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Effects of sunlight and diet on vitamin D status of pulmonary tuberculosis patients in Tbilisi, Georgia

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ABSTRACT

Objective: Vitamin D deficiency is common in tuberculosis (TB) and this may modulate immune responses. This study investigated vitamin D status in patients with TB and examined the sources of vitamin D in Tbilisi, Georgia.

Methods: We measured plasma 25-hydroxyvitamin D (25[OH]D) and dietary vitamin D intake in patients with pulmonary TB ($n = 85$) in Tbilisi, Georgia. To determine the impact of season on vitamin D status, we tested the in vitro conversion of 7-dehydrocholesterol (7-DHC) to previtamin D_3 after sunlight exposure.

Results: In subjects with TB, mean plasma 25(OH)D concentrations were 14.4 ± 7.0 ng/mL, and vitamin D insufficiency (25[OH]D <30 ng/mL) occurred in 97% of subjects. The dietary sources of vitamin D were mainly fish, eggs, and butter. The daily intake was well below recommended daily intakes in subjects with TB (172 ± 196 IU). The conversion of 7-DHC to previtamin D_3 was undetectable from October to March and highest in June and July from 11:00 to 14:00 h.

Conclusion: An insufficient vitamin D dietary intake and a limited production of vitamin D from sunlight for most of the year may explain the high prevalence of vitamin D insufficiency in patients with TB in Tbilisi.

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Introduction

Vitamin D is a secosteroid hormone produced primarily in the skin upon exposure to ultraviolet-B (UVB) light from the sun or obtained from limited dietary sources [1]. The cutaneous production of vitamin D is the major determinant of an individual's vitamin D status [1]. Vitamin D is synthesized in skin when 7-dehydrocholesterol (7-DHC) is exposed to UVB radiation and undergoes photolysis to previtamin D_3, which then undergoes a thermally induced isomerization to vitamin D_3 [2]. After entering the bloodstream, vitamin D_3 undergoes two sequential hydroxylations to form 25-hydroxyvitamin D (25[OH]D), the major circulating form of vitamin D, followed by the hormonal form of vitamin D, 1,25-dihydroxyvitamin D [1]. In addition to cutaneous production, vitamin D can be obtained from dietary sources such as fish, mushrooms, or fortified foods [1]. In addition to skeletal health and calcium homeostasis, vitamin D regulates

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many other biological systems including the immune system [3]. For example, one function of vitamin D is to regulate the production of cathelicidin an antimicrobial peptide involved in the innate immune response to *Mycobacterium tuberculosis* (TB) infection [4]. Vitamin D may have other effects on the immune system including effects on adaptive and innate immunity [4,5].

There is a high prevalence of vitamin D deficiency worldwide. Although the definition of vitamin D deficiency varies, most studies refer to deficiency as a plasma 25(OH)D concentration <20 ng/mL and insufficiency as <30 ng/mL [1]. In the most recent National Health and Nutrition Examination Survey, of 13, 369 non-institutionalized civilians in the United States from 2001 to 2004, 77% of the participants had vitamin D insufficiency [6]. In North America, hypovitaminosis D has been attributed to obesity, decreased outdoor activity, an inadequate dietary intake of vitamin D, and sunscreen usage [6–8]. In other parts of the world, residents are deficient in vitamin D owing to a lack of food fortification, less sunlight exposure, decreased ambulatory capability, and/or institutionalization of elderly adults [9,10].

Given the connection between poor vitamin D status and TB [11,12], we sought to assess circulating plasma 25(OH)D concentrations and dietary vitamin D intake in patients with pulmonary TB residing in Tbilisi, Georgia. We also measured the effect of sunlight on the in vitro conversion of 7-DHC (the vitamin D precursor in skin) to previtamin D_3 in the environment of patients with TB living in Tbilisi.

Materials and methods

Study location, participants, and ethics

Participants were recruited from the National Center for Tuberculosis and Lung Diseases (NCTBLD) and the Tbilisi Physio-Pulmonology Center in Tbilisi as a subset of the initial subjects from a larger, ongoing, double-blinded, randomized, controlled, prospective trial of high-dose vitamin D_3 treatment (www.clinicaltrials.gov, identifier NCT00918086) for patients with pulmonary TB. The inclusion criteria for patients with TB were an age older than 18 y, newly documented smear-positive pulmonary TB, no more than 7 d of anti-TB therapy, an agreement to receive anti-TB therapy in Tbilisi, and signed informed consent. The exclusion criteria for patients with TB was more than 30 days of lifetime TB therapy, a current pregnancy or lactation, a history of organ transplantation, cancer in the previous 5 y (excluding non-melanoma skin cancer), seizures, hypercalcemia, hyperparathyroidism, sarcoidosis, nephrolithiasis, liver cirrhosis, serum creatinine level higher than 250 mmol/L, a requirement for hemodialysis, corticosteroid use in the previous 30 d, the current use of cytotoxic or immunosuppressive drugs, current incarceration, and an inability to complete all study visits in Tbilisi.

