NOTE
Augmentation of Thyrotropin Responses to Thyrotropin-Releasing Hormone Following Inorganic Iodide

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Synopsis

Eight euthyroid subjects were administered 500 μg of thyrotropin-releasing hormone intravenously before and after the administration of 10 mg potassium iodide daily for 7 days. Basal serum concentrations of TSH and the response of TSH to TRH were significantly increased following iodide treatment, while serum levels of T4 and T3 did not differ significantly. It is suggested that the administration of 10 mg/day of potassium iodide can produce similar changes in serum TSH to those in previous reports using large doses of iodide.

It has been demonstrated by Vagenakis and coworkers (Vagenakis et al., 1974) that small decreases in serum thyroid hormone concentrations in response to treatment with 190 mg of inorganic iodide daily for 10 days, were associated with slight increases in basal serum thyrotropin (TSH) concentrations and pronounced increases in the TSH response to thyrotropin-releasing hormone (TRH). Similar results were obtained from experiments in which normal volunteers were given 50 mg or 250 mg of inorganic iodide daily for 13 days (Saberi and Utiger, 1975).

The present study was undertaken to determine whether similar changes in serum thyroid hormone and/or TSH concentrations could be induced with much smaller doses of iodide for a shorter duration than those administered by previous investigators.

Materials and Methods

Studies were performed in eight normal male volunteers ranging in age between 18 and 22 yr. They were asked to restrict their seaweed diets during the experimental period starting one week before iodide treatment. The first TRH test was performed after a week of a seaweed restricted diet. Samples of blood were obtained immediately before an iv injection of 500 μg synthetic TRH, as well as 30, 60, and 90 min thereafter. Subjects were then given 10 mg of potassium iodide daily for one week. On the last day another TRH test was done, as described above. Serum T4 concentrations were measured by Tetrasorb R² (normal range 5.3-14.5 μg/100 ml), and serum T3 and TSH concentrations by radioimmunoassay using T3-RIA Kit R² (0.8-1.8 ng/ml) and Phadebas R TSH Test R³ (<7.2 μU/ml), respectively. Results obtained before and after iodide treatment were analysed by the paired t test.
Results

Base-line serum T₄, T₃ and TSH concentrations and their responses to TRH before and after iodide administration are shown in Table 1. There was no significant change in values for serum T₄ or T₃ following iodide treatment either in the basal levels or in the responses to TRH.

Base-line serum TSH concentration, however, increased significantly, the mean value changing from 1.6±0.1 (mean±SE) to 2.5±0.4 µU/ml (p<0.05). Values for serum TSH less than 1.5 µU/ml were calculated as 1.5 µU/ml. The TSH response to TRH was also augmented significantly 30 min after TRH, the mean value changing from 13.3±1.6 to 19.4±2.8 (p<0.01) and 60 min after TRH, from 10.8±1.6 to 15.0±2.4 (p<0.05) following iodide treatment. Values for TSH 90 min after TRH did not show any significant difference.

Discussion

The average daily intake of iodide in Japan has been reported to amount to several milligrams, ranging between 100 µg and 20 mg (Nagataki, et al., 1967; Nagataki, 1974). It has been shown that 10 mg/day of iodide was effective in the treatment of hyperthyroidism (Harden, et al., 1964; Nagataki, et al., 1970). The present study was performed, therefore, to determine whether significant changes of serum T₄, T₃ and TSH concentrations in basal levels and in their responses to TRH could be obtained with 10 mg/day of potassium iodide in euthyroid subjects.

The results of changes in base-line serum TSH concentrations and in the responses of TSH to TRH following iodide treatment were essentially the same as those of previous investigators (Vagenakis, et al., 1974; Saberi and Utiger, 1975). Base-line serum T₄ or T₃ values, however, did not change significantly in our study, whereas, slight but significant decreases in serum T₄ and

Table 1. The Effect of iodide on serum basal concentrations of T₄, T₃ and TSH and on their responses to TRH*

<table>
<thead>
<tr>
<th></th>
<th>Basal Concentrations</th>
<th>Responses to TRH</th>
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<tbody>
<tr>
<td></td>
<td>30 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Serum T₄** (µg/100 ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>before</td>
<td>10.3±0.6</td>
<td>10.7±0.5</td>
</tr>
<tr>
<td>after</td>
<td>9.9±0.4</td>
<td>9.7±0.4</td>
</tr>
<tr>
<td>difference</td>
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<td>−1.0±0.4</td>
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<tr>
<td>Serum T₃** (ng/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>before</td>
<td>1.10±0.05</td>
<td>1.10±0.03</td>
</tr>
<tr>
<td>after</td>
<td>1.14±0.04</td>
<td>1.20±0.07</td>
</tr>
<tr>
<td>difference</td>
<td>0.04±0.07</td>
<td>0.10±0.07</td>
</tr>
<tr>
<td>Serum TSH** (µU/ml)</td>
<td></td>
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</tr>
<tr>
<td>before</td>
<td>1.6±0.1</td>
<td>13.3±1.6</td>
</tr>
<tr>
<td>after</td>
<td>2.5±0.4</td>
<td>19.4±2.8</td>
</tr>
<tr>
<td>difference</td>
<td>0.9±0.4***</td>
<td>6.1±1.8***</td>
</tr>
</tbody>
</table>

* Samples of blood were obtained immediately before an i.v. injection of 500 µg of synthetic TRH, and 30, 60, and 90 min thereafter.
** Values shown are the mean±S.E. of the results obtained from 8 normal male volunteers, before and after administration of 10 mg of KI daily for 1 week.
*** Significantly different by paired t test (p<0.05).
T₃ levels were observed after iodide administration in the earlier studies (Vagenakis et al., 1974; Saberi and Utiger, 1975). Saberi and Utiger (1975) observed a significant decrease in basal serum T₄ and T₃ concentrations on several days during iodide treatment only when the results were analyzed by the paired t test, using the mean of the 5 pretreatment days as control. They found no significant decrease in the basal serum T₄ or T₃ concentrations on the day when the second TRH test was done after iodide administration. In our study, the serum T₄ and T₃ concentrations were measured only on the day of TRH testing before and after iodide treatment. A significant decrease in serum thyroid hormone levels might also have been detected in the present study if serum thyroid hormone concentrations had been determined daily before and during iodide treatment.

Recent studies demonstrated that clinically undetectable increases in circulating thyroid hormones soon blunt or abolish the rise of serum TSH that TRH normally induces (Snyder and Utiger, 1972; Snyder and Utiger, 1973; Ridgeway, et al., 1973). Conversely, euthyroid patients with very minor degrees of thyroid insufficiency showed augmented TSH responses to TRH (Franco et al., 1973; Evered et al., 1973; Gordin et al., 1974). The present studies provide evidence that increases in responses of TSH to TRH may be induced with much smaller doses of iodide for a shorter duration than those administered by previous investigators. Although we did not observe significant changes in serum T₄ or T₃ levels after iodide, it is not certain whether actual decreases in serum T₄ and/or T₃ concentrations occurred in those patients.

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References