단신
Lab Med Online
Vol. 12, No. 3: 191-194, July 2022
https://doi.org/10.47429/lmo.2022.12.3.191

진단면역학 LMO

한국인에서 혈청 비오틴 농도

Serum Biotin Levels in General Korean Population

문숙인* · 조은혜* · 박성준 · 권민정 · 박효순 · 우희연
Sookin Moon, M.D.*, Eun Hye Cho, M.D.*, Seong Jun Park, M.D., Min-Jung Kwon, M.D., Hyosoon Park, M.D., Hee-Yeon Woo, M.D.

성균관대학교 강북삼성병원 진단검사의학과
Department of Laboratory Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

The risk of biotin interference has been growing, as the intake of biotin for hair, skin, and nail care has increased. Elevated serum biotin concentration can interfere with immunoassays, thereby possibly leading to serious medical problems. In this study, we estimated the risk of biotin interference by investigating the distribution of serum biotin concentration in the general population of Korea. From October 2020 to March 2021, 723 samples were collected from individuals (age: 18–81 years) who underwent a medical checkup. Biotin levels were quantified by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Biotin interference in the thyroid function test and vitamin D immunoassay was assessed for samples with biotin levels above 10 ng/mL. Thyroid function and vitamin D results obtained by a streptavidin-biotin-based electrochemiluminescence immunoassay were compared to those of a chemiluminescent microparticle immunoassay and LC-MS/MS, respectively. A total of 0.41% (3/723) of samples showed serum biotin concentration above the lowest threshold (10 ng/mL) for biotin interference. Vitamin D status in a patient with serum biotin concentration of 130.3 ng/mL was normal according to the immunoassay (30.6 ng/mL) but deficient (29.3 ng/mL) according to LC-MS/MS. Judging by the distribution of biotin concentration in the general population, the risk of biotin interference seems to be low in Korea. Further studies are needed to monitor biotin concentration because biotin intake is increasing.

Key Words: Biotin interference, Thyroid function test, Vitamin D

Biotin is a water-soluble vitamin that is an essential coenzyme for multiple metabolic processes in the human body [1]. In immunoassays, streptavidin–biotin binding is widely used due to its strong affinity. Therefore, increased serum biotin levels can interfere with immunoassays, thereby leading to serious medical problems. Indeed, the United States (US) Food and Drug Administration (FDA) released a safety communication about the potential for biotin interference with laboratory test results in 2017 and updated the documents in 2019 [2].

In general, biotin supplementation is rarely necessary, except for the treatment of metabolic disorders, such as propionic acidemia, biotinidase deficiency, and multiple sclerosis. Recently, in addition to medical indications, biotin intake increased for esthetic indications, such as hair growth, skin health, and nail strength [3]. In the US, the market size for vitamin and mineral supplements is over $30 billion annually [3]. In Korea, the consumption of dietary supplements is growing, and the most frequently consumed dietary supplements are multivitamin mineral supplements, with a prevalence rate of 89.6 per 1,000 persons [4]. According to the 2020 data from the Ministry of Food and Drug Safety (Korea), the top five companies earned approximately $1.1 million from biotin sales alone [5].

There are significant differences in biotin levels in the general population from country to country. According to some studies, 0%–7.4% of patients' samples contain biotin levels above 10 ng/mL: the lowest threshold for biotin interference [6-10]. Nonetheless, serum biotin levels have never been evaluated in Koreans. In

Corresponding author: Hee-Yeon Woo, M.D., Ph.D.
https://orcid.org/0000-0002-1154-3137
Department of Laboratory Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29 Saemunan-ro, Jongno-gu, Seoul 03181, Korea
Tel: +82 2-2001-2387, Fax: +82 2-2001-2364, E-mail: woohyn@gmail.com

*These authors contributed equally to this work.

Received: October 14, 2021
Revision received: 23 December, 2021
Accepted: December 24, 2021

This article is available from https://www.labmedonline.org

this study, we investigated serum biotin levels in the general Korean population and estimated the prevalence of biotin interference in the thyroid function test (TFT) and vitamin D assays.

