



Editorial

Vitamin D supplementation: A treatment with possible benefits in asthma ☆



La suplementación con vitamina D: un tratamiento con posibles beneficios en el asma

The discovery of vitamin D receptors in numerous tissues¹ has led to the study of vitamin D supplementation in various conditions, including respiratory diseases. This vitamin could help strengthen the innate and adaptive immune system², which would explain its potential impact on the defense against respiratory infections. In fact, 25-OH-D3 deficiency has been associated with an increased risk of respiratory infections³, and numerous studies on vitamin D and respiratory diseases are emerging.

There is evidence in COPD that vitamin D supplementation could help reduce the rate of moderate and severe exacerbations in patients with a 25-hydroxyvitamin-D level of less than 20–25 ng/ml⁴. This vitamin could protect against acute respiratory infections and confer greater protection in patients with a serum deficiency of less than 25 ng/ml⁵. In tuberculosis, however, although several polymorphisms of the vitamin D receptor have been identified that would influence the risk of developing this disease and the response to treatment, there are no consistent data on its influence on the course of the disease⁶. Furthermore, there is no evidence for cystic fibrosis, and the lung cancer data are controversial.

The benefits of vitamin D in asthma have been debated for years, but the multiple studies analyzing different clinical variables and highly divergent methodologies have made it difficult to develop meta-analyses.

There are several mechanisms by which vitamin D may act in asthma. It can act on innate immunity, modulating the production of different pro-inflammatory cytokines and increasing the production of antimicrobial peptides. It also acts on adaptive immunity by directly affecting T cells, influencing the Th2 response, reducing IgE production, increasing IL-10 synthesis, and reducing IL-17 levels in patients with severe asthma⁷. Vitamin D can also improve the activity of regulatory T cells, improve response to corticosteroids by restoring IL-10 induction in asthma patients, and reduce the smooth muscle mass of the airways. All of this suggests that it could be beneficial in asthma patients.

A cross-sectional study published in 2013 by Korn et al.⁸ showed that vitamin D deficiency was common in asthmatics (67%). It also showed that the lower the levels of

25-hydroxy-D3, the worse the severity of asthma (intermittent: 31.1 ± 13.0 ng/ml, mild: 27.3 ± 11.9 ng/ml, moderate: 26.5 ± 12.0 ng/ml, severe: 24.0 ± 11.8 ng/ml; p=0.046), and the same was true for control (controlled: 29.5 ± 12.5 ng/ml, partially controlled 25.9 ± 10.8 ng/ml, uncontrolled: 24.2 ± 11.8 ng/ml; p=0.030). The frequency of vitamin D deficiency was significantly higher in severe or uncontrolled asthma and was associated with lower FEV₁, higher FENO levels, higher BMI, and sputum eosinophilia. This would support the hypothesis that improving a suboptimal vitamin D status could be effective in the prevention and treatment of asthma.

Several randomized clinical trials (RCTs) have attempted to demonstrate the benefits of vitamin D in asthma with conflicting results.

None of the pediatric RCTs exclusively selected asthma patients with serum 25-OH-D3 deficiency. There were no differences in asthma control, but there were beneficial effects on the reduction of exacerbations. A meta-analysis that included 3 RCTs performed in pediatric patients showed the protective effect of vitamin D on reducing exacerbations (RR=0.41; 0.27–0.63; p<0.001)⁹. However, in our opinion, the results obtained could have been better if all of the patients included had had vitamin D deficiency. A meta-analysis that included 2 RCTs in which vitamin D was administered in pregnant women showed a 25% reduction in the risk of developing asthma or recurrent wheeze in the first 3 years of life of their children¹⁰.

In adults, multiple RCTs have been published, but with disparate methodologies and main variables. In 2014, the VIDA trial¹¹ analyzed vitamin D supplementation in patients with symptomatic asthma and vitamin D deficiency. Its main variables were the rate of therapeutic failure and the rate of exacerbations. No differences were found, but a 25% reduction was observed in inhaled corticosteroid doses. In the same year, Arshi et al. published another RCT¹² in which asthmatic patients with and without serum vitamin D deficiency were included. The main variable was the effect of vitamin D on lung function, and the authors concluded that it could improve response to inhaled corticosteroids. In 2015, de Groot et al. published an RCT¹³ that included asthma patients with a serum 25-OH-D3 deficiency of less than 40 ng/ml. The main variable was induced sputum eosinophilia. They observed a reduction in the group treated with vitamin D and concluded that this could be a coadjuvant treatment to inhaled corticosteroids in the subgroup of patients with eosinophilic asthma. A meta-analysis¹⁴ published in

☆ Please cite this article as: Andújar-Espinosa R, Salinero-González L. La suplementación con vitamina D: un tratamiento con posibles beneficios en el asma. Arch Bronconeumol. 2021;57:567–568.

2019 concluded that vitamin D could decrease the annual rate of exacerbations in vitamin-deficit patients, with no significant differences in control, FENO determinations, IL-10, or adverse effects.

In 2020, our research group published the ACVID trial¹⁵ which included asthma patients with a serum vitamin D deficiency below 30 ng/ml. A clinically and statistically significant improvement associated with vitamin D was observed in asthma control determined by ACT and in quality of life measured with the MiniAQLQ.

All the studies conducted to date differ widely in terms of methodology and study variables, and this has made it difficult to extract strong, reliable evidence that will help clarify whether vitamin D is beneficial in asthma patients. More standardized multicenter studies with clear objectives are needed to determine the true value of vitamin D in both asthma and other respiratory diseases.

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