Original Research Article

ROLE OF VITAMIN D IN REDUCING THE FREQUENCY OF ASTHMA ATTACKS IN PATIENTS WITH FREQUENT EXACERBATION OF ASTHMA

Abstract

Introduction: Vitamin D deficiency is common among asthmatics with literature suggesting that its low levels in the body may trigger exacerbations and decrease the response to corticosteroid treatment. It has also shown to inhibit the production of cytokines, which in turn enhances the body's response to corticosteroid treatment during an exacerbation. Therefore, maintenance of adequate levels of vitamin D in patients with asthma may reduce the risk of exacerbation and improve their general health. This study aims to explore the role of vitamin D supplementation in preventing asthma exacerbations.

Methods: This single blind parallel arm interventional study was conducted in the pulmonology ward in a tertiary care hospital from June 2018 to April 2020. Two hundred (n= 200) participants with a history of frequent acute exacerbation of asthma were enrolled in the study via consecutive convenient non-probability technique. Participants were divided into two groups; the placebo and the interventional group that received 200,000 IU of vitamin D capsule.

Results: Compared to day 0, mean episodes of exacerbation in the interventional group were significantly lower after 180 days (1.1 ± 0.4 vs. 0.61 ± 0.3; p-value <0.0001). Similarly, number of asthma attacks in past 7 days was significantly lower in intervention group after 180 days (4.4 ± 2.7 vs. 3.1 ± 1.5; p-value 0.0001)

Conclusion: Vitamin D supplementation is a safe and cost-friendly approach to reducing asthma exacerbations. It may also help to improve the condition in severe asthmatics with low vitamin D levels.

INTRODUCTION:

Asthma is a chronic obstructive disease of the respiratory tract [1]. The global burden of asthma has increased over the last two decades whereby it now affects approximately 300 million people worldwide, with a predilection towards industrialized countries. The onset of the disease is mostly early in life, with almost 90% of cases diagnosed before the age of six years [1,2].

Asthma is characterized by the presence of hyper-responsive airways with reversible airway obstruction and inflammation, leading to symptoms of cough, wheeze, breathlessness, and chest tightness [3,4]. The acute onset of these symptoms is commonly referred to as an exacerbation. Although there is no proper definition for an asthmatic exacerbation, the literature suggests that onset of worsening symptoms requiring hospital admission, treatment with systemic steroids, or a more than 25 % reduction in peak expiratory flow (PEF) indicates an exacerbation [1,5]. These exacerbations are a major cause of morbidity and mortality in this group [6]. Several factors can trigger an attack but exposure to allergens and infections of the respiratory tract are seen to be the main culprits [7]. The exacerbations require urgent inpatient management and can lead to death with a mortality rate of approximately 4000 deaths/year [3].

Vitamin D plays an important immunoregulatory and anti-inflammatory role in the body, and is often linked to asthma [4]. It is seen that vitamin D deficiency is common among asthmatics with literature suggesting that its low levels in the body may trigger exacerbations and decrease the response to corticosteroid treatment. Vitamin D has shown to inhibit the production of cytokines, which in turn enhances the body's response to corticosteroid treatment during an exacerbation [8,9]. Its unique antimicrobial properties lower the risk of infections, hence reducing the triggers for the exacerbation [10]. Therefore, maintenance of adequate levels of vitamin D in patients with asthma may reduce the risk of exacerbation and improve their general health. This study aims to explore the role of vitamin D supplementation in preventing asthma exacerbations.

MATERIAL AND METHODS:

This single blind parallel arm interventional study was conducted in the pulmonology ward in a tertiary care hospital from June 2018 to April 2020. Two hundred (n= 200) participants with a history of frequent acute exacerbation of asthma were enrolled in the study via consecutive convenient non-probability technique. Frequent exacerbations were defined as two or more in the previous year. Exacerbation was defined as 25 % reduction in peak expiratory flow. Patients with severe lung diseases such as parenchymal diseases, tuberculosis, chronic obstructive pulmonary disease and other illnesses such as chronic kidney disease and congestive heart failure were excluded from the study. Patients already on vitamin D supplements were also excluded from the study. Patients were randomized into two groups by a 1:1 ratio using an online software research randomizer (https://www.randomizer.org/). The interventional group received 200,000 IU of capsule, each on day 0 and day 90. Placebo group received placebo tablets in addition to their standard treatment for asthma.

A self-structured questionnaire was used to note participants' age, gender, number of asthma attacks in the last 7 days, number of nights with troublesome cough in the past 28 days and number of episodes of acute exacerbation in the last six months were noted at time of enrollment and on day 180. Patients were asked to come for follow up at day 90 and day 180. On day 0 after registration, patients in the interventional group were given a vitamin D capsule and patients in placebo were given placebo and were asked to take the medicine in front of the physician. Similar process was reported on day 90. This was done to ensure compliance to the intervention assigned. 15 participants in the intervention group and 17 participants in the placebo group were lost to follow up. Participants who completed the study were included in final analysis.

Statistical analysis was done using Statistical Package for Social Sciences® software version 23.0 (SPSS; IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean and standard deviation. Categorical variables as percentages and frequencies. Dependent t-test was applied to compare the mean values of the interventional and placebo group on day 0 and day 180. A p-value of less than 0.05 represented a difference between the interventional and placebo group and the null hypothesis was void.

RESULTS:

In this study, the mean age of participants in the interventional group was 34 ± 14 and in placebo, it was 39 ± 16 years. Treatment regime was comparable between both the groups (table 1).

