lectin-type adhesion molecules expressed at the surface of activated leukocytes and endothelium in inflamed tissues (6).

References

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Lipid and Thyroid Changes After Partial Thyroidectomy: Guidelines for l-Thyroxine Therapy?

To the Editor:

Subclinical hypothyroidism, defined as normal concentrations of thyroxine (T4) with increased concentrations of thyrotropin (TSH), could, like overt hypothyroidism (low free T4), be a risk factor of atherosclerosis or coronary heart disease, given its potential for association with an atherogenic profile (increased low-density lipoproteins) (1). Through decreasing the thyroid parenchyma, partial thyroidectomy could induce subclinical or overt hypothyroidism.

The aim of this study was: (a) to confirm that partial thyroidectomy causes changes in blood lipid and lipoprotein concentrations, and (b) to determine whether T4 treatment was necessary after such surgery.

Forty-two patients who underwent partial thyroidectomy were included in this study. We excluded patients with preoperative hypothyroidism, hepatic cholestasis, kidney failure, or diabetes mellitus, and those taking lipid-reducing drugs or oral contraceptives. The patients, 33 women and 9 men (mean age = 45 ± 3 years (range = 19 to 65)) were followed up for 9 months after their surgery. We measured lipids, free T4, free triiodothyronine (T3), and TSH preoperatively and 3 and 9 months postoperatively. Three months after surgery, the subjects were randomized into two treatment groups: those receiving placebo (n = 20) and those taking T4 1 μg/kg body wt. daily (n = 22). All the procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 1983.

Total cholesterol (TC) and triglycerides (TG) were measured in serum with the CHOD-PAP™ and GPO-PAP™ kits, respectively, with a Hitachi 717™ analyzer (all from Boehringer Mannheim, Mannheim, Germany). High-density lipoprotein cholesterol (HDL-c) was assayed after precipitation of the apolipoprotein (apo) B-containing lipoproteins by a phosphotungstic acid–magnesium chloride mixture (Boehringer Mannheim). Low-density lipoprotein cholesterol (LDL-c) was computed according to Friedewald’s formula (2).

Apo A-I and apo B were measured in serum by immunonephelometry with a BN™ analyzer (Behring, Marburg, Germany). Free T4 and free T3 were assayed by immunoassay (Eastman Kodak, Rochester, NY), and TSH was determined with a sensitive immuno-radiometric assay (Behring). Wilcoxon’s test was used to compare the pre- and postoperative results for lipids, free T4, free T3, and TSH. The Mann–Whitney test was used to compare treated and untreated groups for the same analytes. Spearman’s rank correlation test was used to study correlations between thyroid and lipid variables. Results are expressed as means ± SEM.

Free T4 was lower after the operation than before (11.3 ± 0.3 vs 12.6 ± 0.3 ng/L, P < 0.001), whereas TSH was higher (1.9 ± 0.2 vs 0.9 ± 0.1 mIU/L; P < 0.001). Three months after surgery, no patient was in overt hypothyroidism (increased TSH and T4 <10 ng/L), but five patients were in subclinical hypothyroidism: Two had abnormally increased TSH (6.7 and 7.5 mIU/L), and three exhibited exaggerated TSH response to thyrotrpin (TRH) (TSH at 20 min exceeded 20 mIU/L: 21.9, 23.8, 25.7 mIU/L). One of these five patients (TSH = 6.7 mIU/L) was in the T4-treated group, four were in the placebo group. Nine months after surgery, the T4-treated patient had normal TSH and T4 response, two of the four placebo-treated patients had normal TSH and T4 response, and two had normal TSH but still an exaggerated TSH response (TSH at 20 min = 21 and 26.2 mIU/L).

No difference in serum concentrations was found between pre- and postoperative times for TC, TG, LDL-c, HDL-c, LDL-c/HDL-c, HDL-c/TC, apo A-I, and apo B. Lipid-related variables did not differ with treatment 9 months after surgery, except for improved HDL-c in the T4-treated group (+8% vs -2%, P <0.05). Nine months after surgery, the two patients with the highest TSH response to TRH had higher concentrations of atherogenic lipids (Table 1), and TSH was significantly (P <0.05) correlated with TC (r = 0.55), apo B (r = 0.40), and LDL-c (r = 0.59).

The Framingham study (3) has shown the poor prognosis for coronary mortality evidenced by increased atherogenic lipids. Thyroid hormones increase lipoprotein lipase activity.

Table 1. Variation of lipid variables and thyroid function 9 months after partial thyroidectomy.

