Original Article

Lipid Profile Change after Thyroidectomy

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ABSTRACT

Purpose: Thyroid diseases and lipid metabolic abnormalities have been reported to be correlated. In patients with thyroid cancer, thyroid stimulating hormone levels are suppressed to prevent recurrence. Many studies have reported dyslipidemia associated with thyroid function, although its extent before and after thyroidectomy remains to be studied. This study aimed to determine the lipid levels for administering accurate lipid treatment in thyroid cancer patients post thyroidectomy.

Methods: In total, 1,203 patients with thyroid cancer who underwent thyroidectomy between June 1, 2016 and December 31, 2016 at the Thyroid Cancer Center, Gangnam Severance Hospital, Yonsei University, were enrolled in the study. Of these, patients aged <19 years and taking medication for dyslipidemia were excluded. Finally, we enrolled 295 thyroid cancer patients who underwent thyroidectomy and whose lipid profiles were confirmed pre- and post-operatively.

Results: The total cholesterol levels in the lobectomy group without levothyroxine supplementation were significantly increased 1 year after surgery than those before surgery (168.17±29.19 mg/dL vs. 182.50±34.03 mg/dL, P=0.003). Additionally, the triglyceride (TG) levels were significantly decreased in the lobectomy with levothyroxine supplementation and total thyroidectomy groups, whereas cholesterol and low-density lipoprotein-cholesterol (LDL-C) levels showed no significant change. No significant changes in the levels of cholesterol, LDL-C, and TG were observed in all the 3 groups.

Conclusion: Extent of surgery and levothyroxine supplementation had an insignificant impact on the levels of cholesterol, LDL-C, and TG, and high-density lipoprotein-cholesterol compared pre- and post-operatively.

Keywords: Lipid metabolism; Cholesterol; Thyroidectomy; Levothyroxine; Thyroid neoplasms

INTRODUCTION

Thyroid diseases and lipid metabolic disorders have been found to be associated (1). Thyroid hormone stimulates synthesis of cholesterol via the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase activity in the liver. In hyperthyroidism, cholesterol synthesis increases, although serum total cholesterol and low-density lipoprotein-cholesterol (LDL-C) concentrations decrease because of increased LDL-C metabolism (2-7). Atherosclerosis
resembles a plaque with accumulation of substances composed of fat, cholesterol, calcium,
and so on. Moreover, the pathologic effect of lipids (cholesterol, high-density lipoprotein-
cholesterol [HDL-C], and triglyceride [TG]) in hypothyroidism has not been confirmed;
however, the probability of coronary heart disease was increased due to increased lipid levels
(8,9). LDL-C is transported from the liver to peripheral tissues by low-density lipoprotein-
receptor (LDL-R). Thyroid hormone receptor and sterol regulatory-element binding protein
(SREBP)-2 stimulate LDL-R gene expression and increase cholesterol absorption (4-7,10,11).
Activation of SREBP signals the thyroid hormone receptor to increase the expression of
LDL-R, which leads to a decrease in the levels of LDL and TG. This cascade also stimulates
cholesterol synthesis via HMG-CoA reductase activity (4-7,10,11). Excess cholesterol in the
liver is converted into bile acids catalyzed by cholesterol 7 alpha-hydroxylase (CYP7A1).

Therefore, in hyperthyroidism, cholesterol synthesis is increased, but at the same time, serum
total cholesterol and LDL-C levels are reduced because of increased LDL metabolism (2-7).

T3 and T4 show similar functions, although they differ in the rapidity and intensity, with
T3 having 4-times the potential as T4; despite a shorter duration in the blood stream than
T4, T3 is the main hormone that responds at the cellular level (12). After thyroid surgery,
artificially synthesized thyroid hormone is administered instead of the naturally synthesized
thyroid hormone secreted by the existing thyroid. Moreover, in case of thyroid cancer,
hyperthyroidism is often maintained to decrease the concentration of thyroid stimulating
hormone (TSH) (13,14). Most of the efforts have focused on studying dyslipidemia
associated with thyroid function, and no study has addressed the extent of dyslipidemia
by observing lipid levels before and after thyroidectomy. This study aimed to observe the
change in lipid metabolism in patients with thyroid cancer before and after thyroid cancer
surgery; these findings could help in the planning for an appropriate treatment according
to the change in lipid metabolism in patients receiving thyroid hormone.

