



LUNG FUNCTION IN HYPOTHYROID SUBJECTS BEFORE AND AFTER TREATMENT WITH LEVOTHYROXINE

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ABSTRACT Hypothyroidism is a syndrome characterized by clinical and biochemical manifestations of thyroid hormone deficiency in the target tissues of thyroid hormones (1). Studies conducted have shown the negative effect of hypothyroidism on respiratory system. As there is an increased prevalence of hypothyroidism in India, this study is undertaken to know the pulmonary function in hypothyroid subjects before and after treatment with levothyroxine. A non-randomized trial before and after comparison studies which included 40 patients with elevated TSH. Pulmonary function test was recorded using Medical Electronics Construction (M.E.C) body plethysmography, at the time of diagnosis and again when the TSH value returned to normal range. It was found that the PFT parameters significantly improved on treatment compared to before treatment. Correlation of pre-treatment TSH values with the PFT parameters before treatment showed negative correlation of TSH to the PFT parameters before treatment.

The above study thus concludes that hypothyroidism affects the lung functions significantly. Since these effects are reversible on treatment and regular follow up, more emphasis is necessary to assess the lung functions in all the patients of hypothyroidism

KEYWORDS : pulmonary function test, hypothyroidism, TSH, body plethysmography

INTRODUCTION

Hypothyroidism is a syndrome characterized by clinical and biochemical manifestations of thyroid hormone deficiency in the target tissues of thyroid hormones⁽¹⁾. Thyroid hormones being regulated by TSH, play a critical role in cell differentiation during foetal development and help maintain thermogenic and metabolic homeostasis in the adult⁽²⁾.

Prevalence of hypothyroidism in adult population in India is estimated to be 3.9%, with higher prevalence in women at 11.7% compared to men⁽³⁾. Studies conducted have shown the negative effect of hypothyroidism on respiratory system. Hypothyroidism is associated with skeletal muscle myopathy⁽⁴⁾, increased incidence of pleural effusions⁽⁵⁾, sleep apnoea episodes even with normal lung function⁽⁶⁾, produce depression of hypoxic ventilator drive⁽⁷⁾, affects respiratory muscle strength which is linearly related to thyroid hormone levels⁽⁸⁾, cause restrictive changes in respiratory system⁽⁹⁾, and diaphragmatic dysfunction ranging from mild weakness predominantly affecting exercise tolerance to very severe compromise mimicking diaphragmatic paralysis⁽¹⁰⁾. All these effects are reversible with treatment of hypothyroidism⁽⁶⁻¹⁰⁾. Studies documented so far have shown that hypothyroidism cause decrease in lung functions which is reversible on treatment^(8,9).

As there is an increased prevalence of hypothyroidism in India, this study is undertaken to know the pulmonary function in hypothyroid subjects before and after treatment with levothyroxine

OBJECTIVES OF THE STUDY

1. To record the Pulmonary Function Test in hypothyroid subjects with increased TSH.
2. To record the Pulmonary Function Test after normalization of TSH with Levothyroxine.
3. To compare the results of Pulmonary Function Tests in hypothyroid subjects with increased TSH before and after normalization of TSH with treatment.

METHODOLOGY

The intended study is a non-randomized trial before and after comparison studies which included 40 patients with elevated TSH. Institutional ethical committee clearance was obtained before starting the study. Subjects were selected from Victoria hospital attending medicine OPD and diagnosed as hypothyroidism for 1st time and also following later at 6 to 8 weeks as part of treatment review with levothyroxine when TSH values returned to normal.

Subjects were selected according to inclusion and exclusion criteria. Subjects were selected in the age group of 15 – 50 yrs with elevated

TSH. Smokers and tobacco chewers, Subjects with chronic respiratory disease, subjects with signs and symptoms of respiratory infections at the time of test, history of cardiovascular illness and hypertension, any other metabolic disorder except for hypothyroidism, pregnant women, subjects with musculo skeletal chest deformities, Subjects taking drugs which will alter the thyroid hormonal profile were excluded from the study.

