Study on Renal Function in Patients with Subclinical Hypothyroidism. Response to Treatment with Levothyroxine


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Abstract
Chronic Kidney Disease (CKD) has been recently recognized as a public health problem. Subclinical Hypothyroidism (SCH) presents with a low Glomerular Filtration Rate (GFR) due to a reduction in renal blood flow.

Objective: To evaluate renal function in patients with SCH at diagnosis and after treatment with levothyroxine (LT4)

Materials and Methods: Thirty-three patients between 18 and 85 years of age with SCH (TSH 4.5-10 mIU/L and FT4 0.8-1.9 ng/dL, CLIA method), whose GFR was assessed prior to LT4 treatment, and twenty-four patients post average treatment ≥6 months. TPOAb (CLIA VR < at 22 KIU/L), glucose, uremia, creatinine, lipid profile were determined (method: autoanalyzer, Siemens Dimension RXL Max). To calculate the GFR, the MDRD4 formula was applied and patients were grouped into 4 stages, according to the values obtained. We worked with a significance level of 5%. The SPSS version 17 software was used for statistical analysis, applying chi-square test, and calculation of mean and standard deviation for quantitative variables.

Results: The pre- and post-treatment clinical and biochemical aspects are, respectively: 52 vs. 51 years of age, TSH (mIU/mL) 5.42 vs. 1.72, (p < 0.5), FT4 1.13 vs. 1.21 ng/dL, creatinine 0.93 vs. 0.82 mg/dL, glucose 84 vs. 87 mg/dL, total cholesterol 202 vs. 190 mg/dL, triglycerides 127 vs. 124 mg/dL, LDL-c 120 vs. 110 mg/dL, HDL-c 55 vs. 54 mg/dL and uremia 36 vs. 35 mg/dL.
Normalization of TSH and a fall in creatinine were observed (TSH p < 0.0001; creatinine p > 0.036), all other parameters p > 0.5. Only 24% of the patients had an estimated GFR ≥90 ml/min/1.73 m² prior to treatment. Changes in the GFR were observed after the administration of LT4: 74.6 ± 17 vs. 84.5 ± 22 ml/min/1.73 m² p < 0.5.

We recommend studying the renal function in every patient with thyroid dysfunction. Having excluded other causes of kidney failure, an improvement in GFR can be expected in patients with subclinical hypothyroidism after levothyroxine treatment. Rev Argent Endocrinol Metab 49:115-118, 2012.

The authors do not have conflicts of interest.

Key words: hypothyroidism, renal failure, levothyroxine, changes in the glomerular filtration rate

INTRODUCTION AND OBJECTIVE
Chronic kidney disease (CKD) has been recently recognized as a public health problem as over two million people worldwide currently require dialysis treatment or renal transplant because of diabetes, hypertension and population aging (1, 2). The concept of subclinical hypothyroidism (SCH) has emerged in recent decades as an expression of subtle changes in thyroid function with a purely biochemical definition characterized by elevated TSH with normal T4L. There is limited quantitative evidence regarding the prevalence of SCH and its impact on glomerular filtration rate (GFR). The pathophysiogetic mechanism underlying the low GFR associated with primary subclinical hypothyroidism is linked to hemodynamic alterations that lead to a decline in renal blood flow and GFR (3, 4).

The objective of our study is to evaluate the renal function in patients with primary SCH at the time of diagnosis and after treatment with levothyroxine (LT4).
MATERIALS AND METHODS

Subjects and study design

Thirty-three patients of both genders aged 18 to 85 years old with primary SCH defined by TSH values between 4.5 and 10 mIU/L and T4L of 0.8 and 1.9 ng/dL prior to therapy with LT4.

Patients with diabetes mellitus, hypertension, heart disease, nephropathy and collagen disease were excluded.

Treatment with LT4 was instituted for an average period ≥ 6 months, evaluating GFR before and after treatment.

Twenty-four patients completed the study after giving their written informed consent, previously approved by the Education and Training Committee at this institution.

Nine of the patients were excluded for not meeting the analytical requirements.

Lab test required

Lab tests were performed in all patients before and after treatment in a sample collected between 7 AM and 10 AM, after an 8-hour fasting period.

Serum measurements of TSH, T4L (RR 0.8-1.9 ng/dL) were performed by a third-generation chemiluminescent immunometric assay (CLIA). Thyroid peroxidase antibody (TPOab) measurements were performed by third-generation immunometric assay (CLIA) RR < 22KIU/L. The analyzer used for the above measurements was IMMULITE-1000 Siemens Diagnostics. Blood glucose, uremia, blood creatinine and lipid profile (total cholesterol, HDL-c, LDL-c and triglycerides) were assayed on automated analyzer, Dimensión RXL max Siemens.

GFR was calculated using the MDRD4 (Modification of Diet of Renal Disease) formula: 186 x (creatinine)^-1.154 x (age)^-0.203 x (0.7402 if female) x (1.210 if black) and patients were grouped into stages: GF > 90 ml/min (S1 or normal), 89-60 ml/min (S2), 59-30 ml/min (S3) and < 30 ml/min (S4), according to K/DQOI 2002 of the National Kidney Foundation.

Statistical Analysis

Results were expressed as mean ± SD and percentages, with a 5% significance level. T Test and Chi-square test were employed, using SPSS software, version 17.

Design: longitudinal interventional study.

