Chest Heart Journal
Vol. 45, No. 1, January 2021

ORIGINAL ARTICLE

Role of Vitamin D Supplementation on Patients of Severe COPD to Reduce Exacerbations

Md. Habibur Rahman[1], Md. Abdur Rouf[2], Md. Mohiuddin Ahmad[2], Md. Sayedul Islam[2], S M Abdur Razzaque[3], Md. Khairul Anam[3], Nihar Ranjan Saha[3], Prottush Kumar Mondal[4], Shamima Nasrin[5], Mohammad Ashif Iqbal[6], Mohammad Nazmul Hasnine Nawshad[7]

Abstract:

Background: *Vitamin D deficiency is prevalent among patients with chronic obstructive pulmonary disease (COPD) and comes to be more frequent with increased disease severity. Low serum 25-hydroxyvitamin D (25-[OH]D) levels have been associated with lower FEV_1, impaired immunologic control and increased airway inflammation which causes frequent exacerbations of COPD patients.*

Aims: *To evaluate the role of vitamin D supplementation on patients of severe COPD to reduce exacerbations.*

Materials & Methods: *This study was prospective observational study conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from December, 2019 to March, 2021. Total 94 severe COPD patients were enrolled in this study, out of which 46 patients were taken in group A that include vitamin D deficiency (<20 ng/ml) group and 48 in group B that include vitamin D insufficiency (20-30 ng/ml) group.*

Results: *Mean vitamin D level – initial (25.1±2.7 vs 10.9±3.8 ng/ml), at 3rd month (39.4±3.9 vs 32.5±3.2 ng/ml) and at 9th month (34.0±4.5 vs 22.7±4.9 ng/ml) were significantly (p<0.05) higher in group B than group A. Mean vitamin D level - at 9th month were statistically significant (p<0.05) within the group A and group B compare with initially. At 3rd month and at 9th month exacerbation were significantly higher in group A than group B.*

Conclusion: *We concluded that vitamin D level was significantly increased at nine month in both group A and group B respectively. In both group, exacerbation was significantly reduce at nine month follow up than initially. So early supplementation of Vitamin D in exacerbation of severe COPD patients can reduce number of further exacerbation.*

Keyword: *Chronic obstructive pulmonary disease (COPD), Serum 25-hydroxyvitamin D, Exacerbation.*

[Chest Heart J. 2021; 45(1) : 26-30]

DOI: http://dx.doi.org/10.33316/chab.j.v45i1.2019633

1. Medical Officer, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
2. Professor, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
3. Associate Professor, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
4. Registrar, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
5. Residential Medical Officer, *Upazila Health Complex, Belabo*, Narsingdi.
6. Assistant Registrar, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
7. Medical Officer, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.

Correspondence to: Dr. Md. Habibur Rahman, MBBS, MD (Pulmonology),Medical Officer, Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka. E-mail: habibbarca2010@gmail.com, Mobile: 01717734351.

Submission on: 12 December, 2020 **Accepted for Publication:** 20 December, 2020

Available at http.//www.chabjournal.org

Introduction:

Chronic obstructive pulmonary disease (COPD) remains a major public health problem.[1]

The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease and parenchymal destruction (emphysema). Chronic inflammation causes structural changes, narrowing of the small airways and destruction of the lung parenchyma that leads to the loss of alveolar attachments to the small airways and decreases lung elastic recoil.[2] Airflow limitation is usually measured by spirometry as this is the most widely available and reproducible test of lung function.

Vitamin D is a fat soluble hormone precursor that plays an important role in bone metabolism and seems to have anti-inflammatory and immune-modulating properties. Vitamin D is present in two forms. Ergocalciferol or vitamin D2, is present in plants and some fish. Cholecalciferol or vitamin D3, is synthesized from 7-dehydrocholesterol in the skin by sunlight.

Vitamin D deficiency is prevalent among patients of COPD and comes to be more frequent with increased disease severity.[3] In participants with severe vitamin D deficiency at baseline, supplementations may reduce exacerbations.[4]

Recent studies show that a substantial proportion of patients with chronic obstructive pulmonary disease have deficient vitamin D levels (<20 ng/mL).[3,5] Few studies have measured the significance of vitamin D deficiency in COPD by calculating serum levels of 25-hydroxyvitamin D (25-[OH]D), which is the important circulating vitamin D metabolite and recognized as the finest short-term biomarker of entire contact to vitamin D. With disease development, marked by decay in FEV_1, patients grow systemic significances and became prone to infectious exacerbations which are precipitated by concomitants vitamin D deficiency.[3]

Vitamin D supplements halve the number of exacerbations of chronic obstructive pulmonary disease (COPD) in people with low levels of the vitamin, from two per year to one per year. The supplements do not affect exacerbations of COPD in people who are not deficient.[6]

In this study, we have aimed to evaluate the role of vitamin D supplementation on patients of severe COPD to reduce exacerbations.

