Original Article

Relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease (COPD)

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Abstract

Background: Vitamin D deficiency seems to be associated with pulmonary function deterioration. The present study was designed to investigate the relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease (COPD).

Methods: From September 2011 to April 2012 eighty consecutive patients with COPD presented to an outpatient clinic of Babol University- Teaching Hospital entered to the study. Diagnosis of COPD was confirmed according to clinical findings and pulmonary function test. Serum 25-hydroxyvitamin D (25-OHD) was assessed by chemiluminuscence method and postbronchodilator forced expiratory volume in 1s (FEV1) was measured in all patients. The objective of this study was to determine the relationship between serum 25-OHD concentrations and FEV1 value. The patients were classified according to serum 25- OHD concentrations as less 10ng/ml, 10-19.9; 20-29.9; 30-39.9; and 40ng/ml or higher. The mean values of FEV1 for each class of serum 25-OHD were determined and compared.

Results: The mean age of patients was 67.4±11.5 years. The mean FEV1 volume in serum 25-OHD deficient COPD was lower than sufficient COPD (1.550±0.55 vs 1.650±-0.58, p=0.45). Mean FEV1 values increased from 1.55±0.55 L in patients with mean serum 25-OHD <20 ng/ml to 1.94±0.74 L in COPD patients with mean serum 25-OHD ±>40 ng/ml. There was a dose-response pattern of relationship between FEV1 and serum 25-OHD. However, the relationship did not reach to a statistically significant level.

Conclusion: These findings indicated a relationship between serum 25-OHD concentration and FEV1 volume in patients with COPD and suggest optimization of serum vitamin D levels in COPD.

Keywords: COPD, Vitamin D, Supplement, FEV1, Treatment

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Vitamin D deficiency is common across various populations as well as among several skeletal and nonskeletal conditions including autoimmune diseases, diabetes, pulmonary diseases. (1-5). The patients with pulmonary diseases such as asthma and chronic obstructive pulmonary disease (COPD) are at greater risk of vitamin D deficiency (6, 7). In COPD, the risk of vitamin D deficiency is higher than expected and is linked with disease severity (8-10). There is an association between the risk of upper respiratory infection and vitamin D deficiency in particular, the relation is stronger in patients with background respiratory disease (11, 12). Vitamin D in particular calciteriol exerts anti-inflammatory effect and modulates airways reactions in response to several stimulants like gases and noxious particles (13). Vitamin D has been shown to prevent airway inflammation and the development of experimental allergic asthma in mice (14, 6).

It also helps the remodeling of airways and reverses steroid resistance which is important characteristics of COPD (15). Several previously published studies have demonstrated a positive relationship between serum vitamin D and forced expiratory volume in 1 s (FEV1) in patients with COPD and asthma (11, 16-20) as well as in healthy subjects (11, 16-23). Persistent airway inflammation and airway obstruction are a distinguished characteristics of COPD. Regarding the high prevalence rate of vitamin D deficiency in these patients and the impact of vitamin D deficiency on airways, it is reasonable to compare the status of FEV1 volumes in patients with vitamin D deficiency versus patients with vitamin D sufficient COPD. For these reasons, the present cross-sectional study was performed to investigate the relationship between serum vitamin D and FEV1 in patients with COPD.

Patients and methods

Study population: The study population was derived among the COPD patients presented to outpatient pulmonary clinic of Ayatollah Rouhani Hospital, a university affiliated teaching hospital of Babol, north of Iran. These patients were selected prospectively between September 2011 and April 2012. Diagnosis of COPD was confirmed according to clinical pictures concurrent with airflow limitation defined as forced expiratory volume in 1s (FEV1) / forced vital capacity (FVC) less than 0.70 (FEV1/FVC ratio <70%) and FEV <80% predicted (20). The severity of COPD was assessed by Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (21).

All patients with confirmed diagnosis of COPD entered to the study. Exclusion criteria included: presence of pulmonary infection, tuberculosis, pleural effusion, congestive heart failure, primary pulmonary hypertension, pulmonary emboli, restrictive airway disease, and conditions associated with vitamin D metabolism, absorption or taking vitamin D containing medications.

Serum vitamin D was assessed by the measurement of 25-hydroxyvitamin D (25-OHD) using chemiluminescence method according to the manufacturer's instructions. Serum 25-OHD levels of less than 20 ng/ml were considered as vitamin D deficiency, levels at 21-29 ng/ml as insufficient and levels ≥ 30 as sufficient.

Postbronchodilator forced expiratory volume in1s (FEV), and percent predicted FEV1 (FEV2%) were measured for all the patients by a single expert technician in the hospital. The data were collected through an interview in regard to age, previous illness, medication such as beta agonist bronchodilators. Inhaled corticosteroids weight, smoking and opium addiction. All the patients were accepted to participate by giving informed consent. The proposal of this study was approved by the Ethics Committee of Babol University of Medical Sciences, Babol, Iran.

The objective of this study was to determine the relationship between serum 25-OHD concentrations and FEV1 value. In the statistical analysis, the patients were classified according to serum 25- OHD concentrations as less 10 ng/ml, 10-19.9; 20-29.9; 30-39.9; and 40ng/ml or higher. The mean values of FEV1 for each class of serum 25-OHD were determined and compared with Kruskal-Wallis test. In addition, the proportion of serum 25-OHD deficiency was determined according to the severity of COPD by GOLD criteria.

Results

Patients' characteristics: Eighty male patients with mean age of 67.4±11.5 years were studied. The characteristics of study population are presented in table 1. Totally, 78.8 % of participants were smokers, 55.4% were using inhaled bronchodilators such as salbutamol or ipratrupium, and 40% were using inhaled corticosteroids.

