



Major Approaches to the Dosage of Vitamin D in the Elderly: A Systematic Review

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Abstract: Introduction: In the scenario of vitamin D deficiency, this incident is prevalent and with risks to public health in the world, reaching approximately 90% of individuals. Hypovitaminosis D can cause, mainly in the elderly, lower bone mineral density, fractures, muscle weakness, falls, and acute respiratory infection. **Objective:** To evaluate the main clinical results on vitamin D levels in the elderly, as well as to analyze which daily or weekly dose of vitamin D is most effective in the elderly in reducing the number of falls and fractures. **Methods:** The present study developed a systematic review, addressing randomized clinical studies, diverse clinical studies, systematic reviews, meta-analysis, and the latest international consensus, following the rules of PRISMA. **Results and Conclusion:** A total of 152 articles were found involving the dosage and the impact of vitamin D in the elderly. In total, 72 articles were evaluated in full and 30 were included. According to the main literary findings, vitamin D deficiency implies problems with mineralization and bone mineral density, causing fractures and an increase in the number of elderly falls. In this sense, SBEM recommends maintaining vitamin D concentrations above 30 ng/mL. Also, vitamin D deficiency points to the occurrence of neurological diseases such as cognitive decline, risk of Alzheimer's disease, and depression. In the current scenario of the pandemic, vitamin D points as an important modulator of the immune system, and its deficiency promotes the unregulated release of cytokines, leading to complications in patients with COVID-19.

Keywords: Elderly, Vitamin D, 25 (OH) D, Hypovitaminosis, Immunity, Inflammatory Process.

1. Introduction

In the scenario of vitamin D deficiency, this incident is prevalent and with risks to public health in the world, reaching approximately 90% of individuals [1]. Vitamin D deficiency can be understood in the measurement of serum 25-hydroxyvitamin D (25 (OH) D) <50 nmol/L or 20 ng/mL [1,2], with severe deficiency (25 (OH) D <30 nmol/L or 12 ng/mL) is found in more than 10% of Europeans [3].

In this regard, hypovitaminosis D can cause, especially in the elderly, fractures and lower bone mineral density [4,5], falls and acute respiratory infection and muscle weakness [6,7]. In this context, eating foods rich in vitamin D can improve the vitamin D status of the entire population [8]. In addition, genetic studies can help to define individual vulnerability due to vitamin D deficiency [9,10]. In cases of vitamin D deficiency, secondary hyperparathyroidism and increased bone resorption can occur [11]. The vitamin D values for PTH normalization are between 28 and 40 ng/mL [11]. In this sense, it is necessary the action

active vitamin D in the duodenum for calcium absorption [7]. Thus, it is necessary to correctly establish both the identification and treatment of hypovitaminosis D.

In this sense, the Department of Bone Metabolism of the Brazilian Society of Endocrinology and Metabology (SBEM) seeks scientific efforts for the diagnosis and adequate treatment of this population. Therefore, the present study aimed to evaluate the main clinical results on vitamin D dosage levels in the elderly, as well as to analyze which daily or weekly vitamin D dose is most effective in the treatment of osteopenia/osteoporosis, immunity, weakness muscle in the elderly and reducing the number of falls and fractures in the elderly.

2. Methods

2.1. Study Design

The present study developed a systematic review (rules of PRISMA. Available at: [HTTP://www.prisma-statement.org/](http://www.prisma-statement.org/) [12]), addressing

randomized clinical studies, diverse clinical studies, systematic reviews, meta-analysis, and consensus.

2.2. Data sources and research strategy

The descriptors used were elderly, vitamin D, 25(OH)D, hypovitaminosis, immunity, and inflammatory process, with publications from 2000 to 2021. SCOPUS, Cochrane Library, PubMed, Science Direct, and Google Scholar databases were used.

2.2. Study quality and risk of bias

For the analysis of the quality of the studies, the GRADE instrument [13] was used, based on the strata of levels of scientific evidence, according to the nature of each study. For the risk of bias, the Cochrane instrument was used [14].

3. Results and Discussion

A total of 152 articles were found involving the dosage and the impact of vitamin D in the elderly. In total, 72 articles were evaluated in full and 30 were included and evaluated in the present study to compose the systematic review (Figure 1). The overall assessment resulted in 5 studies with a high risk of bias and 3 studies with uncertain risk. The highest risk of bias were related to the number of participants in each study addressed, and the uncertain risk was related to the use of vitamin D in overdosage.

After a thorough analysis of these selected studies, it was found that in the elderly population, there is scientific evidence of the benefits of vitamin D on the risk of fractures. According to meta-analysis and guidelines, the recommended vitamin D doses are those capable of maintaining the patient to plasma 25 (OH) D values above 30 ng/mL, thus avoiding secondary hyperparathyroidism and the increase in bone resorption [15-17].

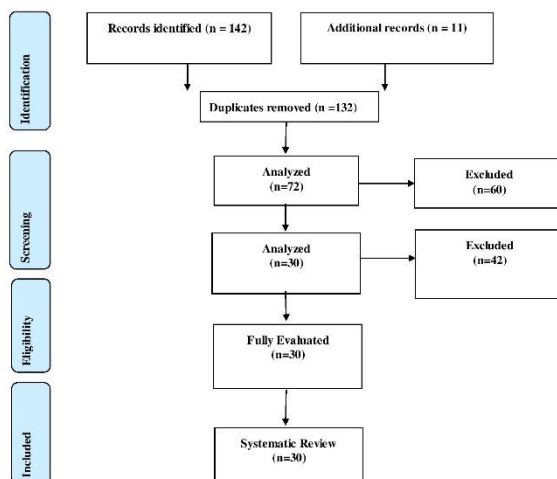


Figure 1. Eligibility of the studies.