Methods:

This study was prospective observational study was carried out in the Department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from December, 2019 to March, 2021. Pulmonary disease other than COPD, malignancy, advanced renal disease, COPD with history of diseases (nephrolithiasis, hypercalciuria, malignancy, tuberculosis, sarcoidosis, Paget's disease, malabsorption syndromes), pregnant women, alcoholics, HIV seropositivity and use of active metabolites of vitamin D within 6 months of screening were excluded.

Of 102 patients with COPD vitamin D deficiency which fulfilled the inclusion and exclusion criteria during the study period. Out of them 1 patient died & 4 patients were lost to follow up in group A (vitamin D <20 ng/ml) and 3 patients were lost to follow up in group B (vitamin D 20-30 ng/ml). Finally, 46 patients were taken in group A and 48 in group B. Both groups of patients received oral vitamin D 40000 IU weekly for 8 weeks followed by 2000 IU daily for 1 month.Vitamin D level was measured at 3 month and 9 months and exacerbation of COPD was recorded.

Statistical Package for Social Science (SPSS) version 23 for windows was used to analyze the data. Chi square test was used for categorical variables as shown cross tabulation. Unpaired t-test and paired t-test was used for continuous variables. A p value d"0.05 was considered to be significant.

Results:

The mean age was found 60.2±10.2 years in group A and 58.2±10.3 years in group B. Majority (87.0%) patients were male in group A and 43(89.6%) in group B. The difference were not statistically significant (p>0.05) between two groups (Table-1).

Mean vitamin D level - initial, at 3rd month and at 9th month were significantly (p<0.05) higher in group B than group A. Mean vitamin D level - at 9th month were statistically significant (p<0.05) within the group A compare with initially. Mean vitamin D level - at 9th month were statistically significant (p<0.05) within the group B compare with initially (Table-2).

At 3rd month, 25(54.3%) patients were found exacerbation in group A and 16(33.3%) in group B. At 9th month, 28(60.9%) patients were found exacerbation in group A and 13(27.1%) in group B. The difference were statistically significantly (p<0.05) between two groups (Table-3).

Table-I

Demographic characteristics of the study patients (n=94)

Demographic characteristics	Group A(n=46)		Group B (n=48)		P value
	n	%	n	%	
Age (years)	41-50	9	19.6	13	27.1
	51-60	17	37.0	17	35.4
	61-70	15	32.6	12	25.0
	71-80	4	8.7	6	12.5
	>80	1	2.2	0	0.0
Mean±SD	60.2	±10.2	58.2	±10.3	[a]0.346[ns]
Range (min-max)	42.0	-85.0	41.0	-80.0	
Sex					
Male	40	87.0	43	89.6	[b]0.692[ns]
Female	6	13.0	5	10.4	

ns= not significant

[a]P value reached from unpaired t-test

[b]P value reached from chi square test

Table-II

Vitamin D level in different follow up (n=94)

Vitamin D level (ng/ml)	Group A(n=46) Mean±SD	Group B (n=48) Mean±SD	P value
Initial	10.9±3.8	25.1±2.7	[a]0.001[s]
Range (min-max)	6.0-19.1	20.1-29.9	
At 3rd month	32.5±3.2	39.4±3.9	[a]0.001[s]
Range (min-max)	24.6-38.0	32.4-47.2	
At 9th month	22.7±4.9	34.0±4.5	[a]0.001[s]
Range (min-max)	15.3-34.2	24.2-44.1	
P value (Initialvs at 9th month)	[b]0.001[s]	[b]0.001[s]	

s= significant

[a]P value reached from unpaired t-test

[b]P value reached from paired t-test

Table-III

Exacerbation in different follow up (n=94)

Exacerbation	Group A (n=46)		Group B (n=48)		P value
	n	%	n	%	
Initial					
Present	46	100.0	48	100.0	
Absent	0	0.0	0	0.0	
At 3rd month					
Present	25	54.3	16	33.3	0.040[s]
Absent	21	45.7	32	66.7	
At 9th month					
Present	28	60.9	13	27.1	0.001[s]
Absent	18	39.1	35	72.9	

s= significant

P value reached from chi square test

Discussion:

This study was Prospective Observational study carried out with an aim to evaluate the role of vitamin D supplementation on patients of severe COPD to reduce exacerbations among the patients in the Department of Respiratory Medicine, NIDCH. Of 102 patients with COPD vitamin D deficiency which fulfilled the inclusion and exclusion criteria during the period from December, 2019 to March, 2021 were included in this study. Out of them 1 patient died & 4 patients were lost to follow up in group A (vitamin D <20 ng/ml) and 3 patients were lost to follow up in group B (vitamin D 20-30 ng/ml). Finally, 46 patients were taken in group A and 48 in group B. The present study findings were discussed and compared with previously published relevant studies.

In this study it was observed that mean age was found 60.2±10.2 years in group A and 58.2±10.3 years in group B. The difference were not statistically significant (p>0.05) between two groups. In a study done by Pourrashid et al.[7] reported mean age was 62.73±8.26 years in vitamin D group and 64.06±8.77 years in placebo group, that was not significant (p=0.54).

