L-Thyroxine in the Treatment of Obesity Without Increase in Loss of Lean Body Mass

By L. Lamki, C. Ezrin, I. Koven, and G. Steiner

The present study compares the loss of body weight and lean body mass observed in obese patients while receiving a restricted (600 cal) diet with that obtained in the same individuals while receiving a more satisfying (1200 cal) diet plus a large dose of L-thyroxine (T₄). Four massively obese male patients were studied. Two patients had one period of 600-cal diet plus T₄ 0.3 mg/day interposed between two periods of 1200-cal diet plus T₄ 0.9 mg/day. The other two patients had one period of 1200-cal diet plus T₄ 0.9 mg/day interposed between two periods of 600-cal diet plus T₄ 0.3 mg/day. Both diets were constant and relatively high in protein. Their activity program did not change when they changed diet and T₄ dose. None of the patients had any serious side effects. There was no significant difference in the amount of weight lost on the two protocols. Each patient lost more body water at the beginning of the study than at the end regardless of the protocol. The average negative nitrogen balance during the two treatments was approximately equal. It appears from the present study that under appropriate circumstances, moderately large doses of T₄ do not necessarily cause erosion of lean body mass. The role of T₄ in the treatment of special cases of obesity is worthy of further trial.

The use of thyroid in the management of obesity has been a subject of controversy. A major objection to the use of pharmacologic doses of this hormone is that the extra weight loss it produces is probably derived from the loss of lean body mass. Ball and Kyle¹² have shown that four obese subjects lost more lean body mass with diet plus large doses of desiccated thyroid than with the diet alone. Sabe et al.³ have shown that administering desiccated thyroid to patients on starvation programs increased their weight loss by almost 40%. However, it did not alter their relative protein loss. This remained about 8% of the body weight lost. Danowski et al.⁴ showed that out of 93 patients a greater number lost more weight on diet plus desiccated thyroid than on diet alone, and that it was well tolerated. Cornman and Alexander⁵ who used up to 300 μg of triiodothyronine (T₃) in the treatment

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of obesity found that it was well tolerated and produced a "satisfactory weight loss." Hollingsworth et al. recommended T3 in pharmacologic doses for treatment of motivated, massively obese patients who do not have hypertension, diabetes requiring insulin, or arteriosclerotic heart disease. Bray et al. have recently reported favorably on the use of T3 anabolic steroids.

The present study compares the loss of body weight and lean body mass observed in obese patients while receiving a restricted (600 cal) diet with that obtained in the same individuals while receiving a more satisfying (1200 cal) diet plus a high of L-thyroxine (T4).
MATERIALS AND METHODS

Four massively obese male patients weighing 134–172 kg were the subjects of this study. They were all seen as out-patients for at least 3 wk prior to admission. During this time, they were given L-thyroxine (T4) 0.3 mg daily p.o. and were on apparently normal diets. The diets contained sufficient calories to maintain each patient’s weight after the initial 10 days. The patients were then admitted to the Clinical Investigation Unit of the Toronto General Hospital. During the first week they continued on T4 (0.3 mg/day) and the same diet that they had received as out-patients. Hereafter, two patients were started on protocol I, and two on protocol II. In protocol I the patients commenced with a 4-wk period during which they received 1200 cal plus T4 (0.9 mg/day), followed by a 3-wk period during which they received 600 cal plus T4 (0.3 mg/day). Finally, they were returned to the first program, 1200 cal plus T4 (0.9 mg/day), for 4 wk. Protocol II was the reverse pattern
of protocol I. In it the patients started on 600 cal plus \( T_4 \) (0.3 mg/day), followed by 1200 cal plus \( T_4 \) (0.9 mg/day) and finished with 600 cal plus \( T_4 \) (0.3 mg/day). The doses of \( T_4 \) were chosen either to supply pharmacologic amounts or to maintain physiologic levels. All patients were free of hypertension, arteriosclerotic heart disease and their fasting and 2-hr p.c. plasma sugars were normal.

