Pulmonary function in hyperthyroidism by spirometry and the effects of antithyroid therapy

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Abstract

Hyperthyroidism is a common endocrine disorder; it affects the function of various body systems particularly respiratory system. However pulmonary function in hyperthyroidism and the effect of antithyroid medication is not thoroughly studied. Therefor this study aimed to evaluate pulmonary function in hyperthyroid patients by measuring spirometric parameters and to study the effect of antithyroid therapy on these parameters. The study was carried out in Al-Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC), Al-Faiha hospital, Basrah, Iraq. The study included 110 subjects, they classified into 3 groups: 1) recently diagnosed hyperthyroid group (n=20, male/female 8/12, age 20-64 year), 2) treated hyperthyroid groups (n=30, male/female 12/18, age 27-67 years) and 3) control group consist of age and sex matched euthyroid subjects (n=60, male/female 25/35, age 22-46 year). Assessment of pulmonary function and thyroid hormones were done to all participants. Age, gender distribution, BMI were comparable in all studied groups. A significantly lower FVC, FVC%, FEV1, FEV1%, PEF, PEF%, FEF25-75 and FEF25-75% were noticed in hyperthyroid groups compared with euthyroid group, these parameters are insignificantly more in treated than in recently diagnosed hyperthyroid group. A significantly more abnormal spirometry tests, mostly of restrictive pattern, were noticed in hyperthyroid groups compared with euthyroid group. It could be concluded that pulmonary function is adversely affected in hyperthyroidism and insignificantly improved by medical therapy.

Keywords: hyperthyroidism, pulmonary function, spirometry, Basrah, Iraq

Introduction

Pulmonary function is frequently affected by systemic diseases including thyroid gland disorders (1, 2, 3). Hyperthyroidism causes dyspnea, hyperventilation and increased pulmonary ventilation in response to hypoxia and hypercapnia (4). Dyspnea results from asthenia of respiratory muscles which can be reversed by antithyroid therapy (5), muscle weakness may be functional (6). Increased pulmonary ventilation is secondary to increased oxygen consumption, mitochondrial synthesis, and respiratory enzymes (7, 8). Hyperthyroidism is associated with increased ventilatory drive in response to hypoxemia and hypercapnia. Excessive increase in pulmonary ventilation during exercise in hyperthyroid patients results from overexpression of β adrenoreceptors (9). An association has been reported between hyperthyroidism and pulmonary hypertension (10). Moreover, pulmonary congestion due to congestive heart failure reduces lung compliance in hyperthyroid patients (11, 12). Studies about the effects of hyperthyroidism and antithyroid medication on spirometric

parameters in Iraq were limited, therefor this study aimed to evaluate pulmonary function in hyperthyroid patients by measuring spirometric parameters and to study the effect of antithyroid therapy on these parameters.

Subjects and methods

Subjects' selections

The study was carried out in Al-Faiha Teaching Hospital, Basrah, Iraq from January to July 2018. All patients in the study were referred from outpatient unit of Al-Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC) by endocrinologist, patients were randomly selected and recruited in the study. Subjects are classified into 3 age and sex matched groups:

1) Euthyroid group: it included 60 apparently healthy adult individuals who are relative of the patients attending the FDEMC, aged 22-64 years and male/female was 25/35, with normal serum TSH and free serum T4 (0.4-4.0 mIU/l, 9.0-25 pmol/l, respectively) (13).
2) Treated hyperthyroid group: it included 30 adult hyperthyroid patients on antithyroid medication, aged 27-67 years and male/female is 12/18.
3) Recently diagnosed hyperthyroid group: it included 20 adult patients, aged 20-64 years and male/female is 8/12, serum TSH < 0.4 mIU/l and serum FT4 level >25 pmol/l.

Thyroid hormones were measured by electrochemiuminescence immunoassay method (Roche's Cobas e411 analyzer; Hitachi High-Technologist Cooperation, Japan). All subjects with a history of smoking, respiratory diseases, or systemic illnesses affecting the pulmonary function are excluded from the study. The study protocol had been approved by the ethical committee in Basrah medical College, Basrah, Iraq. After explaining the aim of the study, a written agreement for enrolment in the study was taken from all participants.

Spirometry

Spirometry was done to all subjects by spirolab III MIR (Medical International Research, Italy) in order to measure forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC, peak expiratory flow rate (PEF), and forced expiratory flow in mid expiration (FEF 25-75). The test done in sitting position at the morning (8-12am), repeated several times, and the best result recorded for evaluation. The predicted values and percentages of spirometric parameters were calculated by the instrument depending on subject age, height, weight, sex, and ethnicity.

