Hypothyroidism in Patients Older Than 55 Years: An Analysis of the Etiology and Assessment of the Effectiveness of Therapy

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Background. Several epidemiological studies on the prevalence of hypothyroidism in the elderly have been reported; however, extensive series of elderly patients with thyroid dysfunction have not been studied. Our aim has been to assess the relative frequency of the diverse causes of hypothyroidism in a group of patients older than 55 years and the adequacy of control of thyroid function attained by levothyroxine therapy.

Methods. We performed a descriptive, observational, cross-sectional study in the setting of a hospital endocrinology clinic. From a total of 1581 patients older than 55 who were complaining of a thyroid disorder, we studied a group of 655 patients with hypothyroidism. There were 559 women (85.3%, age 65.01 ± 7.90 years) and 96 men (14.7%, 65.36 ± 8.39 years). In every patient, we collected etiology, presence of goiter, time of evolution from diagnosis and from therapy prescription, previous and present treatments, current thyroid functional status (free thyroxine and thyrotropin concentration), adequacy of disease control, and thyroid autoimmune status.

Results. The causes of hypothyroidism were as follows: autoimmune thyroiditis, 308 (47.0%); postoperative hypothyroidism, 175 (26.7%); therapy for previous thyrotoxicosis, 63 (9.6%); thyrotropin deficiency, 15 (2.3%); iodine excess, 6 (0.9%); subacute thyroiditis, 2 (0.3%); and unknown etiology, 86 (13.1%) patients. Most patients with autoimmune thyroiditis were positive for thyroid peroxidase antibodies at the time of the study (94.4%). Mean (± SD) age at diagnosis was 61.8 ± 9.4 years in men and 59.8 ± 9.7 years in women. Median (range) duration of hypothyroidism was 1.4 (0–18) years in men and 3 (0–45) years in women (p < .05). Adequacy of therapy was studied in 385 patients treated with replacement doses of levothyroxine. Two hundred and sixty (67.5%) of these subjects attained good control, whereas 125 (32.5%) showed inadequate control of the disease at the time of the study. A model of logistic regression showed that adequacy of therapy was dependent on the duration of therapy, but independent of age, gender, degree of hypothyroidism, etiology, autoimmune status, age at diagnosis, and dose of levothyroxine. A 2-year follow-up study performed in 56 newly diagnosed patients showed that an adequate control of hypothyroidism was attained in 35 (62.5%) patients at 6 months, in 46 (82.1%) patients at 1 year, and in 49 (87.5%) at 2 years of therapy with levothyroxine.

Conclusions. Autoimmune thyroiditis and postoperative hypothyroidism are the main causes of thyroid hypofunction in patients older than 55 years. The time from starting therapy is the main determinant of the adequacy of control of thyroid hypofunction in this population. With effective therapy and appropriate monitoring, more than 80% of the patients showed adequate control within 1 year of follow-up.

It behooves all clinicians who deal with the elderly to understand health problems that occur frequently in patients in this age group in order to improve health services and quality of life of elder people. In this setting, it is well known that thyroid gland dysfunction is a common clinical problem associated with aging (1–3). Both hypothyroidism and hyperthyroidism are easily overlooked or misdiagnosed in elderly patients because of nonspecific or atypical presentation (3–6). Moreover, thyroid function tests may be affected not only by normal aging processes, but also by concurrent nonthyroidal illness and the effect of certain drugs widely used in elderly patients.

Several studies on the epidemiology of thyroid dysfunction in aged people have been performed. The reported prevalence of hypothyroidism has varied from 0.9 to 17.5%, and that of hyperthyroidism from 0.5 to 6% (7–18). The reported prevalence varies widely, depending on the sensitivity of methods used to detect thyroid disease and the population evaluated. The prevalence of thyroid dysfunction has been found to be higher in women (7,11,13) and in hospitalized patients (19). Also, the prevalence of subclinical thyroid dysfunction is higher than that of overt thyroid dysfunction in both hypothyroidism and hyperthyroidism. Nevertheless, extensive series of elderly patients with thyroid dysfunction are not easily available; therefore, the evaluation of several aspects of thyroid dysfunction such as etiology, natural history, and the assessment of treatment effectiveness has not been fully characterized in this age group.

