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Evaluation of Respiratory Functions in Subclinical and Clinical Hypothyroidism

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Abstract

Aim: Subclinical hypothyroidism reflects the earliest stage of thyroid dysfunction with subjects having normal or decreased fT4, normal fT3 and decreased thyroid stimulating hormone levels. Thyroid hormones have effects on the respiratory system functions. It is well known that thyroid hormones have effects on the respiratory system functions however there are few studies concerning the effect of subclinical hypothyroidism on the respiratory system. We aimed to investigate the respiratory functions in patients diagnosed with subclinical and clinical hypothyroidism.

Material and Methods: A total of 61 patients with clinical (n=31) or subclinical (n=30) hypothyroidism and 27 healthy subjects as a control group were included in the present study. Respiratory functions were evaluated by simple spirometry. All respiratory parameters including FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF25-75, FEF25-75%, PEF, PEF% were assessed. Additionally, free triiodothyronine (FT3), free thyroxin (FT4) and thyroid stimulating hormone (TSH) levels were measured in all subjects.

Results: Patients in the clinical hypothyrodism, subclinical hypothyroidism and control groups were homogenous in terms of age and gender distribution. Body mass index (kg/m^2) was determined to be significantly higher in patients with clinical hypothyroidism when compared to control subjects ($p<0.05$). Spirometric evaluation of the respiratory function revealed significantly lower values for FVC (L; $p<0.05$), FVC (%; $p<0.05$), FEV1 (L; $p<0.05$) and FEV1 (%; $p<0.05$) in all hypothyroid patients regardless of the clinical type when compared to control subjects.

Conclusions: Respiratory function tests seem to be beneficial in the evaluation of respiratory functional state in hypothyroidism. We think that community screening with simple spirometry may be helpful for patients with risk of subclinical hypothyroidism.

Key Words: Subclinical Hypothyroidism; Clinical Hypothyroidism; Respiratory Functions.

Klinik Ve Subklinik Hipotiroidizimde Solunum Fonksiyonlarının Değerlendirilmesi

Özet

Amaç: Subklinik hipotiroidizm tiroid disfonksiyonlarının erken evresidir ve hastaların ft4 düzeyleri normal veya düşük, ft3 düzeyleri normal ve tiroid stimulan hormonu düzeyleri azalmıştır. Tiroid hormonlarının solunum sistemi fonksiyonları üzerinde etkileri vardır. Titoid hormonlarının solunum sistemi fonksiyonları üzerine olan etkisi iyi bilinirken, Subklinik hipotiroidinin solunum sistemin üzerindeki etkilerini araştıran çok az çalışma vardır. Biz klinik ve subklinik hipotiroidi tanısı almış hastalarda solunum fonksiyonlarını araştırmayı amaçladık.

Gereç ve Yöntemler: Çalışmamıza, 31 klinik ve 30 subklinik hipotiroidili olmak üzere toplam 61 hasta ve 27 sağlıklı birey kontrol grubu olarak alındı. Solunum fonksiyonları basit spirometrik testler ile ile değerlendirildi. Tüm solunum parametreleri, FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF25-75, FEF25-75%, PEF, PEF% değerlendirildi. Ayrıca, serbest triiodotironin (ST3) ve serbest tiroksin(ST4) ve tiroid stimule edici hormon (TSH) tüm bireylerde ölçüldü.

Bulgular: Klinik hipotroidili, subklinik hipotiroidili hastalar ve kontrol grubu yaş ve cinsiyet dağılımı açısından homojendi. BMI (kg/m^2) klinik hipotiroidili hastalarda kontrol grubu ile kıyaslandığında önemli düzeyde yüksekti ($p<0.05$). Solunum fonksiyonlarının değerlendirilmesinde FVC (L; $p<0.05$), FVC (%; $p<0.05$), FEV1 (L; $p<0.05$) and FEV1 (%; $p<0.05$) değerleri kontrol grubu ile karşılaştırıldığında, tüm hipotiroidili hastalarda klinik tipten bağımsız olarak önemli düzeyde düşüktü.

Sonuç: Solunum fonksiyon testleri, hipotiroidizmli hastaların solunum fonksiyon durumunun değerlendirilmesinde faydalıdır. Basit spirometre ile toplum taramasının subklinik hipotroidi riski taşıyan hastaların tespiti açısından faydalı olacağını düşünüyoruz.

Anahtar Kelimeler: Hipotiroidizm; Klinik Hipotiroidizm; Solunum Fonksiyonları.

