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Spirometry in Patients with Clinical and Subclinical Hypothyroidism

Gulfidan Cakmak

*Haseki Training and Research Hospital, Istanbul,
Turkey*

1. Introduction

Hypothyroidism is defined as a clinical state resulting from insufficient secretion of thyroid hormone from thyroid gland due to some structural or/and functional impairments in thyroid hormone production (Kek PC et al., 2003, Dashe JS & Cunningham FG., 2001). Hypothyroidism affects all of the organ systems. Main clinical findings are fatigue, weakness, dryness and coarseness of the skin, cold intolerance, swelling of the extremities, hair loss, lack of concentration and memory, constipation, weight gain without loss of appetite, dyspnea, hoarseness of speech, menorrhagia, paraesthesia, hearing disorders, diffuse alopecia, bradycardia, delayed relaxation of tendon reflexes, carpal tunnel syndrome and serous cavitory effusions (Kek PC et al., 2003). All of these signs and symptoms recover after replacement of thyroid hormone (Larsen PR & Davies TF, 2003, Fatourechi V., 2001). Subclinical hypothyroidism reflects the earliest stage of thyroid dysfunction with subjects having normal or decreased fT_4 , normal fT_3 and decreased TSH levels. Since diagnosis depends on laboratory values, theoretically, no symptoms or signs are expected but yet patients may suffer from somnolence, weakness and fatigue (Kek PC et al., 2003).

In the English literature there exists several studies revealing the effect of clinical hypothyroidism on respiratory and cardiovascular systems but we were not able to find any comparative effect of subclinical hypothyroidism on these systems. 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 affected in subclinical hypothyroidism by using simple spirometry.

2. Materials and methods

Two hundred and sixty-seven subjects were enrolled in the study. None of the participants had a history of smoking, any respiratory illness or any other systemic pathology affecting the respiratory system. The patients did not suffer from goitre disturbing the respiratory function. The body mass indices (BMI) of all of the participants were under 30 kg/m². Following the approval of the local ethics committee written informed consent was obtained from all of the participants.

Serum fT_3 , fT_4 levels were assessed by Chemiluminescent Competitive Enzyme Immunoassay method with Immulite 2000 of BIODPC. Serum TSH analysis was performed

by Enzyme Chemiluminescent Immunometric Assay method with the same analyser. Normal range for TSH was <4.0 uIU/ml, $1.57-4.71$ ng/ml for fT_3 , and $0.8-1.8$ ng/ml for fT_4 . If the patients' serum fT_3 level was between $1.57-4.71$ ng/ml, fT_4 was between $0.8-1.8$ ng/ml and TSH level was >4.0 uIU/ml, they were included in the subclinical hypothyroidism group. On the other hand, if their serum levels of fT_3 was <1.57 ng/ml, $fT_4 < 0.8$ ng/ml and TSH was >4.0 uIU/ml; they were included in the clinical hypothyroidism group. The control group consisted of subjects having normal fT_3 , fT_4 and TSH values.

Spirometric analysis was performed with Jaeger Master Scope (version 4.5). All respiratory parameters including FVC, FVC %, FEV_1 , FEV_1 %, FEV_1/FVC , FEF_{25-75} , FEF_{25-75} %, PEF, PEF % were assessed.

The mean and standard deviation of parametric values were assessed with Students'-t test and ANOVA. Chi-square test was used when assessing the percentages of the groups and Pearson correlation was used to compare the groups. $P < 0.05$ was considered as significant.

3. Results

Among 120 patients enrolled into the study with subclinical hypothyroidism, 114 of them were women and 6 were men while there were 86 women and 3 male patients with clinical hypothyroidism. Control group consisted of 51 women and 9 men. The mean age of the patients was 43 ± 13 years and 41 ± 13 years with subclinical hypothyroidism and clinical hypothyroidism, respectively. The mean age was 41 ± 12 years in the control group. There was not a significant difference between groups regarding age (Table 1).

| | Subclinical hypothyroidism (n=120) | Clinical hypothyroidism (n=87) | Control group (n=60) |
|-----------|------------------------------------|--------------------------------|----------------------|
| Age/years | 43.68 ± 13.31 | 41.97 ± 13.22 | 41.45 ± 11.98 |
| Gender | | | |
| F | 114 | 84 | 51 |
| M | 6 | 3 | 9 |

Table 1. Demographic features of the participants

Serum fT_3 , fT_4 and TSH values and spirometric parameters of the groups are shown at Table 2 and 3, respectively. Spirometric values were the lowest in the clinical hypothyroidism group while it was higher in subclinical hypothyroidism and the highest in the control group.