**Diet**

Both diets were constant. The 1200-cal diet contained 108 g protein, 50 g fat, 80 g carbohydrate, 100 meq sodium and 80 meq potassium. The 600-cal diet contained 50 g protein, 18 g fat, 60 g carbohydrate, 60 meq sodium and 80 meq potassium. The sodium and potassium contents of the diet were measured by flame photometry using lithium as internal standard, and the nitrogen content by the microKjeldahl method.8

**Urine and Stools**

Sodium, potassium, and nitrogen6 contents were measured in urines collected over 24-hr periods, and in stools collected over 4-day periods. Sodium and potassium were measured by flame photometry as above. The creatinine content of each 24-hr urine was assayed9 in order to ensure adequacy of collection.

**Changes in Body Composition**

By using \( ^{3}H_2O \) (1 mCi in 5 ml saline), total body water (TBW) was measured by the tritium dilution method.10

Changes in lean body mass (LBM) were derived from nitrogen balance studies. It has been indicated11 that 1 g nitrogen represents 27 g of extracellular fluid-free lean body mass. Changes in fat content were derived from the equation of Edelman et al.12

**Activity**

Patients were constantly under supervision throughout their stay in the Clinical Investigation Unit. They had scheduled and constant activity in the physiotherapy unit as well as on the ward. Their activity program did not change when they changed diet and \( T_4 \) dose.

**RESULTS**

**Clinical Effects of Thyroxine**

None of the patients had any serious side effects. Excessive perspiration was observed in all patients while on 0.9 mg \( T_4 \). The blood pressure did not rise. In one patient, the average pulse rate increased from 65 to 85, and in another patient the average pulse rate increased from 70 to 80 with 0.9 mg \( T_4 \). Serum thyroxine concentrations exceeded 20 \( \mu g/100 \) ml with the 0.9 mg \( T_4 \) dose. Weekly electrocardiograms showed no change.

**Weight Loss and Total Body Water**

During the balance studies, patients lost 30–35 kg body weight (Figs. 1-4) and 9–11 kg body water. Each lost more body weight as well as more body water at the beginning of the study than at the end, regardless of the protocol. There was no statistically significant difference in the amount of weight lost on the two forms of treatment (Table 1), except in one patient (F.H.) who lost more weight on the 600 cal–0.3 mg \( T_4 \) program.

**Nitrogen Balance and Lean Body Mass**

Nitrogen balance during the period of 1200-cal high \( T_4 \) treatment was compared with that during the 600-cal normal \( T_4 \) period. In making this
Table 1. Changes in Body Composition

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Lean Mass</th>
<th>Water</th>
<th>Fat</th>
<th>Body Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient D.M.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_4$ (0.3 mg) + 600 cal</td>
<td>131.8</td>
<td>161.0</td>
<td>216.3</td>
<td>509.1</td>
</tr>
<tr>
<td>$T_4$ (0.9 mg) + 1200 cal</td>
<td>150.0</td>
<td>146.4</td>
<td>150.0</td>
<td>446.4</td>
</tr>
<tr>
<td>$T_4$ (0.3 mg) + 600 cal</td>
<td>110.0</td>
<td>95.2</td>
<td>256.7</td>
<td>461.9</td>
</tr>
<tr>
<td><strong>Patient D.B.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_4$ (0.9 mg) + 1200 cal</td>
<td>82.1</td>
<td>166.6</td>
<td>152.0</td>
<td>410.7</td>
</tr>
<tr>
<td>$T_4$ (0.3 mg) + 600 cal</td>
<td>104.7</td>
<td>142.8</td>
<td>242.9</td>
<td>490.4</td>
</tr>
<tr>
<td>$T_4$ (0.9 mg) + 1200 cal</td>
<td>89.3</td>
<td>71.4</td>
<td>150.0</td>
<td>310.7</td>
</tr>
<tr>
<td><strong>Patient F.H.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_4$ (0.9 mg) + 1200 cal</td>
<td>82.2</td>
<td>210.7</td>
<td>139.2</td>
<td>432.1</td>
</tr>
<tr>
<td>$T_4$ (0.3 mg) + 600 cal</td>
<td>97.4</td>
<td>181.8</td>
<td>234.4</td>
<td>513.6</td>
</tr>
<tr>
<td>$T_4$ (0.9 mg) + 1200 cal</td>
<td>60.2</td>
<td>171.4</td>
<td>129.1</td>
<td>360.7</td>
</tr>
<tr>
<td><strong>Patient W.F.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_4$ (0.3 mg) + 600 cal</td>
<td>115.1</td>
<td>243.8</td>
<td>150.1</td>
<td>509.0</td>
</tr>
<tr>
<td>$T_4$ (0.9 mg) + 1200 cal</td>
<td>71.2</td>
<td>140.0</td>
<td>242.3</td>
<td>453.5</td>
</tr>
</tbody>
</table>

