A Report of Hypothyroidism Induced By an Over-the-Counter Fat Loss Supplement (Tiratricol)

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Prior to presentation, two physically fit adults, a 39-year-old male and 40-year-old female, began supplementation with an over-the-counter thyroid preparation marketed as a metabolic accelerator and fat loss aid, tiratricol. Both participants took the supplement for 5 weeks (3000–4000 mcg/d) and 3 weeks (6000 mcg/d), respectively. At presentation, both complained of lethargy, loss of appetite, and muscle weakness. Upon initial laboratory evaluation, results revealed low thyroid stimulating hormone with profoundly elevated T3 values in both patients. After an extensive review of the literature, the cause of the problem was found to be the nutritional supplement they consumed contained tiratricol. After discontinuation of the supplement, thyroid levels slowly returned to baseline 40 days and 5 months later, respectively.

Key Words: triax, supplements, thyroid

Introduction

Tiratricol (3,5,3’-triiodothyroacetic acid) is a weakly active metabolite formed by oxidative deamination and decarboxylation of triiodothyronine (T3; 1). Used clinically in resistant thyroid syndrome, the compound possesses thyromimetic activity at the anterior pituitary, and demonstrates limited calorigenic potency in peripheral tissues (2–4). Bracco et al. found a substantial inhibition of TSH secretion (0.17 mU/L) after only 1 week of 1700 mcg/d tiratricol administration in 14 euthyroid participants (2). These patients failed to show any increase in basal metabolic rate or sleeping energy expenditure, revealing the substantial endocrine but negligible metabolic effects of tiratricol (2). With a half-life of just over 6 hours (5) and no effects in the periphery (2), tiratricol is ineffective in carrying out the normal metabolic actions associated with thyroid hormones. Centrally, tiratricol is a potent inhibitor of thyrotropin (TSH) due to its high binding affinity for transthyretin, the nuclear T3 receptor, and β2-receptors on thyrotroph cells (4). Since tiratricol is metabolized to T3 in the periphery, circulating triiodothyronine levels can become supraphysiologic. Confounding to some physicians, tiratricol will increase laboratory readings for T3 due to its cross reactivity with the T3 detection antibody, while
endogenous T3 levels are suppressed (7, 8). Table 2 shows the percentage of cross-reactivity of various thyroid metabolites. Supraphysiologic levels of T3, consequently, cause negative-feedback inhibition of TSH secretion that eventually results in decreased oxygen consumption, heat production, and basal metabolic rate (9). While decreased TSH level in the presence of suppressed thyroxine level is expected in a hypothyroid state, simultaneous supraphysiologic T3 levels do not follow ordinary thyroid physiology. This confounding example of abnormal thyroid physiology was discovered in the 2 participants described herein.

Physicians who are unfamiliar with the supplement/drug regimens available over the counter may mistakenly misdiagnose an excessive quantity of T3, thyrotoxicosis, which is actually due to tiratricol. A past report warned of possible misdiagnoses of T3 thyrotoxicosis due to tiratricol ingestion in bodybuilders (8). Due to the compound’s inability to support cell metabolism, patients taking tiratricol become peripherally hypothyroid, creating the side effects described in the following report.

Table 1 Post-tiratricol Supplementation Thyroid Function Tests

<table>
<thead>
<tr>
<th>Patient</th>
<th>Dose of tiratricol mcg</th>
<th>Duration of use</th>
<th>T3 uptake %</th>
<th>T3 total ng/dl</th>
<th>T4 total ug/dl</th>
<th>TSH mU/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3000–4000</td>
<td>21 days</td>
<td>46.7</td>
<td>—</td>
<td>1.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>2</td>
<td>6000</td>
<td>56 days</td>
<td>—</td>
<td>465</td>
<td>2.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Reference range</td>
<td>N/A</td>
<td>N/A</td>
<td>22–35</td>
<td>60–181</td>
<td>4.5–12.5</td>
<td>0.4–5.5</td>
</tr>
</tbody>
</table>

Note. Empty cells indicate values missing due to change in thyroid panel by laboratory.

Table 2 Cross-Reactivity of Thyroid Metabolites

<table>
<thead>
<tr>
<th>Analogue</th>
<th>Cross reaction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,3’,5’-Triiodo-L-thyronine (T3)</td>
<td>100</td>
</tr>
<tr>
<td>3,3’,5’-Triiodothyroacetic acid (TRIAC)</td>
<td>100</td>
</tr>
<tr>
<td>L-Thyroxine (L-T4)</td>
<td>0.015</td>
</tr>
<tr>
<td>D-Thyroxine (D-T4)</td>
<td>0.07</td>
</tr>
<tr>
<td>3,3’,5’-Triiodo-L-thyronine (rT3)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

