Egyptian Journal of Chest Diseases and Tuberculosis (2012) **61**, 75–79

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

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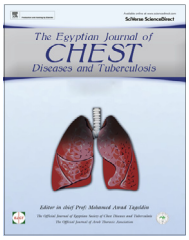

ORIGINAL ARTICLE

Hormonal dysfunction in patients with chronic obstructive pulmonary disease

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Received 3 April 2012; accepted 13 April 2012
Available online 4 February 2013

KEYWORDS

COPD;
Thyroid dysfunction;
Insulin like growth hormone

Abstract *Background:* Systemic response to chronic disease in COPD patients might cause hormonal imbalance which in turn affects the severity of the disease. The severity of hypoxia in COPD patients causes alterations in thyroid function tests and IGF-1 levels.

Methods: This work was carried on 50 COPD patients diagnosed and classified according to GOLD criteria and 20 healthy controlled subjects. All subjected to full clinical history, examination, chest X-ray and spirometry. Levels of TT3, TT4, FT3, FT4, IGF-1 and insulin were measured.

Results: TT4, FT3, FT4, TSH, and insulin levels were normal in all COPD. Despite the TT3 hormone level were normal in all stages of COPD, there is reduction in hormone levels in stage III and stage IV than control subjects. There is also reduction in TT3/TT4 ratio in severe COPD and there is correlation between TT3/TT4 ratio and PaO2 in stage III and stage IV but no correlation between TT3/TT4 ratio and PaO2 in stage I and stage II. IGF-1 hormone levels were variable among different stages of COPD.

Conclusion: There is was no significant difference between some hormonal levels in COPD and in controls, accordingly hormonal replacement therapy in these patients is doubtful.

Introduction

Endocrine changes in chronic obstructive pulmonary disease patients are poorly documented. The pathogenesis and clinical manifestation of chronic obstructive pulmonary disease are not restricted to pulmonary inflammation and structural remodeling. Rather, this disorder is associated with clinically significant systematic and alteration in biochemistry and organ function. This may include alteration in the relative levels or

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

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activities of endocrine hormone such as insulin and growth hormone [1].

The thyroid hormone enhances mitochondrial oxidation and, thus, augments metabolic rate. This effect on metabolic rate is probably responsible for the association between the thyroid hormone and respiratory drive. Limited data on the prevalence of thyroid diseases among patients with COPD are available. Yet, several characteristics of patients with COPD could potentially increase their likelihood of developing hypothyroidism and hyperthyroidism [2].

Little is known about circulating growth hormone or IGF-1 concentration. Some author find a decrease in growth hormone or IGF-1, others an increase. An increase of growth hormone might reflect a nonspecific response of the body to stress (for instance, hypoxemia). Until now, only on controlled study on growth hormone supplementation has been published, which however did not reveal any functional benefits. Before growth hormone supplementation can be advised as part of the treatment in chronic obstructive pulmonary disease, further controlled studies must be performed to investigate its functional efficacy [3].

In this study we measured different hormonal assay including thyroid hormones, IGF-1 and insulin in an attempt to detect some hormonal abnormalities in patients with COPD, we also correlated different hormonal level with severity of COPD.

Methods

This is a prospective study including 50 patients with COPD diagnosed and classified according to GOLD 2009 criteria [4] and twenty healthy non smoker volunteers as control.

Between 2008 and 2010 the patients were recruited from the outpatient clinic of El Mataria teaching Hospitals according to the inclusion criteria which include, symptoms of chronic bronchitis, evidence of airway obstruction according to GOLD study 2009 and no improvement in FEV1 of more than 10% after inhalation of 200 mg of Salbutamol. However, we excluded patients on oral glucocorticoids or with any other drug known to affect thyroid function such as amiodarone or iodine-containing contrast media. Clinical evidence of thyroid disease or coexistence of other diseases altering thyroid function tests. Patients with fasting hyperglycemia, positive urine glucose or renal failure.

Patients were subjected to clinical examination, chest X-ray, spirometry (Spirovit SP-10-Schiller, Switzerland), complete blood picture, fasting and two hours post prandial blood glucose. Hormonal assay using enzyme linked immunosorbent assay technique measuring the following hormonal levels.