MATERIALS AND METHODS

1. Patients
A total of 1,203 patients with thyroid cancer who underwent surgery between June 1, 2016
and December 31, 2016, at the Thyroid Cancer Center, Gangnam Severance Hospital, Yonsei
University, were enrolled in the study. We excluded patients who received dyslipidemia-
related medication, whose lipid profiles were not evaluated pre- and post-operatively, and
who were aged under 19 years. Finally, 295 patients were retrospectively studied. This study
was approved by the Institutional Review Board of Gangnam Severance Hospital (approval
No. 3-2016-0200).

2. Statistical analysis
Descriptive statistics were used to describe the basic characteristics. Continuous variables were
expressed as means±standard deviations (SD) and analyzed by Student’s t-test and one-way
analysis of variance. Pearson’s χ² test and Fisher’s exact test were used for analyzing categorical
variables, which were expressed as numbers and percentages. All statistical analyses were
performed using the SPSS version 23.0 for Windows (SPSS Inc., Chicago, IL, USA). For all
statistical analyses, a 2-sided P value <0.05 was considered statistically significant.
RESULTS

The clinicopathological characteristics of the patients included in the study (n=295) are presented in Table 1: mean age was 42.6±11.8 years; female sex, 80.0% (n=236); and tumor size, 1.2±1.06 cm. Of these, 292 patients had papillary thyroid carcinoma (99.0%) and one had medullary thyroid cancer (0.3%). Furthermore, patients received levothyroxine supplementation after lobectomy (n=114), bilateral total thyroidectomy (n=157), and no Synthroid (levothyroxine sodium tablets; AbbVie Inc., North Chicago, IL, USA) (n=24). Further, in the lipid analysis, the total cholesterol levels in the lobectomy group without levothyroxine supplementation were significantly increased 1 year after surgery than those before surgery (168.17±29.19 mg/dL vs. 182.50±34.03 mg/dL, P=0.003). Additionally, the TG levels were significantly decreased in the lobectomy with levothyroxine supplementation and total thyroidectomy groups, whereas cholesterol and LDL-C levels showed no significant change (Table 2). Finally, no significant changes in the levels of cholesterol, LDL-C, and TG were observed in all the 3 groups, viz. lobectomy without Synthroid, lobectomy with Synthroid, and bilateral total thyroidectomy (BTT) with central compartment neck dissection (CCND) (Table 3).

DISCUSSION

In this study, we confirmed that there were no differences in the levels of cholesterol, LDL-C, TG, and HDL-C before and after surgery for thyroid cancer when comparing them between the treatment modality groups (lobectomy without levothyroxine supplementation, lobectomy with levothyroxine supplementation, and BTT with or without lateral neck dissection). Lipid aberrations affect liver function; however, liver function was not assessed.

Table 1. Baseline characteristics of thyroid cancer patients who underwent thyroidectomy

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Total patients (n=295)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>42.6±11.8</td>
</tr>
<tr>
<td>Female</td>
<td>236 (80.0)</td>
</tr>
<tr>
<td>Size (cm)</td>
<td>1.2±1.06</td>
</tr>
<tr>
<td>Lobectomy without levothyroxine</td>
<td>24 (8.1)</td>
</tr>
<tr>
<td>Lobectomy with levothyroxine</td>
<td>114 (38.6)</td>
</tr>
<tr>
<td>BTT with CCND</td>
<td>157 (53.2)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Papillary</td>
<td>292 (99.0)</td>
</tr>
<tr>
<td>Medullary</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Poorly</td>
<td>2 (0.7)</td>
</tr>
</tbody>
</table>

Data are shown as means±standard deviations or numbers (percentage or range).