We performed a cross-sectional descriptive study in a large cohort of ambulatory patients older than 55 complaining of thyroid disease. Our aim has been to assess in a prospective way the relative frequency of the diverse etiologies of hypothyroidism in adult patients older than 55 years in the setting of an endocrinology clinic of a general hospital. On the other hand, we have assessed the relationships be-
between the age and gender of the patients and the etiology of hypothyroidism, and we have analyzed the evolution of the disease. Determining the adequacy of control obtained in the different groups of studied patients assessed the effectiveness of the levothyroxine therapy.

**METHODS**

**Patients**

A descriptive, observational, cross-sectional study including all patients older than 55 years complaining of any kind of thyroid disease for a period of 6 years starting on October 1994 was carried out. Patients were included in the study in a consecutive way with no restriction criteria. With a comparative purpose, patients were divided into groups A (55 to 64 years) and B (65 years or older). All patients were ambulatory and were studied as outpatients during visits to an endocrinology clinic. A detailed clinical history, review of the previous case record, and complete physical examination were performed in every patient. Serum concentrations of free thyroxine (FT4) and thyrotropin (TSH) were measured in all patients. Other laboratory and complementary investigations were carried out as necessary to obtain a diagnosis.

A total of 1581 patients older than 55 years came into our thyroid clinic. In 157 of them, the designed record could not be fully completed, and these patients were not included in the study. Therefore, the studied population consisted of 1424 patients—1171 women (82.2%) and 253 men (17.8%), aged from 55 to 91 years. Euthyroidism was found in 456 patients (32.0%), whereas 313 patients (22.0%) patients had hyperthyroidism and the remaining 655 (46.0%) had hypothyroidism. In the group of patients with hypothyroidism, there were 559 women (85.3%) and 96 men (14.7%). The age of the women was 65.01 ± 7.90 years, and the age of the men was 65.36 ± 8.39 years (not significant). Three were 335 patients (51.1%) included in group A and 320 (48.9%) in group B. Overt hypothyroidism was diagnosed in 474 patients (72.4%), and subclinical hypothyroidism was diagnosed in the remaining 181 subjects (27.6%). Age distribution was not different in patients classified according to the severity of thyroid hypofunction, but the percentage of patients with overt hypothyroidism was significantly higher in group B in relation to group A (Table 1).

**Criteria for Diagnosis**

Overt hypothyroidism was diagnosed when patients showed simultaneously low serum concentrations of FT4 (<0.75 ng/dl) and high TSH levels (>5.0 μU/ml). Subclinical hypothyroidism was considered in the presence of high TSH levels (>5.0 μU/ml) with normal FT4 (0.75 to 2.0 ng/dl). To establish the diagnosis of secondary or central hypothyroidism, low FT4 levels, low or normal-low TSH levels, and evidence of hypothyalamic-hypophysial lesion, generally a pituitary adenoma, were required. The etiology of thyroid hypofunction was determined, taking into account clinical and analytical data at the time of diagnosis. The presence of thyroid peroxidase autoantibodies (TPOAb) in titer higher than threefold the upper limit of normal range in a patient with primary hypothyroidism was considered to diagnose chronic autoimmune thyroiditis. When patients had suffered a total or subtotal thyroidectomy for nodular goiter and presented with an increase in serum TSH concentration, the diagnosis of postoperative hypothyroidism was settled. Hypothyroidism occurring after definitive therapy for thyrotoxicosis with radioiodine or subtotal thyroidectomy was considered in a separate etiological group. Other causes of hypothyroidism, such as thyroid dysgenesis, infiltrative diseases, iodine deficiency, iodine excess, painless thyroiditis, and subacute thyroiditis, were also considered. Usual clinical, analytical, and morphological procedures were employed to diagnose these disorders.

