Effects of antithyroid medication on the flow-volume loop in patients with hyperthyroidism

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ÖZET

Hipertiroidi olgularında antitroid tedavinin akım-volüm eğrileri üzerindeki etkileri

Astrın tanısta bulunmayan 20 hipertiroidi olgusunda antitroid tedavinin akım-volüm eğrileri üzerindeki etkilerini değerlendirerek üzere prospektif bir çalışma düzenlendi. Antitroid tedavinin başlangıcında ve üçüncü aynın sonunda hastaların tiroid hormonları (Total T3, Total T4 ve TSH), ultrasonografi ile tiroid bezi volümleri, boynun çevresi ölçümleri ve akım-volüm eğrileri değerlendirildi. Propiltiourasil tedavisi ile tiroid bezi volümlünde ve boynun çevresi ölçümlerinde istatistiksel olarak anlamalı azalma görüldü (sarsısla; p < 0.001), Çalışmanın en önemli sonucu maksimal ekspirasyon ortası akım hızı (MMFR) parametrelerinde üç aylık propiltiourasil tedavisi sonrası görülen düzelmeye idi. Vital kapasitenin %25%’indeki ortalama ekspiratuar akım hızı (FEF25) ve vital kapasitenin %75’indeki ortalama ekspiratuar akım hızı (FEF75) parametrelerinde kaydedilen artışlar tüm ekspiratuar akım parametrelerindeki düzelmeye uymadı (sarsısla; p = 0.012). Sonuçta hipertiroidi tedavisi için propiltiourasil kullanılan hastaların akım-volüm eğrilerinde en erken değişiklik eksipitatuar akım parametrelerindeki düzelmeye olarak bulundu.

Anahtar Kelimeler: Hipertiroidizm, akım-volüm eğrisi.

SUMMARY

Effects of antithyroid medication on the flow-volume loop in patients with hyperthyroidism

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This prospective study was designed to evaluate the effects of hyperthyroidism on flow-volume loops in nonasthmatic 20 patients with hyperthyroidism. Thyroid related hormones (Total T3, Total T4 and TSH), thyroid gland volumes with ultrasonography, circumference of neck values and flow-volume loops were obtained at the beginning and after three months of antithyroid treatment. Propylthiouracil treatment was followed by a statistically significant decrease in thyroid gland volume and circumference of neck (p < 0.001 and p > 0.001, respectively). The most significant result was improvement of ma

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ximum midexpiratory flow rate (MMEFR) after propylthiouracil therapy for three months (p = 0.003). Increases in mean forced expiratory flow after 25% of FVC has been exhaled (FEF_{25}), mean forced expiratory flow after 75% of FVC has been exhaled (FEF_{75}) values were found consistent with the overall improvement in expiratory flow parameters (p = 0.044, p = 0.012 respectively). In conclusion, we speculated that improvement of expiratory flow parameters might be the earlier changes in flow volume loops of patients who were treated with propylthiouracil for hyperthyroidism.

**Key Words:** Hyperthyroidism, flow-volume loop.

Previous studies have shown a relation between hyperthyroidism and respiratory function. Abnormalities in pulmonary functions that occur in patients with hyperthyroidism include upper airway obstruction by large goitres, respiratory muscle weakness, increased ventilatory drive and airway resistance (1,2). An association between hyperthyroidism and increasing severity of asthma have also been reported (3,4). It has been shown that treatment of hyperthyroidism resulted with improvement of asthma. These reports have forced the investigators to evaluate the effects of antithyroid medication on the flow-volume loop in patients with hyperthyroidism (1). In a study including both hyperthyroid and euthyroid goitre cases, the primary abnormality in the flow-volume loops was an inspiratory flattening of the curve. That study also showed normalization of all preoperative abnormal curves after thyroidectomy (5). Although several reports showed deterioration of asthma in hyperthyroidism, the effects of hyperthyroidism on the expiratory curve of flow-volume loop in asthmatic and nonasthmatic subjects still have been debated.

The aim of present study is to evaluate the effects of antithyroid medication on flow-volume loop in the nonasthmatic patients with hyperthyroidism.

