Trends in

Medical Research

ISSN 1819-3587

Academic
Journals Inc.

www.academicjournals.com

Trends in Medical Research 6 (3): 184-190, 2011
ISSN 1819-3587 / DOI: 10.3923/tmr.2011.184.190

Relationship Between FEV1 and 25-hydroxy Vitamin D in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD), as the sixth prevalent cause of death in the world, is one of the most important causes of morbidity and mortality worldwide. COPD has been defined as a disease state characterized by airflow limitation that is not fully reversible and includes emphysema, chronic bronchitis, small airways diseases, etc. In this cross-sectional and analytical study, 145 patients having the inclusion criteria were selected using a convenience sampling. The data collection tools included a questionnaire including demographic data and health history as well as paraclinical results. Variables such as age, sex, history of cigarette smoking, hookah using, antibiotics and inhaled corticosteroids consumption, bread baking, serum concentration of vitamin D and FEV1 were evaluated. The collected data were then analyzed using the SPSS software. The study revealed that the mean serum 25-hydroxy vitamin D level was 64.0243.14 ng mL^{-1} and the mean FEV1 was 61.72±16.02%. There was a statistically significant linear relationship between serum 25-OHD level and FEV1. There was not a significant relationship between respiratory infection history in the last month and serum 25-OHD and FEV1 levels. Based on the results of the study, it can be claimed that there is a significant linear relationship between the serum 25-hydroxy vitamin D level and FEV1. Therefore, it seems that measuring vitamins level, particularly vitamin D, can be effective in order to use complementary medicine in the treatment of chronic obstructive pulmonary disease.

Key words: Chronic obstructive pulmonary disease, FEV1, 25-hydroxy vitamin D, spirometry, inhaled corticosteroids

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is the fourth cause of mortality in the United States, which has infected more than 16 million people in the US. The disease is ranked as the sixth most prevalent cause of death in the world, which probably will be the third in 2020 (Reilly Jr *et al*., 2008). Patients with COPD occupy 10% of hospital beds each year and nearly 500 thousand COPD patients are discharged from hospitals yearly (Roman and Briggham, 2007).

COPD refers to a spectrum of diseases characterized by airflow limitation that is not fully reversible and includes emphysema, chronic bronchitis, small airways diseases, etc. New studies have reported new factors in the incidence and exacerbation of the disease, one of which is serum 25-hydroxy vitamin D (25-OHD) level (Janssens *et al*., 2009, 2010). These studies have found various results including a direct relationship between serum 25-OHD level and pulmonary infections, chronic infections, obstructive pulmonary diseases, autoimmune diseases, cancers, etc. Also, some studies have linked this vitamin with symptoms such as weakness of the skeletal muscles, cardiovascular diseases and cancers (Janssens *et al*., 2010; Ginde *et al*., 2009).

In relation to the role of vitamin D in the immune system, it has been stated that vitamin D can regulate the activities of T-cells and products of interleukin-10 (IL-10). In addition, vitamin D reduces the inflammatory response in the airways and reduces the unpleasant effects of the risk factors of COPD and oxidative stresses (Janssens *et al*., 2010; Wright, 2005; Ginde *et al*., 2009; Hughes and Norton, 2009; Janssens, 2009). Moreover, studies have shown that the matrix metalloproteinase enzyme plays a role in the destruction of the lung tissues in patients with COPD and vitamin D can inhibit the production of this enzyme. Additionally, individuals without a history of cigarette smoking but with vitamin D deficiency have a pulmonary function which is 35% lower than the function in those with a history of cigarette smoking but with an ideal serum vitamin D level. The ideal level of vitamin D for adults is at least 75 n mol L^{-1}. Serum vitamin D level decreases in the late middle age. In healthy individuals, around 20-30 mL $year^{-1}$ of the FEV1 amount is reduced and this reduction reaches 50-100 mL $year^{-1}$ in patients with COPD. The reductions in these two cases may be related with each other (Black and Scragg, 2005).