**Assessment of Control of the Hypothyroidism**

Control of the disease was assessed by means of laboratory data obtained in every patient at the time of the study. Hypothyroidism was considered adequately controlled when serum concentrations of both FT4 and TSH were normal. In the case of secondary hypothyroidism, adequate control was considered in the presence of normal values of FT4, regardless of those of TSH. In patients with differentiated thyroid carcinoma, the requirements for adequate control included normal FT4 levels and TSH levels less than 0.4 μU/ml. To assess the autoimmune status, we measured the titer of TPOAb at the time of the study. Patients were classified as positive for TPOAb when the result of this test was higher than threefold the upper limit of normal range, and negative in the opposite case.

**Hormone Assays**

Serum concentrations of TSH and FT4 were measured in all patients. Fasting samples of venous blood were obtained from an antecubital vein between 08:00 and 09:00. Blood samples were centrifuged immediately, and the serum was stored at –20°C until assayed. Plasma TSH and FT4 concentrations were determined by using commercially available immunoenzymatic assay (AIA-PACK TSH and AIS-PACK FT4, respectively). Both assays were performed using the AIA-1200 system (Toosoh Corporation, Tokyo, Japan). For TSH assay, the sensitivity was 0.06 μU/ml, and the maximal intraassay and interassay coefficients of variation were 3.3% and 3.4%, respectively. For the immunoenzymatic assay of FT4, maximal intraassay and interassay coefficients of variation were 9.6% and 7.7%, respectively. The sensitivity of FT4 assay was 0.1 ng/dl.

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**Table 1. Distribution of Patients With Hypothyroidism Classified According to Age and Gender**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Overt Hypothyroidism</th>
<th>Subclinical Hypothyroidism</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55–64 (group A)</td>
<td>230 (68.7)</td>
<td>105 (31.3)</td>
<td>335</td>
</tr>
<tr>
<td>&gt;65 (group B)</td>
<td>244 (76.3)</td>
<td>76 (23.7)</td>
<td>320</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>69 (71.9)</td>
<td>27 (28.1)</td>
<td>96</td>
</tr>
<tr>
<td>Female</td>
<td>405 (72.5)</td>
<td>154 (27.5)</td>
<td>559</td>
</tr>
</tbody>
</table>

*Note: Figures in parentheses indicate the percentage in relation to total in each group of age or gender.*

*p < .05 versus age 55 to 64 years by χ² test.*
Serum TSH concentrations in 82 euthyroid subjects older than 55 years were 1.56 ± 1.07 µU/mL, with a range of 0.48 to 4.53 µU/mL. However, to avoid overdiagnosis in patients with TSH values close to these limits, we set as normal range the values included between 0.4 and 5.0 µU/mL. FT4 concentrations in this group of euthyroid subjects were 1.32 ± 0.28 ng/dl, with a range of 0.78 to 1.89 ng/dl. We fixed upon 0.75 and 2.0 ng/dl the limits of FT4 concentrations in order to diagnose thyroid dysfunction and assess the adequacy of therapy.

Thyroid autoimmune status was studied by the measurement of serum levels of TPOAb using the Enzymun-test from Boehringer Mannheim (Germany). The sensitivity of this test was 1 U/ml. Values obtained in normal subjects were lower than 6.2 U/ml. However, positivity for TPOAb was considered when the titer of this autoantibody was at least 18 U/ml.

Statistical Analysis

For quantitative variables, results are expressed as mean ± SD for normally distributed data and as median (range) for nonparametric data. Adjustment to normal distribution was tested by the Kolmogorov test. Categorical variables are described as ratios or percentages. For comparisons of means between two groups of patients, the Student’s t test was used for normally distributed data, and the Mann-Whitney test was employed for nonparametric data. For comparisons of means in paired groups of data, the paired Student’s t test or the Wilcoxon signed-rank test was employed, as necessary. A repeated measured analysis of variance was used to compare more than two means. Individual comparisons were performed by the Scheffé test. The Kruskal-Wallis analysis of variance by ranks was used to detect differences if data were nonparametric. Regression analysis was used to study the relationship between quantitative variables. For ratio comparisons, the chi-square test or Fisher exact test was used. A model of logistic regression was used to assess the adequacy of therapy as a function of several quantitative and qualitative variables. Differences were considered significant when p < .05.

