

Clinical Study on Thyroid and Insulin Hormonal Dysfunction in Patients with Chronic Obstructive Pulmonary Disease

D Nikethan

Assistant Professor, Department of Medicine, Viswabharathi Medical College, Kurnool, Andhra Pradesh, India

Abstract

Background: Many systemic changes take place in patients with chronic obstructive pulmonary disease (COPD) cause hormonal imbalance which, in turn, affects the severity of the disease. The systemic manifestations of COPD include a number of endocrine disorders such as those involving the pituitary, the thyroid, the gonads, the adrenals, and the pancreas. The fluctuating severity of hypoxia in COPD patients results in alterations in thyroid function tests and insulin-like growth factor-1 (IGF-1) levels.

Aim of the Study: This study aims to evaluate the thyroid function tests, insulin, and IGF-1 levels in patients with chronic COPD disease and analyze the data.

Materials and Methods: Sixty-four COPD patients and 32 normal subjects as control group were included in this study. The COPD group was diagnosed and classified according to Global Initiative for Chronic Obstructive Lung Disease criteria. All were subjected to thorough clinical history, examination, and chest X-ray and spirometry. Hormonal levels of thyroxine hormone (total triiodothyronine [TT3], total thyroxine, free triiodothyronine, and free thyroxine) and IGF-1 and insulin were measured.

Observations and Results: There was a statistically significant difference between patients with COPD and controls in regard with mean values of total T3, but there was no statistically significant difference in regard with mean values of total T4, thyroid-stimulating hormone, free T3 and T4, or insulin levels in this study. Hormonal levels according to the stages of COPD showed no statistical difference between Stage I COPD patients and controls, but there was statistically significant difference in regard to other stages of COPD and control groups, i.e., in the present study, the hormonal level of TT3 was normal in all COPD patients; however, in Stages 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.

Conclusion: There were significant differences between some hormonal levels in COPD and in controls. There were demonstrable thyroid hormonal changes and insulin levels in patients of severe degree COPD patients which could be attributed to as systemic manifestation resulting in cachexia, muscle wasting.

Key words: Chronic obstructive pulmonary disease, Insulin-like growth hormone, Thyroid dysfunction

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a very common and major cause of chronic morbidity and mortality throughout the world. It was ranked as sixth as the cause of death in 1990, especially in industrialized

areas. It was also presumed that it would become the third leading cause of death worldwide by 2020.^[1] The disease is no longer considered to affect not only the lungs and airways but also results in systemic changes in the body. The systemic manifestations of COPD include endocrine disorders involving the pituitary, the thyroid, etc. The thyroid hormone regulates the metabolism of proteins, lipids, and carbohydrates, and controls the activity of membrane-bound enzymes.^[2,3] The thyroid hormone enhances mitochondrial oxidation and thus augments metabolic rate.^[4] This effect on metabolic rate is probably responsible for the association between the thyroid hormone and respiratory drive.^[5] Limited data on the prevalence of thyroid diseases among

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019

Month of Peer Review : 07-2019

Month of Acceptance : 08-2019

Month of Publishing : 08-2019

Corresponding Author: Dr. D Nikethan, Department of Medicine, Viswabharathi Medical College, RT Nagar, Penchikalapadu, Kurnool, Andhra Pradesh, India

patients with COPD are available.^[6,7] There is a potential possibility of increase in developing hypothyroidism and hyperthyroidism in COPD patients and the severity of airway obstruction in these patients affects the rate of survival.^[8] It is associated with impairment of thyroid gland function.^[9] There was every possibility of differences in hormone levels during stable and exacerbation phases in comparison to healthy controls. Some authors found a decrease in growth hormone or IGF-1, others an increase in growth hormone or IGF-1. An increase of growth hormone might reflect a non-specific response of the body to stress (for instance, hypoxemia). Before growth hormone supplementation can be advised as part of the treatment in COPD, further controlled studies must be performed to investigate its functional efficacy.^[10] In this study, hormonal assays including thyroid hormones, IGF-1, and insulin were done to observe and analyze their changes in patients with COPD and a healthy control group.

