Vitamin D and its effects in the prevention of diseases at all stages of life

Vitamina D e seus efeitos na prevenção de doenças

La vitamina D y sus efectos en la prevención de enfermedades en todas las etapas de la vida

RESUMO

Objetivo: Analisar os níveis ótimos de vitamina D no organismo e seus efeitos na prevenção de doenças. Método: Trata-se de um estudo de revisão integrativa. Foram selecionados artigos entre 2016 e 2020 nas bases de dados Pubmed, Scielo, BDENF e Science Direct de março a julho de 2021. A padronização dos descritores foi realizada por meio dos Descritores em Ciências da Saúde e pelo Medical Subject Headings. Foi utilizado o operador booleano "AND". Resultados: Após aplicar todos os critérios de inclusão, houve 14 artigos que compuseram a amostra final, os quais responderam à questão de pesquisa. Estudos demonstraram os efeitos benéficos da vitamina D em diferentes patologias, entre essas para a COVID-19, asma, pneumonia, rinite alérgica, síndrome pré-menstrual, produção de imunidade, fibrose cística e tireoidite de Hashimoto. Conclusão: São muitos os benefícios da vitamina D, tais como potente anti-inflamatório, regulação de infecções e equilíbrio do sistema imune.

DESCRITORES: Vitamina D; Deficiência de Vitamina D; Fatores Imunológicos.

ABSTRACT

Objective: To analyze the optimal levels of vitamin D in the body and its effects on disease prevention. Method: This is an integrative review study. Articles between 2016 and 2020 were selected in the Pubmed, Scielo, BDENF and Science Direct databases from March to July 2021. The descriptors were standardized using the Health Sciences Descriptors and the Medical Subject Headings. The Boolean operator "AND" was used. Results: After applying all the inclusion criteria, there were 14 articles that made up the final sample, which answered the research question. Studies have shown the beneficial effects of vitamin D in different pathologies, including COVID-19, asthma, pneumonia, allergic rhinitis, premenstrual syndrome, immunity production, cystic fibrosis and Hashimoto's thyroiditis. Conclusion: There are many benefits of vitamin D, such as potent anti-inflammatory, infection regulation and immune system balance.

DESCRIPTORS: Vitamin D, Vitamin D Deficiency, Immunologic Factors.

RESUMEN

Objetivo: Analizar los niveles óptimos de vitamina D en el organismo y sus efectos en la prevención de enfermedades. Método: Este es un estudio de revisión integradora. Se seleccionaron artículos entre 2016 y 2020 en las bases de datos Pubmed, Scielo, BDENF y Science Direct de marzo a julio de 2021. Los descriptores se estandarizaron utilizando los Health Sciences Descriptors y los Medical Subject Headings. Se utilizó el operador booleano "AND". Resultados: Después de aplicar todos los criterios de inclusión, fueron 14 los artículos que conformaron la muestra final, los cuales respondieron a la pregunta de investigación. Los estudios han demostrado los efectos beneficiosos de la vitamina D en diferentes patologías, incluyendo COVID-19, asma, neumonía, rinitis alérgica, síndrome premenstrual, producción de inmunidad, fibrosis quística y tiroiditis de Hashimoto. Conclusión: Hay muchos beneficios de la vitamina D, como un potente antiinflamatorio, regulación de infecciones y equilibrio del sistema inmunológico.

DESCRIPTORES: Vitamina D, Deficiência de vitamina D, Factores inmunológicos.

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INTRODUCTION

Vitamin D is a pre-steroid hormone synthesized in the skin through sunlight, some foods and through supplementation. [1] In addition to the functions of regulating calcium, bone formation and resorption, vitamin D has receptors in most cells of our body. 1 These receptors, when functional, provide several functions such as increasing immune defense, tumor apoptosis, inhibition of cell metastasis, cell proliferation and angiogenesis. [2]

Vitamin D deficiency occurs worldwide, causing an increase in chronic, infectious, autoimmune and oncological diseases and depression. [3] Among individuals, Afro-descendants have great difficulty in obtaining adequate doses of vitamin D 4, because melanin blocks much of the synthesis of vitamin D in the skin, requiring greater sun exposure. [4,5]

