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Longitudinal association between vitamin D intake and taking hypertension medications 20 Years Later: The CARDIA study

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Abstract

Previous research has shown high rates of cardiovascular diseases in patients with low levels of vitamin D. This is a retrospective study that used the CARDIA dataset to examine the association between subject-reported vitamin-D intake and subjects taking antihypertensive medications after 20 years, beginning in 1985 through 2006. Multivariate logistic regressions were used to analyze the data. We found that almost 12% (n=150) of subjects reported taking at least one medication for hypertension in 2005-2006. Taking an antihypertensive medication was associated with higher baseline Body Mass Index (BMI), higher age at baseline, being non-white, lower levels of Vitamin D intake at baseline, having an increased BMI after 20 years, and reporting a decline in vitamin D over 20 years. Thus, it may be beneficial for practitioners to examine vitamin D levels in subjects at higher risk of developing high blood pressure.

Introduction

Hypertension is one of the most common conditions in humans, affecting nearly one in three adults in the United States and it is the most common diagnosis in America [1-2]. The Direct costs for hypertension are estimated at almost $50 billion and almost $4 billion in indirect costs [1]. With the most common treatments are lifestyle modifications and antihypertensive medications [1]. Although blood pressure control is a reasonable target, the majority of patients will require at least two antihypertensive medications to achieve control [2]. Adequate blood pressure control is associated with a reduction in hypertension morbidity and mortality [2].

Research has shown that hypertension is a complicated disease and that nutrition is a key factor hampering blood pressure control. Additionally, research has shown that vitamin D may play a key role in hypertension by regulating the renin-angio-

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tensin-aldosterone system [3-4]. Further, vitamin D deficiency is a world-wide phenomenon [5]. Although numerous studies have been conducted to examine the relationship between vitamin D deficiency and cardiovascular disease, but have reported mixed results, have been limited in duration, or focused on particular subgroups [4, 6-10].

To our knowledge, this is the first study to examine the association between vitamin D intake and taking an antihypertensive medication by longitudinally following subjects over 20 years. The objective of this study was to examine the longitudinal association between self-reported vitamin D intake and the incidence of taking at least one antihypertensive medication 20 years later. We hypothesized that subjects who had lower levels of vitamin D intake would be more likely to take an antihypertensive medication at year 20.

Methods

Overview

The Marshall University Institutional Review Board approved this study. This study was a longitudinal secondary analysis of data collected from the CARDIA dataset that followed 5,115 subjects over 20 years, from 1985 through 2005-2006. The original study population was limited to healthy, non-institutionalized young adults living in the United States and was designed to be equally represented across age, race, and gender. The subjects were recruited in Birmingham, Chicago, Minneapolis, and Oakland.

Participants

Subjects were eligible for the analyses if they had not been diagnosed with hypertension at baseline and did not have any secondary causes of hypertension (diabetes, chronic kidney disease, hyperthyroidism, pregnancy, etc.). We used data from 1985-1986 (CARDIA study year 00) as baseline and data from 2005-2006 (year 20) for follow-up data. The study sample includes 1,290 subjects.

Measures

Demographics

The following variables were collected by self-report: age in years, race, and gender. Race was dichotomous (white, non-white). Weight was measured by a Detecto model 439 scale and was recorded to the nearest 0.2 pounds. Height was measured by a vertical mounted centimeter ruler and was recorded to the nearest 0.5 centimeters. Body Mass Index (BMI) was calculated by dividing the subjects' weight in kilograms by height in meters squared. BMI was measured as continuous in all models. Change in BMI was measured by subtracting the baseline BMI from the Year 20 BMI measurement and was treated as a continuous variable. At both baseline and year 20, subjects were asked whether they took an antihypertensive medication. Subjects' report of antihypertensive medication-taking was measured as a dichotomous variable (yes/no).

Nutrition

The CARDIA study analyzed nutrient intake based on a 28-day subject-reported dietary history, utilizing the Western Electric dietary history format. The nutrient database that was selected for the analyses of nutrition data for the CARDIA study was developed by the Nutrition Coding Center. The database is a table that contains values for 60 nutrients in over 1,300 items. The nutrition history consisted of two parts. The first part consisted of 18 questions that asked subjects about their use of fats, consumption of fast foods, and salt use. The second part consisted of questions about the usual intake of various items that were then followed by lists of food items. All foods were divided into food groups to facilitate subject recall. The food groups were: Eggs, dairy, grains/cereals, fruit, ethnic, soups, convenience foods, meat, poultry, fish/shellfish, legumes, vegetables, desserts, nuts/seeds, snack foods, beverages, alcohol, vitamin/mineral supplements, additions (e.g. butter, margarine, jelly, mustard, and ketchup).