MATERIALS AND METHODS

In this study, the subjects were divided into two groups. Group A consisted of 64 patients who were diagnosed as COPD and attending the Department of Medicine, Viswabharathi Medical College, RT Nagar, Panchikalapadu, Kurnool, Andhra Pradesh. An institutional ethical committee clearance was obtained before the commencement of the study. A committee approved consent form was used for the study.

Inclusion Criteria

(1) Patients with COPD belonging to the age group of 35–75 years were included in the study. (2) Patients with COPD and classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2009 criteria were

included in the study. (3) 32 healthy non-smoking volunteers were included in the study. (4) Patients with symptoms of chronic bronchitis, evidence of airway obstruction according to GOLD study 2009, and no improvement in forced vital capacity 1 (FEV1) of more than 10% after inhalation of 200 mg of salbutamol were included in the study.

Exclusion Criteria

(1) Patients who are on oral glucocorticoids or with any other drug known to affect thyroid function tests such as amiodarone or iodine-containing contrast media were excluded from the study. (2) Patients aged below 35 years and above 75 years were excluded from the study. (3) Patients with clinical evidence of thyroid disease or coexistence of other diseases altering thyroid function tests were excluded from the study. (4) Patients with fasting hyperglycemia were excluded from the study. (5) Patients with positive urine glucose or renal failure were excluded from the study. All the patients were subjected to clinical examination, chest X-ray, spirometry, complete blood picture, fasting, and 2 h postprandial blood glucose. Hormonal assay using enzyme-linked immunosorbent assay technique measuring the following hormonal levels: (a) Total thyroxine (TT4), (b) total triiodothyronine [TT3], (c) thyroid-stimulating hormone (TSH), (d) free thyroxine, (e) free triiodothyronine, (f) fasting serum insulin hormone level, and (g) insulin growth factor range (insulin-like growth factor-1 [IGF-1]).

OBSERVATIONS AND RESULTS

The clinical and laboratory parameters of the two groups are summarized in Table 1. It was observed that there was a statistically significant reduction in FEV1, FEV1/FVC, paO_2 , and $paCO_2$ values when compared between patients with COPD ($n = 64$) and controls ($n = 32$).

Table 1: The clinical and laboratory parameters in both the groups (Group A – 64 and Group B – 32)

Characteristics	Chronic obstructive pulmonary disease patients (n=64)	Control (n=32)	P-value
Age range	35–75	40–65	0.081
Mean age	52.75±8.9	47.16±7.10	0.734
Sex	All male	All male	---
BMI	20.2–33.9	21.7–29.3	0.89
Mean BMI	23.9±2.4	25.8±1.18	
Stage of the disease			
Stage I	16 (25%)	--	
Stage II	21 (32.8%)	--	
Stage III	13 (20.31%)	--	
Stage IV	14 (21.87%)	--	
Spirometry			
FEV1%	61.3±15.2	109.1±7.7	0.001
FEV1/FVC	58.5±12.6	98.8±7.45	0.001
Arterial blood gases			
pH	7.4±0.02	7.41±0.02	0.001
paO_2	74±9.33	82.8±4.5	
$paCO_2$	44.6±6.54	38.6±1.3	
Fasting blood sugar	87.72±13.4	83.6±11.1	0.36
2 h postprandial	115.3±26.1	99.9±22.82	0.04

BMI: Body mass index, FEV1: Forced vital capacity 1

There was a statistically significant difference between patients with COPD and controls in regard with mean values of total T3, but there was no statistically significant difference in regard with mean values of total T4, TSH, free T3 and T4, or insulin levels in this study [Table 2].

Hormonal levels according to the stages of COPD showed no statistically significant difference between Stage I COPD patients and controls, but there was a statistically significant difference in regard to other stages of COPD and control groups [Table 3].

