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Case report

Erroneous thyroid diagnosis due to over-the-counter biotin

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ABSTRACT

Objectives: Biotin is a component of the vitamin B complex used in standard immunoassays to detect serum levels of various hormones and non-hormones, including thyrotropin (TSH) and thyroxine. These assays involve a strong bond between streptavidin and biotin, which serves as an anchor for measured analytes. Large doses of exogenous biotin for the treatment of certain medical conditions have resulted in assay interference, causing TSH to be spuriously lowered. Smaller doses of biotin found in dietary supplements also have caused assay interference.

Methods: We describe four cases in which over-the-counter (OTC) biotin caused erroneous thyroid diagnosis and clinical confusion in patients with preexisting thyroid disease. Serum TSH and thyroxine were measured by the Vitros 5600 assay.

Conclusions: Although the biotin–streptavidin interaction is sensitive for detecting serum levels of TSH, it is subject to interference by exogenous biotin at levels found in OTC products. The widespread use of OTC biotin for cosmetic purposes can adversely affect the diagnosis of the entire spectrum of functional thyroid disorders. Physicians must carefully and routinely question for the use of biotin before thyroid function testing.

Introduction

Biotin is commonly used in immunoassays to measure several hormones and non-hormone analytes, including thyroxine (FT4), thyrotropin (TSH), parathyroid hormone, and ferritin [1]. Cases of thyroid function test assay interference have been documented in patients taking high doses of biotin for the treatment of inborn errors of metabolism and progressive multiple sclerosis; euthyroid patients appeared hyperthyroid and a newborn baby with hypothyroidism was misdiagnosed due to the spurious lowering of TSH [2–4]. Assay interference also occurs with the ingestion of lower doses of biotin found in over-the-counter (OTC) products [5]. We expand on this current laboratory phenomenon by documenting instances of biotin-related immunoassay interference in patients with preexisting thyroid dysfunction. We report on four patients encountered during endocrine evaluation in which OTC biotin caused clinical confusion.

Case Series

A recurrence of subacute thyroiditis versus toxic nodular goiter?

A 78-y-old woman with a history of thyroid nodules was evaluated after she developed right-sided neck pain. Laboratory work and radioactive iodine uptake and scintiscan confirmed a diagnosis of subacute thyroiditis. Her neck pain ultimately resolved and she remained otherwise asymptomatic. Four years later, routine labs revealed normal FT4 level and depressed TSH level of 0.2 mIU/L (reference 0.5–5 mIU/L), concerning for disease recurrence. She denied neck pain, fever, or symptoms of hyperthyroidism and appeared clinically euthyroid on physical examination. She reported taking an OTC supplement containing 1000 μg of biotin for hair growth. She was asked to stop biotin, and her TSH rose to 2.8 mIU/L within 72 h.

Non-toxic goiter confused for toxic nodular goiter

A 69-y-old woman was referred for evaluation of thyroid nodules. Initial labs revealed normal FT4, FT4 index, and T3 uptake; however the TSH was low at 0.28 mIU/L. The physical examination was notable for an enlarged, irregular thyroid gland. She appeared otherwise euthyroid. She was suspected of having mild toxic nodular goiter because of the low TSH. She was informed of her condition and the potential progression to clinical hyperthyroidism, as well as possible treatment with radioactive iodine. Three months later, repeat TSH was 0.142 mIU/L with normal FT4. She continued to appear clinically euthyroid. Upon deeper questioning, the patient revealed taking an OTC dietary supplement containing 300 μg of biotin for "thinning hair." She was instructed to stop biotin. A repeat TSH 48-h later revealed a normal level at 0.937 mIU/L, making treatment for hyperthyroidism unnecessary.

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Subclinical hypothyroidism mistaken for Graves' disease

An 84-y-old woman was referred to the endocrinology practice for evaluation of excessive fatigue and depression, suspicious for hypothyroidism. A year previously, the patient's thyroid function tests were within the normal range. Upon current evaluation, TSH was low at 0.13 mIU/L, FT4 was normal, and the serum was positive for antithyroglobulin antibody and negative for antithyroid peroxidase antibody. One month later, repeat TSH was still low at 0.24 mIU/L with normal T3 and free T4. On physical examination, the patient appeared euthyroid. She revealed recently using OTC biotin 1000 μg for "nail breakage." She was asked to stop taking the biotin, and repeat TSH rose to 5.5 mIU/L. Given her symptoms, positive antithyroglobulin antibody, and elevated TSH, the patient was diagnosed with subclinical hypothyroidism due to Hashimoto's thyroiditis. She was prescribed daily Synthroid 25 μg with improvement of her symptoms.

