

# The Effect of Levothyroxin on Pulmonary Function Tests of Hypothyroid Patients

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**T**he aim of the present study was to determine the effect of levothyroxin on the pulmonary function of patients with hypothyroidism.

**Materials and Methods:** In this Quazi-experimental study, all patients who were diagnosed as hypothyroid for first time and had no history of known pulmonary disease or smoking or recent abdominal or chest surgery were recruited. Levothyroxin was prescribed for all patients (1.7 µg/kg). Spirometry was done with the standard methods for all patients at the beginning of the study and again after at least 3 months of euthyroidism.

**Results:** 30 patients (24 females and 6 males) with a mean age of 37.5±12 years were studied. At the beginning of the study, 16 patients had mild restrictive pulmonary abnormalities and 10 patients had moderate restrictive pulmonary disease. 4 patients were normal. At the end of the study, the results of spirometry were normal in 12 patients and mild restrictive abnormalities were found in 14, and moderate restrictive abnormalities in 4 patients. Significant increases in FEV1, FVC and FEF25-75% were found after treatment with levothroxin ( $p<0.05$ ), especially in patients over 40 years of age and those with a body mass index  $<30$  kg/m<sup>2</sup>.

**Conclusion:** This report shows that respiratory restrictive abnormalities are prevalent in hypothyroidism and may be reversible after treatment

with levothyroxin.

**Key Words:** Hypothyroidism, Pulmonary function, Levothyroxine

## Introduction

Many patients with hypothyroidism complain of fatigue and exercise intolerance. These subjective sensations could arise from limited pulmonary reserve, limited cardiac reserve, decreased muscle strength or increased ease of muscle fatigue.<sup>1</sup> Some forms of respiratory abnormalities such as sleep apnea can be seen in hypothyroid patients,<sup>2</sup> but data about probable subclinical changes in their the respiratory systems is insufficient. This study was designed to determine the probable abnormalities in pulmonary function tests of hypothyroid patients and to evaluate the effectiveness of early thyroxin treatment in hypothyroid patients with pulmonary function abnormalities

## Materials and Methods

In this Quazi-experimental study, all patients with hypothyroidism, diagnosed for the first time entered the study.

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Patients were defined as hypothyroid when  $ft_3$  was below 1.6 pg/mL,  $ft_4$  below <0.9 ng/dL and TSH levels above 20 mIU/L. All patients with a history of smoking, pulmonary disorders or recent abdominal or chest surgery were excluded from the study.

All thyroid function tests were performed in one laboratory center. Free  $T_4$  and free  $T_3$  were measured by Radioimmunoassay (RIA) and Immunotech kits. We measured TSH by Immunoradiometricassay (IRMA). Spirometry was performed in all subjects using ATS and ERS standard methods (in Vali-Asr Hospital Zanjan, I.R. Iran) at the beginning of the study. All spirometries were repeated three or more times for each patients to get the best result.

Levothyroxin tablets (1.7  $\mu$ g/kg) were prescribed for all patients by an endocrinologist. Thyroid function tests were repeated after 6 weeks and the levothyroxin dosage was adjusted to normalize TSH levels. After three months of thyroid hormones normalization spirometry was repeated at the same center, using the same methods.

The results were analysed by paired t and chi-square tests.

## Results

This study was conducted on 30 patients (24 females and 6 males). The patients' age ranged between 21 and 61 years, mean age being  $37.5 \pm 12$ . There were not any significant differences between two sexes for their ages ( $36.9 \pm 12$  years in women versus  $37.5 \pm 12$  years in men).

The mean value for TSH levels was  $55.9 \pm 11.7$  mIU/L before treatment and reached  $2.2 \pm 1.2$  mIU/L at the end of the study. Mean  $ft_4$  levels changed from  $0.7 \pm 0.3$   $\mu$ g/dL before treatment to  $1.4 \pm 0.5$   $\mu$ g/dL after treatment with levothyroxin.

There were no significant changes in the BMI of patients after treatment ( $27.5 \pm 5.2$  kg/m<sup>2</sup> before versus  $27.2 \pm 5.2$  kg/m<sup>2</sup> after treatment).

The results of the first spirometry were normal in 4 patients (13%). Mild restrictive abnormality was found in 16 patients (53%) and moderate restrictions were detected in the remaining 10 patients (34%). After treatment with levothyroxin 12 patients (40%) was normal, 14 patients (47%) had mild and 4 patients (13%) showed moderate restrictive abnormalities in their spirometry (Table 1).

**Table 1. Results of pulmonary function tests before and after treatment in hypothyroid patients**

	before		after	
	n	%	n	%
Normal PFT	4	13	12	40
Mild restriction	16	53	14	47
Moderate restriction	10	34	4	13

No forms of obstructive pulmonary diseases were seen in our study. From patients with mild restrictive abnormalities, 7 changed to normal and one of them progressed to moderate restriction after treatment with levothyroxin. Of those who had moderate restrictive abnormalities, only one patient returned to normal and 6 of them changed to mild forms of restrictive pulmonary diseases.