INTRODUCTION

It is well known that respiratory functions are affected at clinical hypothyroidism. The ventilatory response to hypoxia was reported to be significantly lower in hypoxia and hypercapnia in

hypothyroidism (1,2). The main factors responsible for hypoxemia and retention of carbon dioxide in hypothyroidism are respiratory muscle weakness, reduction in lung volumes, disturbed ventilation perfusion balance and obesity. Lower levels of thyroid hormones are associated with respiratory problems during sleep, dyspnea at exercise, inspiratory muscle weakness and disturbed diaphragmatic function (3-5). Subclinical hypothyroidism is an asymptomatic condition characterized by increased serum concentrations for TSH accompanied with normal levels for serum fT3 and fT4 hormones. However, a few patients with a normal fT4 and elevated TSH can present with symptoms and signs of hypothyroidism (6,7). Female gender, advanced age, and high dietary intake were reported to increase the risk of development of subclinical hypothyroidism (6). In the literature there are number of studies concerning the effect of clinical hypothyroidism on respiratory system. However there is no study who evaluates comparative effect of subclinical and clinical hypothyroidism on respiratory system. In this study we evaluated the respiratory function in subclinical hypothyroidism as well as comparing the results with clinical hypothyroidism and healthy control groups. Our aim was to determine if respiratory function was effected in subclinical hypothyroidism by using simple spirometry.

MATERIAL AND METHODS

Patients with subclinical and clinical hypothyroidism and healthy individuals were enrolled in this cross-sectional case-control study. None of the participants had history of smoking, any respiratory illness or any other systemic pathology affecting the respiratory system. The patients did not suffer from goiter disturbing the respiratory function. The body mass indexes (BMI) of all of the participants were under 30 kg/m^2. Written informed consent was obtained from each subject after explaining the objectives and the protocol for the study. The study was approved by the institutional ethics committee.

Measurement of thyroid hormone levels (fT3, fT4 and TSH) were performed in patient and control groups. fT3, fT4 were determined by chemiluminescent competitive enzyme immunoassay method, TSH was determined by chemiluminescent immunometric assay method in same analyzer in the biochemical laboratory of our hospital. Normal levels for TSH, fT4, fT3 were considered to be 0.34-5.6 uIU/ml, 0.58-1.64 uIU/ml and 2.5-3.9 uIU/ml, respectively. Patients with TSH levels >5.6 uIU/ml, fT4 levels of 0.58-1.64 uIU/ml and fT3 levels of 2.5-3.9 uIU/ml were defined as the subclinical group, whereas patients in the clinical hypothyroidism group were selected from patients having TSH levels >5.6 uIU/ml, fT4 levels <0.58 uIU/ml and fT3 levels <2.5 uIU/ml.

Spirometric analysis was performed with KoKo Legend Portable Office Spirometer (Circle-Longmont, CO, Germany). All respiratory parameters including FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF25-75 were assessed.

Statistical analysis was performed using "NCSS 2007". Data were expressed as “mean±standard deviation (SD)” and/or percent (%). Comparison of categorical variables was performed using Chi-square test while students’ t-test and ANOVA tests were used for the numerical data. $p<0.05$ was considered statistically significant.

RESULTS

A total of 61 patients (mean age: 45.86±12.69 years; 85% females) with subclinical (n=30; mean age: 45.3±11.6 years; 86.7% females) or clinical (n=31; mean age: 46.45±13.6 years; 83.9% females) hypothyroidism and 25 healthy individuals as a control group (mean age: 40.81±11.9 years; 66.7% females) were enrolled in the study. Patients in the clinical hypothyroidism, subclinical hypothyroidism and control groups were homogenous in terms of age and gender distribution. BMI (kg/m^2) was determined to be significantly higher in patients with clinical hypothyroidism when compared to control subjects (Table 1).

Serum fT3, fT4 and TSH values and spirometric parameters of the groups were given at Table 2 and Table 3 respectively. Spirometric evaluation of the respiratory function revealed significantly

lower values for FVC, FVC (%), FEV1 and FEV1(%) in all hypothyroid patients regardless of the clinical type when compared to control subjects. There was no difference between clinical and subclinical hypothyroidism in terms of respiratory function. Regardless of the clinical type, control subjects and hypothyroid patients were determined to have similar scores for FEV1/FVC and FEF25-75(%) (Table 3).

