

Vitamin D or Flu Vaccine-Benefits over Adverse Effects

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Abstract

Available data suggest that calcitriol has a role in controlling pulmonary inflammation by inducing the production of natural broad-spectrum antimicrobial peptides, the so-called cathelicidin. Randomized clinical studies reported that vitamin D supplements in a daily-wise manner caused a significant risk reduction in acute respiratory tract viral infections and participants who were given vitamin D supplementations were half less infected with flu than those who were not given the vitamin. Hence, vitamin D3 supplementation may be advantageous when compared with flu vaccine especially when we put in consideration morbidities and complications caused by this vaccine as well as the conditions in which influenza vaccine may be contraindicated like in patients who receive cancer immunotherapies targeting the programmed death-ligand 1 (PD-L1) or its receptor, programmed cell death protein 1 (PD-1).

from the diet and from supplements. Syntheses of vitamin D (specifically cholecalciferol) in the skin in addition to very few foods containing vitamin D are the major natural sources of the vitamin. Dermal synthesis of vitamin D from cholesterol is sun exposure-dependent, specifically UVB radiation [6].

The endocrine impacts of vitamin D are fundamentally entangled in blood calcium homeostasis. Calcium and vitamin D are overwhelmingly mentioned in the same clause because of their interconnecting actions. When present in optimal level, vitamin D has no tangible influence on absorption of calcium although it favors adaptable physiological reverberation to change in calcium requirement [7]. Vitamin D's autocrine and paracrine effects depend upon cellular genetic transcription expressing nuclear vitamin D receptors. These prospective effects comprise cell differentiation enhancement, suppression of cell proliferation, and programmed cell death that occur in response to immunological and neoplastic events [8].

Keywords: Vitamin D; Flu vaccine; Cathelicidin; Influenza virus

Introduction

Vitamin D has been a spectacular field of research in recent years, with more than hundreds of articles appeared by the beginning of 21st century [1]. Some studies had found that vitamin D influences many other cells and tissues. It has reported that the pluripotent steroid hormone 1 α ,25(OH)₂D₃ commences the physiologic responses of \geq 36 cell types that reign the vitamin D receptor (VDR) [2]. Globally, vitamin D insufficiency is experienced by about 1 billion individuals, and deficiencies can be found in all age groups and ethnicities [3-5].

Vitamin D belongs to a group of fat-soluble secosteroids that play a fundamental role in enhancing intestinal absorption of calcium, phosphate, iron, magnesium, and zinc. In humans, the most significant components in this group are vitamin D₃ and vitamin D₂, alleged cholecalciferol and ergocalciferol respectively. Cholecalciferol and ergocalciferol can be taken

Role of Vitamin D in Infection and Immunity

More than 200 human genes are targeted by the end product of vitamin D metabolism [9]. The "non-classic" impact of vitamin D on the body's immunity is mediated by adjustment of adaptive and innate immune system and regulation of cathelicidin, antimicrobial proteins, production that affect inflammatory process [10]. The synthesis of these antimicrobial proteins is highly expressed at integumentary barrier sites such as the respiratory epithelium [11].

The links between Vitamin D deficiency and increased risk severity of infection, particularly of the respiratory tract, have been mentioned by many epidemiological studies in adults and children. However, the mechanisms by which calcitriol may ameliorate immune responses to infection are still debatable. With due considering its impact on immunity and inflammation, vitamin D may have a remarkable promising role against infection [10,12-14].

Alkhedaide et al. tried to show the extent of association of vitamin D insufficiency with competence of immune system.

They concluded that vitamin D insufficiency can be improved by daily oral administration of 4000 IU of the vitamin for 3 weeks. Moreover, Vitamin D might have as an anti-inflammatory activity that impedes autoimmune reactions and ameliorates either innate or adaptive immunity [15]. Vitamin D-mediated adaptive immune system regulation through T cells leads to their differentiation into two distinct subcategories namely the pro-inflammatory TH1 cytokine producing cells including IL2, TNF α and IFN γ as well as the anti-inflammatory TH2 cytokine producing cells including IL-3, IL-4, IL-5, and IL-10 [16].

