

Relationship between Serum Levels of Testosterone and the Severity of Chronic Obstructive Pulmonary Disease

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Background: This cross-sectional study aimed to investigate the relationship between the levels of serum testosterone and the severity of chronic obstructive pulmonary disease (COPD).

Materials and Methods: Using GOLD criteria, 140 male patients with COPD were categorized into mild, moderate, severe and very severe COPD groups of 35 each. Then, serum levels of testosterone, prolactin and LH of patients were compared and the data were analyzed using SPSS version 18 software.

Results: Average age of patients was 67.4 ± 10.1 years (range 41 to 90 years). The prevalence of the secondary hypogonadism was 58.6%. It was shown that the level of serum testosterone was directly correlated with the severity of COPD ($P = 0.04$).

Conclusion: This study found that the prevalence of the secondary hypogonadism in COPD patients was high. The forced expiratory volume in 1 second (FEV₁) was correlated with the level of serum testosterone. Further investigations are required to better evaluate the pathology and treatment of secondary hypogonadism in COPD patients.

Key words: Chronic Obstructive Pulmonary Disease, Testosterone, Serum level

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a group of respiratory diseases characterized by airflow limitation that is not fully reversible, and is associated with cough, sputum production and dyspnea and is defined by reduced forced expiratory volume in 1 second (FEV₁) and FEV₁/FVC ratio on lung function tests. In advanced conditions, COPD is associated with involuntary weight loss and muscle wasting. The association between low body mass index (BMI) and poor prognosis in patients with COPD is a common clinical observation and reduced

BMI is considered as an independent predictor of COPD (1).

It has been shown that men suffering from advanced COPD have lower levels of endogenous testosterone and the changes in the levels of the sex hormone are associated with hypoxia, hypercapnia, and reduced FEV₁ (2-10).

In this study, the FEV₁/FVC ratio in patients suffering from COPD was determined and the correlation between the levels of serum testosterone and the severity of COPD was evaluated. The results can provide a better insight for treatment of hypogonadism following COPD.

MATERIALS AND METHODS

In this cross-sectional study, 140 patients suffering from COPD were investigated.

Using a spirometry test, the patients with COPD who did not respond to bronchodilator were considered eligible to enter the study.

Those who had a history of primary or secondary hypogonadism, pituitary adenomas, or the patients with a benign prostatic hypertrophy requiring surgical intervention or administration of 5-alpha reductase inhibitors, and alcohol consumers or patients with chronic kidney disease were excluded.

To calculate the BMI, the subjects' weight and height were measured. The average levels of total serum testosterone, luteinizing hormone (LH) and prolactin were determined. Pulmonary function was determined using a JAEGER spirometer (CareFusion Corp., CA, USA) and salbutamol inhaler as a bronchodilator. Total serum level of testosterone was measured with an electrochemiluminescence immunosensor (Hitachi ECL, Japan) and using Roche kit (Germany) (with a normal range of 2.8-8.8 ng/ml). The serum levels of LH and prolactin were determined using a gamma counter and Immunotech radioimmunoassay (RIA) kit (Beckman coulter, France) (with a normal range of 0.5-10 mIU/ml and 1-18 ng/ml, respectively).

By using spirometry and according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, the severity of the COPD in patients was classified into mild, moderate, severe and very severe groups. Then, the average levels of serum total testosterone, LH and prolactin in each group were compared. The data were analyzed using one-way ANOVA (SPSS 18) and P values less than 0.05 were considered statistically significant.

RESULTS

In this study, 140 male patients with COPD were investigated. The average age was 10.1 ± 4.67 years (range 41 to 90 years). Demographic characteristics like BMI and number of smokers are listed in Table 1.

From 140 patients, 101 (72.1%) had a smoking history, with an average consumption of 28.5 ± 8.9 packs per year and no significant differences were found for the percentage of smokers between the groups ($P=0.07$).