Table 1. Demographic and antropometric measurements of the participants

	Subclinical hypothyroidism *n=30*	Clinical hypothyroidism *n=31*	Control group *n=27*	p value
Gender		n(%)		
Male	4 (13.3)	5 (16.1)	9 (33.3)	0.102
Female	26 (86.7)	26 (83.9)	18 (66.7)	
Age (years)	45.3±11.6	46.5±13.6	40.8±11.9	0.206
Height (cm)	162.2±5.8	162.4±5.5	163.5±9.2	0.740
Weight (kg)	70.2±9.1	76.9±15.0	70.4±12.5	0.062
BMI (kg/m²)	26.7±3.6	29.2±5.4	26.3±4.3	**0.038***

* p<0.05

Table 2. Thyroid function values of the participants.

	Subclinical hypothyroidism *n=30*	Clinical hypothyroidism *n=31*	Control group *n=27*
fT3(ng/mL)	2.68 ± 0.63	1.56 ± 0.7	3.17 ± 0.94
fT4(ng/mL)	1.04 ± 0.16	0.44 ± 0.21	1.23 ± 0.22
TSH(ulU/m)	12.18 ± 5.23	68.12 ± 56.45	1.50 ± 1.05

Table 3. Spirometry parameters of the participants.

	Subclinical hypothyroidism *n=30*	Clinical hypothyroidism *n=31*	Control group *n=27*	p value
FVC (L)	2.6±0.7	2.7±0.7	3.1±0.8	**0.027***
FVC (%)	83.7±14.6	83.7±16.6	92.7±10.9	**0.029***
FEV1 (L)	2.4±0.7	2.5±0.6	2.9±0.7	**0.018***
FEV1 (%)	92.1±16.3	88.0±16.5	98.2±12.3	**0.043***
FEV1/FVC	114.2±10.3	112.2±12.2	112.6±9.5	0.746
FEF25-75 (%)	97.5±24.8	90.7±28.4	105.4±16.0	0.072

* p<0.05

DISCUSSION

Respiratory problems during sleep, exercise dyspnea, impaired response to hypercapnia, reduction in inspiratory muscle strength and functional disorder of the diaphragm have been reported in patients with low thyroid hormone levels (8,9).

Although the influence of subclinical hypothyroidsm is well defined for many organ systems, its effects on respiratory system is still unclear (10-13). Therefore we aimed to assess the respiratory function of patients with subclinical hypothyroidism in comparison with clinical hypothyroidism and healthy subjects. In our study respiratory functions were measured by spirometry since this method is easier, more available and cheaper than other respiratory function tests. Subclinical hypothyroidism is a common phenomenon seen more often in women with increasing age. The prevalance in women is 6-8% and 3% in men (14). Accordingly in our study 85% of the patients were female.

Limitation in thorax movements, reduction in muscle tonus, reduction in respiratory muscle force and changes in central nervous system may affect lung volumes without disturbing FEV_1/FVC ratio thereby lead to restrictive pattern in pulmonary function test (PFT) (14,15). Accordingly in our study, the patients with clinical and subclinical hypothyroidism had significantly lower forced vital capacity (FVC), forced vital capacity in one second (FEV1) than control group where as normal FEV1/FVC ratio which show

that hypothyroidism is associated with restrictive pattern of respiratory abnormality.

Comparison of pulmonary function parameters in patients with subclinical and clinical hypothyroidism revealed no significant difference despite slightly raised scores obtained in the subclinical hypothyroidism, however pulmonoary fuction scores were lower than healthy subjects which was reaching statistical significance.

We acknowledge a number of limitations. We had a relatively small sample size and thus, we were likely underpowered for some of our assessments particularly in subgroup analyses.

Secondly the spirometry test used to measure the respiratory functions was very limited; we did no have a chance to measure TLC. However, we believe that our data represent an important addition to the literature based on the hypotheses that respiratory system is affected in subclinical hypothyroidism. We believe that the spirometry may have utility in subsequent subclinical hypothyroidism research, potentially as a surrogate outcome measure.

We found that suclinical hypothyroidism may result in restrictive pattern of respiratory anomaly. Spirometry is a reproducible, cheap, widely applicable and simple noninvasive method for the estimation of abnormalities in pulmonary function test in patients with sunclinical hypothyroidism. Since spirometric evaluation of pulmonary function tests seems to be beneficial in the evaluation of respiratory functional state in hypothyroidism, Thereby, we suggest spirometric assessment and scanning for serum levels of T3, T4 and TSH among individuals with high risk of subclinical hypothyroidsm. The results from this study should be further confirmed with several longitudinal studies.

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