

Short Communication

Vitamin D produce antibodies in pandemic response to gripal viruses? A critical analysis

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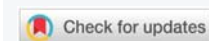
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Abstract

In the evolutionary journey of humanity, it is possible to verify an analysis of pandemics with high occurrences. This study aims to conduct a critical analysis of the role of Vitamin D as an endogenous vaccine in the main viruses present in humanity over the decades. To construct this text, we used the short review methodology through a critical analysis. This study demonstrated the importance of using Vitamin D as an endogenous vaccine when used frequently in both healthcare professionals and patients. Therefore, it is concluded that Vitamin acts protectively in the innate immune system.

Introduction

When carrying out an analysis over time in the history of pandemics such as the “Spanish Flu” it is possible to verify the high occurrence in the period from 1918 to 1920 [1]. For example, in the northern hemisphere, recent documents related to records of pandemic waves in the United States of America and Norway in the spring of 1918 in the months referring to February to April were mild and had low mortality, started in military populations and did not spread to civilian populations [1,2].

However, it was in the period of 1918 [1], specifically in the months of May to September, at that time morbidity occurred in a characteristically urban area in countries well connected with transport, in relation to rural areas it is possible to verify that isolated areas managed to have little pandemic incidence. But it was in the year 1919 [2], specifically in the months of January to March, that several isolated regions that had not previously had contagions were affected with devastating consequences [1,2].

Specifically in the year of the 1918 the H1N1 virus was responsible for pandemics during the winter and autumn wave periods in the United States [1]. What is observed in this period in relation to viral development is the presence of information regarding geographic factors and the host responsible with specific patterns related to age and sex with morbidity, mortality and fatality per wave [1,2].

However, viruses have continued to emerge and bring challenges to the global public health system with emerging viruses with respiratory contagion, for example, in 2002 the coronavirus (CoV) of a viral family, known since the 1960s which is the cause of infection breathing in humans and animals has brought problems to human health [1]. Coronavirus causes mild to moderate respiratory illness and the symptoms are equivalent to a common cold. Generally the coronaviruses that infect humans are the alpha coronavirus 229E, NL63 and beta coronavirus OC43 and HKU1 types [3-7].

In addition, the coronavirus can develop as the disease worsens due to a genetic environmental depression of the



immune system and severe respiratory syndrome, for example, severe acute respiratory syndrome (SARS) which is caused by the coronavirus generally associated with SARS-CoV which is spread rapidly to twelve nations on different continents, in this case, North America, South America, Europe and Asia [8,6]. In addition, in 2002 it caused the infection of more than 8000 people and resulted in the equivalent of 800 deaths and was controlled only in 2003 [2,6]. However, in 2012 another new coronavirus was isolated, but with different genetic traits than the one that caused SARS at the beginning of the past decade [2]. This new coronavirus was unknown as a causative agent of human disease until its recent identification in Saudi Arabia and only a few years later in other countries in the Middle East, Europe and Africa [1,2].

However, the most interesting is that all the cases diagnosed outside the region of the Arabian Peninsula and were carried out after recent trips or contacts with tourists from countries in the Middle East region, specifically Saudi Arabia, Qatar, the United Arab Emirates and Jordan [1,2]. And because the cases occurred in this global region, the disease started to be defined as Middle East Respiratory Syndrome (MERS) and the new virus received the name of MERS-associated coronavirus (MERS-CoV) [1,8-10].

Vitamin D is a potent immune system activator and is considered an absolute and protective component of the natural defense mechanism against microbial invasion and belongs to a group of molecules derived from 7-dehydrocholesterol and are interconnected [4] by means of chemical and enzymatic reactions that take place in different cells of the human organism. And it has been wrongly classified as vitamin D and is considered an essential element in the human diet is a steroidal and fat-soluble prohormone with endocrine, paracrine and autocrine functions. Let us remember that the synthesis of Vitamin D occurs in the skin, however [5], Vitamin D comes from diets or supplementation orally and after ingestion it is transported to the liver and in the liver it under goes hydroxylation of carbon 25 which results in the production of 25-hydroxyvitamin D [25 (OH) D] and molecular compound is the main circulating vitamin D formula [5,6]. The mediation of hydroxylation in the liver occurs by several enzymes known as 25-hydroxylase, the most important being known as CYP2R1 which is a type I of P450 enzyme [5]. And after this hydroxylation the 25 (OH) D is transported to the rins and undergoes a second hydroxylation, in the proximal renal tubule by the action of the mitochondrial enzyme 1- α -hydroxylase (CY2P27B1) and this enzyme is responsible for the conversion of the 25 (OH) D in 1,25-dihydroxyvitamin D [1,25 (OH) 2D] [5] the well-known active hormone responsible for the biological conduct of Vitamin D [11-13]. And that immune response to viral or bacterial infectious agents is complex and influenced by increasing numbers related to biological and metabolic factors [8,12]. Therefore, Vitamin D plays a role in the innate and adaptive immune

response to the infectious process [13,14]. Previous studies have shown that the increase in the incidence of certain viral respiratory infections, including influenza [7], is associated with low levels of Vitamin D [3,15]. So the purpose of this critical analysis is to examine the immune response of Vitamin D against Flu viruses in relation to serum levels of D vitamin [3,13]. Previous studies have shown that viral infections have shown below ideal levels of Vitamin D ($\leq 20\text{ng/ml}$) [5,6] in blood serum for good health in regions of China [3-5,14,15], however, this is consistent with regions in Europe and America, where about 80% of the pre-adolescent population had deficient levels of Vitamin D and in white and obese pre-adolescents the proportions were more reduced [4-6].