(A) Total thyroxin (TT_4).
(B) Total triiodthyronine (TT_3).
(C) Thyroid stimulating hormone (TSH).
(D) Free thyroxine (FT_4).
(E) Free triiodthyronine (FT_3).
(F) Fasting serum insulin hormone level.
(G) Insulin growth factor range (IGF-1).

Results

Between 2008 and 2010, we measured the hormonal levels of thyroid gland, TSH and insulin and IGF-1 in 50 patients with COPD and 20 controls.

The patient characteristics are summarized in Table 1. There was a statistical significant reduction in FEV1, FEV1/FVC, paO2 and paCO2 between patients with COPD (No. = 50) and controls (No. = 20).

There was no statistical significant difference between patients with COPD and controls in total T3 and T4, TSH, Free T3 and T4 or insulin levels in this study (Table 2).

Hormonal levels according to stages of COPD showed a statistical difference between COPD patients and controls in total iodothyrionine (T3) levels. However, no significant differences were detected in other hormonal parameters (Table 3).

Calculated TT3/TT4 did not correlate with paO2 in stage I and stage II, however there was a strong positive correlation

Table 1 Patients characteristic.

Characterestics	COPD patients No. 50	Control No. 20	*P*-value
Age	38–71	40–67	0.09
	56.5 ± 8.1	52.9 ± 8.3	
Sex	All males	All males	
BMI	19.2–33.9	22.9–28.7	0.89
	24.6 ± 3.7	24.5 ± 1.47	
Stage of disease	Stage I No. 12 (24%)		
	Stage II No. 19 (38%)		
	Stage III No. 10 (20%)		
	Stage IV No. 9 (18%)		
Spirometry			
FEV1%	57.6 ± 19.3	107.7 ± 8.9	0.001
FEV1/FVC	57.2 ± 10.9	99.7 ± 9.45	0.001
Arterial blood gases			
pH	7.4 ± 0.02	7.41 ± 0.02	0.012
paO2	74 ± 9.33	82.8 ± 4.5	0.001
paCO2	44.6 ± 6.54	38.6 ± 1.2	0.001
Fasting blood sugar 2 h postprandial	87.72 ± 13.4	83.6 ± 11.1	0.26
	115.3 ± 26.1	99.9 ± 22.8	0.02

Table 2 Different hormonal levels between COPD patients and controls.

Hormones	COPD patients	Controls	P - value
Total T3 (ng%)			
Range	80 – 180	120 – 200	0.027
Mean + SD	140.4 ± 25.7	155 ± 20.9	
Total T4 (μg%)			
Range	5.7 – 12	6.5 – 12	0.16
Mean + SD	8.5 ± 1.55	9.1 ± 1.6	
TSH (μIU/dl)			
Range	0.3 – 3.6	0.09 – 4.5	0.29
Mean + SD	1.8 ± 0.88	1.15 ± 1.16	
Free T3 (pg/ml)			
Range	1.2 – 3.7	1.7 – 4.2	0.3
Mean + SD	2.6 ± 0.4	2.8 ± 0.6	
Free T4 (ng/dl)			
Range	0.68 – 1.9	0.08 – 1.7	0.27
Mean + SD	1.2 ± 0.23	1.12 ± 0.38	
Insulin (μIU/ml)			
Range	6.4 – 24.8	10 – 20	0.5
Mean + SD	15.7 ± 3.7	15 ± 2.4	

between TT3/TT4 ratio and paO2 in stage III and stage IV (Fig. 1).

The IGF1 level in chronic obstructive lung disease was: In mild stage (stage I) (25%) of patients the hormone levels were reduced, while in (75%) of patients the hormone levels were within normal limits. In moderate stage (stage II) (63.16%) of patients the hormone levels were reduced, while in (36.84%) of patients the hormone levels were within normal limits. In severe stage (stage III) (60%) of patients the hormone levels were reduced, while in (40%) of patients the hormone levels were within normal limits. In very severe stage (stage IV) (22.22%) of patients the hormone levels were reduced, while in (77.78%) of patients the hormone levels were within normal limits (Graph 1–4).

Discussion

Systemic response to chronic disease in COPD patients might cause hormonal imbalance which in turn affects the severity of the disease. The severity of hypoxia in COPD patients causes alterations in thyroid function tests and IGF-1 levels [5].