Optimal prescribed vitamin D levels differ in countries such as the United States of America (USA) and Brazil. [6,7] In Brazil, according to the Endocrinology Society, levels of 20 ng/mL are considered normal and do not require replacement 6, however, according to the Brazilian Institute of Geography and Statistics (IBGE) 85% of adults and adolescents do not consume vitamin D properly, which can lead to vitamin D deficiency. In the US, according to the Endocrine Society, serum levels below or equal to 20 ng/mL are deficient and levels >30 ng/mL are considered great 8, and only 24% of the population has insufficient serum levels. [9]

Exposure to UVB rays should be done horizontally, without sunscreen and with good skin exposure. [5] However, due to the difficulties of time availability, latitude and season of the year with little sunlight, and atmospheric pollution increases vitamin D deficiency, evidencing that supplementation would be the most appropriate. [5,7] The doses of daily supplementation indicated by various authorities are as low as 400 to 600 IU per day. [8]

Studies in mice with different types of viruses also showed that vitamin D reduced the replication of dengue, rotavirus and influenza A10 viruses. In COVID-19 studies have shown the essential role of vitamin D acting as a physical barrier in the mucosa, in natural and adaptive immunity. [10] In Spain, 76 patients were hospitalized for COVID-19, of which 50 received doses of approximately 130,000 IU in the first week and 33,000 IU in the following weeks. [11] Of the 26 patients who did not receive vitamin D, [13] went to the Intensive Care Unit (ICU) and 2 died. And of those who received vitamin D, only one patient required an ICU. [11]

Vitamin D deficiency is increasing and prevalent, however, in the literature there is little incentive for its supplementation. [12] Thus, it is necessary to create strategies in primary health care to increase adherence to supplementation with optimized doses and the combination of vitamin D supplementation in vaccination campaigns for children and vitamin D fortification in foods. [12] It is important to emphasize that those responsible for formulating health policies should also educate health professionals on the prevention and prescription of vitamin D supplements, with the monitoring of patients' serum levels of vitamin D. [12]

This work is justified by the need to disseminate more information about the urgency of raising the population's serum levels of vitamin D, in addition to generating greater awareness of the benefits of vitamin D among nursing professionals, who are the most involved in health promotion.

Based on this information, the objective was to analyze the optimal levels of vitamin D and its effects on disease prevention at all stages of life. Therefore, the research question was: What are the benefits of optimal levels of vitamin D in the human body to control pathologies?

METHOD

This is an integrative review study on the effects of vitamin D on the human

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body, focusing on the benefits of high serum levels of vitamin D and its daily dosage in disease prevention.

The criteria established for the inclusion of scientific articles were: studies carried out in humans, articles published between the years 2016 to 2020, with comprehensive information about the function of vitamin D and the benefits of high serum levels. Only articles in English, Portuguese and Spanish were selected. Exclusion criteria were: newspaper article, thesis, reflective study, works in editorial format, integrative or systematic review, book or book chapter, experience report, dissertation and others not being original articles.

Data collection was performed in the following databases: Pubmed, Scielo, BDENF and Science Direct. As descriptors, through the Descriptors in Health Sciences (Decs) and Medical Subject Headings (MeSH): Vitamin D, Vitamin D Deficiency, Receptors Calcitriol, Immunologic Factors, Respiratory Track Disease. All titles and abstracts from the initial search were read and, after this selection, the articles that met the inclusion criteria were read in full, in order to meet the research objective. Articles that agreed with the research question were included in the final sample.

To help the search on the platforms, the Boolean operator "AND" was used to select the articles. The articles selected for the final sample were analyzed and evaluated according to the level of evidence proposed by Ribeiro and Aroni (2019).[13] As it is a review study, with data in the public domain, the research did not need to undergo ethical approval.

RESULTS

A search was performed in PubMed, Science Direct, SciELO and BDENF databases from March to July 2021 and a total of 2983 studies were collected. Chart 1 clarified how the descriptors were crossed in the databases for the acquisition of the initial sample and without the application of inclusion and exclusion criteria.

Chart 1 – Process of searching scientific studies in the databases. Maringá, PR, Brazil, 2022.

Descriptors	PubMed	ScienceDirect	SciELO	BDENF
Vitamin D AND Vitamin D Deficiency AND Receptors Calcitriol	317	439	4	0
Vitamin D AND Vitamin D Deficiency AND Immunologic Factors	173	893	0	0
Vitamin D AND Vitamin D Deficiency AND Respiratory Track Disease	574	583	0	0
Total	1064	1915	4	0

Source: The authors, 2022.