Results

Etiology of Hypothyroidism

Autoimmune thyroiditis was the most frequent etiology of hypothyroidism, being present in 308 patients (47.0%). Of these, 278 (90.3%) showed no goiter, whereas 30 (9.7%) exhibited the goitrous form of the autoimmune thyroiditis (Hashimoto’s disease). Postoperative hypothyroidism was found in 175 patients (26.7%). Thyroid hypofunction following subtotal or total thyroidectomy was found in 89 patients with nontoxic multinodular goiter and in 22 patients with solitary thyroid nodule. Sixty-four patients underwent total thyroidectomy because of malignant tumors. Of them, 58 exhibited differentiated thyroid carcinoma (40 papillary, 16 follicular, and two mixed thyroid carcinoma). There were four cases of medullary carcinoma, one thyroid lymphoma, and one anaplastic thyroid carcinoma. Hypothyroidism after definitive treatment for previous thyrotoxicosis was found in 63 patients (9.6%). Thyroid surgery was employed in eight patients, whereas 55 patients were given radiiodine therapy. Other causes of hypothyroidism were thyrotopin deficiency (2.3%), iodine excess (0.9%), and subacute thyroiditis (0.3%). Etiology could not be established with certainty in 13.1% of the patients (Table 2).

Etiology and severity of thyroid hypofunction were significantly related (p < .001, Table 2). Postoperative hypothyroidism was uncommon among patients with subclinical thyroid hypofunction in relation to those with overt hypothyroidism (3.3 vs 35.7%), whereas the unknown etiology was more frequent in the former in relation to the latter (30.9 vs 6.3%). A significant relationship was also found between etiology of hypothyroidism and gender (p < .01). Central hypothyroidism (8.3 vs 1.3%) and iodine excess (2.1 vs 0.7%) were more frequent in males than in female patients, whereas subacute thyroiditis was found in 0.4% of women and in no men. On the other hand, etiology of hypothyroidism and the age of the patients were unrelated variables.

Thyroid Autoimmunity

TPOAb was measured in 529 patients. Autoimmunity was positive in 301 (56.9%) and negative in 228 patients (43.1%). Etiology of hypothyroidism and thyroid autoimmunity status were clearly and significantly related (p < .001, Table 3). Most patients with autoimmune thyroiditis were positive for TPOAb at the time of the study (270 out of 286, 94.4%), whereas most patients with postoperative hypothyroidism showed negative autoimmunity (101 out of 110, 91.8%).

Duration of Disease

Time of evolution of hypothyroidism since diagnosis was 2.8 years (0–45) in the whole population, 1.4 years (0–18) in men and 3 years (0–45) in women (p < .05). Sixty-two percent of patients had been diagnosed in the past 5 years and 80.0% in the past 10 years. Only 4.0% of patients showed duration of hypothyroidism longer than 20 years. Mean age at diagnosis was 60.1 ± 9.7 years (61.8 ± 9.4 in men and 59.8 ± 9.7 in women, NS). Two hundred seventy-eight patients (42.4%) were diagnosed between the ages of 0 and 5 years, whereas 56 (13.1%) presented between 5 and 10 years, 33 (8.1%) were diagnosed between 10 and 15 years. Another 39 (9.6%) had been diagnosed between 15 and 20 years, whereas 44 (10.8%) were diagnosed between 20 and 25 years.

Table 2. Etiology of Hypothyroidism in Patients Classified According to the Degree of Thyroid Hypofunction

<table>
<thead>
<tr>
<th>Classification</th>
<th>Overt Hypothyroidism (n = 474)</th>
<th>Subclinical Hypothyroidism (n = 181)</th>
<th>Total (n = 655)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune Thyroiditis</td>
<td>203 (42.8)</td>
<td>106 (58.6)</td>
<td>308 (47.0)</td>
</tr>
<tr>
<td>Postoperative Hypothyroidism</td>
<td>169 (35.7)</td>
<td>6 (3.3)</td>
<td>175 (26.7)</td>
</tr>
<tr>
<td>Treatment of Hyperthyroidism</td>
<td>53 (11.2)</td>
<td>10 (5.5)</td>
<td>63 (9.6)</td>
</tr>
<tr>
<td>Thyrotopin Deficiency</td>
<td>15 (3.2)</td>
<td>0 (0)</td>
<td>15 (2.3)</td>
</tr>
<tr>
<td>Iodine Excess</td>
<td>4 (0.8)</td>
<td>2 (1.1)</td>
<td>6 (0.9)</td>
</tr>
<tr>
<td>Subacute Thyroiditis</td>
<td>1 (0.2)</td>
<td>1 (0.6)</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Unknown Etiology</td>
<td>30 (6.3)</td>
<td>56 (30.9)</td>
<td>86 (13.1)</td>
</tr>
</tbody>
</table>

