

ASSESSMENT OF PULMONARY FUNCTION TESTS IN PATIENTS OF HYPOTHYROIDISM AND OF THE EFFECTS OF LEVOTHYROXINE ON THEIR PULMONARY FUNCTION TESTS

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ABSTRACT

BACKGROUND

Hypothyroidism is a condition resulting from inadequate thyroid hormone secretion from the thyroid gland due to the structural and functional impairment. Many patients with hypothyroidism present with dyspnoea. Hypothyroidism causes a restrictive pattern of lung disease due to respiratory muscle weakness, hypoxic alveolar hypoventilation and decrease in maximal breathing capacity.

Aims and Objectives- The objective of the present study is to evaluate spirometry in patients with hypothyroidism, supplement them with levothyroxine according to protocol and reassess their spirometry after three months and compare the two sets of spirometry parameters.

MATERIALS AND METHODS

An uncontrolled clinical trial with supplementation of levothyroxine for a period of four and a half months to the newly diagnosed hypothyroid patients was carried between February 2017 and October 2017 in Biochemistry Department and Chest Department in College of Medicine and Sagore Dutta Hospital, Kamarhati. Thirty-two patients with hypothyroidism were followed up till the end. Serum TSH and total T4 levels were measured at the beginning and repeated after six weeks of levothyroxine therapy to normalise the TSH and total T4 levels. Simple spirometry was done at the beginning and repeated after three months of normalisation of TSH level. Height (cm) and weight (kg) of all the participants were noted at the beginning and end.

RESULTS

The results were analysed by paired t-test and chi-square tests using SPSS version 20. Hypothyroid patients showed a significant increase in FEV1, FVC and FEF 25%-75% after treatment ($p < 0.05$), but the change in FEV1/FVC ratio was not statistically significant. From eight hypothyroid patients with mild restriction, six changed to normal but one progressed to moderate restriction after treatment. All seven hypothyroid patients with moderate restriction changed to mild restriction (100%).

CONCLUSION

In conclusion, respiratory system can be affected in a restrictive pattern in hypothyroid patients and most of these are completely reversible with levothyroxine.

KEY WORDS

Spirometry; FEV1, FVC, FEF 25% - 75%, FEV1/FVC; Hypothyroidism.

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BACKGROUND

Hypothyroidism is a clinical condition, which results from inadequate secretion of thyroid hormones from the thyroid gland because of various primary and secondary causes.^[1,2] It is a relatively common disorder worldwide, particularly in the sub-Himalayan region. The prevalence of hypothyroidism is found to be common in both male and female. Deficiency of iodine in the diet is the most common cause of hypothyroidism.

Autoimmune mechanisms, e.g. Hashimoto's thyroiditis and certain drug-induced hypothyroidism are also important.

Hypothyroidism is a disease which involves multiple systems of the body and is clinically manifested as weight gain, easy fatigue, dry skin, intolerance to cold, constipation, swelling of the limbs, dyspnoea, hoarseness of voice, menorrhagia, bradycardia, hair fall, multiple neurological symptoms and infertility etc.^[3]

Respiratory system like other body systems is also involved in hypothyroidism. Patients of hypothyroidism often complain of weakness, shortness of breathing and exercise intolerance. These subjective symptoms could be due to limited pulmonary reserve, limited cardiac reserve and increased muscle fatigue involving respiratory muscles.^[4] The type of disease may range from mild dyspnoea to severe respiratory failure.^[5,6] Dyspnoea in hypothyroidism looks secondary to limited cardiac reserve.^[7] So assessment of pulmonary function by spirometry in patients suffering from hypothyroidism is of great importance.

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The present study was designed to determine the probable abnormalities in pulmonary function tests of newly diagnosed hypothyroid patients and to assess the effect of levothyroxine on their pulmonary function tests after three months of normalisation of their TSH levels.

Aims and Objectives

- To assess the baseline pulmonary function by spirometry in newly diagnosed hypothyroid patients not having any known lung diseases.
- To reassess the pulmonary function by spirometry in those patients after three months of normalisation of their TSH levels by levothyroxine treatment.
- To compare the two sets of data if there were any significant increase in FEV1, FVC, FEF 25% - 75% and FEV1/FVC ratio.

MATERIALS AND METHODS

In this uncontrolled clinical trial all patients with hypothyroidism, diagnosed for the first time participated in the study after obtaining written consent from them. Patients were defined as a TSH level > 20 $\mu\text{IU/mL}$ and T4 level <5 $\mu\text{g/dL}$.^[8]

Exclusion Criteria Included

- Smokers and ex-smokers.
- Chronic respiratory diseases.
- Pregnant mothers.
- Diabetes mellitus.
- Obesity, BMI > 30 kg/m².
- Patients underwent recent chest and abdominal surgeries.

