Research Article

Dynamics of airway functions in untreated hypothyroidism

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ABSTRACT

Background: Hypothyroidism is a hormonal disorder, more prevalent in females, affects respiratory systems at early stage. **Objectives:** Present study was carried out to observe the expiratory and inspiratory dynamics of airway functions in recently diagnosed hypothyroid females without medication and its comparison with hypothyroid females with hormonal therapy and euthyroid females. Parameters studied were forced vital capacity (FVC), forced expiratory volume (FEV1), FEV1%, forced inspiratory vital capacity (FIVC), FIV1, FIV1%, forced expiratory flow (FEF25-75%), FEF0.2-1.2%, FEF25%, FEF50%, FEF75%, peak expiratory flow (PEF), and peak inspiratory flow. **Materials and Methods:** Twenty-one ($n = 21$) recently diagnosed hypothyroid women without medication (Group-1) and 19 hypothyroid women taking medication for the last 6-8 months (Group-2) were studied. Hypothyroidism was diagnosed on the basis of serum thyroid-stimulating hormone level (<5IU). Total 22 apparently euthyroid subjects (Group-3) were studied as control. Data were analyzed by one-way ANOVA with *post hoc* Tukey honestly significant difference and alpha error was set at 5% level. **Results:** The mean values for FVC, FEV1, FIVC, and FIV1 were less in Group-1 in compare to Group-2 and 3 and the differences were statistically significant ($P < 0.05$). Large airway functions as FEF25-75%, FEF25%, and PEF also found the same decrease as above. Small airway functions as FEF50%, FEF75% may preserve except FEF 0.2-1.2. **Conclusion:** Untreated hypothyroidism extremely alters the respiratory dynamics and can be reversed by hormonal therapy. Large airway functions get diminished, but small airway functions remain unaltered. Study in large population with more disease duration will help to determine the severity of disease. Lung functions can be used as a tool to assess the effectiveness of treatment of hypothyroidism.

KEY WORDS: Forced Vital Capacity; Forced Expiratory Volume 1; Peak Expiratory Flow; Thyroid-stimulating Hormone; Hypothyroid; Euthyroid

INTRODUCTION

Hypothyroidism is a common phenomenon and reported the incidence of hypothyroidism is 5 times greater in women than men.[1] Respiratory system like other body systems is affected by hypothyroidism. The spectrum of diseases involvement can range from mild-to-severe dyspnea to respiratory failure.[2,3] Prevalent subjective complain of exercise intolerance, dyspnea, and fatigue in hypothyroid may arise from limited pulmonary reserve, limited cardiac reserve, decreased muscle strength, or increased muscle fatigue.[4] Majority of systemic effects are present due to reduction in metabolic activity and deposition of glycosaminoglycans in interstitial tissues.[5] Hypothyroidism may depress the central ventilator control and affects respiratory muscle strength which is linearly related to the thyroid hormone levels.[6,7]

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In hypothyroidism, respiratory muscle weakness is present in both inspiratory and expiratory muscles both affects pulmonary functions accordingly.[7-9] Researchers reported

that pulmonary functions may decrease in hypothyroid females and after thyroid hormone replacement these values may increase significantly,[10-13] but studies are limited to the expiratory respiratory functions only. Moreover, the effect of hormone deficiency on expiratory and inspiratory flow rates was not found place in literature. The objectives were to evaluate the expiratory and inspiratory respiratory functions in hypothyroid females diagnosed at least before 6 months and their comparison with hypothyroids with medication and euthyroid group.

MATERIALS AND METHODS

After ethical clearance (SVIEC/ON/MEDI/RP/14133), the present study was conducted in the Department of Physiology, Dhiraj General Hospital, Vadodara. In a cross-sectional study, total 62 females aged between 30 and 50 years were studied in three groups.

- Recently diagnosed hypothyroid women without medication (serum thyroid-stimulating hormone [TSH] level >5 μIU/ml) were studied as Group-1 (n = 21).
- Hypothyroid women (based on history) taking medication for the last 6 months were studied as Group-2 (n = 19).
- Euthyroid subjects as Group-3 (n = 22).