Variables	**Interventional group (n=85)**	**Placebo group (n=83)**	**p-value**
Mean + SD (in years)	34 ± 14	39 ± 16	NS
Male	45 (52.9%)	46 (55.4%)	NS
Smoking	16 (18.8%)	11 (13.3%)	NS
Exercise	11 (12.9%)	12 (14.5%)	NS
NSAIDs more than 30 days in last 180 days	01 (1.2%)	02 (2.4%)	NS
Beta blockers	03 (3.5%)	02 (2.4%)	NS
Family history of asthma	05 (5.9%)	05 (6.0%)	NS

Treatment			
Short acting beta agonists	72 (84.7%)	74 (89.2%)	NS
Long acting beta agonists	35 (41.2%)	36 (43.4%)	NS
Montelukast	51 (60.0%)	55 (66.3%)	NS
Inhaled corticosteroids	36 (42.4%)	38 (45.8%)	NS
Oral corticosteroids	06 (7.1%)	7 (8.4%)	NS

Table 1: Comparison of demographics and treatment regime of both groups

Compared to day 0, mean episodes of exacerbation in the interventional group were significantly lower after 180 days (1.1 ± 0.4 vs. 0.61 ± 0.3; p-value <0.0001). Similarly, the number of asthma attacks in the past 7 days was significantly lower in the intervention group after 180 days (4.4 ± 2.7 vs. 3.1 ± 1.5; p-value 0.0001) (Table 2).

Variables (Mean ± SD)	**Interventional Group (n=85)**			**Placebo Group (n=83)**		
	Day 0	**Day 180**	**p-Value**	**Day 0**	**Day 180**	**p-value**
Episodes of acute exacerbation in last 180 days	1.1 ± 0.4	0.61 ± 0.3	< 0.0001	1.2 ± 0.4	1.1 ± 0.4	0.107
Number of asthma attacks in the past 7 days	4.4 ± 2.7	3.1 ± 1.5	0.0001	4.5 ± 2.6	4.7 ± 2.9	0.63

Number of nights with troublesome cough in past 28 days	10.1 ± 6.2	7.7 ± 3.1	0.0017	12.2 ± 8.1	11.1 ± 7.9	0.37

Table 2: Comparison of asthma attacks in both groups on day 0 and day 180.

In Kaplan-Meier survival analysis, the survival probability of not having an event (acute exacerbation) was significantly higher in the intervention cohort than in the placebo cohort (log-rank test, p-value= 0.029) (figure 1).

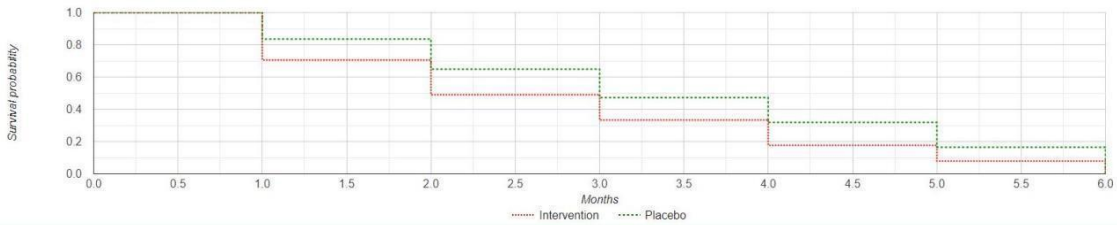

Figure 1: Kaplan-Meier survival analysis showing comparison between both groups in terms of not having acute exacerbation

DISCUSSION:

Our study demonstrated that the group that received vitamin D supplementation showed a significant decrease in the frequency of acute exacerbation. This group also experienced less number of asthma attacks, and the problem of onset of troublesome cough at night was also solved. These results were further analyzed to point towards the fact that vitamin D supplementation could potentially result in favor of not having an asthma exacerbation.

There is sufficient evidence supporting the results of our study, stating that vitamin D supplementation is a safe and useful approach in the treatment of asthma [11]. However, Hall et al. reviewed studies and concluded that the intake of vitamin D to cure asthma is controversial [12]. A study suggested that administration of vitamin D for 4 months would potentially lead to

better lung functioning, not taking the level of vitamin D into account [13]; on the other hand, other studies did not prove a positive result [14,15]. Moreover, Musharraf et al. reported that asthma exacerbation could be avoided by the help of vitamin D supplementation [16]; whereas some other studies reported quite the opposite [17,18].

The results found in our study can be backed by proof provided by a number of studies that vitamin D affects the cells of innate and adaptive immune systems in addition to the cells of the respiratory tract. Its deficiency triggers inflammation, and its increase via supplements aid in relieving these effects [19,20]. This idea has been supported by many studies that are of the idea that vitamin D supplementation is capable of reducing asthma exacerbations, and helps to improve the condition in severe asthmatics with low vitamin D levels [21-23]. This could also be explained by a fact that people who have low levels of a micronutrient will most likely respond to its substitution.

To the best of our knowledge, this is first study from local setting that studies the role of vitamin D in reducing asthma exacerbation. However, there were some limitations as well. First since, the study was conducted in single center, sample size was less diverse. Secondly, most of lack of resources, patients were followed up for only six months. Further large scale multicenter studies are needed to assess role of vitamin D in asthma.

CONCLUSION:

In conclusion, our study has proved that vitamin D supplementation is a safe and cost-friendly approach to reducing asthma exacerbations. However, further large scale studies and clinical trials are required to further provide a guideline to the doctors in order to make the best possible use of this supplementation.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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