It was observed in this study that the calculated TT3 and TT4 ratio did not correlate with paO₂ levels in Stage I and Stage II of COPD group; however, there was a strong positive correlation between TT3 and TT4 ratio and paO₂ in Stage III and Stage IV of COPD. The IGF1 level in chronic obstructive lung disease was: In mild stage (Stage I) 2/10 (20%) of patients in Group A, the hormone levels were reduced, while in the remaining 8/64 (80%) of patients, the hormone levels were within normal limits. In moderate stage

(Stage II), 11/18 (61.11%) of patients, the hormone levels were reduced, while in 7 (36.88%) of patients, the hormone levels were within normal limits. In severe stage (Stage III), 12/20 (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), 9/16 (56.25%) of patients, the hormone levels were reduced, while in 7/16 (43.75%) of patients, the hormone levels were within normal limits.

DISCUSSION

The severity of the COPD disease produces systemic response in patients such as hormonal imbalance which, in turn, affects the homeostasis. Hormonal imbalance in thyroid function tests and IGF-1 levels varies with the degree of hypoxia in COPD patients.^[5] The present study was conducted to observe the hormonal levels of TT3, TT4, free T3, free T4, TSH, IGF-1, and insulin in severe stages of COPD patients. The patients with COPD presenting a spectrum in disease severity were included in the study as indicated by the various degrees of airway obstruction and hypoxia. There was a statistically significant difference between patients with COPD and controls in regard with mean values of total T3, but there was no statistically significant difference in regard with mean values of total T4, TSH, free T3 and T4, or insulin levels in this study. Hormonal levels according to the stages of COPD showed no statistically significant difference between Stage I COPD patients and controls, but there was a statistically significant difference in regard to other stages of COPD and control groups, i.e., in the present study, the hormonal level of total triiodothyronine (TT3) was normal in all COPD patients; however, in Stages III and IV, there was a reduction in the hormone level in these stages than control subject and in comparison to Stages I and II. Similar results were observed with other studies.^[6,7] However, few authors found that TT3 is reduced in all COPD patients, especially those with hypoxemia than control subjects.^[8] The calculated TT3–TT4 ratio was used, as this ratio has been proven to be a useful tool in studying the peripheral conversion of thyroxine to triiodothyronine

Table 2: The range and mean values of different hormonal levels between COPD patients and controls (Group A – 63 and Group B – 32)

Hormones	COPD patients Group A	Controls Group B	P-value
Total T3 (ng %)			
Range	78–176	198–224	0.023
Mean	140.4±25.7	155.6±23.65	0.012
Total T4 (µg)			
Range	5.2–11.7	6.1–11.3	0.16
Mean	8.1±1.24	8.9±1.0	
TSH (µIU/dl)			
Range	0.3–3.8	0.08–4.5	0.24
Mean	1.7±0.98	1.15±1.16	0.06
Free T3 (pg/ml)			
Range	1.2–37	1.7–4.2	0.21
Mean	2.6±0.4	2.8±0.6	
Free T4			
Range	0.68–1.9	0.07–1.8	0.22
Mean	1.07±0.25	1.09±0.39	
Insulin			
Range	6.1–24.3	9.90–19.02	0.4
Mean	14.90±3.9	14.7±2.35	

COPD: Chronic obstructive pulmonary disease

Table 3: The different hormonal level in relation to disease stages of COPD in comparison to control group (Group A – 64 and Group B – 32)

Hormonal level	Stage I (10)	Stage II (18)	Stage III (20)	Stage IV (16)
Total triiodothyronine mean+SD	162.9±20.6	142.6±17.9	127±21.5	120.6±28.1
Total thyroxine mean+SD	0.82±1.4	0.82±1.6	0.81±1.8	0.84±1.8
Thyroid-stimulating hormone mean+SD	2.1±0.8	1.6±0.7	1.9±1.4	2.01±0.8
Free triiodothyronine mean+SD	2.7±0.4	2.7±0.3	2.6±0.4	2.6±0.6
Free thyroxine mean+SD	1.2±0.2	1.2±0.1	1.2±0.3	1.2±0.3
Insulin mean+SD	14.4±5.4	16.3±1.7	16.2±5.4	16±1.5
P-value	0.12	0.049	0.004	0.02

