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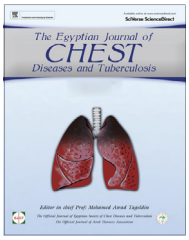

Thyroid dysfunction and inflammatory biomarkers in chronic obstructive pulmonary disease: Relation to severity and exacerbation

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KEYWORDS

Thyroid dysfunction;
Non-thyroidal illness syndrome;
Chronic obstructive pulmonary disease;
Interleukin-6;
Tumor necrosis factor alpha

Abstract *Background:* Thyroid dysfunction or non-thyroidal illness syndrome (NTIS) is frequently detected in chronic, systemic diseases. The systemic manifestations of chronic obstructive pulmonary disease (COPD) include a number of endocrine disorders. The severity of hypoxia and airway obstruction in COPD patients might cause alterations in thyroid function.

The aim of this study is to assess serum levels of thyroid hormones and the inflammatory biomarkers; IL-6, TNF-α in COPD patients during stability and acute exacerbation of the disease, and also to assess the relation between severity of COPD and levels of thyroid hormones.

Subjects and methods: Forty stable COPD patients and twenty COPD patients with acute exacerbation were included in this study as patient groups and twenty healthy age-matched non smoker subjects with normal pulmonary function as a control group. The diagnosis of COPD and acute exacerbation of COPD were established according to GOLD (2011) criteria. Stable COPD patients were further subdivided into Mild-to-moderate COPD patient group (FEV1 $\geqslant$ 50% of predicted value, which included 14 patients) and Severe COPD patient group (FEV1 $<$ 50% of predicted value, which included 26 patients). All enrolled patients were subjected to measurements of pulmonary function tests (FEV1%, FVC% and FEV1/FVC ratio), arterial blood gases (ABGs) (PaO_2, $PaCO_2$, pH), serum levels of thyroid hormones (TSH, total T3, total T4, free T3 and free T4) and the inflammatory biomarkers IL-6 and TNF-α on the first day of admission to RICU or first visit to the outpatient clinics.

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Results: There was a significant decrease in serum total T3 and free T3 levels in stable COPD patients when compared to control subjects. Also, there was a significant decrease in serum total T3, free T3, TSH levels and TT3/TT4 ratio in the COPD exacerbation patient group when compared to control subjects and when compared to stable COPD patients. There were no statistically significant differences in serum levels of total T4, free T4 between the studied groups. Regarding disease severity, serum total T3, free T3 levels and TT3/TT4 ratio were significantly decreased in severe COPD patients when compared to mild-to-moderate COPD patients. There were significant positive correlations between PaO_2 and both serum total T3 and TT3/TT4 ratio in the stable COPD group. Serum IL-6 and TNF-α levels were significantly increased in both stable and exacerbation phase COPD patient groups when compared to control subjects.

Conclusion: COPD is a systemic disease that may produce significant alterations in serum levels of thyroid hormones, especially in severe COPD patients and during exacerbation phases of COPD where NTIS is more evident. There was a significant decrease in serum total T3 and free T3 levels in stable COPD patients and this decrease was more significantly evident with a superadded significant decrease in serum TSH levels during the exacerbation phase of COPD. The hormonal alterations are especially related to severity of the disease and hypoxemia. Serum IL-6 and TNF-α levels were increased even in stable COPD and this rise is magnified with increased disease severity and during exacerbation phases of COPD.

Introduction

Chronic obstructive pulmonary disease (COPD) is associated with low grade systemic inflammation that may be responsible for the systemic effects of the disease; malnutrition, muscle wasting, osteoporosis, cardiovascular disease, type II diabetes mellitus, anemia and depression [1]. COPD is no longer considered to affect only the lungs and airways but also the rest of the body. The systemic manifestations of COPD include a number of endocrine disorders such as those involving the pituitary, thyroid, gonads, adrenals and pancreas [2]. 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 [3]. The terms ''Non-thyroidal Illness Syndrome (NTIS)'' and ''Euthyroid Sick Syndrome (ESS)'' have been used to describe alterations in thyroid function tests in critical illness, such as starvation, sepsis, surgery, myocardial infarction, and also in chronic, systemic diseases including chronic heart failure, chronic liver or hematologic diseases, cancer, diabetes, connective tissue diseases and COPD [4]. Proinflammatory cytokines, especially IL-6, IL-1β, TNF-α and IFN-γ have inhibiting effects on peripheral thyroid hormone metabolism [5,6].These mediators may also be involved in the pathogenesis of NTIS [4].

Limited data on the prevalence of thyroid diseases among patients with COPD are available [4,7], yet, several characteristics of patients with COPD could potentially increase their likelihood of developing hypothyroidism and hyperthyroidism [2]. Also the severity of airway obstruction in these patients is associated with impairment of thyroid gland function [8].

The aim of this study is to assess serum levels of thyroid hormones and the inflammatory biomarkers IL-6 and TNF-α in COPD patients during stability and acute exacerbation of the disease, and also to assess the relation between the severity of COPD and levels of thyroid hormones.

Subjects and methods

This cross-sectional prospective study was conducted between October 2011 and February 2013 at Internal medicine, Chest and Medical Biochemistry Departments, Zagazig University Hospitals.

This study comprised 40 stable COPD patients and 20 COPD patients with acute exacerbation as patient groups and 20 healthy non smoker age-matched subjects with normal pulmonary function as a control group.

Stable COPD Patients (had been clinically stable for at least 3 months) were recruited from the outpatient clinics of Chest and Internal Medicine Departments. Patients with acute exacerbation of COPD (had clinical signs of COPD exacerbation as increased dyspnea, increased cough and sputum, wheezing and chest tightness, fever. tachycardia and tachypnea) were admitted to the respiratory intensive care unit (RICU). In both patient groups, all males were ex-smokers, but females were non smokers. The diagnosis and acute exacerbation of COPD were established according to Global Initiative for Chronic Obstructive Lung Disease (GOLD 2011) criteria [9].

Spirometric classification of disease severity in stable COPD patients (Stage I ''mild'', Stage II ''moderate'', Stage III ''severe'' and Stage IV ''very severe'') was done according to GOLD criteria [9].

Stable COPD patients were further subdivided into Mild-to-moderate COPD patient group (Stage I and Stage II, FEV1 $\geqslant$ 50% of predicted value, $n = 14$) and Severe COPD patient group (Stage III and Stage IV, FEV1 < 50% of predicted value, $n = 26$).

Stable COPD patients had been receiving inhaled bronchodilator therapy in the form of long-acting β2-agonists and/or anticholinergic agents. Severe/very severe COPD patients were on inhaled corticosteroids.