Note: Figures in parentheses indicate the percentage of each etiologic group in relation to the number of patients with overt or subclinical hypothyroidism or the total number of patients.

*p < .001 (χ² analysis) for the distribution of etiologies in groups of overt and subclinical hypothyroidism.
was slightly higher in patients with overt hypothyroidism \((n = 354, 98.7 \pm 32.9 \mu g/d\) day) in relation to patients with the subclinical form of thyroid hypofunction \((n = 31, 80.24 \pm 39.0 \mu g/d, p < .01)\).

**Control in Patients With Hypothyroidism**

Adequacy of therapy was studied in the group of 385 patients (mean age 65.2 \(\pm 8.1\) years, 49 men and 336 women, 200 group A and 185 group B) with hypothyroidism due to other causes than differentiated carcinoma. All of these patients had been treated with replacement doses of levothyroxine for more than 0.2 years at the time of the study. Adequate control of thyroid hypofunction was obtained in 260 subjects (67.5%). However, 125 patients (32.5%) showed inadequate control of the disease at the time of the study. Nineteen of them (4.9%) presented with analytical data suggesting excess levothyroxine dose, whereas in 106 (27.5%), the prescribed dose was insufficient. Doses of levothyroxine employed in these three groups of patients, as well as percentages of patients at each dose, are given in Table 4. Mean values for serum TSH at each dose of levothyroxine in patients classified according to the degree of control of hypothyroidism are shown in Figure 1.

Chi-square analysis demonstrated that adequacy of treatment did not show any significant relationship with gender, age (groups A, B), degree of thyroid hypofunction (subclinical, overt), and autoimmune status (positive, negative). However, adequacy was significantly related to etiology of hypothyroidism \((p < .01, \chi^2\)-square), time since the start of therapy, and age at diagnosis. In fact, inadequately controlled patients showed a significantly lower duration of therapy \([2 (0.2–23) vs 7 (0.3–45) years, p = .001]\) and higher age at diagnosis \((69.2 \pm 8.4 vs 56.4 \pm 10.1 years, p < .001)\) than that found in correctly controlled patients. Age \((64.3 \pm 7.3 vs 65.6 \pm 8.4 years, NS)\) was similar in both groups of patients. A model of logistic regression was performed to study the dependence of the variable adequacy of therapy as a function of several independent variables. We studied age, gender, degree of hypothyroidism, etiology, autoimmune status, age at diagnosis, duration of therapy, and dose of levothyroxine as covariates. Results of this analysis

### Table 3. Results of Test for Thyroid Peroxidase Autoantibodies in Patients Classified According to the Etiology of Thyroid Hypofunction

<table>
<thead>
<tr>
<th>Thyroid Peroxidase Autoantibodies</th>
<th>Classification</th>
<th>Positive ((n = 301))</th>
<th>Negative* ((n = 228))</th>
<th>Total ((n = 529))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune Thyroiditis</td>
<td>270 (94.4)</td>
<td>16 (5.6)</td>
<td>286</td>
<td></td>
</tr>
<tr>
<td>Postoperative Hypothyroidism</td>
<td>9 (8.2)</td>
<td>101 (91.8)</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>Treatment of Hyperthyroidism</td>
<td>21 (51.2)</td>
<td>20 (48.8)</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Unknown Etiology</td>
<td>0 (0)</td>
<td>79 (100)</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Other Causes</td>
<td>1 (7.7)</td>
<td>12 (92.3)</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

*Note: Figures in parentheses indicate the percentage of patients with positive or negative results within each etiologic group.