Statistical analyses

Continuous data were tabulated as mean ± SD, and assessed by one way analysis of variance, Post Hoc test followed by Bonferroni procedure. Categorial data tabulated as number (%) and Chi square (χ^2) test was used to compare between group's percentages, Fisher's exact test was used when the expected values in any of the cells of the table are below five. A significant difference is considered if $P< 0.05$.

Results

Data in Table 1 shows no significant difference in age, gender, height, weight, and body mass index (BMI) between the three studied groups. TSH is significantly more in euthyroid than in recently diagnosed hyperthyroid group (2.62±3.6 mU/L ver. 0.37±0.73 mU/L, P=0.006), while no significant difference between treated hyperthyroid and euthyroid or recently diagnosed hyperthyroid group (P>0.05). Serum fT4 is significantly more in recently diagnosed (4.09±2.34 µg/dl) and in treated hyperthyroid groups (2.32±1.66 µg/dl) compared with that in control group (1.06±0.17 µg/dl) (P<0.001). Moreover, it's significantly more in recently diagnosed than in treated hyperthyroid group (P<0.001).

Table 1. Demographic features and thyroid hormones level of participants (mean ± SD)

Parameter	Euthyroid group (1) n=60	Treated hyperthyroid group (2) n=30	Recently diagnosed hyperthyroid group (3) n=20	P value (χ^2 value)
Age (year)	41.9±8.8	41.4±10.8	42.7±11.0	[a]P=1.000 [b]P=1.000 [c]P=1.000
Gender Male/female	25 (41.7%) / 35 (58.3%)	12 (40%) / 18 (60%)	8(40%) / 12(60%)	[a]P=1.000 (0.023) [b]P=1.000 (0.017) [c]P=1.000 (0.000)
Height (cm)	163.0±8.4	162.1±8.6	163.1±8.2	[a]P=1.000 [b]P=1.000 [c]P=1.000
Weight (kg)	77.1±13.8	72.5±11.7	77.6±14.8	[a]P=0.384 [b]P=1.000 [c]P=0.514
BMI (kg/m^2)	29.0±4.9	27.7±4.4	29.5±4.7	[a]P=0.603 [b]P=1.000 [c]P=0.546
Serum TSH (mU/L)	2.62±3.6	1.27±1.48	0.37±0.73	[a]P=0.102 [b]P=0.006* [c]P=0.725
Serum fT4 (µg/dl)	1.06±0.17	2.32±1.66	4.09±2.34	[a]P<0.001* [b]P<0.001* [c]P<0.001*

Post Hoc test (Bonferroni correction) for age, height, weight, BMI, serum TSH, and serum freeT4. Chi square test for gender distribution: BMI= body mass index, TSH= thyroid-stimulating hormone, fT4= free thyroxine. [a]P, [b]P and [c]P, illustrates the differences between group 1and 2, 1 and 3, and 2and 3, respectively. P <0.05 is considered statistically significant.

The results in Table 2 show significantly higher pulse rate (PR), systolic blood pressure (SBP) and lower diastolic blood pressure (DBP) in recently diagnosed hyperthyroid group (91.5±15.3 beat/min, P=0.004 for PR, 128.4±13.5 mmHg, P=0.015 for SBP, 76.1±12.1 mmHg, P=0.029 for DBP) compared with euthyroid group (82.2±10.1beat/min for PR, 120.6±13.9 mmHg for SBP, 83.2±16.4 mmHg for DBP). While, PR, SBP, and DBP were not significantly different between euthyroid and treated hyperthyroid group (P=0.069 for PR, P=0.075 for SBP, P=0.340 for DBP), and between treated and recently diagnosed hyperthyroid group (P= 0.230 for PR, P=0.765 for SBP, P= 0.189 for DBP).

Table 2. Results of pulse rate and blood pressure of the participants (mean ± SD)

Parameter	Euthyroid group (1) n=60	Treated hyperthyroid group (2) n=30	Recently diagnosed hyperthyroid group (3) n=20	P-value
PR (beat/ min)	82.2±10.1	87.2±13.9	91.5±15.3	[a]P=0.069 [b]P=0.004* [c]P=0.230
SBP (mmHg)	120.6±13.9	127.2±16.5	128.4±13.5	[a]P=0.075 [b]P=0.015* [c]P=0.765
DBP (mmHg)	83.2±16.4	79.7±9.5	76.1±12.1	[a]P=0.340 [b]P=0.029* [c]P= 0.189

Post Hoc test (Bonferroni correction): PR= pulse rate, SBP= systolic blood pressure, DBP, diastolic blood pressure. [a]P, [b]P and [c]P, illustrates the differences between group 1and 2, 1 and 3, and 2and 3, respectively. P <0.05 is considered statistically significant.

