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Thyroid Function Tests Assessment in Patients with Chronic Obstructive Pulmonary Disease

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Annotation: BACK GROUND: Chronic obstructive pulmonary disease (COPD) is the term used to describe slowly progressive airways obstruction, usually associated with smoking, that is not reversible and associated with lifelong morbidity with metabolic and several endocrine disturbances.

AIM OF STUDY: To evaluate thyroid function tests (TFT) in patients with COPD.

PATIENTS AND METHODS: Pulmonary function test (PFT) was done to 40 patients with obstructive lung disease and twenty age and sex matched healthy control individuals to confirm diagnosis of COPD and assess the severity of disease.

For all these patients SPO2 with oximetry was measured and TT3, TT4 and TSH were assessed with ELISA test.

RESULTS: The values of PFT (vital capacity, forced vital capacity, forced expiratory volume in 1s and peak expiratory flow), TSH and SPO2 were lower in the COPD than control group (P value 0.001).

In severe COPD (FEV1 < 50%) there was a significant reduction in T3 but not T4 or TSH in comparison with mild-moderate COPD patients.

CONCLUSION: Thyroid dysfunction is observed in patients with COPD, and with increasing severity of COPD, there is a decrease in all thyroid function parameters pointing to a metabolic response, and patients with lower weight indices have lower drive for TSH and consequently T3..

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world [(1)]. The Global Burden of Disease Study has projected that COPD which ranked sixth as the cause of death in 1990, will become the third leading cause of death worldwide by 2020 [(2)]. It is characterized by chronic airflow limitation that progresses slowly and by definition the airflow obstruction is poorly reversible [(3)] , the severity of airway obstruction in these patients affects the rate of survival [(4)] . The most important complaints of patients with COPD are dyspnea and an impaired exercise performance [(5)].

Diagnosis of COPD generally depends on clinical presentation but objective demonstration of airflow obstruction by spirometry where the post-bronchodilator FEV1, less than 80% of the predicted value and FEV1, FVC < 70% is also needed, the presence of an FEV1 /FVC < 70% in the presence of an FEV1 of 80% or more suggests the presence of mild disease [(6)] , assessment of the severity of COPD is different among references, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification is the most widely applied [(7)].

At present, medical treatment of COPD is predominantly focused on the primary problem, but despite optimal medication, there is a weak relationship between the primary organ impairment on one hand and disability on the other. Association with impairment of thyroid function is postulated in patients with COPD who developed hypoxemia and hypercapnia [(8,9)]. chronic hypoxemia affects various

endocrine organs, it was found that hypoxia can produce abnormalities of hypothalamic-pituitary function, but this alteration does not cause significant changes in hypothalamic-thyroid axis [10] .

There is now increasing evidence available to say that COPD is a systemic inflammatory response to identifiable stimuli, affecting predominantly lungs and numerous other organs like thyroid, pituitary etc. The thyroid hormone regulates the metabolism of proteins, lipids and carbohydrates, and controls the activity of membrane bound enzymes.[11,12]

1. Patients and methods

This study was conducted in Baghdad Teaching Medical city from September 2022 – December 2022. A clinical history was obtained and a physical examination performed on the patients.

The study group included sixty subjects; twenty of them were control, forty patients with clinically stable COPD with or without chronic symptoms such as cough, sputum production and dyspnea. Patients with other respiratory diseases (Asthma, bronchiectasis), known thyroid diseases or previous thyroid surgery, and other endocrine system diseases, neuromuscular system diseases were excluded, patients were not receiving iodine-containing drugs or other drugs which may disturbs thyroid gland function but Patients on medications of COPD were not excluded.

To confirm diagnosis of COPD we send all of them for post-bronchodilator spirometry at morning to measures FEV1, PEF and VC with spirolab-II-MIR S/N 504244. In this study and on the basis of FEV1, patients were divided into two groups: group 1, with an FEV1 less than 50% of predicted, having severe COPD, and group 2, with an FEV1 more than 50% of predicted, having mild-to-moderate COPD. SPO_2 was measured with pulse oximeter to determine blood O_2 saturation and send them later for hormonal study of T3, T4 and TSH at the same day just after spirometry to be calculated with ELISA test in the teaching laboratories of Baghdad medical city and according to its following normal values.

1.1. Statistical analysis:

Statistical analysis was performed using((SPSS, Inc., Chicago, IL, USA)) version 23 program.

Correlation analysis was also performed.

A P value < 0.05 was considered significant. Values are expressed as mean± Standard Deviation (SD).

RESULTS

Expectedly there was a significant difference with respect to O_2 saturation, FEV_1 and VC between COPD and control groups and with regards to TFT there was significant decrease in TSH in the COPD group as compared to the control group (p value = 0.001), But there was no difference between these two groups according to T3, T4 level and BMI (table 1).

T3 was significantly lower in group of Thirty two patients of COPD with FEV1<50% (P value = 0.01), also VC was significantly lower in this group than those with FEV1 ≥50% (P value = 0.002) as shown in (table 2).

According to O_2 saturation five had O_2 saturation < 92 % and the remainder had O_2 ≥92%, we found that there was no differences between these two groups regarding PFT and TFT (table 3).

In (table 4) we found that there are no differences regarding PFT and TFT in study group whether to have or not other asymptomatic comorbidities like hypertension, ischemic heart disease, and diabetes mellitus.

In (table 5) and according to different BMI (Kg/m^2) we have three groups, normal weight (BMI 18.5-24.9), over weight (25-29.9) and obese (>30), there is significant differences in T3 were it is higher in obese patients (p value =0.05).

In the last two tables there is no significant correlation between T3/T4 ratio and COPD severity (table 6) or degree of hypoxia (table 7).