In some studies, a statistically significant relationship has been found between serum 25-hydroxy vitamin D (25-OHD) level of lower than 20 ng mL^{-1} and the severity of COPD in the third and four stages of the disease according to the Gold Criterion. Therefore, the present study investigated the relationship between FEV1 amount and serum 25-hydroxy vitamin D (25-OHD) level in COPD patients.

MATERIALS AND METHODS

This cross-sectional study included all the COPD patients having the inclusion criteria who presented to Shohada Ashayer Hospital of Lorestan University of Medical Sciences (west of Iran) from April 2011 to July 2011. A convenience sampling method was applied and the following formulae were used to calculate the sample size:

$$n = \left(\frac{z_{1-\alpha/2} + z_{1-\beta}}{c}\right)^2; \quad c = 1.2 \quad \frac{(1+r)}{(1-r)} \text{ Ln}$$

Considering r = 0.28, the sample size was calculated to be 170 patients.

The inclusion criteria of the study included having the age of over 18 years old, being infected with COPD, undergoing spirometry under standard instructions, being monitored by one physician, not using oral corticosteroids and not having a history of vitamin D supplements.

The COPD patients admitted to the Special Clinic of Shohada Ashayer Hospital of Lorestan University of Medical Sciences were selected based on the inclusion criteria of the study. After informed consents were obtained from the patients, spirometry was performed in each patient. Spirometry was performed in all the patients considering the conditions of not having a heavy meal 3-4 h before the spirometry, not being in the acute phase of COPD, having stable hemodynamic conditions, being in the sitting position 15 min prior to the spirometry and not consuming bronchodilator sprays during the last 12 h.

Then the patients were referred to a laboratory which cooperated in measuring serum 25-hydroxy vitamin D (25-OHD) level for the study. The data were gathered using the patients' evaluation forms and the tables of spirometry and 25-OHD values. The patients' evaluation form consisted of two parts of demographic data and health and disease history with an emphasis on recent diseases of the respiratory tract, consumption of antibiotics and inhaled corticosteroids and so on. The collected data were then analyzed by the SPSS software and statistical analyses were performed.

RESULTS

The present study included 170 patients admitted to the Special Clinic of Shohada Ashayer Hospital of Khorramabad (west of Iran). The data of 145 patients were finally evaluated and analyzed statistically based on the two major variables of the study including serum 25-hydroxy vitamin D level and FEV1 amount. Moreover, the values of $p<0.05$, $0.05\leq p<0.08$ and $p\geq 0.08$ were considered as significant, fairly significant and insignificant.

The results showed that the means of 25-OHD and FEV1 of the subjects were 64.02±43.14 and 61.72±16.02 respectively. Most of the patients (63.5%) had normal 25-OHD level. Most of them (66.7%) were in the moderate phase (II) and only 5% were in the severe phase (IV) of the disease.

The t-test results showed no significant difference between males and females in terms of 25-OHD level ($p = 0.083$). Moreover, there was a fairly significant difference between FEV1 means of males and females ($p = 0.061$). In addition, there were no significant differences between means of 25-OHD ($p = 0.230$) and FEV1 ($p = 0.293$) in cigarette smoking and non-smoking groups. Also, no statistically significant differences were found between means of 25-OHD ($p = 0.917$) and FEV1 ($p = 0.837$) in the group with a history of smoking with hookah and the one without a history of smoking with hookah. A statistically significant difference was found between means of 25-OHD level ($p = 0.024$) in the group with a history of bread baking and the one without a history of bread baking while no significant difference was found between these two groups in terms of FEV1 means ($p = 0.110$). The t-test results also revealed no significant differences in terms of 25-OHD ($p = 0.181$) and FEV1 ($p = 0.712$) means between the group with a history of respiratory infection in the last month and the one with no respiratory infection history.

The results of independent t-tests showed a statistically significant difference between the group with a history of antibiotics consumption in the last month and the group with no history of antibiotics consumption ($p = 0.034$). Moreover, no statistically significant difference was found between these two groups in terms of FEV1 means ($p = 0.891$) (Table 1).