Table1. Characteristics of study population with chronic obstructive pulmonary disease (COPD).

Characteristics		No
No of patients		80
Age (mean±SD)		67.4±11.5
Weight (Kg)		66.3±12.3
FEV1 (%) (mean±SD)		49±25.7
FEV1 (L) (mean±SD)		1.676±0.579
Mean serum 25-OHD (ng/ml)		27.8±8.7
Smoking, No (%)		51 (78.8)
Opium addiction, No (%)		5 (6.5)
Aspirin users No, (%)		7 (8.1)
Hypertension No (%)		5 (6.5)
Inhaled bronchodilators, No (%)		44 (55.4)
Inhaled corticosteroids, No (%)		32 (40)
Staging No (%)	1	8 (10)
	2	51 (63.8)
	3	20 (25)
	4	1. (1.3)

All the patients with stage 2 COPD or higher received long-acting beta agonist bronchodilators. The proportion of patients in stages 1 and 2 of GOLD was 10% and 63.8% and proportion of COPD in stages 3 and 4 2.5%, and 1.3% respectively. Nearly eleven percent of patients had serum 25-OHD deficiency. Mean FEV1 in serum 25-OHD deficient COPD was lower than sufficient COPD but the difference did not reach to a statistically significant level (1.550±0.55 vs 1.650±0.58, p=0.45). Table 2 presents the values of FEV1 according to serum 25-OHD levels. As shown in table 2, mean FEV1 volumes increase with raising serum 25-OHD concentrations. However, the mean FEV1 differences between various groups of serum 25-OHD did not reach to a statistically significant level (p=0.149)

Table 2. Mean forced expiratory volumes in 1 s in patients with chronic obstructive pulmonary disease (COPD) according to serum 25-hydroxyvitaminD 25-OHD) levels.

Serum 25-OHD Levels (ng/ml)	No	FEV1 (L)
< 20	10	1.55±0.55
20-29.	41	1.64±0.55
30-39.	22	1.71±0.59
≥40	7	1.94±0.74

Pvalue= 0.149, Kruskal –Wallis test was used between the groups for comparison

There was no association between serum 25-OHD concentrations and smoking, weight, hypertension, and taking inhaled bronchodilators or inhaled corticosteroids

Discussion

The findings of this study indicated that a proportion of patients with COPD had serum 25-OHD deficiency. There was a positive relationship between serum 25-OHD concentrations and FEV1 volumes indicating higher FEV1 values in patients with greater concentrations of serum 25-OHD. These findings signify that sufficient levels of serum 25-OHD in patients with COPD exert beneficial effects on patency airways and lead to pulmonary function improvement. The relationship between serum vitamin D and pulmonary function has been investigated in many previous studies (11, 16-18). In the elderly and healthy subjects, there was a relationship between serum 25-OHD levels or vitamin D intake and FEV1 value (21-23). Low levels of serum vitamin D may lead to pulmonary function test deterioration and peak exacerbation of COPD, winter and early autumn have been attributed to low concentration of serum 25-OHD. The patients with COPD are liable to vitamin D deficiency due to lower duration of outdoor activities and inadequate sunlight exposure.

In addition, increased catabolism of vitamin D by glucocorticoids, lower capacity of vitamin D storage due to wasting of muscle and fat in COPD are known causes of vitamin D deficiency in these populations (24). Long-term oxygen therapy is a predisposition factor of vitamin D deficiency (20). In patients with more severe COPD, vitamin D deficiency is more prevalent and serum 25-OHD concentrations are lower. In a study of Janssens et al., 74% of COPD in stage 4 and 60% of patients in stage 3 had vitamin D deficiency (24).

In a study of patients with COPD who participated in pulmonary rehabilitation program, 19.6% had serum 25-OHD concentrations less than 10 ng/ml. In this study, vitamin D deficient patients had a higher rate of dropout from rehabilitation program and tended to show poorer improvement compared to sufficient participants (20). A relationship between serum vitamin D and FEV1 has been observed in patients of the Third National Health and Nutrition Examination Survey. In this study, FEV1 and FVC were greater for the highest quantile of serum 25-OHD level compared with the lowest quantile. There was a dose-response relationship between serum vitamin D status and FEV1 (18).

Likewise, in the present study, there was also a dose-response pattern of relationship between serum 25-OHD concentrations and FEV1 volumes but the relationship did not reach to a statistically significant level which should be attributed to a small sample size. However, the results of our study indicate a trend toward higher improvement of FEV1 at greater concentrations of serum 25-OHD. In other aspects, this pattern of relationship is in agreement with previous studies indicating higher levels of serum 25-OHD is associated with better pulmonary function values (17, 18, 24). Several characteristics of vitamin D including its anti-inflammatory effects are in consistent with the results of our study (13).

Vitamin D can be produced locally within the lungs, and confers many immunomodulatory actions including secretion of antimicrobial peptides cathelicidin, reduces

chemokine production and inhibits dendritic and T-cell activation (25). The findings of our study indicate that awareness of serum 25-OHD levels in patients with COPD is important and suggests raising serum 25-OHD to sufficient levels may be associated with higher improvement of FEV1. However, the results of our study suffer from a small sample size, in particular, the small number of more severe COPD for the detection of significance between groups' differences. Nevertheless, the strength of our study is based on the patients' selection which was done prospectively among those presented to a single hospital and all tests were performed by a single technician and so the results are subjected to less bias.

In conclusion, the results of this study indicate a positive relationship between serum 25-OHD levels and FEV1 in patients with COPD and suggest awareness and optimization of serum 25-OHD status in these patients. However, these findings are required to be confirmed in further studies comprising a larger sample size.

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