Data were analyzed by one-way ANOVA with *post- hoc* Turkey honestly significant difference. After informed consent and all details fulfilled, inclusion and exclusion criteria's were filled in the pro forma. Demographic details and detailed history including clinical, personal, and drug intake was taken. Spirometry was done for all subjects on a PC-based Spirometer SpiroWin + (genesis medical, made in India), and as per the American Thoracic Society guidelines, every female was investigated for pulmonary function test (PFT) at least thrice. Before the actual test for respiratory parameters, instrumental training was given to all participants. All participants were examined for instantaneous flow and expiratory and inspiratory flow rates both at large and small lung volumes. Subjects with unsatisfactory training and recording with the instrument were excluded.

RESULTS

Table 1 summarizes the demographic profile of all three groups. The mean values for weight showed highly significant differences between all groups (ANOVA $P < 0.05$). Difference between 1 and 2 Group is highly significant, while Group 2 and 3 showed insignificant difference. The mean values for age and height did not show any significant differences between groups.

Expiratory and inspiratory respiratory variables in all three groups are shown in Table 2. All parameters showed a highly significant decrease in Group-1 compared to Group-2 and Group-3. The difference in forced vital capacity (FVC) and forced expiratory volume (FEV1) was highly significant between Group-1 and Group-2 and between Group-1 and Group-3 ($P < 0.001$). Difference for FEV1% and forced inspiratory vital (FIV) was not significant.

The expiratory and inspiratory flow rates are shown in Table 3. Large airway functions forced expiratory flow (FEF25%), FEF25-75%, and peak expiratory flow rate (PEFR) showed a significant difference in all three groups (ANOVA $P < 0.05$) and also found less in untreated hypothyroids compared to treated hypothyroids and euthyroid controls. Small airway function FEF50% and FEF75% values showed significant difference in all the groups except FEF0.2-1.2. Peak inspiratory flow rate showed highly significant difference in all three groups (ANOVA $P < 0.05$) and found to be less in Group-1 when compared with Group-2 and 3.

DISCUSSION

In our study, we found that the values for FVC and FEV1 were significantly lower in recently diagnosed hypothyroid group (Group-1) as compared to treated hypothyroid group (Group-2) and euthyroid group (Group-3), but the same parameters were not significantly decreased between Group-2 and Group-3. Large airway functions get diminished in untreated hypothyroidism, shown by FEF25-75%, FEF25%, and PEFR. Small airway functions were not affected much as shown by unaltered FEF50%, FEF75%, and FEF 0.2-1.2. Inspiratory functions also showed decrease as depicted by the values of FIV capacity (FIVC), FIV1 while FIV1% remains unaltered.

Our findings for FVC, FEV1, FIVC, and FIV1 are in concordance with various previous researchers as Koral *et al*. and Cakmak *et al*.[10,12] Studies reported the effects of lack of thyroid functions on various body system including nervous, respiratory, and cardiovascular. Thyroid hormone is one of the hormone affects respiration, centrally as well as locally and respiratory functions can be affected by deficiency as well as excess secretion of thyroid hormone.[14-16] Hypothyroidism is associated with diminished ventilatory drive for both hypoxia and hypercapnia.[17,18] Supporting studies shown no change between the treated hypothyroid group and euthyroid group, explain that hormonal therapy can reverse the respiratory changes.[7,19,20] In a study on six hypothyroid patients, maximal expiratory and inspiratory pressures were reduced and improved with hormone treatment. Respiratory muscle strength is reduced in patients with hypothyroidism, although improves with treatment, is caused by both myopathy and neuropathy.[21] Impaired respiratory functions and muscle weakness are frequently observed in untreated hypothyroidism, more significantly in females of older age, although reversible after treatment with levothyroxine.[10-13] Respiratory infections are more common in hypothyroid patients than healthy people, which might be the cause of

Table 1: Demographic profile of all three groups involved in study

Variables	Group-1	Group-2	Group-3	*P* (ANOVA)
Age (years) Mean±SD	35.03±2.45	37.32±2.5	34.7±2.65	*P*>0.05, NS
Height (cm) Mean±SD	156±5.4	156±6.5	153±7.1	*P*>0.05, NS
Weight (kg) Mean±SD	59±7.33	48.29±6.52	46.74±6.5	*P*<0.05, S

S: Significant, NS: Non-significant. SD: Standard deviation

Table 2: Expiratory and inspiratory respiratory volume and capacities in all three groups