In previous studies, it is possible to verify that levels below 20 ng/ml of Vitamin D in blood serum are associated with a lower antibody response in viral infections [11-13], however, there is already evidence that the low level of Vitamin D is related to the appearance from autoimmune diseases, for example, systemic lupus erythematosus, multiple sclerosis and type I diabetes [14].

Vitamin D plays a role in innate and adaptive immunity [8] as it is essentials for the regulation of human genes and stimulates the production of catelicidin which increases the production of HCAP-18 and thus improves the function of cells such as macrophages and immunity innate. This relationship is associated between Vitamin D levels [12,13], for example, the expression of increased catelicidins and the intracellular death of Mycobacteria Tuberculosis and yet [2], there is an inverse association between low Vitamin D levels and increased infections in the upper respiratory tract [2,14,15] by flu viruses. Let's remember that Vitamin D also influences the development of adaptive immunity by inhibiting the proliferation of B cells with differentiation and secretion of immunoglobulins that will supply the proliferation of T cells and thus results in a more pro-inflammatory response change from TH1 to anti-inflammatory TH2 cells [4,12]. In previous studies, it was observed that inadequate vitamin D nutrition is endemic among children [13], the elderly and populations with a history of pre-existing autoimmune diseases, especially in winter [8]. During the development of studies in the systematic review and meta-analysis model it was possible to high light that the deficit in serum levels of Vitamin D [25 (OH) D] are below the limit of 20 ng/ml in blood serum [4,5] and this risk factor increases in people of all ages who live in temperate latitudes [9], especially in the north in long winter regions [4,5]. We have observed in previous published studies that the human being tends to acquire Vitamin D mostly by exposure to occasional sunlight to a degree that is a function of the exposed surface area of the skin [6,9]. For example, older people have less than 25% vitamin D production when compared to a 21-year-old youth after the same amount of exposure to sunlight [4,13]. It is possible to observe that in the world there is a seasonal variation in relation to the deficit



of Vitamin D which is related to subtropical and a tropical latitudes. Generally, this elderly person can supplement 10 mcg/day [16,17] of vitamin D by sun exposure, and yet [4,9,13] it does not prevent vitamin D insufficiency in winter, with oral supplementation being necessary and when we talk about influenza or coronavirus pathology [1] we emphasize that it involves a complex interaction between the virus and innate and acquired immunity [4,5] the defense action of the organism occurs by macrophages that rapidly release cytokines in the infected respiratory tissue and virucidal antimicrobial peptides try to prevent viral replication and thus it prevents the organism from being infected [7]. Studies have shown that the release of pro-inflammatory cytokines as well as the virulence of the virus is possible to determine the clinical phenotype of viral infection, for example, flu [6,15]. This is because clinical flu phenotypes can positively correlate with the amount of cytokines released [15]. During years of studies it was possible to observe that the severity of the illness induced by influenza viruses, for example, influenza is correlated with the virus's ability to induce the production of cytokines by macrophages. Let us remember that in avian influenza, for example, the innate immune response in relation to the release of cytokines can be dominant, since the levels of this cytokine are high and with lethal results. A study recently [4,5] reported that Vitamin D has a modulating role in the release of macrophages and thus prevents the release of many inflammatory cytokines and chemokines [5,9]. It was also found that the vitamin D deficit also shows negative changes in the macrophages' ability to mature and thus produce surface antigens specific for macrophages and thus produces the acid phosphatase of the lysosomal enzyme and secrete H₂O₂ through an integral function of their abilities [4,10,13] functional antimicrobial [8]. It is possible to report with studies published in the last five years that Vitamin D supplementation increases the expression of specific surface antigens, for example, macrophages and the acid phosphatase of the lysosomal enzyme by stimulating its oxidative burst function [2,13]. This is due to the stimulation of gene expression of antimicrobial peptides (AMP) in human monocytes, neutrophils and other human cell lines [4,15]. It is possible to report that this endogenous antibiotic, such as defensin and catelicidins, is able to directly destroy the invasive viral microorganism [1,6], since the broad-spectrum antimicrobial peptide can include antiviral activities and inactivate the flu virus, for example, influenza [6]. Neutrophils, macrophages are considered natural killer cells which secrete antimicrobial peptides, however, the epithelial cells that line the upper and lower respiratory tract can also secrete this immune cell origin as a lung defense [8,14]. If Vitamin D has the capacity to stimulate the production of viral antimicrobial peptides with a primary function in the defense against infectious agents, and this defense occurs through the stimulation of antimicrobial peptides which can intensify the reduction of catelicidins [4,8], it is concluded that the vitamin deficit is able to cause imbalance of the immune system and the

supplementation of pharmacological doses of 250-500 mcg/day [16,17] of vitamin D can be useful in the treatment of viral infections by influenza or coronavirus. Thus, it is reinforced that vitamin D should be used by health professionals through pharmacological doses to prevent vitamin D deficiency and avoid viral infectious risks [6,8], therefore, it is possible to conclude that daily pharmacological doses have the benefit of improving symptoms of viral respiratory infections [9,14]. However, the nutritional potential of vitamin D remains untapped by scientific evidence [4,9,18].

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