RESULTS

Table I shows clinical and biochemical parameters assessed before and after treatment with LT4, where TSH normalization and a decrease in blood creatinine are observed after treatment (for TSH p < 0.0001 and blood creatinine p < 0.036), with no significant changes in all other parameters studied.

All patients tolerated the LT4 replacement dose administered for normalization of TSH.

Figure 1 shows percent distribution of the various GFR stages before treatment with levothyroxine, with only 24% being normal.

Table 2 shows changes in GFR after levothyroxine replacement therapy. We highlight the improvement in GFR in the whole population studied (74 ± 16.8 ml/min/1.73 m² to 84.5 ± 22.5 ml/min/1.73 m² with p < 0.042).

Figure 2 illustrates renal function before and after treatment with LT4 expressed by GFR calculation estimated in ml/min/1.73 m².
TABLE I. Clinical and biochemical characteristics of patients before and after treatment with levothyroxine

<table>
<thead>
<tr>
<th></th>
<th>Subclinical hypothyroidism</th>
<th>Subclinical hypothyroidism</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Without treatment N = 33</td>
<td>Treated N = 24</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.4 ± 16.5</td>
<td>50.6 ± 18.5</td>
<td>0.70</td>
</tr>
<tr>
<td>Gender F/M %</td>
<td>84.4 % (28)/15.2 % (5)</td>
<td>87.5 % (21)/12.5 % (3)</td>
<td>0.77</td>
</tr>
<tr>
<td>TSH (mIU/L)</td>
<td>5.42 ± 0.87</td>
<td>1.72 ± 0.56</td>
<td>0.0001</td>
</tr>
<tr>
<td>T4L (ng/dL)</td>
<td>1.13 ± 0.15</td>
<td>1.21 ± 0.16</td>
<td>0.07</td>
</tr>
<tr>
<td>Blood glucose (mg/dL)</td>
<td>84.4 ± 17.4</td>
<td>87.7 ± 7.5</td>
<td>0.40</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>202.3 ± 38.2</td>
<td>190.3 ± 32.5</td>
<td>0.21</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>127.3 ± 54.2</td>
<td>124.6 ± 70.5</td>
<td>0.87</td>
</tr>
<tr>
<td>LDL-c (mg/dL)</td>
<td>120.1 ± 35.9</td>
<td>110.5 ± 24.1</td>
<td>0.25</td>
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<tr>
<td>HDL-c (mg/dL)</td>
<td>55.6 ± 11.9</td>
<td>54.1 ± 9.7</td>
<td>0.50</td>
</tr>
<tr>
<td>Uremia (mg/dL)</td>
<td>36.1 ± 10</td>
<td>35.3 ± 5.9</td>
<td>0.73</td>
</tr>
<tr>
<td>Blood creatinine (mg/dL)</td>
<td>0.93 ± 0.19</td>
<td>0.82 ± 0.14</td>
<td>0.036</td>
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</table>

Figure 1. Patients grouped according to glomerular filtration rates calculated by MDRD4 formula expressed in ml/min/1.73 m², illustrating the impact of SCH on renal function.

TABLE II. Renal function before and after treatment with levothyroxine

<table>
<thead>
<tr>
<th>SCH Pretreatment n = 33</th>
<th>SCH Pretreatment n = 24</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated GFR (ml/min/1.73 m²)</td>
<td>74.6 ± 16.8</td>
<td>84.5 ± 22.5</td>
</tr>
<tr>
<td>≥ 90</td>
<td>24.2 % (8)</td>
<td>29.2 % (7)</td>
</tr>
<tr>
<td>60-89</td>
<td>57.6 % (16)</td>
<td>62.5 (15)</td>
</tr>
<tr>
<td>30-59</td>
<td>18.2 % (6)</td>
<td>8.3 % (2)</td>
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<tr>
<td>&lt; 30</td>
<td></td>
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</table>
DISCUSSION

The most common conditions associated with hypothyroidism are elevated serum creatinine levels, decreased plasma renal flow and reduced GFR\(^{(5)}\). Elevation of serum creatinine levels has also been reported in association with subclinical hypothyroidism as reported by Verhetsl et al\(^{(6)}\).

Montenegro et al. reported 75.8% of different stages of renal dysfunction associated with primary hypothyroidism\(^{(5)}\).

Several reports show an increased prevalence of subclinical and clinical hypothyroidism in people with CKD\(^{(3)}\). Conversely, there are limited reports reflecting the impact of subclinical hypothyroidism on the renal function of healthy individuals\(^{(7)}\).

The importance of our observations lies in the fact that only 24% of patients with subclinical hypothyroidism had a GFR equal to or above 90 ml/min/1.73 m\(^2\).

An adequate renal plasma flow has been positively associated with normal thyroid function\(^{(8)}\). The reasons for the decline in renal plasma flow include an increased vascular resistance and a decrease in cardiac output\(^{(9)}\).

In agreement with Adrees M. et al., who showed the effect of levothyroxine with an increase in GFR in hypothyroid patients and a decrease in GFR on discontinuation of the thyroid hormone, we observed an pre- and posttreatment impact expressed as an improvement in mean estimated GFRs\(^{(10)}\).

Our findings and the evidence found in medical literature encourage us to recommend that all patients with different stages of thyroid hypofunction should have their kidney function tested.

In the absence of other causes of renal failure, an improvement in GF can be expected in patients with subclinical hypothyroidism treated with replacement doses of levothyroxine.

REFERENCES