Surprisingly, vitamin D has an inhibitory action on TH1 cytokine producing cells and a stimulatory action on TH1 cytokine producing cells proliferation. These actions are mediated by activating vitamin D receptors (VDR) of T-cells [16,17]. It is also becoming increasingly clear that microbes slow down immune reactivity by deregulating the VDR ultimately to increase their chance of survival [18]. Moreover, vitamin D streamlines the inflammatory cascade by regulating the nuclear factor kappa B (NF- κ B) which is induced by activation of pathogen associated molecular patterns (PAMPs) derived from pathogens like protozoa, viruses, bacteria, and fungi. This causes Toll-like receptors (TLRs) existed on various immune cells to induce NF κ B pathway and upregulate pro-inflammatory cytokines expression [19]. Vitamin D upregulates I κ B α , which decreases NF- κ B signaling by binding to NF- κ B sub units, hence decrease many pro-inflammatory cytokines proliferation during viral infection in the airway epithelium [20].

Vitamin D and Influenza

Vitamin D deficiency and respiratory tract infection are common health problems in children in many countries [21]. There was likewise a correlation between vitamin D levels and incidence and severity of lower respiratory tract infections (LRTI) since children with LRTI were found to have significantly less mean vitamin D levels as compared to normal controls [22]. Although the mechanisms by which calcitriol exerts beneficial effects on the incidence of respiratory tract infection still needs further research, available data suggest vitamin D plays a role in controlling inflammation in the lungs.

However, to date, vitamin D induced production of cathelicidin [9], a naturally occurring broad-spectrum antibiotic, has not been detected to have any obvious influence on the burden pathogenic particles like bacteria or viruses [23]. Wayse and colleagues [24] found that children with serum vitamin D levels <10 ng/ml were 11 times more likely prone to lower respiratory infections. In contrast, Tse et al. reported that neither vitamin D insufficiency nor deficiency was associated with adverse respiratory outcomes [25].

Now, it is obvious that vitamin D is an immunomodulator and is locally produced in lung tissues via 1 α -hydroxylase which is expressed by lymphocytes, dendritic cells, alveolar macrophages and airway epithelium. These immunomodulatory effects are accomplished by increasing cathelicidin secretion, suppressing dendritic cell activation, modulating T-cell activation, and lowering chemokine production within pulmonary tissues in response to allergic lung diseases and infections (Figure 1) [26].

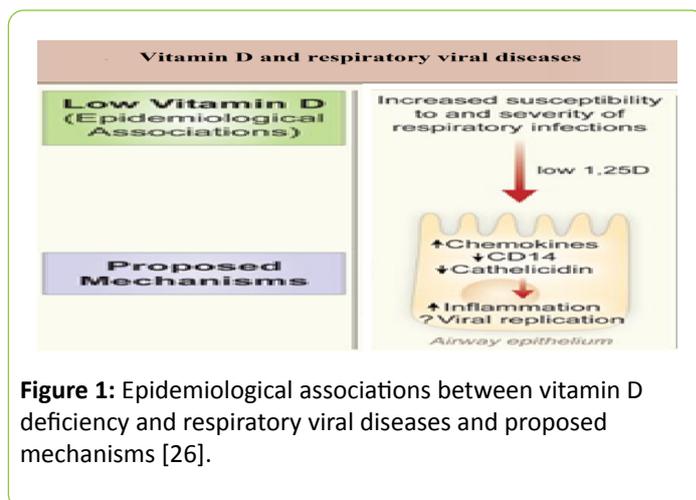


Figure 1: Epidemiological associations between vitamin D deficiency and respiratory viral diseases and proposed mechanisms [26].

Zittermann et al. showed that randomized clinical studies (RCTs) indicate a significant risk reduction by vitamin D supplements in regard to acute respiratory tract infection and there is evidence that daily administration of vitamin D is more effective than high-dose bolus administration [27] while Bergman et al. revealed that supplementation with vitamin D3 may reduce disease burden in patients with frequent respiratory tract infections [28]. Cell culture studies propped the suggestion that vitamin D has forthright anti-viral efficacy that may be linked to vitamin D's capability to up-regulate human beta defensin 2 and the anti-microbial peptides LL-37 [29].

Influenza researches were broadly established to find obvious associations between flu and vitamin D status especially in individuals that are likely to have insufficient vitamin D concentrations [30]. There is a proposed direct correlation between vitamin D and epidemic influenza. About four decades ago, Hope-Simpson submitted his proposal that a 'seasonal stimulus' closely linked to sun radiation expounded the significant seasonality of epidemic influenza. As solar radiation triggers sturdy seasonal vitamin D biosynthesis in the skin, its insufficiency is common in the winter.