TABLE 1: Results of PFT, TFT, O2 saturation and BMI in patients with COPD and control group.

	GROUP	NO.	Mean± SD*	P value
AGE	COPD	40	61.4±7.0	0.0001
	CONTROL	20	55.2±3.9	
O2 SATURATION	COPD	40	93.0±1.6	0.0003
	CONTROL	20	95.3±1.9	
FEV1	COPD	40	36.7±16.4	0.0005
	CONTROL	20	90.8±11.2	
PEF	COPD	40	28.2±16.5	0.0004
	CONTROL	20	83.3±19.6	
VC	COPD	40	48.9±22.1	0.0002
	CONTROL	20	87.3±11.8	
TSH	COPD	40	1.3±1..05	0.001
	CONTROL	20	3.4±0.79	
T3	COPD	40	0.8±0.33	0.566
	CONTROL	20	0.9±0.97	
T4	COPD	40	5.5±1.69	0.240
	CONTROL	20	6.0±0.97	
BMI	COPD	40	24.7±4.2	0.742
	CONTROL	20	25.1±3.5	

*; Standard deviation

TABLE 2: Results of PFT and TFT in patients with COPD according to severity (FEV1 <50% , FEV1 > 50%).

	SEVERITY	NO.	Mean± SD	P value
TSH	< 50%	32	1.2 ±0.9	0.566
	>50%	8	1.5 1±.4	
T3	< 50%	32	0.7± 0.2	0.01
	>50%	8	1.1± 0.3	
T4	< 50%	32	5.4 1±.7	0.65
	>50%	8	5.8± 1.3	
VC	< 50%	32	41. ±0 16.7	0.002
	>50%	8	80.5 ± 7.6	

TABLE 3: Results of PFT and TFT in patients with COPD according to O2 saturation.

	O2 SATURATION	NO.	Mean± SD	P value
TSH	<92%	5	0. ±6 0.6	0.198
	>92%	35	1.4± 1.0	
T3	<92%	5	0.7 0±.2	0.419
	>92%	35	0.8 ±0.3	
T4	<92%	5	4.9 ±2.1	0.453
	>92%	35	5.6 ±1.6	
FEV1	<92%	5	36.2 ±17.2	0.943
	>92%	35	36.9 ±16.6	

VC	<92%	5	43.5 ±26.3	0.604
	>92%	35	49.8 2±1.8	

TABLE 4: Results of PFT and TFT in patients with COPD according to presence of asymptomatic comorbidities.

	COMORBIDITIES	NO.	Mean± SD	P value
TSH	YES	16	1.3± 1.0	0.945
	NO	24	1.3± 1.0	
T3	YES	16	0.8± 0.4	0.472
	NO	24	0.9± 0.2	
T4	YES	16	5.3 ±1.8	0.555
	NO	24	5.6 ± 1.6	
FEV1	YES	16	39.2± 15.4	0.517
	NO	24	35.2 ± 17.2	
VC	YES	16	52.1 ± 19.2	0.527
	NO	24	46.8 ± 24.1	

DISCUSSION

a lot of controversy occurred with regards to thyroid function abnormalities and chronic obstructive pulmonary diseases, the role of thyroid dysfunction in cachexia associated with COPD is still needs for further study and assessment[34], in this study there was a significant decrease in the level of TSH in COPD group as compared to the control group, but there was no significant differences in the values of T3 and T4, pechatnikov [35] had found that T3 and T4 concentrations were low and TSH concentrations was high in patients with COPD, and he suggested that this occurred probably as a result of a compensatory (secondary) mechanism, on the other hands NHLBI/WHO [29] report a positive association between $PaCO_2$ and T3, and no association between TSH and T4 on one hand and pulmonary function tests and arterial blood gasses on the other, a clear reasoning for these dissimilarities is not easy and the population differences may play a role.

In this study, also we found that there is no significant correlation between T3/T4 ratio and COPD severity or degree of hypoxia.

Dimopoulou *et al*.[16] reported that there was a strong positive correlation between total T3/total T4 ratio and spO_2, and that severity of the disease through hypoxemia was important in determining the peripheral metabolism of thyroid hormones, this wasn't consistent with previous reports [8,9,34,36,37], Gow *et al*.[9] did not find any correlation between arterial blood saturation measurements and thyroid hormone concentrations in patients with COPD.

In this study, the values of SPO_2 was correlated with significant changes in T3, and when the patients with COPD in this study were divided in a group with mild to moderate COPD (FEVI >50%) and group with more severe COPD (FEVI <50%), a positive association was found between PFT (FEV_1 and VC) and T3, where it is more lower in more severe COPD, this finding is consistent with that of Bratel *et al* [8] who found low FEV_1 level is associated with low TSH level, conversely Funda *et al* [34] found negative correlation between FEV1 and freeT4 where Free T4 level were significantly higher in patients with severe COPD than normal subject and this is supported by the findings of Okutan *et al* [37] where T3 level was higher in patients with severe COPD, on the other hand significant association wasn't found with regards to TSH concentration.

However, Banks and Cooper [36] found no relationship between hormonal levels and lung function in patients with chronic lung disease, and they suggested that most of endocrine dysfunction ascribed to COPD was probably due to factors other than hypoxia or hypercapnia.

The diversity of hormonal changes in COPD patients must point to the fact that COPD must be considered a systemic disease, and the extra pulmonary manifestations must be considered in the

assessment of its severity and follow-up as the treatment of these manifestations could modify the prognosis of these patients . [38]

Interestingly TSH and T3 levels were getting higher with increasing weight in this patients sample, this is most likely to be the effect of TSH suppression with loosing weight because of hyper metabolic state in some patients with low weight and COPD .[16,29]

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