Table 2. Lipid profile (cholesterol, LDL-C, and TG) result analysis (preoperative vs. 1-year postoperative) using the paired t-test

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Lobectomy without levothyroxine supplementation (n=24)</th>
<th>Lobectomy with levothyroxine supplementation (n=114)</th>
<th>BTT with CCND (n=157)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Op 1-year P value</td>
<td>Pre-Op 1-year P value</td>
<td>Pre-Op 1-year P value</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>168.17±29.19 182.50±34.03 0.003</td>
<td>179.33±31.24 183.96±23.31 0.122</td>
<td>179.20±29.56 180.27±30.02 0.612</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>108.09±24.06 114.04±26.37 0.079</td>
<td>119.68±23.05 118.61±21.68 0.611</td>
<td>118.67±23.22 116.39±24.37 0.152</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>163.39±148.80 122.22±78.70 0.128</td>
<td>156.35±125.44 110.48±58.85 &lt;0.001</td>
<td>153.24±109.93 113.11±50.08 &lt;0.001</td>
</tr>
<tr>
<td>TSH (mciU/mL)</td>
<td>1.62±0.81 2.95±1.30 &lt;0.001</td>
<td>2.44±1.77 1.12±1.83 &lt;0.001</td>
<td>2.23±1.47 0.64±3.27 &lt;0.001</td>
</tr>
</tbody>
</table>

Data are shown as means±standard deviations.

BTT, bilateral total thyroidectomy; CCND, central compartment neck dissection; LDL-C, Low-density lipoprotein-cholesterol; TG, triglyceride; pre-Op, preoperative; TSH, thyroid stimulating hormone.
in this and previous studies. Ghadir et al. (15) measured the lipid profile (HDL-C, LDL-C, cholesterol, and TG) according to liver function test results in 50 patients with liver cirrhosis and found that the severity of liver damage was significantly correlated with a decrease in serum lipid levels. Thus, this study suggests the disease to be directly related to liver function among other parameters of the patients’ history (15). In mice study, TSH increased the hepatic triglyceride content, indicating an essential role for TSH in the pathogenesis of non-alcoholic fatty liver disease through SREBP-1, a key regulator involved in triglyceride metabolism. Another study showed that TG and LDL-cholesterol were independent predictors of serum TSH levels, whereas cholesterol was negatively correlated with TSH. Study of Korean population revealed that TSH showed significantly positive correlations with serum total cholesterol, TG, and LDL-C regardless of sex, age, season, obesity, or menopausal status (16-18).

Levothyroxine is an artificially derived hormone from the body’s natural thyroid hormones. Levothyroxine increases the absorption with higher efficiency and can affect absorption when taking products containing iron or calcium. With respect to pharmacokinetics, levothyroxine can affect the metabolism of thyroid hormones, such as decrease the overall concentrations of T3 and T4 in patients with impaired new functions. Moreover, TSH levels are increased in patients with obesity, an effect that can be attributed to the leptin hormone produced by adipose tissue. The secretion of T4 and T3 and metabolism of T4 to T3 decreases in healthy elderly patients, although the levels of rT3 increase; the half-life for elimination of T4 can be checked for longer duration (19,20).

Considering the limitations described above, the action of several drugs is affected by the metabolism (absorption, synthesis, secretion, catabolism, protein binding, and target test response) and pharmacokinetics of thyroid hormones (21). Additionally, the therapeutic response of levothyroxine may differ according to a person’s physical status. Moreover, the follow-up duration in our study was only 1-year, and a prolonged duration of observation would be required. Nevertheless, these results have several practical implications in the clinical settings. Therefore, clinicians can consider treatment for lipid metabolism abnormalities after thyroid surgery.

**CONCLUSION**

The study indicated no difference in the levels of cholesterol and LDL-C, TG, and HDL-C before and after surgery (lobectomy and total thyroidectomy) in patients with thyroid cancer.
REFERENCES