\(p < .001\) for comparison between adequate control versus insufficient control (analysis of variance followed by Scheffé test).

### Table 4. Dose of Levothyroxine (L-T4) in 385 Treated Patients Classified According to the Degree of Control of Hypothyroidism With Expression of the Number and Percentage of Patients at Each Dose

<table>
<thead>
<tr>
<th>Group of Control</th>
<th>Dose of L-T4 ((\mu g/d))*</th>
<th>12–25</th>
<th>25–50</th>
<th>50–75</th>
<th>75–100</th>
<th>100–125</th>
<th>125–150</th>
<th>150–200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate Control</td>
<td>99.0 ± 32.9(^a)</td>
<td>(1.2)</td>
<td>(14.6)</td>
<td>(18.1)</td>
<td>(35.4)</td>
<td>(16.5)</td>
<td>(11.9)</td>
<td></td>
</tr>
<tr>
<td>((n = 260))</td>
<td>(25 to 200)</td>
<td>(23.6)</td>
<td>(19.8)</td>
<td>(33.0)</td>
<td>(13.2)</td>
<td>(7.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excess Control</td>
<td>115.8 ± 30.3(^b)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>((n = 19))</td>
<td>(50 to 150)</td>
<td>(5.3)</td>
<td>(10.5)</td>
<td>(31.6)</td>
<td>(21.1)</td>
<td>(31.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insufficient Control</td>
<td>89.3 ± 32.4(^c)</td>
<td>2</td>
<td>25</td>
<td>21</td>
<td>35</td>
<td>14</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>((n = 106))</td>
<td>(12.5 to 175)</td>
<td>(1.9)</td>
<td>(23.6)</td>
<td>(19.8)</td>
<td>(33.0)</td>
<td>(13.2)</td>
<td>(7.5)</td>
<td>(0.9)</td>
</tr>
<tr>
<td>All Patients</td>
<td>97.2 ± 33.2</td>
<td>5</td>
<td>64</td>
<td>70</td>
<td>133</td>
<td>61</td>
<td>45</td>
<td>7</td>
</tr>
<tr>
<td>((n = 385))</td>
<td>(12.5 to 200)</td>
<td>(1.3)</td>
<td>(16.6)</td>
<td>(18.2)</td>
<td>(34.5)</td>
<td>(15.8)</td>
<td>(11.7)</td>
<td>(1.8)</td>
</tr>
</tbody>
</table>

*Values are mean ± SD. Figures in parentheses indicate the range.

1. Each interval indicates a dose ≥ inferior limit and ≤ superior limit of the interval. Figures in parentheses indicate the percentage of patients in each group.
2. \(p < .05\) for comparison between adequate control versus insufficient control. \(p < .01\) for comparison between excess control versus insufficient control (analysis of variation followed by Scheffé test).
show that the only significant variable in the model was the duration of therapy (odds ratio 1.6270, \( p < 0.0001 \)). Figure 2A shows the relationship between duration of therapy and the percentage of patients who attained an adequate control of the disease.

**Follow-up Study**

Throughout the duration of the study, we diagnosed 163 new cases of hypothyroidism. We could perform a 2-year follow-up study in 56 of these patients. This group (mean age 64.7 ± 7.3 years, 12 men and 44 women, 26 group A and 30 group B) was composed of 46 patients with overt hypothyroidism and 10 with subclinical hypothyroidism. Etiology of thyroid hypofunction was autoimmune thyroiditis in 45, radioiodine therapy in two, iodine excess in one, and unknown in eight patients. As shown in Figure 2B, we could attain an adequate control of hypothyroidism in 35 patients (62.5%) at 6 months, in 46 patients (82.1%) at 1 year, and in 49 patients (87.5%) at 2 years of therapy with levothyroxine.