Table 3 show significantly more FVC, FVC%, FEV1, FEV1%, PEF, PEF%, FEF, and FEF% in euthyroid group (3.06±0.68 L, 86.9±11.2 %, 2.59±10.61 L, 86.6±12.7 %, 5.69±1.32 L/sec, 80.1±13.3 %, 3.37±0.87 L/sec, and 88.9±19.8 %, respectively) compared with those in treated hyperthyroid group (2.45±0.50 L, P<0.001; 71.1±12.6 %, P<0.001; 2.12±.0.48 L, P<0.001; 72.9±14.0 %, P<0.001; 5.06±0.87 L/sec, P=0.039; 72.6±16.9 %, P=0.034; 2.91±0.61 L/sec, P=0.029 and 78.3±14.6 %, P=0.031) and in recently diagnosed hyperthyroid groups (2.44±0.81 L, P=0.001; 68.5±12.1 %, P<0.001; 1.99±.0.64 L, P<0.001; 67.4±14.1%, P<0.00; 4.86±0.76 L/sec, P=0.015; 69.0±16.0 %, P=0.009; 2.82±0.69 L/sec, P=0.023; 78.0±23.5 %, P=0.016, respectively). Although spirometric parameters were more in treated than in recently diagnosed hyperthyroid group, but the difference was not statistically significant. Moreover, no significant difference exists in FEV1/FVC between the three studied groups.

Table 3. Comparison of spirometric parameters between hyperthyroid and euthyroid groups (mean ±SD)

Parameter	Euthyroid group (1) n=60	Treated hyperthyroid group (2) n=30	Recently diagnosed hyperthyroid group (3) n=20	P-value
FVC (L)	3.06±0.68	2.45±0.50	2.44±0.81	[a]P<0.001* [b]P=0.001* [c]P=1.000
FVC %	86.9±11.2	71.1±12.6	68.5±12.1	[a]P<0.001* [b]P<0.001* [c]P=1.000
FEV1(L)	2.59±10.61	2.12±.0.48	1.99±.0.64	[a]P=0.001* [b]P<0.001* [c]P=1.000
FEV1 %	86.6±12.7	72.9±14.0	67.4±14.1	[a]P<0.001*

				[b]P<0.001*
				[c]P=0.465
FEV1/FVC	85.0±8.5	86.6±10.4	82.7±11.6	[a]P=1.000
				[b]P=1.000
				[c]P=0.471
PEF (L/sec)	5.69±1.32	5.06±0.87	4.86±±0.76	[a]P=0.039*
				[b]P=0.015*
				[c]P=1.000
PEF%	80.1±13.3	72.6±16.9	69.0±16.0	[a]P=0.034*
				[b]P=0.009*
				[c]P=1.000
FEF (25-75) (L/sec)	3.37±0.87	2.91±0.61	2.82±0.69	[a]P=0.029*
				[b]P=0.023*
				[c]P=1.000
FEF (25-75) %	88.9±19.8	78.3±14.6	78.0±23.5	[a]P=0.031*
				[b]P=0.016*
				[c]P=1.000

Post Hoc test (Bonferroni): FVC=forced vital capacity, FEV1=forced expiratory volume in one second, PEF= peak expiratory flow, $FEF_{(25-75\%)}$ = forced expiratory flow in mid expiration. [a]P, [b]P and [c]P, demonstrates the differences between group 1and 2, 1 and 3, and 2and 3, respectively. P <0.05 is considered statistically significant.

A significantly more percentage of normal spirometry has been reported in euthyroid group (75%) compared with treated (23.3%, P<0.001) and recently diagnosed hyperthyroid groups (10%, P<0.001). Although higher percentage of normal spirometry has been found in treated than in recently diagnosed hyperthyroid group, but the difference between the two groups was not significant (P=0.569) (Table 4).