Table 1. Demographical parameters and the level of serum hormones in COPD patients

Parameter	COPD severity stage				P Value
	Mild	Moderate	Severe	Very severe	
Age (years)	67.3 \pm 7.5	69.4 \pm 11.6	66.9 \pm 11.5	66.2 \pm 9.2	0.58
BMI (kg/m ²)	25.6 \pm 3.01	25.5 \pm 4.5	24.6 \pm 3.4	23.1 \pm 3.4	0.02*
Smoking (%)	71.4	62.9	65.7	88.6	0.07
Testosterone level (ng/ml)	3.4 \pm 1.09	2.4 \pm 1.7	2.36 \pm 1.6	2.35 \pm 0.96	0.04*
LH level (mIU/ml)	11.2 \pm 2.1	8.2 \pm 2.5	7.2 \pm 3.3	6.6 \pm 2.1	0.001*
Prolactin (ng/ml)	9.2 \pm 3.1	10.02 \pm 3.9	10.2 \pm 3.2	11.2 \pm 4	0.13

*P values with significant differences.

Subjects who had a FEV₁/FVC <0.70 were classified into four COPD severity groups (35 patients each) based on GOLD criteria: FEV₁ \geq 80% of predicted (mild stage), 50% \leq FEV₁ <80% of predicted (moderate stage), 30% \leq FEV₁ <50% of predicted (severe stage), FEV₁ <30% of predicted (very severe stage). All patients in each group were compared for age, BMI, blood levels of testosterone, LH and prolactin. There was no significant difference in the average age ($P=0.58$) and number of smokers ($P=0.07$) between groups (Table 1).

In our study, from 140 patients with COPD, 82 cases (58.6%) had a testosterone level of less than 2.8 ng/ml, indicating a hypogonadism in these patients.

The results showed that serum levels of testosterone in patients with severe stage of COPD were the lowest and in the group with mild stage of COPD, it was the highest; this difference was statistically significant ($P=0.04$).

There was a significant correlation between BMI and FEV₁ in all groups ($P=0.02$).

The serum level of LH in all patients was lower or within the normal range and its average was significantly different between the groups ($P<0.001$).

Twenty-eight out of 140 patients (20%) in this study had an addiction to opium, of those, 19 patients had hypogonadism and 9 patients were eugonadal. Using the Post-Hoc analysis, the paired-comparison of groups showed a significant difference between the mild and very severe groups ($P<0.001$), mild and severe groups ($P=0.02$) and between the mild and moderate groups ($P=0.005$).

The serum levels of prolactin in the very severe group were higher than in the mild group, but it was not statistically significant ($P=0.13$).

DISCUSSION

In the current study, 140 patients with COPD were investigated using spirometry and were categorized into 4 groups based on GOLD criteria.

The average age of patients was not significantly different between the groups. Thus, since the patients in all groups were matched for age and smoking habit, the findings regarding blood levels of testosterone appear not to be biased by these factors.

It was shown that the BMI in the patients with very severe stage of COPD was lower than in others, indicating a progressive and chronic state of losing weight and muscle wasting in these patients.

The percentage of COPD patients with hypogonadism was 58.6%. Different prevalence for hypogonadism in patients with COPD reported in previous studies (7,11) may be due to the differences in sex, age and race.

In an investigation by Mulligan et al., 36.2% of 2,152 over 45 year-old male patients with COPD had hypogonadism (12). In a review by Balasubramanian, the prevalence of hypogonadism in COPD patients was indicated to be 22-69% (13).

In the current study, it has been shown that in patients suffering from very severe COPD with the lowest FEV1, the testosterone level was less than in other groups, while it was greater than the group with mild COPD and the highest FEV1 ($P<0.001$). Similar correlation between the FEV1 and the serum levels of testosterone has been shown previously (4).

COPD is associated with secondary hypogonadism, which is characterized by normal or low range of serum LH levels (14). Similar pattern was shown by the current study.

Chronic illnesses, COPD, steroids, opium and hyperprolactinemia can suppress the gonadotropin secretion by central nervous system (15). As shown in our study, the percentage of hypogonadism in opium addicts was higher than in those with eugonadism (23.2% vs.15.5%).

Except for the very severe COPD group, the serum level of prolactin was within normal range. The greater amount of prolactin level in patients with very severe COPD could be caused by regulatory effect of nicotine on the secretion of prolactin (16). The increased prolactin can reduce the secretion of LH and testosterone by affecting the hypothalamic-pituitary pathway.

In conclusion, the current study showed that COPD patients had a high prevalence of secondary hypogonadism (58.6%). As the hypogonadism is associated with increased rates of depression in patients with osteoporosis and impairs life quality, performing further prospective and interventional investigations on COPD patients with hypogonadism might provide better insights for understanding its pathology and treatment.

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