From October 2020 to March 2021, 723 samples were collected from medical checkup examinees. After centrifugation, serum was separated and stored at 4°C. All stored serum samples were analyzed within 7 days on the basis of our preliminary study indicating that the change of biotin levels at 4°C is less than 6% after 7 days of storage. Biotin levels were quantified by the method described by Song [11] with modifications; the method is based on liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) on a Xevo TQD instrument (Waters Corporation, Milfold, MA, USA). Purified biotin (Sigma-Aldrich, St. Louis, MO, USA) served as a standard material, and Biotin-d4 (IsoSciences, Ambler, PA, USA) was used as an internal standard. The lower limit of quantitation was 5 ng/mL. Biotin interference in the TSH, free-T4, and vitamin D immunoassays that are based on biotin was assessed for samples with biotin levels >10 ng/mL. The threshold of biotin interference claimed by a manufacturer is 1,200 ng/mL for TSH, 30 ng/mL for vitamin D, and 100 ng/mL for free T4, respectively. To assess the interference, TSH, free-T4, and vitamin D results obtained by a streptavidin-biotin-based electrochemiluminescence immunoassay (ECLIA) using a Cobas c702 analyzer (Roche Diagnostics, Mannheim, Germany) were compared to those of a chemiluminescent microparticle immunoassay (CMIA) by means of ARCHITECT (Abbott Laboratories, Abbott Park, IL, USA) and LC-MS/MS, respectively. The following reagents were employed: Elecsys TSH (Roche Diagnostics) and ARCHTECT TSH (Abbott Laboratories) for TSH, Elecsys FT4 III (Roche Diagnostics) and ARCHITECT Free T4 (Abbott Laboratories) for free T4, and Elecsys Vitamin D total II (Roche Diagnostics) and the MSMS Vitamin D Kit (PerkinElmer, Waltham, MA, USA) for vitamin D. The study protocol was approved by the Kangbuk Samsung Hospital Institutional Review Board (approval number: KBSMC 2020-08-011). Because this study involved anonymized residual samples, the requirement to obtain informed consent was waived.

The median age of examinees was 48 years (range: 18–81 years). The proportions of males and females were 50.5% and 49.5%, respectively. Of all the samples analyzed, 99.6% (720/723) showed biotin levels lower than the lowest interference threshold. Two samples contained biotin levels of 5–10 ng/mL, and 718 samples contained biotin at concentrations lower than 5 ng/mL. Only three (0.4%) samples showed biotin levels >10 ng/mL: 12.0, 14.1, and 130.3 ng/mL. Among these three samples, only one featured a biotin level higher than the threshold of biotin interference with free-T4 (100 ng/mL) and vitamin D assays (30 ng/mL). There were no samples with a biotin concentration above the interference threshold for TSH (1,200 ng/mL). For the three samples with biotin levels >10 ng/mL, biotin interference in free-T4 and vitamin D immunoassays was evaluated (Table 1). For the sample with the biotin level of 130.3 ng/mL, vitamin D status was normal in ECLIA (30.6 ng/dL) but deficient in LC-MS/MS (29.3 ng/dL). For all three samples with biotin levels above 10 ng/mL, free-T4 values were slightly higher in ECLIA than in CMIA but were within the reference ranges of both methods. Interference with the TSH assay was not evaluated because no samples contained more biotin than the interference threshold for TSH (1,200 ng/mL).

Other studies on the prevalence of biotin interference have involved patients visiting clinics and emergency rooms. To the best of our knowledge, this is the first study on the prevalence of biotin interference in the general Korean population. The prevalence of biotin above the interference threshold varies among studies. Studies in the United Kingdom, the Netherlands, Australia, and the US point to prevalence rates of 0%, 0.2%, 0.8%, and 4.1%–7.4%, respectively [6-10]. In the present work, the prevalence was found to be 0.4%, which is much lower than that in the US and similar to that in the Netherlands. According to the observed biotin levels in the general population, the risk of biotin interference may be low in Korea. The prevalence may depend on population characteristics, such as age, socioeconomic status, and health management knowledge.