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Case Reports

Case 1

A 39-year-old male athlete presented with fatigue, loss of appetite, sweats, chills, lethargy, and inability to exercise in accordance with his normal regimen. The patient was questioned about any over-the-counter or prescription medicines consumed but admitted to only taking the tiratricol-containing supplement. No signs or symptoms of preexisting medical conditions were present upon physical examination and health history. Lab values upon initial evaluation revealed abnormal levels of all thyroid regulatory hormones. Serum T3 uptake was 46.7%, total T4 was 1.7 ug/dl, and free T4 was 0.8 mg/dl. TSH was < 0.01 mU/L. Upon review of his presentation lab data, he was further questioned about his use of over-the-counter supplements, in particular tiratricol. The patient stated that he took the preparation at a daily dose of 3000 to 4000 mcg for 1 month, which he discontinued 2 months prior to presentation. The dosage consumed was in accordance with the directions labeled on the bottle by the manufacturer. After his initial evaluation, the time course necessary for the patient to return to normal was 5 months. Blood serum T4 total and TSH levels returned to normal, reaching 3.6 and 1.7, respectively, after the 5-month period.

Case 2

A 40-year-old female, weighing 59 kg and 64 in. in height, began taking tiratricol in association with resistance training and a dietary program directed toward body fat loss. The patient exercised 4–5 times per week and consumed a low-fat diet sufficient in protein and moderate intake of complex carbohydrates. The patient showed no signs or symptoms of preexisting medical conditions upon physical examination and health history. At presentation to the physician, she was taking no over-the-counter supplements or prescription medications. Prior to supplementation of the compound, laboratory values were absent of any thyroid abnormalities and within normal laboratory reference ranges (T3 total 86 ng/dl, T4 8.3 mcg/dl, TSH 0.62 mU/L). During follow-up, the patient complained of weight gain accompanied by decreased appetite and severe lethargy despite stringent dieting and exercise. Physician consultation found that the patient was taking no prescription medications or over-the-counter supplements other than Triax (tiratricol). Blood pressure and pulse recordings showed normal values of 129/78 and 87 bpm, respectively. The patient ingested 6000 mcg/d of the product for 21 days prior to follow-up. Blood work showed the following abnormalities: T3 total 465 ng/dl, T4 total 2.9 mcg/dl, and TSH < 0.01 mU/L. Initial therapy consisted of discontinuation of the Triax. Follow-up blood analysis 40 days after discontinuation of tiratricol showed a T4 total value slightly below normal limits (4.2 ug/dl), with TSH (2.7 mU/L) and T3 returning within normal reference ranges.

Discussion

At face value, laboratory analysis of a patient administering tiratricol would lead one to assume an overproduction of T3 from the thyroid. However, suppressed thyroxine values in conjunction with suppressed TSH conflict with this assumption. Impossible in a normal hypothalamus-pituitary-thyroid axis (HPTA), secondary
measurements or interpretations must be made in light of the confounding laboratory results. Although supraphysiologic T3 levels, thyrotoxicosis, would normally result in an elevated basal metabolism, increased body temperature, tachycardia, and possibly weight loss, such is not the case with tiratricol. Since the thyroid metabolite acts centrally and minimally in the peripheral, it’s influence is limited to suppression of the body’s thyroid regulating axis. As this occurs, the body will fall into a hypothyroid state, experiencing a low basal metabolic rate, decreased body temperature, diminished appetite, and weight gain. The use of tiratricol as a method of reducing adipose tissue and increasing basal metabolic rate has obviously proven to be contradictory to its mechanism of action.

The interesting aspect about tiratricol lies not just in its unique pharmacology, but that the compound is marketed as a “nutritional” supplement in both the United States and Europe (brand names TRIAX, Tri-Cuts, and Tricana). The supplement industry’s advertising campaigns have ignored, and in some cases attempted to contradict, peer reviewed scientific literature that demonstrates detrimental effects of tiratricol both to energy metabolism and mechanisms of thyroid regulation when given to euthyroid individuals (2, 7, 10).

The science behind tiratricol reveals it is not a nutritional supplement, but a potent drug capable of inducing thyroid abnormalities when consumed inappropriately. While the supplement industry has in the past been guilty of misrepresenting science, never has there been such a blatant disregard of public health as in the case of those companies selling tiratricol. On November 11, 1999, the Food and Drug Administration (FDA) issued a warning to consumers who have consumed or purchased any products containing the compound. Through the aid of the Medwatch program <http://www.fda.gov/medwatch> and the FDA, the State of Missouri initially embargoed the product and its distributor. Although this stopped production of tiratricol-containing supplements in Missouri, sales continued around the country. On November 21, 2000, the FDA issued a warning to consumers concerning tiratricol (11). Since the initial warning in 1999, four recalls have taken place. Despite action by the U.S. government, tiratricol remains available at some health food stores and on the Internet. The product is still being manufactured and sold in Europe. It is imperative that government organizations and physicians continue efforts in educating the public on the true effects of this and similar compounds that may be harmful.

Health professionals must be diligent about asking patients, athletes in particular, about supplement use. Kaye et al. (12) found that 32% of patients in an ambulatory surgery setting confessed to using herbal medications. It was then discovered that over 70% of these patients failed to disclose their herbal medicine use during routine preoperative assessment (12). The potential dangers of this type of lack of communication are obvious. With products like Triax still available to consumers, it is up to the health care professionals to discover and condemn their use whenever possible.

References