The institutional review boards from Emory University (Atlanta, GA, USA) and the NCTBLD in Tbilisi approved the study protocol. All subjects provided written informed consent for participation in the study. All data for this study were collected from November 1, 2009 to October 31, 2010.

Study design

Evaluation of seasonal production of vitamin D from sunlight

Glass ampules containing 5 mL of synthetic 7-DHC in methanol were placed in direct sunlight for 1 hour each from 10:00 to 17:00, monthly from November 2009 to October 2010. The investigators recorded the corresponding weather conditions. The ampule studies were completed during the days when the weather forecast predicted at least 50% to 100% sunny in attempt to capture the peak amount of vitamin D conversion during each month (www.weather.com). Two dates were studied each month, and the most representative sunny day from the month was used for the analysis. The ampules were protected from light and stored in a −20° Fahrenheit freezer before and after the hour-long sunlight exposure. The amount of previtamin D_3 converted from 7-DHC was determined by standard high-performance liquid chromatographic methods using previously published methods at the Boston University School of Medicine (Boston, MA, USA) [2].

Vitamin D status in participants

Subjects provided demographic information on age, gender, and mean daily time spent outdoors. Participants were recruited throughout the year, and each subject provided a blood specimen upon enrollment into the study. Vitamin D status was determined by plasma 25(OH)D concentrations that were measured by enzyme-linked immunosorbent assay (Immunodiagnostics, Ltd., Fountain Hills, AZ, USA) at the Vitamin D and Bone Research Laboratory, Emory University. The laboratory participates in the International Vitamin D External Assessment Scheme (DEQAS) to ensure quality control of the plasma 25(OH)D determinations.

Assessment of vitamin D content in the Georgian diet

Baseline nutritional status included body weight measured on a digital scale (Tanita Co., Arlington Heights, IL, USA) and height measured using a stadiometer to calculate a body mass index (kilograms per meter squared). To define habitual daily vitamin D intake, one-on-one interviews were conducted by trained physicians who used a 3-day food recall questionnaire designed to capture all food and beverage intakes, including staple foods and recipes common in the Georgian diet. Models were used to accurately determine the portion sizes of reported items. The vitamin D intake from the reported intakes was quantitated by a registered dietitian J. K. F. at the Atlanta Clinical and Translational Science Institute Bionutrition Research Unit (Atlanta, GA, USA) using Nutrition Data System for Research software (NDS-R 2009, University of Minnesota, Minneapolis, MN, USA).

Statistical analysis

Descriptive statistics were performed for the demographic information. Student's *t* tests were used to determine the mean plasma 25(OH)D concentrations, daily vitamin D intake, and daily intake of specific foods containing natural vitamin D in subjects with TB.

Results

Seasonal production of vitamin D from sunlight

The in vitro ampule studies demonstrated that the largest amount of previtamin D_3 production from 7-DHC occurred from May through August, and that no detectable previtamin D_3 was produced from October through March (Fig. 1). The peak production of previtamin D_3 occurred from 11:00 to 14:00 h (Fig. 2).

Demographics and vitamin D status in subjects with TB

The demographic information of the subjects with TB is presented in Table 1. Most subjects were ethnic Georgians (91%). The mean plasma 25(OH)D concentrations were in the vitamin D–deficient range (25[OH]D <20 ng/mL) in 83% of subjects with TB. Vitamin D insufficiency (25[OH]D <30 ng/mL) was present in 97% of participants (Table 2). There were no differences in plasma 25(OH)D in the ethnic Georgian subjects compared with the non-ethnic Georgian subjects (14.4 ± 7.0 versus 14.8 ± 7.0,

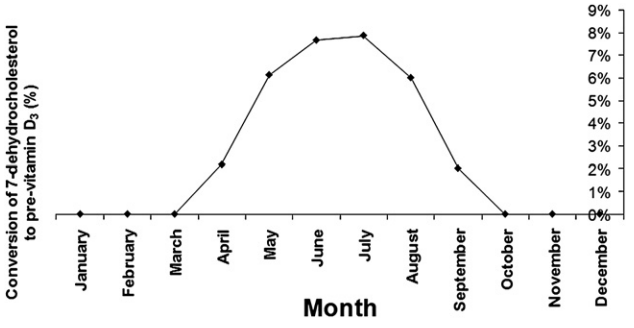

Fig. 1. The percentage of conversion of 7-dehydrocholesterol to previtamin D_3 by the month of the year in Tblisi, Georgia. Ampules containing 7-dehydrocholesterol were placed in direct sunlight hourly from 10:00 to 17:00 h twice a month for 1 y in Tbilisi. The most representative day is presented. The percentage of conversion to previtamin D_3 was analyzed using high-performance liquid chromatography. The mid-day conversion rates (12:00–13:00 h) are presented for each month. The most efficient conversion of 7-dehydrocholesterol to previtamin D_3 occurred from May to August. There was no detectable production of previtamin D_3 from September to March.