Table 2 – Screening of studies in databases according to selection criteria. Maringá, PR, Brazil, 2022.

Database	Eligible Articles	ElectedArticles	Duplicate studies excluded	Primary studies included	Studies for Sample
PubMed	1064	168			
Science Direct	1915	22			
SciELO	4	0			
BDENF	0	0			
Total	2983	190	27	163	14

Source: The authors, 2022.

At this stage, all titles and abstracts were read, and 190 articles were chosen that matched the initial inclusion criteria. Subsequently, a search for duplicate articles was carried out, from which 27 studies were excluded, resulting in a total of 163 studies to be analyzed according to the selection criteria (Chart 2).

A total of 163 articles were read in their entirety, among which 14 studies were selected that responded to the objective, constituting the final sample. All articles in the final sample were found in the PubMed database. The year 2020 had a higher prevalence of publications, predominantly in English.

DISCUSSION

The selected studies demonstrated the beneficial effects that vitamin D provides in different pathologies, including for COVID-19, asthma, pneumonia, allergic rhinitis, premenstrual syndrome, immunity production, cystic fibrosis and Hashimoto's thyroiditis.

Kaufman et al. conducted a study to detect the association of COVID-19 with circulating levels of vitamin D, evidencing that levels < 20ng/ml had a 54% higher positivity rate compared to those at levels 30-34 ng/ml. 20 Confir-

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Chart 3 – Synthesis of the studies of the final sample. Maringá, PR, Brazil, 2022.

AUTHORS	TITLE	MAIN RESULTS
Ahmed et al. (2020) [14]	Analysis of 25-hydroxy cholecalciferol, immunoglobulin E, and vitamin D receptor single nucleotide polymorphisms (Apa1, Taq1, and Bsm1), among sample of Egyptian children with bronchial asthma: A case-control study	He observed that the vitamin D of asthmatic children was 13.46 ng/mL with IgE of 99.83 ku/L and healthy children 37.53 ng/mL with IgE of 7.52 ku/L, demonstrating the susceptibility of the organism without the ideal levels of the supplement.
Chahardoli et al. (2019) [15]	Can supplementation with vitamin D modify thyroid autoantibodies (Anti-TPO Ab, Anti-Tg Ab) and thyroid profile (T3, T4, TSH) in Hashimoto's thyroiditis? A double blind, randomized clinical trial	The group that received vitamin D raised levels from 25.38 ± 11.02 ng/ml to 50.16 ± 14.98 ng/ml while the placebo group continued with insufficient levels, showing that vitamin D decreases the activity of Hashimoto's disease.
Haugen et al. (2016) [16]	Vitamin D status is associated with treatment failure and duration of illness in Nepalese children with severe pneumonia	Vitamin D of <50 nmol/l was associated with increased risk of treatment failure and longer time to recovery.
Heidari et al. (2019) [17]	Vitamin D supplementation for premenstrual syndrome-related inflammation and antioxidant markers in students with vitamin D deficient: a randomized clinical trial	Through supplementation vitamin D levels increased from 21 to 40 ng/ml and interleukin 12 mediated inflammatory levels decreased from 18 to 7 Pg/ml.
Jain et al. (2020) [18]	Analysis of vitamin D Level among asymptomatic and critically ill COVID-19 patients and its correlation with inflammatory markers	Among the 154 patients, 91 were asymptomatic and 63 were critically ill in the ICU. Asymptomatic patients had mean levels of 27.89 ± 6.21 ng/mL and critically ill patients admitted to the ICU had mean levels of 14.35 ± 5.79.
Kanhere et al. (2018) 19	Bolus weekly vitamin D3 supplementation impacts gut and airway microbiota in adults with cystic fibrosis: A double-blind, randomized, placebo-controlled clinical trial	Individuals with insufficient levels had their intestinal microbiota enriched by pathological bacteria and the group that received vitamin D had the best response by enriching the bacteria that help in the health of the gut.
Kaufman et al. (2020) [20]	SARS-COV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels	Vitamin D levels < 20ng/ml were 54% higher in positive tests than patients with levels 30-34 ng/ml.
Liu et al. (2017) [21]	Vitamin D regulates immunoglobulin mucin domain molecule-4 expression in dendritic cells	Rhinitis patients had lower vitamin D levels than healthy subjects. The exposure of dendritic cells to calcitriol increased the expression of the vitamin D receptor, which repressed the transcription and expression of the mucin gene.
Miroliaee et al. (2017) [22]	The study of vitamin D administration effect on CRP and Interleukin-6 as prognostic biomarkers of ventilator associated pneumonia	Vitamin D administration can significantly reduce IL-6-mediated inflammation from 112.98 ± 121.87 pg/ml to 55.44 ± 57.51 pg/ml.
Mohammadzadeh et al. (2020) [23]	Association of serum 25-OH vitamin D3 with serum IgE and the pediatric asthma severity score in patients with pediatric asthma	Low vitamin D is associated with asthma severity, as it showed an increase in immunoglobulin E, leukocytes and eosinophils in vitamin D deficient patients.
Mulrennan et al. (2018) [24]	Vitamina D and Respiratory health in the Busselton healthy ageing study	There was a prevalence of vitamin D deficiency <50 nmol/L. It was significantly associated with asthma, bronchitis, wheezing and chest tightness. Higher levels were associated with higher levels of lung function.