**MATERIALS and METHODS**

Twenty consecutive patients with hyperthyroidism were included in to the study. There were 19 females and one male. The mean age was 47 ± 13 years. Patients with a history or clinical evidence of chronic obstructive pulmonary disease (COPD) or asthma and smokers were excluded. None of the patients had clinical evidence of Graves’ disease. Eight of the patients were hypertensive and one of all patients was diabetic.

All patients were evaluated for hyperthyroidism by serum concentrations of total thyroxine (TT₄), total triiodothyronine (TT₃) and thyroid stimulating hormone (basal TSH). The results of the ultrasonographic measurements of thyroid glands and circumference of neck were also obtained. With ultrasonographic evaluation 13 (65%) of the patients had multinodular goitre, 1 (5%) of them had cystic goitre and 6 (30%) of them had diffuse goitre.

Assessment of respiratory status were made in all patients by pulmonary function tests, oxygen saturation measurements and chest radiographs. Pulmonary function tests were performed with a dry rolling spirometer (Morgan Spiro 232, Gillingham-England). Parameters studied included; FVC, FEV₁, FEV₁/FVC, MMEFR, PEF, FEF_{25}, FEF_{50}, FEF_{75}, FIV₁, PIF, FIF_{50}, FEF_{50}/FIF_{50}. Each patient performed at least three respiratory maneuvers and the best results were recorded. All volumes were corrected to BTPS and expressed as the percentage of predicted values. Measurements of oxygen saturation were performed with pulse oxymeter (Criticare Pulse 503 Oximeter, USA). Chest radiographs were evaluated as normal in all patients.

Tests which were detailed above were performed in all patients at the beginning of study and after three months of propylthiouracil treatment (300 mg/day). No beta blockers were given during this period. All patients gave informed consent.

Statistical analysis was made using Student’s paired t-test to evaluate statistically significant differences in the mean values between pretreatment and post-treatment data in patients. A p value less than 0.05 was considered to indicate statistical significance.

**RESULTS**

Serum TT₃ and TT₄ levels and basal TSH levels before and after propylthiouracil treatment are shown in Table 1.
Table 1. Thyroid related hormones.

<table>
<thead>
<tr>
<th>Hormone level</th>
<th>Reference ranges</th>
<th>Pretreatment (n= 20)</th>
<th>Post-treatment (n= 20)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT4 (ng/dL)</td>
<td>4.5-12.5</td>
<td>12 ± 4.87</td>
<td>9 ± 19.81</td>
<td>0.028</td>
</tr>
<tr>
<td>TT3 (ng/dL)</td>
<td>82-179</td>
<td>242 ± 120.06</td>
<td>166 ± 44.91</td>
<td>0.854</td>
</tr>
<tr>
<td>TSH (μIU/mL)</td>
<td>0.4-4.0</td>
<td>0.71 ± 4.80</td>
<td>0.64 ± 6.22</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* p< 0.05 indicated statistical significance.

There was a significant decrease in the serum TT4 level after propylthiouracil treatment (p= 0.028). Decrease in serum TT3 level was not statistically significant (p= 0.854). Expected increase in the level of mean TSH after antithyroid treatment was not observed. Possible explanation for this conflicting result might be the relatively short period of antithyroid treatment in this study. At the end of study 6 (30%) patients were still remaining in thyrotoxic status.

Values of mean thyroid gland volumes, circumference of neck and oxygen saturation are seen in Table 2.

Propylthiouracil treatment was followed by a statistically significant decrease in thyroid gland volume and circumference of neck (p< 0.001 and p< 0.001, respectively). Oxygen saturation significantly increased (p< 0.001).

Changes of mean flow-volume parameters are shown in Table 3.

Statistically significantly differences were observed in mean FVC, MMEFR, FEF25, FEF75, FIV, PIF and FIF50 values after antithyroid treatment. Whereas MMEFR, FEF25, FEF75, PIF and FIF50 increased, FVC, FIV decreased. No significant changes in FEV1, FEV1/FVC, PEF, FIF50 were observed after treatment.