| | Subclinical hypothyroidism (n=120) | Clinical hypothyroidism (n=87) | Control group (n=60) |
|----------------|------------------------------------|--------------------------------|----------------------|
| fT_3 (ng/ml) | $2,82 \pm 0,76$ | $1,65 \pm 0,85$ | $3,12 \pm 1,01$ |
| fT_4 (ng/dl) | $1,06 \pm 0,16$ | $0,52 \pm 0,22$ | $1,17 \pm 0,23$ |
| TSH (uIU/m) | $10,19 \pm 6,22$ | $74,17 \pm 140,78$ | $1,60 \pm 1,07$ |

Table 2. Thyroid function values of the participants

The comparison between clinical hypothyroidism and control group demonstrated that all of the spirometric parameters were higher in control group; but only the differences among FVC, FVC %, FEV₁, FEF₂₅₋₇₅ reached statistical significance

($p < 0.05$); the others were not statistically significant.

According to the comparison between subclinical hypothyroidism and control group, spirometric parameters were higher in the control group and lower in patients with subclinical hypothyroidism and there was a statistical significant difference regarding FVC, FVC %, FEV₁ and FEF₂₅₋₇₅ ($p < 0.05$).

Statistically significant positive correlation was found between FT₄ and FVC % in patients with subclinical hypothyroidism ($r = 0.198$, $p = 0.030$).

| | Subclinical hypothyroidism (n=120) | Clinical hypothyroidism (n=87) | Control group (n=60) |
|---------------------------|------------------------------------|--------------------------------|----------------------|
| FVC(ml) | 3284±574* | 3218±767* | 3565±806 |
| FVC % | 109±18* | 105±19* | 115±15 |
| FEV ₁ (ml) | 2661±529* | 2614±623* | 2866±706 |
| FEV ₁ % | 103±16 | 100±21 | 106±14 |
| FEV ₁ /FVC | 80±9 | 80±7 | 78±6 |
| FEF ₂₅₋₇₅ (ml) | 4716±1415* | 4534±1470* | 9034±13162 |
| FEF ₂₅₋₇₅ % | 81±22 | 79±26 | 81±20 |
| PEF(ml) | 4966±1413 | 4940±1337 | 5374±1932 |
| PEF % | 77±20 | 77±21 | 80±21 |

Table 3. Spirometry parameters of the participants

There was a positive correlation between FT₃ and FEF₂₅₋₇₅ ($r = 0.484$, $p = 0.0001$), FEF₂₅₋₇₅ % ($r = 0.490$, $p = 0.0001$), PEF ($r = 0.419$, $p = 0.0001$) and PEF% ($r = 0.432$, $p = 0.0001$) in the clinical hypothyroidism group. There was also a positive correlation between FT₄ and FEF₂₅₋₇₅ ($r = 0.211$, $p = 0.05$), FVC ($r = 0.251$, $p = 0.019$) and FVC% ($r = 0.248$, $p = 0.021$). On the other hand, there was a negative correlation between TSH and FVC% ($r = -0.249$, $p = 0.02$).

4. Conclusion

Hypothyroidism and subclinical hypothyroidism is a clinical disorder occurring frequently in community. Literature research reveals many studies regarding the effects of clinical hypothyroidism on respiratory and cardiovascular systems. But there exists no study concerning the effect of subclinical hypothyroidism on respiratory system nor there exists any study comparing healthy subjects to clinical hypothyroid patients in terms of respiratory function tests. Therefore we aimed to assess the respiratory function of patients

with subclinical hypothyroidism in comparison with clinical hypothyroidism and healthy subjects.

The incidence of primary hypothyroidism is 2% in women and 0.2% in men. Hypothyroidism affects all of the organ systems (Kek PC et al., 2003, Larsen PR & Davies TF, 2003). The clinical presentation of thyroid hormone deficiency alters from one person to another depending on the duration, cause and the degree of deficiency. The decrease in both expiratory and inspiratory muscle strength (Siafakas NM et al., 1992), alveolar hypoventilation due to depression of hypoxic and hypercapnoic ventilatory drives (Kahaly GJ, 2000) and decrease in maximal breathing and diffusing capacity (Zwillich CW et al., 1975) are evident in patients with hypothyroidism. These impairments are reversible with hormone replacement therapy. Respiratory infections are more common than healthy people (Harrison RN & Tattersfield AE., 1984, Krishnan R et al., 1984). Obstructive sleep apnea syndrome is common in severe hypothyroidism but it is reversible with restoration of a euthyroid state (Larsen PR & Davies TF, 2003). The prominent features like somnolence, apathy and lethargy may also recover with replacement therapy (Krishnan R et al., 1984, Jameson JL & Weetman AP, 2001). Muscle strength measurement and sleep investigation is not routine analysis in these patients, so simple spirometric evaluation is preferred. Thus, we used only spirometric measurements in our study since this method is easier, more available and cheaper than other respiratory function tests.

