients with discouraged T-cell work, for example following organ transplantation). CMV is the commonest genuine viral pathogen that influences immunocompromised patients. Flu, parainfluenza, rSV, measles, and adenovirus may likewise cause pneumonia in the immunocompromised, despite the fact that analysis of these infections is troublesome and contamination is generally undetected [3].

- Shen Wei Lim in ERS Handbook of Respiratory Medicine wrote on influenza and pandemic which can rephrased as follows: Flu is profoundly transmissible. Human-to human transmission happens through huge bead spread and direct contact with emissions (or fomites).

Treatment: There are two principle classes of medication that are dynamic against flu. The M2 particle channel inhibitors, amantadine and rimantadine, are viable against flu A. Be that as it may, their utilization is thwarted by the quick rise of protection from these medications together with a high rate of symptoms.

Antibiotics are generally prompted for patients with flu related pneumonia or patients with serious flu disease who are at high danger of creating auxiliary bacterial contaminations. The utilization of corticosteroids in serious flu can't be routinely supported dependent on current information; observational accomplice contemplates led during the 2009 H1N1 pandemic have detailed blended outcomes including expanded mischief [4].

Therefore, it seems we can conclude for now that even though there are recommended for such a viral pneumonia, there is no clear suggestion for treatment in a pandemic situation.

In this regards, inspired by a recent video lecture by Prof. Luc Montagnier, a renowned virus expert, we will discuss immunomodulatory effect and other advantages of Vitamin D, especially D3.

[3]Source: https://japantoday.com/category/world/all-16-of-vietnam%27s-coronavirus-sufferers-cured

Short review of immunomodulatory effect and other advantages of vitamin D/D3

In this section, we will review some advantages of Vitamin D and D3 for possible treatment of Covid-19.

Jeremy Beard., *et al*. wrote on major role of Vitamin D in regulating immune system, which can be rephrased as follows: Nutrient D has for some time been perceived as fundamental to the skeletal framework. More current proof recommends that it additionally assumes a significant job managing the invulnerable framework, maybe including safe reactions to viral contamination. Interventional and observational epidemiological investigations give proof that nutrient D insufficiency may give expanded danger of flu and respiratory tract contamination. Cell culture tests bolster the postulation that nutrient D has direct anti-viral impacts especially against enveloped viruses. In spite of the fact that nutrient D's enemy of viral instrument has not been completely settled, it might be connected to nutrient D's capacity to up-manage the counter microbial peptides LL-37 and human beta defensin 2. Extra examinations are important to completely clarify the efficacy and mechanism of vitamin D as an anti-viral agent [6].

We continue with a review of inflammatory research. Mag Mangin., *et al*. wrote on relation between Vitamin D and inflammatory disease, which can be rephrased as follows: Inflammation is accepted to be a contributing element to numerous constant maladies. The influence of nutrient D deficiency on inflammation is being investigated however examines have not exhibited a causative impact. Inflammation is associated with numerous incessant illnesses and concern has been raised about the influence of nutrient D deficiency on inflammatory forms. At the point when studies found a relationship between inflammatory infections and low serum 25-hydroxyvitamin D (25(OH)D), further research discovered proof of low nutrient D in a huge fragment of everybody. This drove a few specialists to announce an overall pandemic of nutrient D deficiency and to prescribe nutrient D supplementation. Specialists are discussing the definition of nutrient D deficiency and the fitting nutrient D portions, while further research is being done to decide whether nutrient D supplementation has the expected impact [5].

A possible mechanism of vitamin D metabolism is shown in figure 1 below.