Calcitriol has profound effects on human immunity by acting as an immune system modulator, suppressing the excessive expression of inflammatory cytokines and raising the 'oxidative burst' potential of macrophages. It spectacularly promotes the production of efficient anti-microbial peptides, which present in monocytes, neutrophils, natural killer cells, and in epithelial cells lining the respiratory tract where they play a substantial role against pulmonary infection. Volunteers injected with influenza vaccine were more likely to develop wintertime fever and serological evidence of an immune response [31].

Influenza is one of several respiratory viral pathogens that reveal a distinct predilection for infection in the wintertime [32]. More than 200 viruses cause the common cold, which, as the name implies, also shows a distinct wintertime excess [33]. Pro-inflammatory mediators are likely the major culprit of mortality given rise by the highly pathogenic influenza A virus strains and infected individuals may get benefits from vitamin D by alleviation of the Th1 immune response [34]. Children who experienced regular artificial UVB radiation exposure had approximately two times less incidence rates of sore throat,

upper respiratory tract infections, and influenza than non-exposed ones and dosages of exposure are positively correlated with macrophages' phagocytic activity [35].

Juzeniene et al. assumed the seasonality of pandemic influenzas even in temperate areas. This finding supported the postulation that UVB radiation-dependent vitamin D is protective against flu in summertime [36]. Concordantly, a case-control study showed that black, postmenopausal ladies, who were daily supplemented with 800 IU of vitamin D, experienced three times less susceptibility to flu symptoms than control group and 2000 IU daily supplementation for one year caused efficacious protection against wintertime influenza [37]. Another placebo-controlled study suggested that daily supplementation of 1200 IU of vitamin D caused two folds reduction of seasonal influenza A incidence in school children [38]. Although debatable findings have been reported, many clinical and observational studies supported the protective evidence of vitamin D against viral respiratory infections and HIV [39,40].

During the winter of 2008-2009, researchers from Jikei University School of Medicine in Tokyo conducted a placebo-controlled study on 354 children. They found that 1200 IU of daily supplementation of vitamin D efficaciously diminished flu infection risk by 50 percent when compared with who were given placebo. This decline in infection rate coincided with an elevation in vitamin D plasma levels. In contrast, vaccines had conquering rates significantly less than that accomplished by calcitriol. In addition, antiviral drugs declined influenza rates by only 8 percent [41]. This made the suggestion that vitamin D3 supplementation during the winter may reduce the incidence of influenza A, especially in specific subgroups of school children [38], and thence, healthcare workers and patients should strongly be tested and treated for vitamin D deficiency to prevent the spread of the H1N1 virus [42].

Egalitarianly, Dutch scientists indicated that vitamin D3 supplementation may prevent or possibly treat influenza viruses. However, the optimal daily dosage regimen of the vitamin has yet to be specified [43]. With a due concordance, Indian researchers studied the effect of treatment with vitamin D3 on bronchial cells infected with influenza A virus, specifically the H1N1 strain, and found that the vitamin reduced the severity of H1N1 influenza [44]. Moreover, Surman et al. described the individual and combined effects of vitamin A and D insufficiency in mice immunized with an attenuated influenza virus vaccine. They proposed that healthy immune responses to respiratory virus vaccines in vitamin-deficient subjects may be clinically enhanced by vitamin supplementation programs [45].

A report released from the Department of Justice in June 15, 2014, revealed that the flu vaccine is the most perilous vaccine in America. Most complications due to the flu shots were for Guillain-Barré Syndrome. Other flu vaccine complications encompassed rheumatoid arthritis, chronic Inflammatory demyelinating polyneuropathy, shingles, lichenoid drug eruption, brachial plexus neuropathy, transverse myelitis, brachial neuritis, Bell's Palsy, and narcolepsy [46].

Conclusion

Vitamin D is a secosteroid hormone that possesses a significant non-classic impact on the body's immune system to enhance the secretion of endogenously important peptides with antimicrobial potentials like cathelicidin. Many researchers reported that vitamin D3 supplementation may be advantageous when compared with the flu vaccine. It is worthy to put in consideration morbidities and complications caused by influenza vaccine as well as the conditions in which this vaccine may be contraindicated like in individuals who receive cancer immunotherapies targeting the programmed death-ligand 1 (PD-L1) or its receptor, programmed cell death protein 1 (PD-1). Nevertheless, setting the recommended efficient dosage of which to fight flu remains yet unspecified. As flu vaccination encountered many health complications and morbidities, the search for other alternative solutions against respiratory viruses became a great premonition for researchers in this field.

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