Stable Hashimoto's thyroiditis mistaken for progression to Graves' disease

A 66-y-old woman with a history of autoimmune thyroiditis was seen for routine follow-up. The TSH was low at 0.193 mIU/L, concerning for progression to Graves' disease. Eight weeks later, thyroid function tests were in the normal range. The patient revealed that she had intermittently been taking an OTC supplement containing 5000 μg of biotin, resulting in occasional falsely low TSH levels.

Discussion

Biotin is a small, water-soluble B vitamin that serves as a cofactor for carboxylase enzymes [6]; it is present in minute quantities in every human cell. In recent years, biotin has been marketed as an OTC supplement for improving hair, skin, and nail growth. The US Food and Drug Administration recommends a daily intake of 30 μg for adults [6]. Doses of biotin found in OTC products range from a few hundred micrograms to milligrams, suggesting that many people may be consuming excessive amounts of biotin. Biotin also has been used extensively in biotechnology as a key component of immunoassays. Streptavidin, a protein produced by the bacteria *Streptomyces avidinii,* binds biotin with an extremely high affinity [6]. This bond has been exploited in vitro during testing of various hormones. The biotin–streptavidin immunoassay is a principal method of measuring serum levels of thyroid hormones, TSH, and thyroid-specific antibodies (Fig. 1). Therefore, excess exogenous biotin can interfere with the assay. Depending on the specific type of assay used (competitive versus sandwich), the results of serum hormones and proteins may be falsely elevated or depressed.

In the aforementioned patients, TSH and FT4 were measured using the Vitros 5600 assay from Ortho Clinical Diagnostics (Rochester, NY, USA), which employs a biotin–streptavidin interaction [6]. The cases described are of significant clinical importance. First, they confirm the finding that exogenous biotin can interfere with this common clinical assay at levels found in OTC products, including multivitamins. Given their widespread use for cosmetic purposes, and their easy accessibility in drug stores, these products have the potential to affect a large number of people. Second, the interference can confuse the clinical diagnosis of the entire spectrum of functional thyroid disorders, not solely euthyroid patients who appear to have Graves' disease. As they routinely undergo surveillance thyroid function testing, these patients are at increased risk for experiencing assay interference.

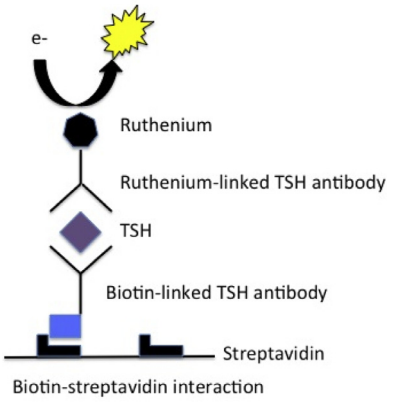

Fig. 1. A schematic of the "sandwich" thyrotropin (TSH) assay used in the cases. Note the biotin–streptavidin interaction used to affix TSH to the solid phase. The chemiluminescence produced when a voltage is applied to the ruthenium will be directly proportional to the TSH level in the serum sample.

Our case series was small, and the laboratory derangements were mild (FT4 was normal in all four cases, whereas TSH depression was minimal). Nevertheless, our experience demonstrates the clinical challenge of interpreting thyroid function tests in patients who ingest exogenous biotin, especially those who have a history of preexisting thyroid disease.

Conclusion

The biotin-streptavidin immunoassay is sensitive for detecting serum levels of several hormones and non-hormone analytes, including TSH. The assay is subject to interference by exogenous biotin. The use of OTC biotin can confuse and complicate the clinical picture by skewing laboratory results critical to diagnosis and management. We recommend that clinicians routinely and carefully question their patients about using OTC biotin before TSH testing. Biotin must be discontinued 48 to 72 h before assaying for TSH by the commonly used biotin-streptavidin immunoassay [6].

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