Table 4. Pattern of spirometry in hyperthyroid and euthyroid groups

Diagnosis	Euthyroid group (1) n=60	Treated hyperthyroid group (2) n=30	Recently diagnosed hyperthyroid group (3) n=20	P-value
Normal spirometry	**45(75%)**	**7 (23.3%)**	**2 (10%)**	[a]P<0.001

Abnormal spirometry	**Restrictive**	13 (21.7%)	21 (70 %)	17 (85%)	[b]P<0.001 [c]P=0.569
	Obstructive	2 (3.3%)	1 (3.3%)	0 (0%)	
	Combined	0 (0%)	1 (3.3%)	1 (5%)	
	Total	**15 (25%)**	**23(76.6%)**	**18 (90%)**	

Fisher's exact test: [a]P, [b]P and [c]P, demonstrates the differences between group 1and 2, 1 and 3, and 2and 3, respectively. P <0.05 is considered statistically significant.

Discussion

The effect of hyperthyroidism and antithyroid medication on pulmonary function were not adequately studied. Thyroid hormones are important for pulmonary development and surfactant secretion (14). Thyroid disorders are associated with altered pulmonary ventilation due to anatomical location of thyroid gland and the metabolic effect of their hormones (15). Therefore, the current study was carried out to illustrate the effects of excess thyroid hormone secretion on spirometric parameters as compared with those in euthyroid subjects as well as to evaluate the effect of antithyroid medication on these parameters. No significant differences were observed in age, sex, height, weight and BMI among studied groups indicating that groups are well matched (Table 1). The significantly higher fT4 in recently diagnosed hyperthyroid patients compared with treated hypothyroid and euthyroid groups was reduced by antithyroid therapy (treated hypothyroid group) but its level still significantly more than that in euthyroid group. This may be attributed to inadequate dose or short duration of therapy or poor compliance of patients, the insignificantly different TSH level between recently diagnosed and treated hyperthyroid group support this explanation (Table 1).

The significantly more heart rate (P=0.004), and SBP (P=0.015) and less DBP (P=0.029) in recently diagnosed hyperthyroid groups compared with euthyroid groups is probably secondary to increase in metabolic activity and cardiac output as well as from enhancement of cardiac β adrenoreceptors (Table 2) (16).

In the current study, spirometric parameters in treated and recently diagnosed hyperthyroid groups are significantly decreased compared with euthyroid group (P<0.001; P=0.001 for FVC, P<0.001; P<0.001for FVC %, P=0.001; P<0.001for FEV1, P<0.001; P<0.001 for FEV1%, P=0.039; P=0.015 for PEF, P=0.034, P=0.09 for PEF%; P=0.029; P=0.023 for FEF and P=0.031; P=0.016 for FEF %), while no significant difference in FEV1/FVC among studied groups. Comparable results were reported by Siafakas et al. (1992) (17). A significant decrease in FVC% in hyperthyroid patients was observed by Ali (2016) [3]. While, Eltrawy et al. (2020) found a significant decrease in FEV1% and FEF25-75% (18).

The results in Table 4 shows that the abnormality in pulmonary function test in treated and recently diagnosed hyperthyroid patients was of restrictive type (70%, 85%, respectively). Kim et al. (19) found s significant association between reduced FVC in hyperthyroidism and level of antithyroid antibodies. Therefore, the restrictive pattern of spirometry in those patients may be attributed to autoimmunity. Moreover, an association between interstitial lung diseases and autoimmune thyroiditis has been found (20). Hyperthyroidism is associated with myopathic and neuropathic manifestation; the most common manifestation of muscular involvement is chronic thyrotoxic myopathy which may result from low muscle carnitine level (21, 22). Thyroid hormones increase the sensitivity of pulmonary vessels to catecholamine leading to pulmonary vasoconstriction and consequently pulmonary hypertension (23). The cardiovascular complications of hyperthyroidism like high cardiac output heart failure and pulmonary edema lead to reduced pulmonary compliance (24, 25). Therefor low spirometric parameters in hyperthyroid patients in this study may be attributed to low pulmonary compliance and weakness of respiratory muscle.

Although spirometric parameters are improved by antithyroid therapy but they are still not significantly different from those in recently diagnosed hyperthyroid group and significantly lower than that in euthyroid group (Table 3). These results are not in agreement with the results of Siafakas et al. (17), who found an improvement in FVC and FEV1 in hyperthyroid patients after three months of medical therapy. Arbak et al.

(26) reported an improvement in expiratory flow parameters of hyperthyroid patients treated with propylthiouracil. Mahajan et al. (27) mentioned that the reduced FVC and PEF in hyperthyroidism are reversed when euthyroid state is achieved by medical therapy.

Conclusion

Pulmonary function is adversely affected in hyperthyroidism and partially improved by medical therapy

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Ethical approval

The present study has been done after obtaining informed consent and approved by the College Research Ethics Committee of Medicine, The University of Basrah at its meeting No.1 on November 26, 2017.

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