Thyroid Screening with Triiodothyronine Assay

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ABSTRACT

The relative independence of serum T-3 from changes in thyroid binding protein levels makes it a more effective screening test for hyper- and hypothyroidism than the T-4 assay alone. In fact, it’s efficiency is comparable to that of the free T-4 index.

Introduction

The purpose of this study was to determine whether or not the serum triiodothyronine by radio-immunoo assay (RIA) can be used as a thyroid function screening procedure. Presently, serum thyroxine is the most commonly used thyroid function screening assay; however, it has two disadvantages. First, it is not specific because serum levels of total thyroxine are affected by a wide variety of drugs and non-thyroid related illnesses. Consequently, large numbers of euthyroid individuals, usually women who are on oral contraceptives, have abnormal T-4 values. This, of course, is because only the unbound circulating thyroid hormones are physiologically active. Total thyroxine levels provide a measure of thyroid activity only in patients who have normal levels of thyroid-binding proteins. The total thyroxine levels do not accurately reflect thyroid activity in those patients whose normal ratios of free thyroxine to protein-bound thyroxine are upset by estrogens, other anabolic and catabolic steroids, kidney disease or hepatitis. The second problem is that the unusual cases of T-3 thyrotoxicosis are missed.

On the other hand, serum levels of free thyroxine are directly related to thyroid activity. This unbound thyroxine is usually estimated by performing a T-4 test and resin T-3 uptake or thyroid globulin assay and calculating the free thyroxine index (FTI). The free thyroxine index, therefore, is more specific. However, it generally requires performing two separate assays. Even then, it will miss the cases of T-3 thyrotoxicosis.

Triiodothyronine is less firmly bound than T-4 to thyroid binding globulins (TBG) and also has greater physiologic activity than thyroxine. Consequently, it
is much less affected by changes in the concentration of TBG and those drugs which produce changes in the TBG levels. If estrogen, in particular, affects the levels of T-3 less than T-4, then perhaps the T-3 RIA is a more reliable indicator of thyroid status than the total thyroxine assays. In fact, it might be nearly as reliable as a free thyroxine index. If so, the T-3 RIA can be used not only to detect cases of T-3 thyrotoxicosis, as it presently is used, but also can be used as a screening procedure and replace the T-4, RT-3U combination.

If done in quantity, the serum triiodothyronine assays would not only be simpler to perform but less expensive than the present screening combinations.

Methods

Simultaneous determinations of T-3 by RIA, resin uptake and thyroxine by RIA were performed on sera from 500 patients. The normal range of these assays is listed in table I. Free T-4 (FT-4I), free T-3 (FT-3I) and combined thyroid hormone (CTI) indices were calculated (table II).

Demers and Krieg1 have reported a combined thyroid hormone index, based on measurements of thyroxine, triiodothyronine and T-3 resin uptake. In contrast to previous thyroid hormone indices, the combined thyroid index incorporated both T-3 and T-4 measurements. They reported that the CTI appears to have superior predictive value in terms of clinical correlation with thyroid disease.1

Thyroid stimulating hormones (TSH) and I-131 uptakes were also performed when indicated.

Results

Of the 500 patients studied, 420 were euthyroid. Of these 420 euthyroid patients, 332, or 79 percent, had all of their assay levels falling within normal range. In addition, 88 (21 percent) of these euthyroid patients had one or more of their thyroid assays falling out of the normal range. These 88 euthyroid patients, who were incorrectly classified by one or more of the assays, are depicted in figure 1. A total of 53 patients had a diagnosis of hyperthyroidism based on a combination of elevated FT-4 I, FT-3 I and characteristic clinical findings relieved by surgery or anti-thyroid medication. Twenty-seven patients had a diagnosis of hypothyroidism confirmed by an elevated serum TSH. These hyper- and hypothyroid patients are appropriately depicted in figure 1.

All 53 hyperthyroid patients had high levels by at least one of the assays; however, nine patients had normal values by at least one assay.

All 27 hypothyroid patients had low values by at least one assay method; however, six patients also had normal values by at least one assay method.

In table III it is shown that the T-3 detected not only as many abnormal patients as did the T-4, FT-3I or FT-4I but had fewer false positives. Only by performing and evaluating all three tests

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>Range of Thyroid Function Assays</th>
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<tbody>
<tr>
<td>Assay</td>
<td>Mean</td>
</tr>
<tr>
<td>T-3 (ng per dl)</td>
<td>130 ± 35</td>
</tr>
<tr>
<td>T-4 (µg per dl)</td>
<td>8.4 ± 2.2</td>
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<tr>
<td>FT-3I</td>
<td>3.4 ± 0.8</td>
</tr>
<tr>
<td>FT-4I</td>
<td>2.2 ± 0.5</td>
</tr>
<tr>
<td>CTI</td>
<td>7.1 ± 1.4</td>
</tr>
</tbody>
</table>

*1 S.D. calculated for all euthyroid patients.

<table>
<thead>
<tr>
<th>TABLE II</th>
<th>Thyroid Function Indices</th>
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<tbody>
<tr>
<td>FT-4I</td>
<td>T-4 × RT-3U</td>
</tr>
<tr>
<td>FT-3I</td>
<td>T-3 × RT-3U</td>
</tr>
<tr>
<td>CTI</td>
<td>(T-3 + T-4) / 60 × RT-3U</td>
</tr>
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(RT-3U, T-3 and T-4) together, via the CTI, was it possible to reduce the number of false negatives. On the other hand, the CTI had a greater number of false positives than did the T-3. The T-3 was quite good in separating hyperthyroidism from euthyroidism. No euthyroid patient had an elevated T-3 value, whereas 52 euthyroid patients had elevated T-4 values and 17 had an increased FT-4I. The T-3 assay did not detect mild hyperthyroidism in five patients with thyroiditis. The T-4 did not detect four other hyperthyroid patients. The T-3 was not quite as good as the T-4 in separating euthyroid from hypothyroid patients. However, the nine euthyroid patients with low T-3 levels either had a malignancy, a severe renal disease or were elderly. The T-4 did not detect four hypothyroid patients, whereas the T-3 assay failed to detect only two hypothyroid patients.

The T-3 assay is at least as sensitive as the T-4 assay (table IV). In addition, it has a much greater specificity than the T-4. In fact, this study suggests that the T-3 assay alone is as specific and as sensitive as the FT-4I. The sensitivity of the calculated CTI was slightly better than that of the T-3 assay. However, the predictive value of a positive result was greater for the T-3 than for any of the other assays or indices.

**Discussion**

The fewer false positives obtained using the T-3 assay instead of the T-4 assay as a screening test obviates the need for performing additional studies on many euthyroid individuals, particularly women who are pregnant or who are on oral contraceptives.

By using the T-3 assay as a thyroid function screening test, large numbers of individuals with normal T-3 levels can be effectively identified as being euthyroid.
Only the remaining small number of individuals with abnormal T-3 results need have further testing in order to confirm or rule out a diagnosis of hyper- or hypothyroidism. The T-3 by radio-immuno assay is recommended as a screening procedure for thyroid disease. If the results are low or borderline low, a TSH can be performed to confirm or rule out primary hypothyroidism. An elevated T-3 level appears to be diagnostic of hyperthyroidism, but it can be confirmed with a T-4 and resin uptake and/or an I-131 uptake. Patients who have a normal T-3 but clinical evidence of hyperthyroidism or thyroiditis should also have a T-4 and/or an I-131 uptake.

References