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Normal (n = 40)</th>
<th>Exaggerated (n = 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC, mmol/L</td>
<td>5.45 (0.17)</td>
<td>7.30 (1.79)*</td>
</tr>
<tr>
<td>TG, mmol/L</td>
<td>0.89 (0.07)</td>
<td>1.15 (0.15)</td>
</tr>
<tr>
<td>LDL-c, mmol/L</td>
<td>3.51 (0.17)</td>
<td>5.11 (0.98)*</td>
</tr>
<tr>
<td>HDL-c, mmol/L</td>
<td>1.59 (0.07)</td>
<td>1.69 (0.16)</td>
</tr>
<tr>
<td>APO A-I, g/L</td>
<td>1.63 (0.05)</td>
<td>1.74 (0.10)</td>
</tr>
<tr>
<td>APO B, g/L</td>
<td>1.07 (0.06)</td>
<td>1.53 (0.48)*</td>
</tr>
</tbody>
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* Significantly different: P <0.05.
and LDL turnover by stimulating the synthesis of LDL receptors and the degradation of LDL (4). Therefore, overt hypothyroidism can increase the concentrations of TC and (or) TG (5). Subclinical hypothyroidism would thus constitute a risk factor for coronary failure by the lipidemic modifications it induces (1). Some authors have reported that subclinical hypothyroidism could be an isolated increase of TSH, increase of TC (1), LDL-c (6), and TC/HDL-c and decrease of HDL-c (7); however, this was not fully confirmed by other authors (6, 8). The effects of T4 on lipid-related variables in patients with subclinical hypothyroidism are also controversial: Some authors have shown that hormone replacement therapy, besides decreasing serum TSH, could also decrease concentrations of blood apo B and TC (9), LDL-c (10), and TC/HDL-c (7) and increase HDL-c (7, 9) or apo A-I (7, 11); these notions, however, were not confirmed by other studies (11–14). Our study has confirmed previous results involving lipids, i.e., that the increase of TSH 9 months after surgery was related to increased atherogenic lipids (1, 6) and that the benefit of T3 therapy would be restricted to increased HDL-c (7, 9). Our study also showed that partial thyroidectomy had little influence on thyroid functions in the mid-term (9 months): At that stage, only 2 patients of 42 exhibited persistent subclinical hypothyroidism, whereas it had spontaneously disappeared between 3 and 9 months after surgery in the other affected patients.

Hormone replacement therapy after partial thyroidectomy should therefore be indicated only in the presence of obvious persistent hypofunction 9 months after surgery.

References

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Functional Sensitivity of Thyrotropin Assays

To the Editor:

The interlaboratory performance of thyrotropin (TSH) assays has been the focus of several recent studies. In this issue Spencer et al. (1) examine the "functional sensitivity" of six TSH methods under typical laboratory conditions and assess the reliability of subnormal TSH measured concentrations by a broader range of 16 TSH methods. This study raises many questions about results from a variety of clinical sites when compared with results obtained by the manufacturer.

Improved performance by manufacturers compared with that at clinical sites may be attributed to many variables, such as calibrations and sample conditions rather than the "sensitivity potential" ascribed to them by Spencer et al. Published reports have shown that there are many ways to improve in between-run precision (2).

The study design and data interpretation are questionable. Although the development of precision profiles under laboratory conditions is reasonably presented, some conclusions are unsupported. Objective interpretation would be facilitated by including the number of reagent lots and calibrations used by individual laboratories, as well as confidence intervals for the precision profiles.

Although not surprising in light of previous publications where K-30 (Kodak TSH-30) and NIC (Nichols) have failed, in practice, to yield "third-generation" functional sensitivity (3, 4), Spencer et al. correctly point out that all three third-generation TSH assays cited fail to reliably meet this criterion. Indeed, two of the assays (K-30, NIC only) marginally meet the third-generation criteria in the manufacturers' hands. Contrary to the authors' conclusions, the precision profiles generated in clinical laboratories by these two methods are essentially equivalent to that of Ciba Corning Diagnostics Corp. (CCD; Medfield, MA) ACS™ TSH (referred to as COR by Spencer et al.). The CCD insert claims a minimal detectable sensitivity of 0.03 mIU/L, a claim that has been independently substantiated (see Fig. 1), reliably yielding better than second-generation functional sensitivity. The results reported by Spencer et al. for COR agree with CCD low-end precision studies on new instruments and those of the College of American Pathologists (CAP), the French Pro-Qual-Bio Programme and two UK EQAS studies.