Procedure was explained and a written informed consent obtained. Pulmonary function test was recorded using Medical Electronics Construction (M.E.C) Body Plethysmography, at the time of diagnosis and again when the TSH value returned to normal range. PFT measurements included Forced vital capacity (FVC), Forced expiratory volume in 1sec (FEV₁), FEV₁/FVC, The average mid maximal expiratory flow (FEF₂₅₋₇₅), Peak expiratory flow rate (PEFR). Three recordings were taken at an interval of 15 minutes apart and the best value was considered.

RESULTS AND ANALYSIS

Study design: A non-randomized trial before and after comparison study consisting of 40 subjects with elevated TSH was undertaken to study the pulmonary function test before and after treatment with Levothyroxine

Statistical Methods:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

+ Suggestive significance (P value: 0.05 < P < 0.10)

* Moderately significant (P value: 0.01 < P < 0.05) ** Strongly significant (P value: P < 0.01)

Table 1: Distribution of subjects in accordance with TSH value before treatment

TSH (mIU/l)	No. of subjects	%
<10	2	5.0
10-15	9	22.5
>15	29	72.5
Total	40	100.0

Table 2: An evaluation of TSH (mIU/l) in study group before and after treatment

	Before treatment	After treatment	P value
TSH (mIU/l)	27.43±22.45	2.11±0.85	<0.001**

Table 2 shows the TSH value in study group before and after treatment with levothyroxine. As shown in the table, after treatment the TSH has reduced to mean of 2.11 ± 0.85 mIU/l

Table 3: Comparison of PFT parameters of study group before and after treatment

PFT parameters	Before treatment	After treatment	Difference	P value
FEV1 (l)	2.10±0.41	2.44±0.40	0.344	<0.001**
FVC (l)	2.59±0.55	2.93±0.50	0.334	<0.001**
FEV1/FVC %	80.69±5.17	83.61±4.36	2.921	0.006**
PEFR (l/s)	4.93±1.08	5.42±1.00	0.481	<0.001**
FEF25-75(l/s)	2.51±0.45	2.85±0.40	0.337	<0.001**

Table 3 shows the comparison of PFT parameters of study group with elevated TSH before treatment with PFT parameters after normalisation of TSH following treatment. As shown in the table, FEV1, FVC, FEV1/FVC, PEFR, FEF25-75 are increased after treatment which is statistically significant.

Table 4: Correlation of TSH value with PFT parameters in study group before treatment using Pearson's correlation.

Pair	Before treatment	
	r value	p value
TSH (mIU/l) vs FEV1 (l)	-0.314	0.048*
TSH (mIU/l) vs FVC (l)	-0.190	0.242
TSH (mIU/l) vs FEV1/FVC %	-0.309	0.052+
TSH (mIU/l) vs PEFR (l/s)	-0.447	0.004**
TSH (mIU/l) vs FEF25-75 (l/s)	-0.224	0.164

Table 4 shows correlation of TSH values with the PFT parameters in subjects with elevated TSH before treatment. As shown in the table, TSH is negatively correlated to the PFT parameters with FEV1 showing moderate significance ($P=0.048$), FEV1/FVC showing suggestive significance ($P=0.052$) and PEFR showing strong significance ($P=0.004$).

DISCUSSION

Hypothyroidism is a syndrome characterized by clinical and biochemical manifestations of thyroid hormone deficiency in the target tissues of thyroid hormones⁽¹⁾. Hypothyroidism affects all the organ systems. Respiratory system like other body systems and organs is affected by hypothyroidism. Many studies documented so far have shown that hypothyroidism cause decrease in lung functions which is reversible on treatment^(9,10).

As per aims and objectives of this study, effort has been made to study the pulmonary function tests in hypothyroid subjects before and after treatment with levothyroxine. The parameters of Pulmonary function tests (FEV₁, FVC, FEV₁/FVC, PEFR, FEF₂₅₋₇₅) were performed before treatment in 40 subjects with elevated TSH and performed again after treatment with levothyroxine. Correlation of TSH values with the PFT parameters was done. The results were tabulated and statistically analyzed.