The study was carried out after obtaining permission from the Institutional Ethics Committee. A written consent form was taken from all the patients. Personal and family history was taken. All patients selected underwent digital chest x-ray examination to exclude any chest related pathology. Besides general examination, anthropometric measurements like height in centimetres (cm) and weight in kilograms (kg) were taken at first contact and at the end of the study.

Fasting blood samples maintaining full aseptic precautions were drawn for fasting blood glucose estimation by glucose oxidase peroxidase method using EM 360 autoanalyser by Transasia. Thyroid functions were assessed in the Departmental Biochemistry Laboratory of College of Medicine and Sagore Dutta Hospital, Kamarhati, Kolkata. Serum TSH and T4 (total) levels were measured using validated ELISA kit of Accubind™ in ERBA LISA ELISA reader using a two level immuno-control (Supplied by Biorad) for comparison. Spirometry was performed in all the patients in the chest OPD, College of Medicine and Sagore Dutta Hospital, Kamarhati using Spirolab III, Ver 3.7 SN 311909, manufactured by Cipla Company by trained technician at the beginning of the study. All the spirometries were repeated three times to get the best possible result.

Levothyroxine tablets were prescribed by an endocrinologist as per protocol to all the newly diagnosed hypothyroid patients with the predominant symptom of shortness of breath. Repeat serum TSH and total T4 tests were done in the blood samples 6 (six) weeks after initiation

of levothyroxine therapy. Majority of the patients gave a history of improvement in their respiratory symptoms. After three months of normalisation of thyroid hormone status, spirometry was repeated at the same centre using the same instrument Spirolab III, Ver 3.7 SN 311909 by Cipla.

The results were analysed by paired t-test and chi-square tests using SPSS version 20. Quantitative variables were expressed as mean $\pm$ standard deviation. Results were considered significant if the 'p' value was < 0.05.

RESULTS

The study started with 50 patients at the beginning. At different intervals of their follow-up, there was a dropout of 18 patients (36%). Finally, 32 patients (26 females and 6 males) continued till the end of the study. The patient's age ranged between 18 and 61 years. The mean age was 36.38 ± 14.9 years. The BMI of the patients were 23.64 ± 2.41 metre/kg².

The mean value of TSH was 30.08 ± 7.63 $\mu\text{IU/mL}$ before treatment, which reached 3.09 ± 0.95 $\mu\text{IU/mL}$ after treatment with levothyroxine for six weeks. The mean T4 level changed from 3.09 ± 1.42 $\mu\text{g/dL}$ before treatment to 9.41 ± 2.17 $\mu\text{g/dL}$ after treatment (Table 1).

Serial No.	Variables	Mean $\pm$ SD
1.	TSH in $\mu\text{IU/mL}$ (Before treatment)	30.08 ± 7.63
2.	TSH in $\mu\text{IU/mL}$ (After six weeks of treatment with levothyroxine)	3.09 ± 1.42
3.	Total T4 in $\mu\text{g/dL}$ (Before treatment)	3.77 ± 0.96
4.	Total T4 in $\mu\text{g/dL}$ (After six weeks of treatment with levothyroxine)	9.41 ± 2.17

Table 1. Results of Thyroid Function Test Parameters (TSH, Total T4)

Values presented as Mean $\pm$ SD; SD = Standard Deviation

Serial No.	Variables	Mean $\pm$ SD	T-test (Two Sample Equal Variance)
1.	FEV1 in Lit (Before treatment)	1.91 ± 0.44	0.01766
2.	FEV1 in Lit (After treatment)	2.17 ± 0.41	
3.	FVC in Lit (Before treatment)	2.21 ± 0.51	0.007835
4.	FVC in Lit (After treatment)	2.56 ± 0.49	
5.	FEF 25-75% in Lit/S (Before treatment)	2.47 ± 0.93	0.00966
6.	FEF 25-75% in Lit/S (After treatment)	3.08 ± 0.9	
7.	FEV1/FVC Ratio (Before treatment)	0.87 ± 0.09	0.435543
8.	FEV1/FVC Ratio (After treatment)	0.85 ± 0.07	

Table 2. Results of Pulmonary Function Test Parameters (FEV1, FVC, FEF 25% - 75% and FEV1/FVC Ratio)

Values presented as Mean $\pm$ SD; SD = Standard Deviation

The results of first spirometry were normal in 17 patients (53%). Mild restriction in pulmonary function was found in 8 patients and moderate restriction in remaining 7 patients. After levothyroxine treatment 21 patients were normal (66%), 10 patients (31%) had mild and 1 (3%) patient had moderate restrictive abnormalities in their spirometry (Table 3).