DISCUSSION

Flow volume loop curves were found as a simple noninvasive method when assessing upper airway obstruction due to the different causes (6). Miller and associates showed goitre related upper airway obstruction in 31% of patients and improvement of upper airway obstruction with thyroidectomy was also reported by these authors (7). In a later study by Melissant and associations it was concluded that both routine lung function tests and CT scan depicted upper airway obstruction due to goitre but both techniques were not well correlated to each other (2). When compared with the study by Melissant and associations, present study was not performed with sophisticated techniques; and upper airway obstruction was evaluated by flow-volume loop curves. Thyroid gland volume and circumference of neck parameters were used to assess the changes of thyroid size after three months of antithyroid treatment. Decrease of both thyroid gland volume and neck circumference parameters after antithyroid treatment were statistically significant (p< 0.001 and p< 0.001 respectively). Generally, an alteration in the contour of the flow-volume loop is considered to be the most reliable abnormality for the detection and localization of upper airway disorders (5,8). One patient’s flow-volume loop was found consistent with variable extrathoracic obstruction in present study. After three months of antithyroid treatment no detectable change was observed in that flow-volume loop curve. In contrast with the study by Thusoo and associations, lower incidence of upper airway obstruction detected with

Table 2. Mean values of thyroid volume, neck circumference and oxygen saturation.

<table>
<thead>
<tr>
<th>Value</th>
<th>Pretreatment (n= 20)</th>
<th>Post-treatment (n= 20)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid volume (cm³)</td>
<td>60.55 ± 41.93</td>
<td>59.15 ± 48.21</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Circumference of neck (cm)</td>
<td>35 ± 3.77</td>
<td>35 ± 3.58</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Oxygen saturation (%)</td>
<td>97 ± 2.35</td>
<td>98 ± 1.15</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* p< 0.05 indicated statistical significance.
flow-volume loop was observed in present study (60% and 5% respectively) (5). Since the aim of present study was to evaluate the effects of antithyroid medication on the flow-volume loop curves, hyperthyroidism (with or without thyroid enlargement) was the primary selection criteria. An unexpected decrease in mean FIV value consistent with a decrease in mean FVC value was observed in this study. This result might be related to effort dependence of forced maneuvers and technical aspects in some way. An additional explanation for decreases in FIV and FVC might be related to the relatively short period of antithyroid treatment in this study. At the end of study 6 (30%) patients were still remaining in thyrotoxic status.

Though present study had some limitations when evaluating the effects of hyperthyroidism on flow-volume loops, some significant changes in MMEFR, FEF<sub>25</sub>, FEF<sub>50</sub>, FEF<sub>75</sub> were observed after propylthiouracil therapy for three months. It is well known that MMEFR reflects airflow during the effort-independent part of the FVC. Especially, abnormal values for MMEFR in association with normal values for FEV<sub>1</sub> and FVC are useful in identifying small airway disease (9).

Previous studies have proposed some mechanisms to explain the effects of hyperthyroidism on small airways. Reduced pulmonary breakdown of the prostaglandins PGE<sub>2</sub> and PGF<sub>2α</sub> due to the hyperthyroidism caused to bronchoconstriction in rat model (10). Other studies showed that hyperthyroidism increased the conversion of hydrocortisone to its inactive derivative (11,12). Settipane and associations suggested that hyperthyroidism causes to an overall decrease in cyclic AMP and so worsens asthma (13). In contrast to previous reports discussed above, Wieshammer and associations showed increased nonspecific bronchial reactivity in nonasthmatic subjects with acute hypothyroidism (14).

Like previous studies that showed a relation between hyperthyroidism and small airways, an increase in MMEFR after propylthiouracil therapy was detected in present study. Increases in mean FEF<sub>25</sub>, FEF<sub>50</sub>, FEF<sub>75</sub> values were found consistent with the overall improvement in expiratory flow parameters.

In conclusion, we speculated that improvement of expiratory flow parameters by antithyroid treatment might be the earlier changes in flow-volume loops.

**REFERENCES**