The results of independent t-tests also showed no statistically significant differences between the group with a history of inhaled corticosteroids consumption and the group with no history of inhaled corticosteroids consumption in terms of 25-OHD level ($p = 0.1$) and FEV1 level ($p = 0.303$). In addition, the results of one-way ANOVA did not show significant differences between different age groups in terms of 25-OHD level ($p = 0.286$) while significant differences were found between different age groups in terms of FEV1 means ($p = 0.000$) (Table 2).

The positive Pearson correlation coefficient between age and 25-OHD levels showed a direct linear relationship, but it was not statistically significant ($p = 0.183$). However, the negative Pearson correlation coefficient between age and FEV1 values showed an inverse linear relationship that was strongly statistically significant ($p = 0.000$) (Table 3).

The non-linear regression showed that the relationship between age and vitamin D levels could be shown approximately as a third-degree curve ($p = 0.078$). Also, the linear regression showed that

Table 1: FEV1 and 25-OHD values in terms of a history of antibiotics consumption in the last month

	25-OHD			FEV1		
Antibiotics consumption	Frequency	Mean	SD	Frequency	Mean	SD
No	90	65.52	41.09	97	61.41%	16.56%
Yes	40	50.87	19.68	47	61.81%	15.31%
Total	130	61.01	36.45	144	61.54%	16.11%
p-value	0.034			0.891		

Table 2: FEV1 and 25-OHD values in terms of a history of inhaled corticosteroids consumption

	25-OHD			FEV1		
Inhaled corticosteroids consumption	Frequency	Mean	SD	Frequency	Mean	SD
No	109	58.70	28.49	122	62.13%	15.77%
Yes	21	73.02	63.26	22	58.27%	17.91%
Total	130	61.02	36.45	144	61.54%	16.11%
p-value	0.1			0.303		

Table 3: Correlation coefficient between age, 25-OHD, and FEV1

	25-OHD			FEV1		
	Pearson correlation coefficient	Frequency	PV	Pearson correlation coefficient	Frequency	PV
Age	0.110	148	0.183	-0.369	159	0.000

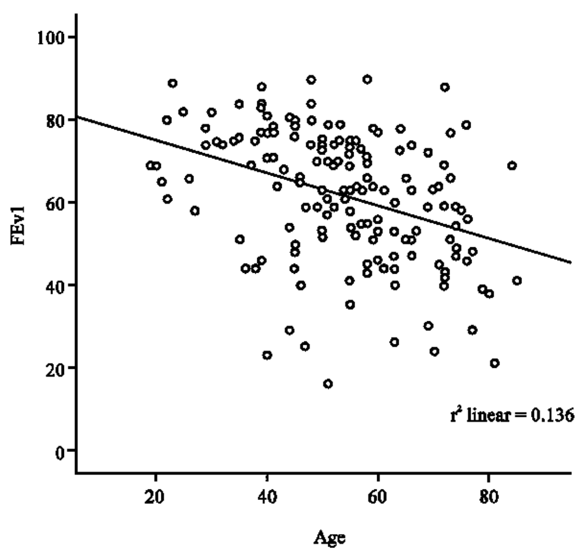

Fig. 1: Graph 1: FEVI in terms of age

the relationship between age and FEV1 values could be shown as a linear plot with a negative slope (p = 0.000) (Fig. 1).

The positive Pearson correlation coefficient showed a direct and linear relationship between 25-OHD and FEV1, which was statistically significant (p = 0.009) (Table 4).

Table 4: Correlation coefficient between 25-OHD and FEV1

	FEV1		
	Pearson correlation coefficient	Frequency	PV
25-OHD	0.217	145	0.009

DISCUSSION

Concerning the major aim of the study, a direct linear relationship was found between serum 25-OHD levels and FEV1 values in the patients, which was statistically significant ($p = 0.009$). Therefore, the first hypothesis of the study, stating a significant relationship between the means of serum 25-OHD levels and FEV1 values, was approved. A direct relationship was found between serum 25-OHD level and FEV1 value (COPD severity) in a study carried out on 414 smoking patients aged over 50 by Janssens *et al.* (2009) that investigated the relationship between serum 25-OHD level and COPD severity ($p<0.0001$; $r = 0.28$) and this result was consistent with the result in our study.