Most studies on biotin interference have been conducted via experiments such as spiking of serum samples with biotin or com-

Table 1. Assessment of biotin interference with free-T4 and vitamin D immunoassays

Biotin (ng/mL)	FreeT4 (ng/dL)*		Vitamin D (ng/mL)†	
	ECLIA (RI: 0.84–1.74)	CMIA (RI: 0.70–1.48)	ECLIA (RI: 30–39)	LC-MS/MS (RI: 30–39)
130.3	1.39 (N)	1.16 (N)	30.6 (N)	29.3 (D)
14.1	1.30 (N)	1.15 (N)	30.4 (N)	30.3 (N)
12.0	1.23 (N)	1.12 (N)	31.6 (N)	34.8 (N)

*The biotin threshold for interference with free-T4 assays is 100 ng/mL; †The biotin threshold for interference with vitamin D assays is 30 ng/mL.
Abbreviations: ECLIA, electrochemiluminescence immunoassay; CMIA, chemiluminescent microparticle immunoassay; LC-MS/MS, liquid chromatography coupled with tandem-mass spectrometry; RI, reference interval; N, normal; D, decreased.

https://doi.org/10.47429/lmo.2022.12.3.191

paring results before and after biotin ingestion [12]. Therefore, the prevalence of this interference has not been estimated accurately. We evaluated biotin interference by comparing the results of two methods without a biotin intervention. Although the difference was not sufficient to be regarded as interference, vitamin D status was affected in the sample with biotin at 130.3 ng/mL. Although free T4 was slightly higher in biotin-based ECLIA than in CMIA, the interpretation of the TFT did not change. If more samples with free-T4 values near the reference limit had been included, then the interpretation could have been affected. Although biotin ingestion can pose a risk of interference, clinically significant interference is uncommon. There has been biotin interference in TFT and vitamin D assays in a few cases of high-dose biotin treatment [12, 13]. Two cases of misdiagnosed Graves' disease due to biotin interference were reported in 2 years at a Swiss institution [14]. The two patients were treated with high-dose biotin for multiple sclerosis. Although their TFT results were compatible with hyperthyroidism, there were no symptoms or signs of hyperthyroidism.

The current study has some limitations. First, the study was conducted by a single institution. Biotin levels can vary from region to region even in the same country depending on population characteristics. Therefore, multicenter studies are necessary to confirm that the results of this report represent the biotin levels of the general Korean population. Second, evaluation of biotin interference was limited because only three samples showed biotin levels above the lowest threshold of biotin interference. Future studies focusing on individuals taking biotin supplements can help to evaluate biotin interference. Third, biotin interference was not evaluated in samples with biotin levels <10 ng/mL. Therefore, it is not clear whether the differences observed in samples with biotin concentration >10 ng/mL are due to the interference or a difference in analytical methods.

In conclusion, we investigated serum biotin levels in the general Korean population and biotin interference in TSH, free-T4, and vitamin D assays. According to these biotin interference assessments, the risk of biotin interference appears to be low in Korea. Studies on other analytes are needed to ascertain the impact of biotin interference.