**DISCUSSION**

It is generally recognized that autoimmune thyroid disease is the main cause of thyroid failure in elderly people. Nevertheless, to our knowledge, few data to support this assumption are available in the literature (1,2,20). Results of this study clearly show that autoimmune thyroiditis, especially in its nongoitrogenous form, is the most frequent cause of thyroid hypofunction in patients older than 55 years (47.0%). As expected, the presence of TPOAb was significantly related to the diagnosis of autoimmune thyroiditis. However, 5.6% of patients in this etiological group did not show positivity for TPOAb, thus indicating a negativeization of autoimmunity in some patients, as reported by others (1,2,4,20–22). It is also possible that a number of patients in the group of unknown etiology may correspond to true autoimmune thyroiditis without detectable antibodies at the time of the study (23).

Postoperative hypothyroidism was the second etiology in our series. Motives for operation were mainly multinodular goiter and thyroid carcinoma. Most patients with hypothyroidism as a consequence of therapy of hyperthyroidism were treated by radioiodine, and a minor percentage were treated by surgery, thus reflecting the present tendency to consider radioiodine as first-line therapy in elderly patients with thyrotoxicosis (5). Frequency of central hypothyroidism was similar to that reported by others (1). Excess iodine administration may cause hypothyroidism (24) as was the case in 0.9% of our patients. Lastly, subacute thyroiditis was detected in only 0.3% of patients, thus suggesting a low frequency of this disorder in aged people (20). We found a low proportion of patients with subclinical hypothyroidism (27.6%) in comparison with data reported in epidemiological surveys (7,9,13,25). This discrepancy may be explained by the fact that our population comes from patients who present in a thyroid clinic and not from the general population.

Most studied patients were diagnosed at an advanced age and therefore exhibited a relatively short duration of the disease. This suggests that most patients developed hypothyroidism at advanced stages of life. This is of interest because hypothyroidism in the elderly frequently is the result of an insidious process of thyroid failure that only has clinical manifestations in late stages (26), hence the need to make efforts to detect thyroid hypofunction in the elderly.

Therapy for hypothyroidism in the elderly has peculiarities (2–4,6,20,27). It must be started with low doses of levothyroxine (12.5–25 \( \mu \)g/day), and changes must be every 4 to 6 weeks (28). Therefore, time to attain adequate control of thyroid hypofunction may be longer than that in a young population. The replacement dose in our patients with hypothyroidism not due to previous thyroid carcinoma was al-
most 100 μg/day, which is within the recommended doses for elderly patients (23,27).

Sawin and colleagues (29) have reported an inadequate control of thyroid hypofunction in 37% of elderly patients treated with levothyroxine. We found that 31.5% of our patients were in defective control. This finding suggests that achieving adequate control in elderly people is not an easy task. It is advisable to avoid overtreatment with levothyroxine, because patients are at risk for the development of cardiac complications (20). However, only 15.2% of uncontrolled patients exhibited an excess of thyroxine dosage, whereas most of them (84.8%) were treated with an insufficient dose of thyroxine. Our results also suggest that most patients can be adequately controlled, provided that effective therapy is administered for a sufficient period of time. In fact, adequacy of therapy did not depend on age, gender, etiology, degree of hypofunction, or autoimmune status. The cross-sectional study showed that about 60% of patients treated for 2 to 5 years attained adequate control, whereas most patients who were treated for more than 5 years were in good control. This relationship was also studied in a prospective 2-year follow-up study. We obtained better results—62.5% of patients showed normalization of TSH and FT4 at 6 months and more than 80% maintained adequate control at 1 and 2 years of therapy. Differences between results in cross-sectional and longitudinal studies may be accounted for by the more intensive monitoring of patients in the latter. Results of our survey are limited because we could not analyze the effect of some variables that may influence the adequacy of therapy. Some of these are poor compliance to therapy, variability in absorption, or influence of drugs in TSH concentrations. Other important issues are changes in thyroxine content or in biological activity in manufactured tablets, as reported by some authors (30).

In summary, the present survey, performed in 655 ambulatory hypothyroid patients older than 55 years, shows that autoimmune thyroiditis and postoperative hypothyroidism are the main etiologies of thyroid hypofunction. The time from starting therapy is the main determinant of the adequacy of control of thyroid hypofunction in this population. Our results suggest that more than 80% of the patients will have adequate control within 1 year of follow-up, provided that appropriate monitoring and effective therapy are given.

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