In another study by Franco *et al.* (2009), the relationship between vitamin D and FEV1 was reported as a significant linear relationship. The serum vitamin D level was used as a marker to determine the severity of COPD and this result was consistent with our study as well. In a study by Black and Scragg (2005), a strong significant correlation was found between serum 25-OHD level and FEV1 values ($p<0.0001$), being consistent with the result in our study.

In relation to the aim of the study regarding the determination of a history of the upper and lower respiratory infection in the last month, the majority of the patients (52.8%) had no history of respiratory infection. Therefore, no significant relationship was found regarding the relationship between the upper respiratory infection and serum 25-OHD level ($p = 0.181$).

The study conducted in 2009 by Ginde *et al.* (2009) reported that in the patients with low levels of vitamin D, the prevalence of influenza and respiratory infections increases. Additionally, the Third National Health and Nutrition Study in the US carried out on 19 thousand adult patients with COPD reported the normal range of vitamin D to be = 30 ng mL^{-1}. Moreover, the prevalence of the upper and lower respiratory tract infections increased by 40% in patients with vitamin D levels lower than 10 ng mL^{-1} (Hu and Cassamo, 2000). But in the present, study the majority of the patients (63.5%) had normal levels of vitamin D and only few patients had serum vitamin D levels lower than 10 ng mL^{-1}. One the other hand, since the sampling was performed in a season of the year when the prevalence of viral, bacterial and other respiratory infections is lower, no significant relationship was found between these two variables in our study.

The following results were obtained regarding other effective variables in the study which were evaluated and analyzed.

A statistically significant relationship was not found between sex and serum 25-OHD levels ($p = 0.083$) and different results may be achieved in other studies with larger sample sizes due to the proximity of the P-value in our study to the level of significance. In the present study, there was a fairly significant relationship between gender and the mean FEV1 ($p = 0.061$). Moreover, in Mannino (2003) study carried out , a significant relationship was found between sex and FEV1 level, so that, the level of FEV1 was lower in males due to more cigarette smoking which was consistent with our result.

In this study, a significant inverse linear relationship was found between age and FEV1 ($p = 0.000$), so that, the relationship between age and FEV1 value can be presented as a linear plot with a negative slope. Moreover, a linear relationship was revealed between age and levels of 25-OHD, which was not statistically significant ($p = 0.183$) and the relationship between age and vitamin D based on non-linear regression was presented approximately as a third-degree curve ($p = 0.078$). Black and Scragg (2005) did not report a significant relationship between age and 25-OHD levels ($p = 0.12$).

The present study showed no statistically significant relationship between smoking and mean of 25-OHD level ($p = 0.23$) while Black and Scragg (2005) showed that serum 25-OHD level was lower in smokers who smoked more than 20 cigarettes daily in comparison to non-smokers and a relative relationship was found between serum 25-OHD and FEV1 levels in smokers and non-smokers ($p = 0.059$).

In addition, in the present study, no statistically significant relationships were found between FEV1 values and other variables such as smoking, use of hookah, history of baking bread and consumption of inhaled corticosteroids and antibiotics.

Black and Scragg (2005) reported in 2005 that although smoking, age, sex and race, etc. are important factors in determining the lung function, they do not justify all the differences among people. Regarding the variable of smoking, Agarwal *et al.* (2010) reported that although COPD is more common in smokers, not all smokers will suffer from COPD and a decrease in FEV1 and only 15% of smokers developed COPD while 20% of COPD patients did not mention a history of tobacco consumption.

CONCLUSION

After considering the effects of variables such as age, sex, smoking, hookah smoking and antibiotics and inhaled corticosteroids consumption, etc. that can affect the lung function (FEV1) and serum 25-OHD level, the study showed that there is a significant linear relationship between serum 25-hydroxy vitamin D level and values of FEV1 in patients with chronic obstructive pulmonary disease ($p = 0.009$). In other words, our results showed that COPD patients without inhaled corticosteroids consumption have lower vitamin D level that is closely related with COPD severity. It means that serum vitamin D level can be used as a marker to determine the severity of COPD. Thus, it seems that determining the level of vitamins, particularly vitamin D, can be helpful in applying complementary medicine in the treatment of chronic obstructive pulmonary disease.

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