This work was carried out to investigate thyroid function, insulin hormone level, and insulin like growth factor-1 (IGF-1) levels in patients with chronic obstructive pulmonary disease COPD, presenting a spectrum in disease severity, as indicated by the various degrees of airway obstruction.

In the present study the hormonal level of total triiodothyronine (TT3) were normal in all COPD patients, however in stage III and IV there was a reduction in the hormone level in these stages than control subject and in comparison to stage I and II. These results agree with other studies that found no significant differences between levels of TT3 in COPD and controls [6,7]. Other investigators found that TT3 is reduced in all COPD patients especially those with hypoxemia than control subjects [8]. Regarding total thyroxine (TT4) the hormone level was normal in COPD patients with no statistical difference in comparison with control, this agrees with other studies [6,7].

The calculated TT3 to TT4 ratio was used, as this ratio has been proven to be a useful tool in studying the peripheral conversion of thyroxin to triiodothyronine in various disease states [9]. In the present study there is reduction in TT3/TT4 ratio in stage III and stage IV COPD patients and there was a strong positive correlation between TT3/TT4 ratio and PaO2 in stage III and stage IV ($r = 0.475$, and $P = 0.040$), this agree with the results in other studies [6,8].

This pattern of hormonal changes suggests that hypoxemia acts not only at the central levels of hypothalamic-pituitary-

Table 3 Different hormonal level in relation to disease stage and its significance with controls.

Hormonal level	Stage I	Stage II	Stage III	Stage IV
TT3				
Mean + SD	162.9 ± 20.6	142.6 ± 17.9	127 ± 21.5	120.6 ± 28.1
p-value	0.3	0.05	0.002	0.001
TT4				
Mean + SD	8.9 ± 1.7	8.5 ± 1.4	8.5 ± 1.6	8.4 ± 1.8
p-value	0.6	0.1	0.29	0.3
TSH				
Mean + SD	2.2 ± 0.9	1.8 ± 0.8	1.8 ± 1	1.4 ± 0.9
p-value	0.1	0.4	0.5	0.6
FT3				
Mean + SD	2.7 ± 0.4	2.7 ± 0.3	2.6 ± 0.4	2.6 ± 0.6
p-value	0.7	0.6	0.3	0.3
FT4				
Mean + SD	1.2 ± 0.2	1.2 ± 0.1	1.2 ± 0.3	1.2 ± 0.3
p-value	0.6	0.2	0.7	0.7
Insulin				
Mean + SD	14.4 ± 5.4	16.3 ± 1.7	16.2 ± 5.4	16 ± 1.5
p-value	0.1	0.1	0.5	0.3

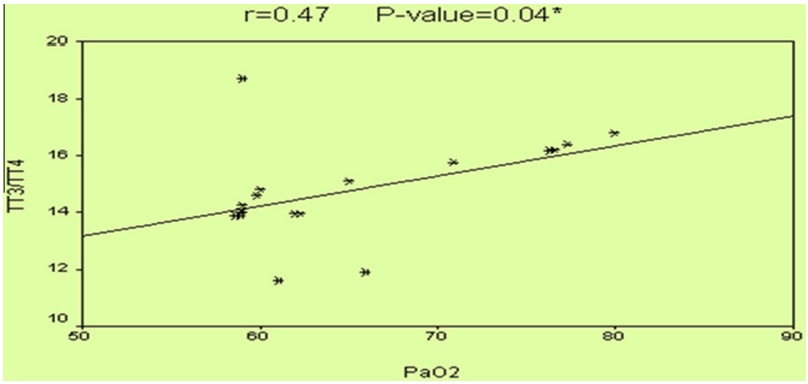
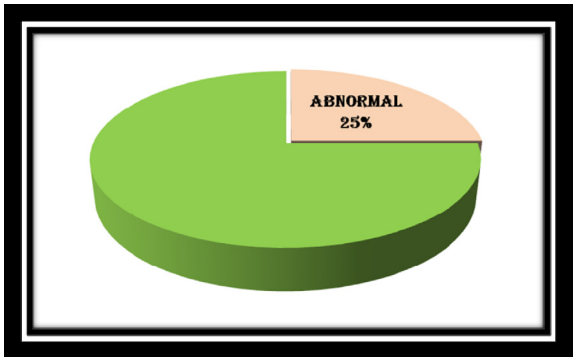
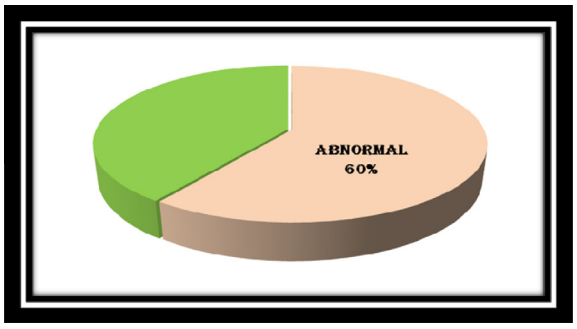