SD: Standard deviation

in various disease states.^[9] In the present study also, there was 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 agrees with the results in other studies.^[6,8] Such pattern of hormonal changes suggests that hypoxemia acts not only at the central levels of hypothalamic pituitary thyroid but also interferes with the peripheral metabolism and turnover of thyroid hormone. The free T3 and T4 levels were normal in the present study in all stages of COPD in comparison to the controls; this was the results in other researches.^[7,10] Review of literature showed that free T3 and T4 were higher in COPD than the control and the authors could not explain their observation.^[7,9] The TSH and insulin levels in this study were normal in all COPD patients, and this agrees with other studies also.^[6,9] It could be concluded that thyroid dysfunction may be ascribed to chronic COPD as a confounding factor and related to hypoxemia or hypercapnia. However, there needs to be further investigation done before concluding that there is definite evidence of thyroid dysfunction in COPD patients. Circulating 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.^[11] In this study, it was observed that there was reduction in IGF-1 level in different stages of COPD. Little information is available regarding circulating growth hormone or IGF-1 levels in COPD in literature.^[6] However, the data that exist suggest that IGF-1 levels in stable COPD patients tend to be low, consistent with the impression that the growth hormone axis is suppressed by chronic disease.^[11] 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.

CONCLUSION

There were demonstrable thyroid hormonal changes and insulin levels in patients of severe degree COPD patients which could be attributed to as systemic manifestation resulting in cachexia, muscle wasting. However, more sophisticated investigation should be done, especially to evaluate the role of hormonal replacement therapy.

REFERENCES

1. Roberto R, Antonio A, Jean B, Gershon AS, Warner L, Cascagnette P, Victor JC, *et al.* Pocket Guide to COPD Diagnosis, Management and Prevention: Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2010.
2. Yen PM. Genomic and nongenomic actions of thyroid hormones. In: Braverman LE, Utiger RD, editors. *The Thyroid. A Fundamental and Clinical Text.* 9th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2005. p. 135-50.
3. Silva JE. Intermediary metabolism and the sympathoadrenal system in hypothyroidism. In: Braverman LE, Utiger RD, editors. *The Thyroid. A Fundamental and Clinical Text.* 9th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2005. p. 817-23.
4. Silva JE. Thermogenesis and sympathoadrenal system in thyrotoxicosis. In: Braverman LE, Utiger RD, editors. *The Thyroid. A Fundamental and Clinical Text.* 9th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2005. p. 607-20.
5. Saaresranta T, Polo O. Hormones and breathing. *Chest* 2002;122:2165-82.
6. Karadağ F, Özcan H, Karul AB, Yılmaz M, Cildag O. Correlates of non-thyroidal illness syndrome in chronic obstructive pulmonary disease. *Respir Med* 2007;101:1439-46.
7. Dimopoulou I, Ilias I, Mastorakos G, Mantzos E, Roussos C, Koutras DA, *et al.* Effects of severity of chronic obstructive pulmonary disease on thyroid function. *Metabolism* 2001;50:1397-401.
8. Beers MH, Berkow R. *The Merck Manual.* 17th ed. Whitehouse Station: Merck; 1999. p. 575.
9. Gow SM, Seth J, Beckett GJ, Douglas G. Thyroid function and endocrine abnormalities in elderly patients with severe chronic obstructive lung disease. *Thorax* 1987;42:520-5.
10. Coşkun F, Ege E, Uzaslan E, Ediger D, Karadağ M, Gözü O, *et al.* Evaluation of thyroid hormone levels and somatomedin-C (IGF-1) in patients with chronic obstructive pulmonary disease (COPD) and relation with the severity of the disease. *Tuberk Toraks* 2009;57:369-75.
11. Olivieri O, Girelli D, Stanzial AM, Rossi L, Bassi A, Corrocher R, *et al.* Selenium, zinc, and thyroid hormones in healthy subjects: Low T3/T4 ratio in the elderly is related to impaired selenium status. *Biol Trace Elem Res* 1996;51:31-41.

How to cite this article: Nikethan D. Clinical Study on Thyroid and Insulin Hormonal Dysfunction in Patients with Chronic Obstructive Pulmonary Disease. *Int J Sci Stud* 2019;7(5):12-15.

Source of Support: Nil, **Conflict of Interest:** None declared.