Siafakas et al. found a significant decrease in the strength of inspiratory and expiratory muscles in patients with clinical hypothyroidism. In the mentioned study, vital capacity (VC), forced vital capacity (FVC), forced vital capacity one second (FEV_1), FEV_1/FVC were significantly lower in patients with clinical hypothyroidism compared to healthy controls. In our study, the patients with clinical hypothyroidism had significantly lower spirometric parameters such as vital capacity (VC), forced vital capacity (FVC), forced vital capacity in one second (FEV_1), FEV_1/FVC , peak expiratory flow (PEF) and forced expiratory flow 25-75 (FEF 25-75) than control group.

Subclinical hypothyroidism reflects the earliest stage of thyroid dysfunction. Chronical autoimmune thyroiditis, subacute thyroiditis, thyroidectomy, radioactive iodine treatment, insufficient thyroid hormone replacement therapy may be the cause of subclinical hypothyroidism. The rate of progression to clinical hypothyroidism from subclinical hypothyroidism is about 7,8 %-17,8 %. Initiating therapy doesn't change the natural course of the illness, but it prevents the progression of clinical hypothyroidism (Biondi B et al., 2002, Surks MI & Ocampo E., 1996).

Subclinical hypothyroidism is a common phenomenon seen more often in women with increasing age. The prevalence in women is 6-8 % and 3 % in men (Kek PC et al., 2003, Surks MI & Ocampo E., 2004). In our study 114 female and 6 male patients had subclinical hypothyroidism. Theoretically no symptoms or findings are expected in subclinical hypothyroidism. On the contrary, almost all of our patients suffered from at least one or more of the symptoms like fatigue, weakness and somnolence. This situation revealed that clinical findings also associated to spirometric abnormalities. Fatigue is observed in subclinical hypothyroidism because of muscle dysfunction. Diagnosis

depends on laboratory evaluation. (Kahaly GJ, 2000, Biondi B et al., 2002, Biondi B et al., 2002).

The effect of subclinical hypothyroidism on several organ systems are well known, whereas the effect on respiratory system is not fully understood (Col NF et al., 2004, Beyer IW et al., 1998). The study we designed led us to the conclusion that the measurements of spirometric variables are higher in subclinical hypothyroidism than in clinical hypothyroidism but lower than healthy subjects reaching statistical significance.

In conclusion it is possible to claim that respiratory system is effected in subclinical hypothyroidism. Since subclinical hypothyroidism is common in general population, the patients at high risk who had clinical signs and symptoms may be screened with simple spirometry.

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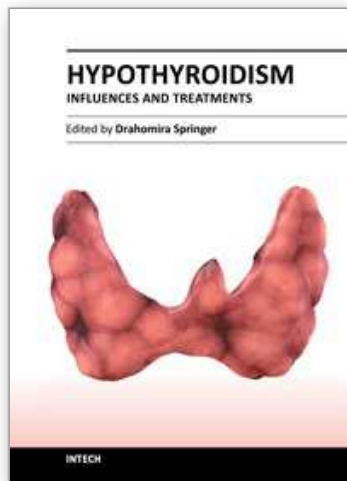
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Hypothyroidism is the most common thyroid disorder and it is significantly more frequent than presented - millions of people suffer from this disease without knowing it. People with this condition will have symptoms associated with slow metabolism. Estimates of subclinical hypothyroidism range between 3 to 8 %, increasing with age, whereas it more likely affects women than men. About 10% of women may have some degree of thyroid hormone deficiency. Hypothyroidism may affect lipid metabolism, neurological diseases or other clinical conditions. The book includes studies on advancements in diagnosis, regulation and replacement therapy, thyroid ultrasonography and radioiodine therapy for hypothyroidism. "Hypothyroidism - Influences and Treatments" contains many important specifications, results of scientific studies and innovations for endocrine practice.

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InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
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Fax: +86-21-62489821

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