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Ohaegbulam et al. (2020) [25]	Vitamin D supplementation in COVID-19 patients: A clinical case series	Patients who received vitamin D supplementation achieved normalization of levels, clinical recovery evidenced by shorter hospital stays, lower oxygen requirements, and reduced inflammatory marker status.
Solidoro et al. (2017) 2[6]	Asthmatic patients with vitamin D deficiency have decreased exacerbations after vitamin replacement	Patients with vitamin D deficiency after receiving supplementation had a reduction in exacerbations, circulating eosinophils, and improvement in airway obstruction.
Tayel et al. (2018) [27]	Vitamin D deficiency and vitamin D receptor variants in mothers and their neonates are risk factors for neonatal sepsis	Septic newborns had much higher vitamin D polymorphism than healthy ones. These genotypes may increase the risk of sepsis.

Source: The authors, 2022.

ming these data, it was found that patients with probable levels of vitamin D deficiency were 1.77 more likely to have COVID-19 compared to patients with sufficient levels [28], in another analysis, clarified that patients with vitamin D deficiency were 4.6 times more likely to be positive for COVID-19.[29]

Jain et al. confirmed an association between vitamin D levels and symptom severity in patients with COVID-19, where 56.05% of asymptomatic patients had levels > 30ng/ml, whereas critically ill patients admitted to the ICU had mean levels of 14.35 ± 5.79. [18] Studies argue that in response to other viral infections, vitamin D plays a role in activating antimicrobial peptides, including cathelicidins and defensins with the potential to inactivate the virus 30 and that individuals with low vitamin D and a weakened antiviral response may be due to low production of these antiviral molecules. [31]

Ohaegbulam et al. followed patients hospitalized for COVID-19 and with vitamin D deficiency, of those who received supplementation (50,000 IU daily for 5 days) their serum vitamin D levels doubled and on the sixth day there was a decrease in oxygen requirements. [25] These results can be attributed to a study that demonstrated that vitamin D supplementation in groups that received a high dose provided a 7.6-fold reduction in the fraction of inspired oxygen. [32] Another study clarified that the effect of vitamin D helps in reducing viral replication and survival, increasing cathelicidins, defensins and free ACE2, thus preventing the virus from entering cells. [33]

Mulrennan et al. found that patients with vitamin D levels < 20 ng/mL were associated with asthma, bronchitis, wheezing, and chest tightness. [24] Mohammadzadeh I et al. presents similar findings, in which pediatric patients with asthma and vitamin D < 20 ng/mL had increased immunoglobulin E (IgE). [23] Ahmed AE et al. showed that the mean vitamin D levels of asthmatic children were 13.46 ng/mL and IgE 99.83 ku/L and healthy children 37.53 ng/mL with IgE 7.52 ku/L. 14 A study showed that the group with vitamin D deficiency had a greater number of annual asthma exacerbations, as well as length of stay and admission to a High Dependency Unit. [34]

Solidoro et al. and Wang et al. performed a study with long-term vitamin D supplementation in asthmatic patients and with vitamin D < 20 ng/mL, later showing that there was a significant reduction in asthma exacerbations. 26,35 In contrast with these data, they analyzed that vitamin D supplementation in children with asthma and vitamin D levels < 30 ng/ml was not significantly associated with changes in lung function measures, asthma control or asthma-related quality of life. [36]