There were significant increases in FEV1, FVC and FEF25-75% after treatment with levothyroxin ( $p < 0.05$ ), but the changes in FEV1/FVC were not statistically significant.

The mean increase in FEV1 was  $0.21 \pm 0.38$  lit, FVC  $0.21 \pm 0.42$  lit and FEF25-75%  $33 \pm 0.7$  Lit (Table 2). The results demonstrated that changes in the FEV1 and FEF25-75% were significant only in females and in those with BMI <30 kg/m<sup>2</sup> and above 40 years.

**Table 2. Mean rise in FEV1, FVC and FEV1/FVC after treatment with levothyroxin in hypothyroid patients**

Spirometric parameters	Mean	SD
FEV1 (Lit)	0.216*	0.387
FVC (Lit)	0.218*	0.429
FEV1/FVC ratio	1.29	7.28

SD: standard deviation; Lit: liter

\*  $p < 0.01$  compared to before treatment

## Discussion

This study showed that most patients with hypothyroidism have some degrees of restrictive abnormalities in their respiratory systems that are reversible in most cases, especially in females above 40 and in those with BMI  $< 30$  kg/m<sup>2</sup>.

Clinical symptoms of the respiratory system in most hypothyroid patients have been reported to be limited to sleep apnea and some nasal and laryngeal mucus edema.<sup>3</sup> Dyspnea, as a subjective sensation, is prevalent in hypothyroidism,<sup>4</sup> seems to be secondary to limited pulmonary reserve or limited cardiac reserve. True objective dyspnea is not prevalent in hypothyroidism and can be due to myocardial dysfunction or pericardial effusion.<sup>5</sup> Both obese and non-obese hypothyroid patients may develop diaphragmatic muscle weakness that can range from mild impairment, which limits exercise tolerance to severe dysfunction, with marked resting dyspnea and chronic hypercarbia.<sup>6</sup> Although lung function is not seriously impaired in the majority of patients with hypothyroidism hypoventilation and even respiratory failure have been reported.<sup>7</sup> The most consistent finding in both obese and non obese hypothyroid patients is that some have a markedly blunted ventilatory response to hypoxia,<sup>8</sup> which improves significantly, and often within weeks

of initiation of thyroid replacement. Hypercarbic ventilatory response is also blunted in some, but not all, patients with hypothyroidism.<sup>9</sup> Analysis of changes in pulmonary function is complicated by an increased frequency of obesity in hypothyroid patients. Lung volumes have been reported normal or mildly decreased in mixed populations of obese and non obese hypothyroid patients.<sup>10</sup> In one case series<sup>11</sup> a subset of hypothyroid non obese patients had normal lung volumes and arterial blood gases, however the diffusion capacities for carbon monoxide were significantly reduced at baseline and improved to near normal after therapy. In the same study moderate pulmonary restriction was found in the hypothyroid, obese patients that normalized with weight loss. Several older studies of patients with hypothyroidism have shown increased capillary wall thickness in the skin; however, no morphologic studies of lung capillaries have been published. Freedman and his colleagues<sup>10</sup> in 1987 studied 9 patients including 6 thyrotoxic and 3 hypothyroid patients. In this study some increases in lung volumes were reported in 50% of thyrotoxic patients but there were no significant changes in lung volumes of hypothyroid patients after treatment. The patient number in this study was too limited. Harrison<sup>12</sup> studied the airway responses of hypothyroid and hyperthyroid patients to salbutamol before and after treatment. The results showed that changes in FEV1 and tidal volume were not statistically significant in hypothyroid patients. They reported more sensitive sites to salbutamol (AUC) in hyperthyroid patients and a reversal relation between thyroid hormones and responses to salbutamol that can be due to elevated  $\beta$ -adrenergic receptors in hypothyroid patients. Peltari<sup>5</sup> in 1994 in a case control study on 26 hypothyroid patients showed nocturnal respiratory problems in 50% of hy-

pothyroid patients versus 29% of normal people. They reported severe obstruction of upper respiratory system and sleep apnea in 7.7% of the patients and 1.5% of normal subjects respectively. These problems were found with a higher prevalence in men and in the more obese patients. Mirsadraei in 1994 studied 17 patients with hypothyroidism and reported some improvement in FEV1, FVC and FEF25-75% after one month of treatment with levothyroxin. Obstructive pulmonary dysfunctions were found in 17% of their patients. We did not find any obstructive pulmonary abnormalities in our study. This difference can be due to our criteria for patient selection and the excluding of all patients with a history of pulmonary disease.

In this study, the changes in the pulmonary function tests after treatment were significant

only in females. This can be due to limited numbers of males in our study. Also significant changes in pulmonary function tests were seen in the patients with BMI less than 30 kg/m<sup>2</sup>. The additive effects of obesity on spirometric parameters can be the cause of this result. Obese patients have some restrictive forms of respiratory dysfunctions due to increased thickness of chest wall.

The results of this study showed that hypothyroidism could cause restrictive changes in respiratory system that are reversible after treatment with levothyroxin. These changes are more significant in females of older ages. Although these changes are not significant clinically, they can cause problems in patients with other pulmonary or chest wall disorders.

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