Data represent average losses in various compartments and in total body weight (g/day) in patients D.M., D.B., F.H., and W.F. Patient W.F. decided to opt out of the study in the middle of the second period of $T_4$ (0.3 mg) plus 600-cal diet.

The combination of this with the greater nitrogen intake, on the 1200 cal diet, indicates that this regimen was probably associated with an increased nitrogen turnover, but that there was no change in the net nitrogen balance.

### DISCUSSION

We have compared a fairly standard form of treatment of obesity (600 cal − 0.3 mg $T_4$) in a small, uncontrolled study of 4 individuals. The average negative nitrogen balance during periods of treatment with 1200 cal − 0.9 mg $T_4$ did not exceed that during treatment with 600 cal − 0.3 mg $T_4$. The latter regimen was probably associated with an increased nitrogen turnover, but the former regimen was not associated with a significant change in the net nitrogen balance.

Table 2. Nitrogen Balance Studies

<table>
<thead>
<tr>
<th>Patient</th>
<th>Thyroxine (0.3 mg/day) + 600 cal</th>
<th>Thyroxine (0.9 mg/day) + 1200 cal</th>
</tr>
</thead>
<tbody>
<tr>
<td>F.H.</td>
<td>3.56 ± 0.36</td>
<td>3.06 ± 0.28</td>
</tr>
<tr>
<td>W.F.</td>
<td>4.21 ± 0.22</td>
<td>2.69 ± 0.30</td>
</tr>
<tr>
<td>D.M.</td>
<td>4.84 ± 0.33</td>
<td>5.48 ± 0.50</td>
</tr>
<tr>
<td>D.B.</td>
<td>4.02 ± 0.40</td>
<td>3.02 ± 0.36</td>
</tr>
<tr>
<td>Mean of all patients combined</td>
<td>4.09 ± 0.14</td>
<td>3.45 ± 0.17</td>
</tr>
</tbody>
</table>

Data represent mean values (± SEM) for negative nitrogen balance (g N lost/day) on each patient, and for all patients combined. Means are calculated from individual daily data, obtained as outlined in Materials and Methods. W.F. completed only one period on 0.3 mg $T_4$. 
cal) with a thyroxine-induced hypermetabolic state (1200 cal + 0.9 mg T4). During the 600-cal period, physiologic amounts of T4 (0.3 mg/day) were given in order to maintain a steady physiologic supply of this hormone. Both forms of treatment induced approximately equal body weight loss, lean body mass loss and total body water loss. It is possible that either the extra 600 cal, or the extra protein, or both prevented the erosion of LBM previously reported with pharmacologic dose of T4.

It appears from the present study that, under appropriate circumstances, moderately large doses of L-thyroxine do not necessarily cause erosion of lean body mass. Therefore this particular objection to thyroxine may not be valid provided caloric and protein intake are carefully selected. As the patients in this study were more content on the 1200-cal diet than on the 600-cal diet, thyroxine may be a useful adjunct in the treatment of obesity; however, its long-term effects and possible cardiac toxicity remain to be assessed. Thyroxine can never replace self-discipline and retraining towards good nutritional habits, but its role in the treatment of special cases of obesity is worthy of further trial.

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