In the study by Miroliaee et al. observed adult patients hospitalized for ventilator-associated pneumonia (VAP) with vitamin D deficiency, those who received supplementation showed a decrease in inflammation mediated by Interleukin 6 (IL-6) from 112.98 ± 121.87 pg/ml to 55.44 ± 57.51 pg/ml, as well as the mortality rate of treated patients was significantly lower than that of the placebo group.22 However, an observational and prospective study in patients with VAP, where 78.6% of them had a low serum level of vitamin D, however, this did not demonstrate significant differences in blood culture, sepsis-associated mortality, duration of mechanical ventilation, or SOFA (Sequential Organ Failure Assessment) scores. [37]

Haugen et al. performed a study with children hospitalized with severe pneumonia, identifying that vitamin D status <50 nmol/l had higher risks of treatment failure and longer duration of illness. 16 These data corroborate another research, in which the level of vitamin D in the blood of children with pneumonia (52.14 ± 21.87 nmol/l) was low compared to children without pneumonia (60.91 ± 32.65 nmol/l) and the number of children with low blood vitamin D levels (≤75.0 nmol/l) was higher in the pneumonia group, indicating that low vitamin D was associated with an increased risk of acute pneumonia. [38]

Liu et al. found in his study on allergic rhinitis analyzing that dendritic cells expressed fewer receptors for vitamin D, however, when exposed to greater amounts of vitamin D these receptors increased in the cells. [21] Another study corrobo-

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rates this result, confirming that vitamin D deficiency is significantly related to severe symptoms of allergic rhinitis, whereas the mean level of IgE and vitamin D was 326.3 and 10.2 ng/ml in the allergic rhinitis group, respectively, and 30.8 and 23.3 ng/ml in the control group. [39]

Heidari et al. conducted a study on inflammation in premenstrual syndrome in which participants had insufficient levels of vitamin D (21 ng/ml), of which one group received 50,000 IU fortnightly, decreasing interleukin 12 inflammation from 18 to 7 Pg/mL and luteal phase antioxidant levels increased from 13 to 21 U/mL. 17 In agreement with this information, an analysis of adolescent girls who received nine high-dose vitamin D supplements (50,000 IU/week) found that premenstrual syndrome fell from 14.9% to 4.8% after the intervention. [40]

Taylor et al. found that the more deficient the mother's vitamin D level was, the lower the neonate's. [27] The absence of vitamin D supplementation in the gestational period was able to influence the immunological resistance of the newborn. [41] Complementing this study, they analyzed that vitamin D insufficiency during pregnancy is capable of favoring low fetal bone development, favoring the recurrence of rickets in this population. [42]

Kanhere et al. carried out a study on the intestinal microbiota of patients with cystic fibrosis and vitamin D supplementation, with a better response due to the enrichment of bacteria that help in the health of the intestine. 19 In addition, they have shown in other studies that the levels of calcium present in the body are directly related to the availability of vitamin D, therefore, individuals with cystic fibrosis, as they are more susceptible to osteoporosis and osteopenia, must have a rigorous supplementation of both components. [43]

Chahardoli et al. performed a study on women with Hashimoto's thyroiditis and vitamin D supplementation, raising levels from 25.38 ± 11.02 ng/ml to 50.16 ± 14.98 ng/ml. Anti-thyroglobulin antibody decreased significantly after supplementation from 192.6 ± 161.8 to 140.2 ± 134.3 showing that vitamin D decreased disease activity. 15 In agreement with this analysis, findings showed that adherence to a balanced diet by patients with Hashimoto's thyroid favored the stimulus in the production of pre-hormones capable of synthesizing vitamin D and, consequently, reducing the inflammatory factors caused by the disease. [44,45]

CONCLUSION

It was found with the findings the beneficial effects that vitamin D provides in different pathologies, being a potent anti-inflammatory, regulator of infections and balance of the immune system, which can be achieved through supplementation or balanced diet, varying this according to the pathology and age characteristic of the individual. Furthermore, many divergent studies have been shown as to the adequate levels of vitamin D for the body.

The optimal level of vitamin D is imperative for health promotion, disease prevention and for a better prognosis of diseases. Therefore, it is extremely important that health professionals update their knowledge about the importance of vitamin D in order to guide, as these professionals are very close to the population.

In addition, it is important to mobilize health authorities and make society aware of the need to maintain habits that benefit the production of vitamin D in the body, such as dietary balance, sun exposure and, if necessary, adherence to vitamin D supplementation.

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