요 약

모발, 피부 및 손톱 관리를 위한 비오틴 섭취가 증가함에 따라 비오틴 간섭의 위험이 증가하고 있다. 혈청 비오틴 농도가 높을 경우 면역측정법에 간섭을 일으켜 심각한 의학적 문제를 야기할 수 있다. 본 연구에서는 한국인을 대상으로 혈청 비오틴 농도 분포를 조사하여 비오틴 간섭의 위험성을 추정하였다. 2020년 10월부터 2021년 3월까지 건강검진을 받은 사람들(18–81세)로부터 수집한 잔여검체 723개를 대상으로 하였다. 모든 검체에서 액체크로마토그래피-탠덤질량분석법(liquid chromatography tandem mass spectrometry, LC-MS/MS)을 이용하여 비오틴 농도를 측정하였다. 갑상샘기능검사 및 비타민 D 면역측정법에 대한 비오틴 간섭은 비오틴 농도 10 ng/mL 초과 검체에 대해 평가하였다. 총 0.41% (3/723)의 검체에서 비오틴 간섭을 일으키는 최저값인 10 ng/mL을 초과하는 혈청 비오틴 농도를 보였다. 혈청 비오틴 농도가 130.3 ng/mL인 환자의 비타민 D 농도는 면역측정법으로는 정상(30.6 ng/mL)이었으나 LC-MS/MS법에서는 결핍(29.3 ng/mL)에 해당하였다. 본 연구에서 확인된 일반 인구의 비오틴 농도를 고려하였을 때, 한국에서 비오틴 간섭의 위험은 낮아 보인다. 하지만 비오틴 섭취가 점차 증가함에 따라 비오틴 농도를 모니터링하기 위한 추가 연구가 필요하다.

Conflict of Interest

None declared.

REFERENCES

1. Zempleni J and Mock DM. Biotin biochemistry and human requirements. J Nutr Biochem 1999;10:128-38.
2. U.S. Department of Health and Human Services Food and Drug Administrations. UPDATE: The FDA warns that biotin may interfere with lab tests: FDA safety communication. https://www.fda.gov/medical-devices/safety-communications/update-fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication (Updated on Nov 2019).
3. Chun KY. Biotin interference in diagnostic tests. Clin Chem 2017;63:619-20.
4. Park HA. Which types of dietary supplements are used in Korea? Data from the 2015 Korea national health and nutrition examination survey. Korean J Health Promot 2018;18:107-12.
5. Ministry of Food and Drug Safety. Food and other production performance statistics in 2020. https://www.mfds.go.kr/brd/m_374/view.do?seq=30205&srchFr=&srchTo=&srchWord=&srchTp=&itm_seq_1=0&itm_seq_2=0&multi_itm_seq=0&company_cd=&company_nm=&page=1 (Updated on Jul 29 2021).
6. Gunsolus IL, Matias M, Prostko J, Mohr P, Sokoll LJ. Prevalence of de-

tectable biotin in five US emergency department patient cohorts. Clin Biochem 2021;93:26-32.
7. IJpelaar A, Beijers A, van Daal H, van den Ouweland JMW. Prevalence of detectable biotin in The Netherlands in relation to risk on immunoassay interference. Clin Biochem 2020;83:78-80.
8. Katzman BM, Lueke AJ, Donato LJ, Jaffe AS, Baumann NA. Prevalence of biotin supplement usage in outpatients and plasma biotin concentrations in patients presenting to the emergency department. Clin Biochem 2018;60:11-6.
9. Sanders A, Gama R, Ashby H, Mohammed P. Biotin immunoassay interference: A UK-based prevalence study. Ann Clin Biochem 2021;58:66-9.
10. Trambas CM, Liu KC, Luu H, Louey W, Lynch C, Yen T, et al. Further assessment of the prevalence of biotin supplementation and its impact on risk. Clin Biochem 2019;65:64-5.
11. Song DY. Quantitative measurement of biotin by LC-MS/MS in human serum and the effect of multivitamin and renal function on biotin concentration [master's thesis]. Seoul: Seoul National University, 2019.
12. Li D, Ferguson A, Cervinski MA, Lynch KL, Kyle PB. AACC Guidance Document on Biotin Interference in Laboratory Tests. J Appl Lab Med 2020;5:575-87.
13. Piketty ML, Prie D, Sedel F, Bernard D, Hercend C, Chanson P, 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;55:817-25.
14. Giovanella L. The impact of biotin interference on laboratory testing and patient diagnosis in clinical practice. Int J Pharmacokinet 2019;4:IPK01.

https://doi.org/10.47429/lmo.2022.12.3.191