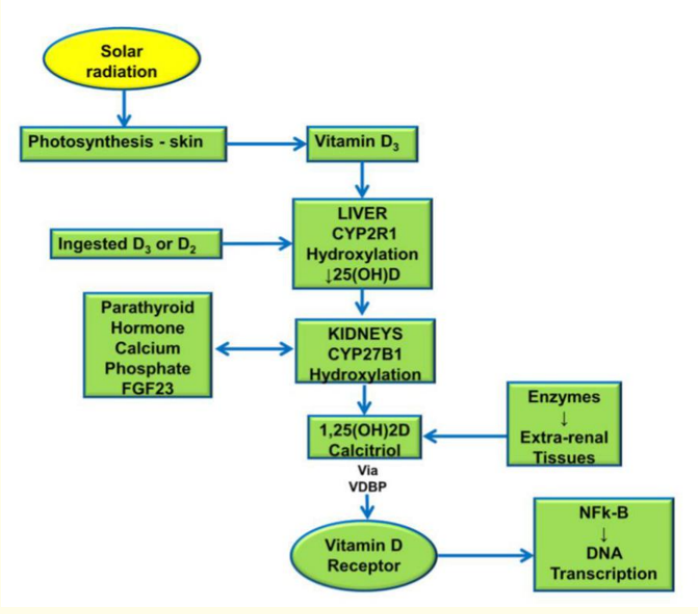

Figure 1: *Synthesis and metabolism of Vitamin D. Sequential metabolic processes convert biologically inactive, parental vitamin D into active metabolites [5].*

Another paper studies the interplay between vitamin D and viral infections and its metabolism mechanism is as shown in figure 2 below.