Variables	Group-1	Group-2	Group-3	*P* (ANOVA)
FVC (Ltr) Mean±SD	1.662±0.36	2.123±0.31	2.221±0.37	*P*<0.05, S
FEV1 (Ltr) Mean±SD	1.311±0.35	1.791±0.31	1.860±0.35	*P*<0.05, S
FEV1 (%) Mean±SD	78.62±8.29	80.33±8.69	83.14±6.89	*P*>0.05, NS
FIVC (Ltr) Mean±SD	1.491±0.41	1.954±0.345	2.231±0.41	*P*>0.05, S
FIV1 (Ltrs) Mean±SD	1.383±0.64	1.643±0.72	1.801±0.74	*P*>0.05, S
FIV1 (%) Mean±SD	77.85±10.12	74.82±11.32	72.24±12.29	*P*>0.05, NS

S: Significant, NS: Non-significant. SD: Standard deviation, FVC: Forced vital capacity, FEV1: Forced expiratory volume, FIVC: Forced inspiratory vital capacity, FIV: Forced inspiratory vital

Table 3: Expiratory and inspiratory flow rates and instantaneous flow rates in all three groups

Variables	Group-1	Group-2	Group-3	*P* (ANOVA)
FEF 0.2-1.2 Ltr Mean±SD	2.005±0.73	2.595±1.03	2.684±0.90	*P*<0.05, S
FEF 25-75% Mean±SD	2.061±0.57	2.428±0.81	2.503±0.68	*P*<0.05, S
FEF 25% Mean±SD	2.098±0.88	2.431±1.12	2.546±1.02	*P*<0.05, S
FEF 50% Mean±SD	2.229±0.70	2.379±0.91	2.234±0.80	*P*>0.05, NS
FEF75% Mean±SD	1.413±0.37	1.442±0.46	1.341±0.46	*P*>0.05, NS
PEFR (Ltr/sec) Mean±SD	2.031±1.09	2.591±0.98	2.673±0.96	*P*<0.05, S
PIFR Mean±SD	2.150±0.846	2.264±0.58	2.212±0.51	*P*>0.05, S

FEF: Forced expiratory flow, SD: Standard deviation, PIFR: Peak inspiratory flow rate, PIFR: Peak expiratory flow rate

low PFT parameters.[21,22] Unchanged FEV1% is may be due to the proportionate decrease in both FVC and FEV1. The Group-2 showed improvement in respiratory functions as compared to Group-1, although no correlation was found between respiratory parameters and serum TSH level.

The author found during literature search that the findings of various studies for respiratory parameters studied are the same but the given explanations are different. Low level of thyroid hormones secondary to the negative feedback control of TSH may cause respiratory muscle weakness and decreased

contractile strength result in decreased values for FVC, FEV1, PEF, and other flow rates in untreated hypothyroid females as compared to treated hypothyroids and healthy controls. Researchers explained that respiratory center depression, interference in neuromuscular transmission, and poor nerve conduction in hypothyroidism may cause alveolar hypoventilation which may affect central ventilatory control.[7,23] Moreover, fibrosis and thickening of the alveolar wall secondary to mucopolysaccharide deposition may increase the work of breathing. All these changes may reduce ventilatory lung functions.[24] Skeletal muscles of hypothyroid person have more glycogen consumption secondary to impaired free fatty acid utilization, thereby reducing skeletal muscle endurance. In addition reduced surfactant phospholipid, phosphatidylglycerol and phosphatidic acid along with increase in surface active lipids phosphatidylserine and phosphatidylinositol in alveolar epithelium may decrease alveolar septation and reduce lung compliance and surfactant adsorption.[25]

Swami *et al*. reported study on respiratory muscle strength in hypothyroidism found that there was a decreased level of FVC, FEV1, and PEFR were significantly lower in hypothyroid subjects, but flow rates and instantaneous flows were not studied.[26] Frequently reported findings include decreased VC, FEV1, FVC, and TLC, which some authors have explained as occurring through alveolar hypoventilation and inspiratory muscle power weakness.[27,28] One of the major inspiratory muscles that are involved in hypothyroidism is the diaphragm, and its weakness is associated with hypoventilation.[29]

Present study studied the PFT extensively and elaborated the discussion to each of the possible facets with supporting evidence. Indian literature is lacking of such studies. This study is limited for the number of participants. Author suggested more studies with inspiratory parameters with hormonal assessment and more number of subjects.

CONCLUSION

Hypothyroidism affects the pulmonary functions, expiratory and inspiratory both. Early hormone therapy can reverse the deterioration; thus, the fall is responsive to hormone replacement therapy. Spirometric studies in large population and long-term studies are required to generate evidence and will be used for evaluating the effectiveness of treatment of hypothyroidism.

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