In the current study, only elevated TSH is taken, T3 and T4 is not taken because a normal TSH level excludes primary hypothyroidism and T3 is normal in 25% of patients. TSH is the most sensitive and is considered the single best screening test for hypothyroidism and the dose of Levothyroxine is adjusted on the basis of TSH levels⁽²⁾.

Table 3 shows the comparison of FEV1, FVC, FEV1/FVC, FEF25-75 before treatment with FEV1, FVC, FEV1/FVC, FEF25-75 after treatment. As shown in the table, above indicated parameters have increased after treatment with statistical significance of $P<0.001$ except FEV1/FVC which increased with $P<0.01$.

The study is in accordance with the study done by Sharifi F et al⁽⁹⁾ to determine the effect of levothyroxine on pulmonary function of patients with hypothyroidism who found out that there were significant increase in FEV1, FVC, FEF25-75, after treatment compared to before treatment except FEV1/FVC which did not show significant difference. The study is also in accordance with the studies done by Saifakas NM et al⁽⁹⁾ and Bassi R et al⁽²⁹⁾ who also found similar results.

Hypothyroidism produces depression of hypoxic ventilatory drive that is responsive to replacement therapy. This alteration in ventilator control may contribute to the hypoventilation seen in hypothyroidism⁽⁷⁾. Hypothyroidism cause respiratory muscle

weakness which is proportional to the degree of thyroid dysfunction⁽⁹⁾.

It also causes diaphragmatic dysfunction ranging from mild weakness predominantly affecting exercise tolerance to very severe compromise mimicking diaphragmatic paralysis⁽¹⁰⁾. These may be the reasons for the improvement of FEV1, FVC, FEV1/FVC, FEF25-75 after treatment seen in the current study.

Table 3 shows comparison of mean peak expiratory flow rate of study group before and after treatment. As shown, there is a significant increase in peak expiratory flow rate after treatment ($P<0.001$ **).

This is in agreement with the study done by Bassi R et al to know the effect of thyroid hormone replacement on Respiratory function tests in hypothyroid women who found out that there was significant increase in PEF ($P<0.001$ ** in treated hypothyroid group compared to non-treated group⁽¹¹⁾.

Peak expiratory flow is the maximum flow achieved during an expiration delivered with maximal force starting from the level of maximal lung inflation. PEF may be impaired by obstruction in intrathoracic airways,

Conditions which limit chest expansion or which affect respiratory muscle function⁽¹²⁾. Both inspiratory and expiratory respiratory muscles are weakened in hypothyroidism in a direct linear relationship to the thyroid hormone level and it is reversible with thyroxine therapy⁽⁹⁾. Furthermore, thyroid deficient muscles have impaired free fatty acid utilisation, which enhances their glycogen consumption, thereby reducing skeletal muscle endurance⁽¹⁵⁾. All these changes may be responsible for increase in PEFR after treatment which is seen in the current study.

Table 4 shows correlation of TSH values with the PFT parameters in subjects with elevated TSH before treatment. As shown in the table, TSH is negatively correlated to the PFT parameters with FEV1 showing moderate significance ($P<0.05$), FEV1/FVC showing suggestive significance ($0.01<P<0.05$) and PEFR showing strong significance ($P<0.05$). The decreased PFT parameters seen in this study and improvement with treatment could be attributed to the elevated TSH levels.

The above study thus concludes that hypothyroidism affects the lung functions significantly. Since these effects are reversible on treatment and regular follow up, more emphasis is necessary to assess the lung functions in all the patients of hypothyroidism. The study was conducted on a limited sample and comparison with after treatment was done within short span of weeks to months on reaching the normal range of TSH.

Large scale study over longer duration of reaching the normal range of TSH is required to observe the changes with time.

CONCLUSION

The results of the study showed significant increase in FVC, FEV₁, PEFR, FEV₁/FVC, FEF₂₅₋₇₅ after treatment with levothyroxine when compared to before treatment in hypothyroid subjects.

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