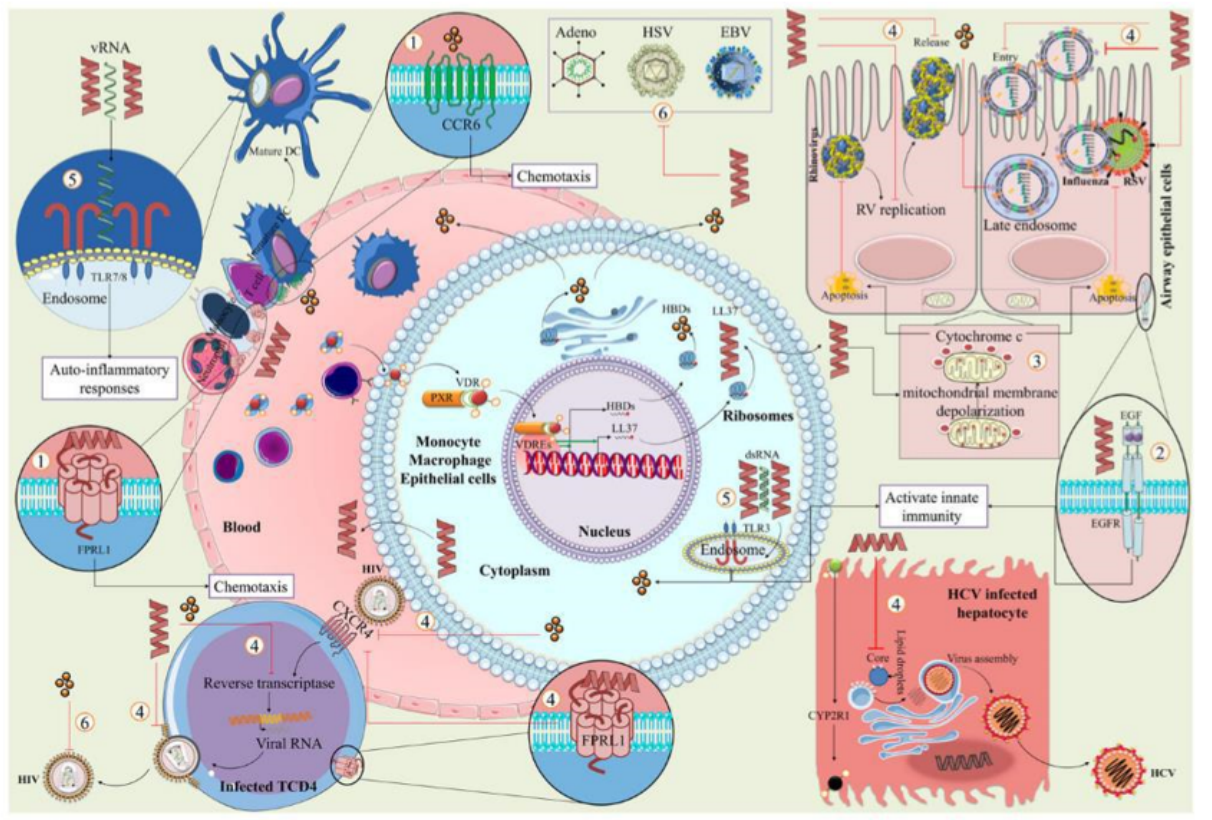

Figure 2: V*itamin D and induction of antimicrobial peptides against viral infection. Vitamin D-induced antimicrobial peptides (LL37 and HBDs) via VDR and RXR dimerization act against viral infections through (1) binding to FPRL1 and CCR6 for recruiting immune cells to site of infection; (2) activation of innate immunity by transactivation of the EGFR; (3) clearance of viral infection through mitochondria! membrane depolarization and release of cytochrome c; (4) down-regulation of cell entry, replication, and viral release; (5) protection of viral RNAs from degradation and induced immunity response through TLRs activation; (6) and direct effects on virions. Abbreviation: Epidermal growth factor receptor (EGFR), formyl peptide receptor-like 1 (FPRL1), human p-defensins (HBDs), retinoic X receptor (RXR), toll-like receptor (TLR), and vitamin D receptor (VDR). After Teymoori-Rad., et al [9].*

And for the last quote is from a not-peer-reviewed manuscript by William B Grant., *et al*. which can be rephrased as follows: Low nutrient D status in winter licenses viral pandemics. During winter, individuals who don't take nutrient D supplements are probably going to have low serum 25-hydroxyvitamin D [25(OH)D] fixations. Nutrient D can diminish the danger of viral plagues and pandemics in a few different ways. To start with, higher 25(OH)D focuses decrease the danger of numerous constant ailments, including tumors, cardiovascular ailment, interminable respiratory tract diseases (RTIs), diabetes mellitus, and hypertension. Patients with interminable illnesses have fundamentally higher danger of death from RTIs than in any case solid individuals. Second, nutrient D decreases danger of RTIs through three components: keeping up tight intersections, killing encompassed infections through acceptance of cathelicidin and defensins, and

diminishing creation of proinflammatory cytokines by the inborn safe framework, along these lines lessening the danger of a cytokine storm prompting pneumonia [7].

In their abstract, they conclude: "From the accessible proof, we estimate that raising serum 25(OH)D fixations through nutrient D supplementation could lessen the rate, seriousness, and danger of death from flu, pneumonia, and the current COVID-19 scourge" [7].

Despite all of the above advantages of Vitamin D/D3 for human immune system, one of the problems is that there is seemingly deficiency of Vitamin D, as reported in Poland's recent guideline, which can be rephrased as follows: Nutrient D insufficiency is a significant general medical issue around the world. Nutrient D lack presents a noteworthy hazard for both skeletal and non-skeletal disarranges and various long lasting negative wellbeing results. The targets of this proof based rules archive are to give social insurance experts in Poland, a refreshed suggestion for the counteraction, finding and treatment of nutrient D lack [8].

How to get a daily intake of Vitamin D and D3 as per required [10]

We have reviewed possible efficacy of Vitamin D/D3 in improving human immune system, including from Covid-19. Now the question is how we can obtain rapid medicine for daily intake of the entire population. The answer could be quite simple: sunbathing (exposing your body to sunlight in the morning) and nutrition and/or with vegetables.

Sunbathing

At the point when our progenitors were living in the tropics, daylight on-skin was their fundamental wellspring of nutrient D. At the point when daylight sparkles on skin it produces nutrient D3. All things considered, just a segment of ultra-violet in daylight carries out the responsibility, known as UV-B. The frequencies for UV-B go from 280 to 315 nanometres and nutrient D is best-delivered by light in the range 295 to 297 nanometres. Uncovering the vast majority of your skin to solid daylight for around 20 minutes can deliver somewhere in the range of 10,000 and 20,000 IU of nutrient D3, in the event that your skin is reasonable. By and large (In the event that you are darker looking, you may take an hour or more to create a similar sum).

Vegetables

Nutrient D nourishment sources can be either vegetable or creature. Vegetable sources are chiefly green growth (which a great many people don't eat, yet it gets into the natural way of life through fish) mushrooms. Wild mushrooms can create very considerable measures of nutrient D2 (ergocalciferol) in the event that they have been presented to solid daylight.

