WHAT YOU NEED TO KNOW ABOUT BIOTIN

Source of Biotin and Its Metabolism

Biotin is known as a water soluble vitamin B7 that is primarily found in organ meats such as beef liver and kidney. The biotin level is low in most vegetables and fruits compared to most water-soluble vitamins[1]. The adequate intake recommended by the Food and Nutrient Board is between 0.005 and 0.035 milligrams per day (mg/day) for different age groups[2].

Dietary biotin is absorbed in the small intestine and chiefly stored in the liver[3]. In the human body, biotin plays a role as an essential coenzyme for carboxylases in the transfer of one-carbon units to targeted substrates[4], which are involved in neuronal energy production, long-chain fatty acid biosynthesis and insulin secretion[5].

The clearance of biotin from the circulation is rapid and mainly through urine, which can be affected by patient population, biotin level, chronicity of biotin exposure, and renal function. A recent study in healthy volunteers demonstrated that the biotin concentration returned to baseline one week after a 10-mg/day 7-day course[6]. Other pharmacokinetics studies showed that the half-life of biotin ranged from 1.8 to 18.8 hours following single oral dose of 0.6 mg, 1 mg and 300 mg[7, 8].

Clinical Needs for Biotin Supplements

Patients may take biotin supplements for different reasons.

Biotin is often promoted to maintain healthy hair and nails. Many people buy over-the-counter biotin supplements dosing from 0.5 to 15 mg that are widely available in capsule or tablet form. Biotinidase deficiency is a rare genetic condition in neonates that need biotin supplements to prevent health problems. Studies have shown that biotin may be good for controlling blood glucose and nerve damage in patients with diabetes[9] and progressive multiple sclerosis. High doses of biotin up to 300 mg per day, which is more than 10,000 times than the adequate daily intake of 0.03 mg, have been found to be a potential therapeutic option in patients with multiple sclerosis[10].

Clinicians should be vigilant of other clinical conditions that are prone to biotin deficiency, such as inflammatory bowel disease, patients treated with antiepileptic medications, pregnant women and alcoholism. Patients with these conditions could benefit from biotin supplementation.

Mechanism of Potential Biotin Interference in Laboratory Testing

Streptavidin is a homotetramer from the bacterium *Streptomyces avidinii* that can bind up to four biotin molecules[11]. The highly selective and stable interactions between streptavidin and biotin make it a popular choice in molecular science for detection, immobilization and labelling. In many immunoassays, streptavidin is bound to the microparticle to immobilize the biotinylated antibody complex or is incorporated into the detection system to increase the sensitivity of the assay. In general, immunoassays have two forms of design formats: sandwich assays and competitive assays. Presence of high levels of biotin in patient's sample can cause falsely low results in sandwich assays and falsely high results in competitive assays[12].

However, the adoption of the streptavidin-biotin technology in the assay format does not necessarily lead to biotin interference. In some immunoassays, biotin labeled antibody is pre-coupled to the Streptavidin solid phase which reduces or eliminates the observed interference to exogenous biotin.

Approaches to Investigate Biotin Interference

Every day, laboratories need to handle thousands of samples, many of which might be susceptible to pre-analytical or analytical interferences. Each lab should consider adding biotin interference testing into their routine protocol for the investigation of aberrant lab results. Concurrently, clinicians need to be vigilant of those patients who are more likely to take biotin supplements for various needs.

If a clinically discordant test result prompts further investigation into assay interference, including biotin interference:

- Review manufacturer's labeling for specific assay susceptibility to biotin interference to understand which assays are sensitive to biotin interference
- Inquire about any supplements patients are taking that contain biotin. The Food and Drug Administration (FDA) recommends clinicians to ask their patients about biotin supplementations when observing discrepancies between clinical symptoms and lab results[13]. Clinicians should always interpret the lab results in the clinical context
- Discontinue use of biotin supplements in the ambulant setting when these supplements are not being used to achieve an immediate clinical outcome. Studies have shown different time duration needed for biotin to clear from the blood stream, ranging from 24 hours to 7 days from the last dose[6]
- Use an alternative assay that is free of biotin interference if the suspected assay is STAT or critical for directing immediate treatment for patients who are in urgent conditions
- Contact manufacturers for more support because manufactures have internal procedures set up for the investigation of samples sent by the labs

Enhancement of communications between laboratorians and clinicians is the most effective approach to mitigate the error caused by all forms of analytical interference including biotin.

References

1. Staggs CG, Sealey WM, McCabe BJ, et al. Determination of the biotin content of select foods using accurate and sensitive HPLC/avidin binding. Journal of food composition and analysis: an official publication of the United Nations University, International Network of Food Data Systems 2004;17:767–76.
2. Institute of Medicine. Food and Nutrition Board. Dietary Reference Intakes: Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington, DC: National Academy Press; 1998.
3. Said HM. Biotin: biochemical, physiological and clinical aspects. Subcell Biochem 2012;56:1–19.
4. McMahon RJ. Biotin in metabolism and molecular biology. Annual Review of Nutrition 2002; 22:221–39.
5. Samarasinghe S, Meah F, Singh V, et al. Biotin interference with routine clinical immunoassays: understand the causes and mitigate the risk. Endocrine Practice 2017;23(8):989–98.
6. Li D, Radulescu A, Shrestha RT, et al. Association of biotin ingestion with performance of hormone and nonhormone assays in healthy adults. JAMA 2017;318(12):1150–60.
7. Mardach R, Zempleni J, Wolf B, et al. Biotin dependency due to a defect in biotin transport. J Clin Invest. 2002;109:1617–23.
8. Peyro Saint Paul L, Debruyne D, Bernard D, et al. Pharmacokinetics and pharmacodynamics of MD100 (high-dose biotin) in the treatment of progressive multiple sclerosis. Expert Opin Drug Metab Toxicol 2016;13(3):327–44.
9. Maebashi M, Makino Y, Furukawa Y, et al. Therapeutic evaluation of the effect of biotin on hyperglycemia in patients with non-insulin dependent diabetes mellitus. J Clin Biochem Nutr 1993;14:211–18.
10. Sedel F, Papeix C, Bellanger A, et al. High doses of biotin in chronic progressive multiple sclerosis: a pilot study. Multiple Sclerosis and Related Disorders 2015;4:159–69.
11. Dundas CM, Demonte D, Park S. Streptavidin-biotin technology: improvements and innovations in chemical and biological applications. Appl Microbio Biotechnol 2013;97:9343–53.
12. Colon PJ and Greene DN. Biotin interference in clinical immunoassays. JALM 2018;5:941–51.
13. FDA Biotin Safety Communication. https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm586641.htm

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