In this sense, it is recommended to keep vitamin D concentrations above 30 ng/mL to prevent secondary hyperparathyroidism, requiring daily doses between 1,000 and 2,000 IU [18]. A relationship between low vitamin D levels and falls and fractures has been described [19]. As a corollary of this, a meta-analysis study showed a decrease in fracture prevention with the use of calcitriol, similar to that obtained with doses above 700 IU of vitamin D3 per day [20].

In this context, eldcalcitol has a strong inhibitory effect on bone resorption and increases bone mineral density, showing a 26% reduction in the incidence of new vertebral fractures in three years and 71% in the risk of wrist fracture compared to alfacalcidol [21-25]. In addition, a meta-analysis examined the effect of vitamin D3 supplementation. Thus, 47 randomized controlled trials with 58,424 participants were evaluated. The main populations were elderly women under the age of 80 years. Vitamin D3 supplementation showed a significant effect in reducing falls. However, vitamin D3 supplementation decreased the incidence of falls, but only in the presence of calcium supplementation. Furthermore, vitamin D together with calcium supplementation can significantly reduce fracture rates [26].

Also, a cross-sectional study recruited 60 patients (mean age 65 years) and looked at vitamin D deficiency and hip fractures. Approximately 10% had vitamin D deficiency and another 53.33% had vitamin D insufficiency. In addition, hip fracture patients had lower serum vitamin D3 levels compared to those patients without osteoporosis [27].

3.1 Cognitive Function in the Elderly

The central nervous system has several vitamin D receptors in several areas. In this regard, studies have shown that low vitamin D intake is associated with cognitive decline, with greater chances of developing Alzheimer's disease and depression. This is due to the formation and aggregation of β -amyloid, dysregulation of the GABAergic system, and increased calcium influx in neurons [28]. Thus, vitamin D plays an important role in pathophysiological pathways that occur with aging [29,30].

3.2 Vitamin D and Immune Function in the Elderly

In the current pandemic scenario for COVID-19, in genomic terms, SARS-CoV-2 targets in human cells

identified that vitamin D is among the three molecules with the highest mitigation score for this infection, ie, vitamin D supplementation may improve the prognosis of COVID-19 [18].

In this context, a study of 260 participants aged ≥ 65 years with COVID-19 compared the effect of a single high oral dose of cholecalciferol versus a single standard oral dose on the mortality rate in elderly patients with COVID-19. Participants were randomized to high-dose cholecalciferol (2 vials of 200,000 IU) or standard-dose cholecalciferol (vials of 50,000 IU). The results showed that high-dose vitamin D supplementation can be an effective, well-tolerated, easily, and immediately accessible treatment for COVID-19 [30].

Besides, one study hypothesized that vitamin D deficiency (<20 ng/mL) could increase the risk of developing severe COVID-19 infection. Eighty patients were included, of which 31 (39%) had the outcome. Vitamin D deficiency pointed to an increased risk of developing severe COVID-19 for age, sex, obesity, heart disease, and kidney disease [31].

In addition, there is evidence of a relationship between vitamin D deficiency and unregulated cytokine release in COVID-19. Mean vitamin D levels in older adults suggest a role for vitamin D in reducing the mortality rate [18]. Thus, a recently published prospective cohort study in the United Kingdom assessed the importance of vitamin D deficiency in elderly patients with COVID-19. Findings showed that patients with lower vitamin D concentrations (≤ 30 nmol/L) at the time of acute infection had a greater release of cytokines and were more likely to become hypoxic and on ventilatory support [32]. In this context, therefore, vitamin D deficiency and the worst hospitalization outcomes of patients infected with COVID-19 are shown to be closely related [32].

Therefore, it is established that there is an interaction between vitamin D and various components of the innate and adaptive immune responses to infections. In addition to its anti-inflammatory properties, vitamin D has a protective effect on alveolar epithelial cells, preserving endothelial integrity and reducing vascular permeability. Despite this, vitamin D can induce ACE-2 expression. However, while the increase in ACE-2 expression was initially predicted to amplify the risk of infection and severity, ACE-2 has also been shown to protect against acute lung injury [33].

4. Conclusion

According to the main literary findings, vitamin D deficiency implies problems with mineralization and bone mineral density, causing fractures and an increase in the number of elderly falls. In this sense, SBEM recommends maintaining vitamin D concentrations above 30 ng/mL (1,000 and 2,000 IU per day). Besides, vitamin D deficiency is associated with neurological diseases such as cognitive decline, risk of Alzheimer's disease, and depression. Vitamin D points as an important modulator of the immune system, and its deficiency promotes the unregulated release of cytokines, leading to complications in patients with COVID-19.

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Data sharing statement

No additional data are available

Ethics Approval

Approval was sought and granted by the Departmental Ethics Committee.

Informed consent

Informed written consent obtained from the participant

Conflict of interest

The authors declare no conflict of interest.

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