Pulmonary Function (PFT)	Before		After	
	n	%	n	%
Normal	17	53	21	66
Mild Restriction	08	25	10	31
Moderate Restriction	07	22	01	03

Table 3. Results of Pulmonary Function Tests before and after Treatment in Hypothyroid Patients

Any forms of obstructive abnormalities were not found in the spirometry in our study. In patients with mild restrictive abnormalities at the beginning six patients progressed to normal, but one of them progressed to have moderate restriction after treatment with levothyroxine. Of those who had moderate restrictive abnormalities, all seven (100%) improved to have mild restriction in their pulmonary function at the end of four and a half months.

However, two patients who had normal spirometry at the beginning of the study, progressed to a mild restrictive form of spirometry after four and a half months of levothyroxine therapy.

Spirometry Parameters	Mean $\pm$ SD	T-test P value
FEV1 (Lit)	0.255 $\pm$ 0.253	0.01766
FVC (Lit)	0.346 $\pm$ 0.32	0.0078
FEF 25-75% (Lit/S)	0.61 $\pm$ 0.7	0.009
FEV1/FVC Ratio	0.02 $\pm$ 0.07	0.43

Table 4. Mean Rise in FEV1, FVC, FEF 25% - 75% and FEV1/FVC Ratio after Treatment with Levothyroxine in Hypothyroid Patients

SD= Standard Deviation.

There was a statistically significant increase in FEV1, FVC and FEF 25% - 75% after treatment of hypothyroid patients with levothyroxine ($p < 0.05$) for four and a half months, but the change in FEV1/FVC ratio was not statistically significant ($p = 0.43$).

The mean increase in FEV1 was 0.255 ± 0.253 lit. The mean increase in FVC was 0.346 ± 0.32 lit and that of FEF 25% - 75% was 0.61 ± 0.7 lit/s (Table 4).

DISCUSSION

This study showed that few patients with hypothyroidism have some degree of restrictive abnormalities in their pulmonary function, which are reversible in most cases when treated with levothyroxine. These restrictive abnormalities are usually assessed by pulmonary function tests with the help of a spirometer. In the spirometry report, FEV1 represents the Forced Expiratory Volume in the first second; FVC represents the Forced Vital Capacity of the patient, while FEF 25 - 75 refers to the mean of the forced expiration during 25% - 75% intervals of the middle portion of the forced expiration. In restrictive pattern of lung disease, both the

FEV1 and FVC are proportionately decreased as a result of reduced pulmonary compliance.

Hypothyroidism has numerous effects on the respiratory system. Fatigue and shortness of breathing are the most common and most frequent symptoms in the absence of other pulmonary diseases.^[9] Hypothyroidism does involve the respiratory system which includes respiratory muscle weakness, hypoxic alveolar hypoventilation, upper airway obstruction, central and obstructive sleep apnoea and even pleural effusion with respiratory failure have been reported.^[10] The most consistent finding in hypothyroid patient is that some have a markedly blunted ventilatory response to hypoxia,^[11] which improves significantly after within weeks of initiation of levothyroxine therapy.

FEV1 is the volume of air exhaled in the first second and it is the most reproducible and most useful measure of lung function and that is according to the study conducted by Valjevac et al,^[12] who suggested that the cause of reduced respiratory function is due to decreased respiratory muscle strength, hypoventilation which is related to the degree and duration of hypothyroidism, while Cakmak et al^[13] observed a significant reduction in FEV1 and FVC in patients with hypothyroidism as compared to control. Even in asymptomatic patients with hypothyroidism, respiratory system can be dangerously and insidiously affected. Many studies investigated the effect of hypothyroidism on pulmonary function and effect of hormone replacement therapy. Some of these studies documented decreased pulmonary function in hypothyroidism, which improved with hormonal replacement.^[14] In our present study, levothyroxine treated euthyroid patients after three months of their euthyroid conversion showed significant increase in FEV1 and FVC ($p < 0.05$), but an insignificant increase in FEV1/FVC ratio.

Beyer IW et al^[15] conducted a study on muscle dysfunction in hypothyroidism showed that central nervous system responses, respiratory and cardiovascular performances that there was decrease in both inspiratory and expiratory muscles strength among hypothyroid patients, limitation in the thoracic movement, reduction in muscle tone reduces the respiratory force which affects the lung volume without disturbing the FEV1/FVC ratio thereby showing a restrictive pattern.

In the present study a significant increase in FEV1, FVC in euthyroid patients reflect that levothyroxine increases the respiratory muscle strength that is responsible for an improvement in the lung function as indicated by the lung function test parameters.

CONCLUSION

- There is a restrictive pattern of lung function abnormality in some hypothyroid patients.
- Most of the restrictive abnormalities in lung function are completely reversible with an early initiation of levothyroxine therapy.

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