Business mushrooms are developed inside and not exposed to UVB light. Therefore they contain no nutrient D. Nonetheless, it merits realizing that on the off chance that you illuminate developed mushrooms that you purchase at a store, by setting them in solid daylight for 30 minutes or something like that, you can create around 1500 IU of nutrient D2 per medium-sized punnet. So, this sort of nutrient D can happen normally in our eating routine. We can utilize it, yet it's not the perfect structure for us. Our bodies are upgraded for nutrient D3, the thoughtful our skin produces. In any case, getting all your nutrient D as vegetable-sourced nutrient D2 would be a whole lot better than getting no nutrient D by any means.

Animal source of vitamin D

Cod liver oil (just a couple of teaspoons daily for a grown-up) can be utilized to give some nutrient D3. Common cod liver oil contains around 5000 IU of nutrient A, however just 500 IU of nutrient D per teaspoon. If you somehow managed to drink a few teaspoons every day (not suggested), the nutrient A would arrive at dangerous levels before you got enough nutrient D. Some cod liver oils are handled to expel the regular nutrients. At that point in the wake of preparing, manufactured nutrient An and nutrient D2 are included go into the

oil. The regular extents of nutrient A to nutrient D may likewise be changed in such oils. Likewise, nutrient A may vie for ingestion with nutrient D, so on the off chance that you are attempting to raise your nutrient D levels, taking additional nutrient A (retinol) could be counter-profitable.

Vitamin D supplement

The most straightforward and maybe most secure approach to build your nutrient D level is to utilize nutrient D3 (cholecalciferol) supplements. Enhancements of nutrient D2 (ergocalciferol) are likewise accessible, yet are presumably less powerful. Nutrient D3 supplements are broadly accessible in many nations. In most first-world nations you would now be able to get nutrient D3 in case estimates extending from 400 IU to 10,000 IU, or even 50,000 IU. Unfortunately, a few nations limit the most extreme nutrient D case size to 400 IU or 1000 IU. This makes it harder, and progressively costly to take a successful portion. Yet, even in those nations, you can for the most part request nutrient D on the web.

Sunlamps

One final other option, for individuals with profound pockets – you can utilize a sheltered tanning bed to give UV-B to your skin lasting through the year, in absolutely controlled portions. UV lights are likewise accessible to do something very similar. The gear needs to give precisely the correct frequencies of UV light, in the correct extents, so as to be sheltered. Purchase from a trustworthy maker and use carefully as per their directions. Additionally, know that tanning beds and sunlamps may not create a similar nature of light for an incredible duration. So, follow producer's proposal for recharging tubes.

We hope that we made it quite clear that certain treatments do exist for Covid-19 based on existing knowledge on the major role of Vitamin D in human immune system, in particular for anti-viral treatment.

So, what is the best way to keep daily intake of Vitamin D/D3?

Presently you recognize what your choices are for getting the nutrient D your body needs. The vast majority should focus on daylight and supplementation, which isn't to dishearten you from eating fish! Fish - from unpolluted waters - is a solid nourishment, yet it can just go so far in meeting your nutrient D needs, except if it frames an enormous piece of your eating regimen. Both daylight and supplementation should be utilized with care and comprehension, for various reasons. Daylight can harm your skin in the event that you take a lot at once. Learn and read more about safe Vitamin D from sunlight. Nutrient D Supplements must be taken in suitable dosages, which are not the equivalent for everybody. At last, while expanding your degree of nutrient D to approach ideal, it is significant that different supplements are likewise taken in the correct amounts, especially calcium, magnesium, nutrient K and nutrient A [10].

For other sources of information regarding nutrition and phytomedicine, see [11-13].

Concluding Remarks

We reviewed a major role of Vitamin D and D3 in human immune system. This is just an early schematic paper, it would need more study to establish which the suggested medicinal plants or nutrition related to Vitamin D/D3 are the most beneficial for improving human immune system.

We hope that this short review article can be found useful for policy makers of health in reducing the effect of Covid-19 in many countries.

Acknowledgement

The authors are grateful to Sibylle Gabriel who informed us a recent video lecture by Prof Luc Montagnier [1].

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflict of interest.

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Volume 16 Issue 6 June 2020