In the present study it was observed that most of the patients were males in both groups that (87.0%) group A and 43(89.6%) in group B. Whereas, female was 6(13.0%) and 5(10.4%) in group A and group B respectively. The difference were not statistically significant (p>0.05) between two groups. Rezk et al.[8] observed that 86.7% patients were male and 13.3% were female. Male to female ratio was 6.5:1.

Regarding vitamin D level in different follow up it was observed that mean vitamin D level – initial (25.1±2.7 vs 10.9±3.8 ng/ml), at 3rd month (39.4±3.9 vs 32.5±3.2 ng/ml) and at 9th month (34.0±4.5 vs 22.7±4.9 ng/ml) were significantly (p<0.05) higher in group B than group A. Mean vitamin D level - at 9th month were statistically significant (p<0.05) within the group A compare with initially. Mean vitamin D level - at 9th month were statistically significant (p<0.05) within the group B compare with initially. Pourrashid et al.[7] consisted that at baseline, mean±SD of serum 25(OH)D levels were 10.59±3.39 ng/mL and 11.12±3.17 ng/mL in vitamin D and placebo groups respectively and did not differ in between groups comparison ($p = 0.82$). Vitamin D supplementation resulted in a statistically significant increase in serum 25(OH)D levels in vitamin D group (36.85±11.80 ng/mL) versus placebo group (12.30±3.66 ng/mL), by day 120 [$p = 0.000$, (CI -30.0, -18.90)]. Rezk et al.[8] observed that mean vitamin D was found 11.8±2.4 nmol/L in before vitamin D replacement and 55.3±5.65 nmol/L in 1 year after vitamin D replacement (p <0.001).

In the present study it was observed that at 3rd month, 25(54.3%) patients were found exacerbation in group A and 16(33.3%) in group B. At 9th month, 28(60.9%) patients were found exacerbation in group A and 13(27.1%) in group B. The difference were statistically significantly (p<0.05) between two groups. Khan et al.[9] reported that at baseline, exacerbation was present all patients in both groups. Whereas, at 2nd month follow up exacerbation present 39(65.0%) patients in group A and 40(66.7%) in group B. At 6th month follow up exacerbation was not found in group A but 4(6.7%) found in group B. According to a recent meta-analysis, the benefits of supplementation were only present when baseline 25-OHD levels are very low (<10 ng/ml).[10]

Conclusion:

We concluded that vitamin D level was significantly increased at nine month in group A and group B respectively. In both group, exacerbation was significantly reduce at nine month follow up than initially. Exacerbation rate was significantly higher in group A than group B. Vitamin D can be beneficial in reducing exacerbations in patients with severe COPD.

References:

1. Devine JF. Chronic obstructive pulmonary disease: an overview. American health & drug benefits. 2008;1(7):34.
2. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Last edited 02/2021 and last reviewed 02/2021.
3. Janssens W, Bouillon R, Claes B, Carremans C, Lehouck A, Buysschaert I, et al. Vitamin D deficiency is highly prevalent in COPD and correlates with variants in the vitamin D-binding gene. Thorax. 2010;65(3):215-20.

4. Lehouck A, Mathieu C, Carremans C, Baeke F, Verhaegen J, Van Eldere J, et al. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease: a randomized trial. Annals of Internal Medicine. 2012;156(2):105-14.

5. Forli L, Halse J, Haug E, Bjortuft O, Vatn M, Kofstad J, et al. Vitamin D deficiency, bone mineral density and weight in patients with advanced pulmonary disease. Journal of Internal Medicine. 2004;256(1):56-62.

6. Jolliffe DA, Greenberg L, Hooper RL, Mathyssen C, Rafiq R, de Jongh RT, et al. Vitamin D to prevent exacerbations of COPD: systematic review and meta-analysis of individual participant data from randomised controlled trials. Thorax. 2019;74(4):337-45.

7. Pourrashid MH, Dastan F, Salamzadeh J, Eslaminejad A, Edalatifard M. Role of Vitamin D Replacement on Health Related Quality of Life in Hospitalized Patients with" Acute Exacerbation of Chronic Obstructive Pulmonary Disease". Iranian Journal of Pharmaceutical Research (IJPR). 2018; 17(2):801.

8. Rezk NA, Aly NY, Hewidy AA. Effect of vitamin D replacement in chronic obstructive pulmonary disease patients with vitamin D deficiency. Egyptian Journal of Chest Diseases and Tuberculosis. 2015;64(2):353-7.

9. Khan DM, Ullah A, Randhawa FA, Iqtadar S, Butt NF, Waheed K. Role of Vitamin D in reducing number of acute exacerbations in Chronic Obstructive Pulmonary Disease (COPD) patients. Pakistan Journal of Medical Sciences. 2017;33(3):610.

10. Stockton KA, Mengersen K, Paratz JD, Kandiah D, Bennell KL. Effect of vitamin D supplementation on muscle strength: a systematic review and meta-analysis. Osteoporosis International. 2011;22(3):859-71.