Biotin interference

Underrecognized patient safety risk in laboratory testing

Jessica L. Gifford PhD S.M. Hossein Sadrzadeh PhD DABCC FACB Christopher Naugler MD MSc FCFP FRCPC

Dietary supplementation with biotin is increasingly recognized as a patient safety risk, as it might lead to incorrect results for various common laboratory tests.

Biotin (also known as *vitamin H, vitamin B7,* and *coenzyme R*) is a water-soluble vitamin that acts as an enzyme cofactor in fatty acid biosynthesis, the citric acid cycle, and metabolism of odd-numbered fatty acids and branched-chain amino acids. It has additional roles in gluconeogenesis and gene expression. In the diet, biotin is bound to proteins found in organ meats, such as liver, kidney, and pancreas, as well as in eggs, yeast, and milk. Cereal grains, fruits, most vegetables, and muscle meat are poor sources of biotin. In Western populations, dietary biotin intake is estimated to be 35 to 70 µg daily, a level in line with the recommended dietary allowance. Most multivitamin pills contain about 30 µg of biotin. High-dose supplementation (doses greater than 1 mg/d) plays a role in therapy for several diseases, including biotinidase deficiency, mitochondrial metabolic disorders, and multiple sclerosis.[1] Doses up to 10 mg a day are frequently encountered in nutritional supplements taken to improve hair, skin, and nail health.

The problem is that many common blood tests employ a biotin-streptavidin reaction as part of the test procedure. While the amount of usual dietary biotin intake is not expected to be high enough to affect these tests, biotin supplementation at doses greater than 1 mg per day can cause either falsely low or falsely high test results, depending on the analyte and platform used for testing.

Biotin interference is particularly dangerous for patients in emergency situations who do not know they are taking high doses of biotin or when the treating physician does not know the patient is taking high doses. A literature search revealed an increasing number of published cases, most describing the problem of biotin interference in thyroid function tests.[2] High-dose biotin can produce a dangerous combination of positive and negative interference among the thyroid tests (free thyroxine, free triiodothyronine, thyroid-stimulating hormone, and thyroid-stimulating hormone receptor antibodies) and paint a picture of Graves disease in patients who have either no clinical symptoms or unrelated symptoms. Without good clinical observations, this could lead to unnecessary procedures and treatments. Interference of high-dose biotin with thyroid tests is particularly troubling for patients with multiple sclerosis, as large doses of this vitamin are emerging as a new treatment.[3] Interference with parathyroid hormone, follicle-stimulating hormone, luteinizing hormone, sex-hormone binding globulin, estradiol, progesterone, testosterone, cortisol, folate, vitamin B12, and ferritin testing has also been reported.[2]

The list of affected immunoassays varies for each analytic platform, and for a given test the manufacturer-supplied product information must be consulted to determine if biotin is an interferent. For some platforms, the list is extensive and includes the aforementioned tests, as well as those for cardiac function, β–human chorionic gonadotropin, and cancer biomarkers.[4] In many of these immunoassays, biotin was an established interferent, but at doses thought to be rarely encountered in the general population. While manufacturers are aware of the increasing use of high-dose biotin and its potential effects on patient care, they have not, to date, suggested any concrete solutions beyond having patients abstain from this vitamin. Solutions proposed by local clinical laboratories include diluting the specimen with a validated assay diluent, running specimens on a different platform known to be unaffected by biotin, and using streptavidin-agarose beads to remove the biotin before the sample is run on the affected analyzer.[5] All of these solutions will increase the costs associated with testing and highlight the potential financial implications of high-dose biotin on the health care system.

Interference of high-dose biotin on immunoassays in the clinical laboratory is an emerging issue. Many questions have not been addressed. What is the prevalence of high-dose biotin in a given patient population? What are the pharmacokinetics of high-dose biotin? How effective is the use of streptavidin-agarose beads to remove biotin interference? For many laboratories, the current solution is basic: It is recommended that patients abstain from taking biotin for at least 48 hours before specimen collection. The most effective approach, however, is an extensive communication campaign to educate physicians and patients.

Dr Gifford is a clinical biochemistry fellow in the Clinical Biochemistry Section for Calgary Laboratory Services and in the Department of Pathology and Laboratory Medicine at the University of Calgary in Alberta. **Dr Sadrzadeh** is Chief of the Clinical Biochemistry Section for Calgary Laboratory Services and Clinical Professor in the Department of Pathology and Laboratory Medicine at the University of Calgary. **Dr Naugler** is Associate Professor and Head of the Department of Pathology and Laboratory Medicine at the University of Calgary and Calgary Laboratory Services.

Competing interests
None declared

References

1. Tourbah A, Lebrun-Frenay C, Edan G, Clanet M, Papeix C, Vukusic S, et al. MD1003 (high-dose biotin) for the treatment of progressive multiple sclerosis: a randomised, double-blind, placebo-controlled study. *Mult Scler* 2016;22(13):1719-31. Epub 2016 Sep 1.
2. Elston MS, Sehgal S, Du Toit S, Yarndley T, Conaglen JV. Factitious Graves' disease due to biotin immunoassay interference—a case and review of the literature. *J Clin Endocrinol Metab* 2016;101(9):3251-5.
3. Siddiqui U, Egnor E, Sloane JA. Biotin supplementation in MS clinically valuable but can alter multiple blood test results. *Mult Scler* 2017;23(4):619-20. Epub 2016 Dec 7.
4. Piketty ML, Polak M, Flechtner I, Gonzales-Briceño L, Souberbielle JC. False biochemical diagnosis of hyperthyroidism in streptavidin-biotin-based immunoassays: the problem of biotin intake and related interferences. *Clin Chem Lab Med* 2017;55(6):780-8.
5. Piketty ML, Prie D, Sedel F, Bernard D, Hercend C, Chanson, et al. High-dose biotin therapy leading to false biochemical endocrine profiles: validation of a simple method to overcome biotin interference. *Clin Chem Lab Med* 2017;55(6):817-25.

This article has been peer reviewed.
Can Fam Physician 2018;64:370