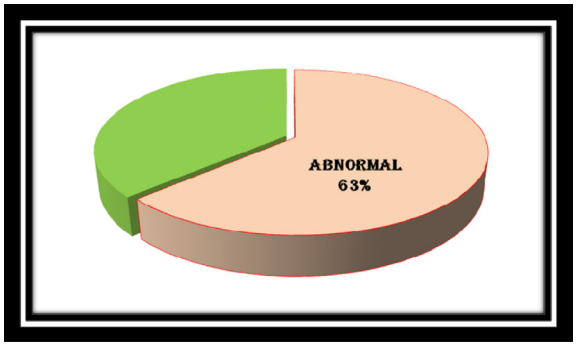
Figure 1 Correlation between calculated TT3/TT4 ratio and paO2.



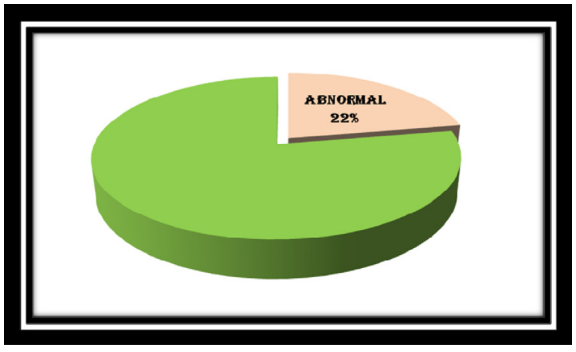
Graph 1 Percentage of patients with abnormal IGF-1 in stage I.



Graph 3 Percentage of patients with abnormal IGF-1 in stage III.



Graph 2 Percentage of patients with abnormal IGF-1 in stage II.



Graph 4 Percentage of patients with abnormal IGF-1 in stage IV.

thyroid, but also interferes with the peripheral metabolism and turnover of thyroid hormone.

In this study the free T3 and T4 levels were normal in all stages of COPD in comparison to the controls, this was the results in other researches [7,10]. Other authorities found that free T3 and T4 were higher in COPD than the control and the authors could not explain their observation [11,12]. However, other studies could demonstrate lower level of FT3 during exacerbations and partially regress after one month when the disease is stabilized [8].

In this study the level of TSH and insulin were normal in all COPD patients, and this agrees with other studies [6,12,13].

It was concluded that thyroid dysfunction ascribed to chronic COPD is probably related to confounding factors and not to hypoxemia or hypercapnia. So far, there is no evidence that thyroid function is consistently altered in COPD, except perhaps in a subgroup of patients with severe hypoxemia.

Circulating insulin like growth factor-1 (IGF-1) level was used as a marker of growth hormone (GH) action because IGF-1 has a longer half life than GH, and its concentration integrates the pulsatile release of GH [1]. In our study we observed the reduction in IGF-1 level in different stages of COPD. Little information is available regarding circulating

growth hormone or insulin like growth factors-1 (IGF-1) levels in chronic obstructive pulmonary disease (COPD). The data that exist suggest that insulin like growth factors-1 (IGF-1) levels in stable chronic obstructive pulmonary disease (COPD) patients tend to be low consistent with the impression that the growth hormone axis is suppressed by chronic disease. [14].

The mechanisms by which COPD alters endocrine function are incompletely understood but likely involve hypoxemia, hypercapnia, and systemic inflammation. Altered endocrine function can worsen the clinical manifestations of COPD through several mechanisms.

In this study we demonstrated some hormonal changes in patients of COPD which could be attributed to systemic manifestation of COPD e.g. cachexia, muscle wasting, however more sophisticated investigation should be done especially to evaluate the role of hormonal replacement therapy.

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