Vitamin D, alcohol, fiber, sucrose, copper, zinc, total carbohydrates, total fats, and thiamine intake was derived from the questionnaires. Alcohol was measured as a continuous variable in milliliters. Vitamin D was measured as a continuous variable in micrograms. Dietary fiber, sucrose, total carbohydrates, and total fats were measured as continuous variables in grams. Copper and zinc were measured as continuous variables in milligrams. Change in vitamin D intake was measured by subtracting the baseline vitamin D intake measurement from the year 20 follow-up measurement and was treated as a continuous variable.

Statistical Analysis

All analyses were conducted using SAS v9.3. First, we present descriptive statistics for the demographic and nutrition variables. We used multivariate logistic regression models to examine how patient and nutrition characteristics were associated with subjects reporting the use of an antihypertensive medication. An alpha level of 0.05 was used to assess statistical significance.

Results

Table 1 presents the subject demographic characteristics of our sample at baseline. The mean age of subjects at baseline was 25.22 (SD=3.55, Range: 18-30) years. The majority of subjects were white (56.43%, n=728) and male (64.96%, n=838). The mean BMI at baseline was 24.00 (SD=3.92, Range: 17.03-45.35). The mean dietary vitamin D intake was reported to be 7.20 (SD=6.30, Range: 0.05-71.85) mcg.

At the 20 year follow-up, 11.63% (n=150) of subjects reported taking at least one antihypertensive medication. The mean BMI at the 20 year follow-up was 28.79 (SD=5.76, Range: 18.79-51.70). The mean BMI change was 4.79 (SD=4.00, Range: -15.88-24.25), meaning that on average, BMI increased almost 5 units per patient over 20 years. The mean dietary intake of vitamin D was reported to be 5.90 (SD=5.08, Range: 0.35-73.56) mcg at follow-up. The mean change of vitamin D intake was -1.29 (SD=6.99, Range: -66.29-69.85) mcg, meaning that on average, vitamin D intake decreased about 1.29mcg per patient. Vitamin D intake at baseline and at year 20 were significantly associated (ρ=0.29, $p<0.0001$).

Multivariate Results

Table 1: Demographic Characteristics of Sample at Baseline (N=1,290)

	Percent (n)-Baseline
Age	
Mean (SD), Range	25.22 (3.55), 18-30
Male	64.96 (838)
Race-White	56.43 (728)
BMI	
Mean (SD), Range	24.00 (3.92), 17.03-45.35
Vitamin D (mcg)	
Mean (SD), Range	7.20 (6.30), 0.05-71.85

Table 2 presents the multivariate logistic regression results examining whether subject-reported vitamin D levels, along with demographic characteristics, were associated with taking at least one antihypertensive medication after 20 years. Subjects were significantly more likely to report taking at least one antihypertensive medication when they: had higher BMI (OR=1.10, 95% CI=1.06-1.15) at baseline, were older (OR=1.08, 95% CI=1.02-1.15) at baseline, were non-white (OR=0.48, 95% CI=0.32-0.72), reported lower levels of vitamin D at baseline (OR=0.92, 95% CI=0.87-0.99), had an increase in BMI over 20 years (OR=1.10, 95% CI=1.06-1.15), and reported a decrease in vitamin D levels over 20 years (OR=0.94, 95% CI=0.90-0.99).

Discussion

Table 2: Multivariate logistic regression predicting patients taking an antihypertensive medication after 20 years (N=1,290)

Variable	OR	95% CI	p-value
BMI at baseline	1.10	1.06-1.15	<0.0001
Age	1.08	1.02-1.15	0.01
Race-white	0.48	0.32-0.72	0.00
Gender-Male	0.84	0.55-1.28	0.41
Vitamin D-Baseline	0.92	0.87-0.99	0.02
Fiber-Baseline	1.05	0.97-1.12	0.23
Sucrose-Baseline	1.01	1.00-1.01	0.06
Copper-Baseline	1.16	0.91-1.48	0.23
Zinc-Baseline	0.96	0.90-1.03	0.24
Alcohol (ml)-Baseline	1.00	1.00-1.01	0.47
Total Carbohydrates-Baseline	1.00	1.00-1.00	0.17
Total Fat-Baseline	1.01	1.00-1.01	0.15
Thiamine-Baseline	1.07	0.87-1.30	0.53
Change in BMI over 20 years	1.10	1.06-1.15	<0.0001
Change in Vitamin D over 20 years	0.94	0.90-0.99	0.02

In our sample, vitamin D intake was low at baseline and declined over 20 years. The National Institutes of Health have stated that optimal vitamin D intake values should be between 15mcg-20mcg per day [11]. Sources of vitamin D include sunlight, vitamin D-fortified dairy products, cod liver oil, and fatty fish [11].

There are many human health consequences of vitamin D deficiency, ranging from various cancers to schizophrenia and depression [12]. Research has shown an association between low serum vitamin D levels and high systemic inflammation in colorectal cancer [13] and a deficiency of vitamin D caused an impaired ability to control intracellular growth of M. tuberculosis in type 2 diabetic patients [14]. Lally et. al., reported a correlation between vitamin D deficiency and psychosis in over half of their study sample [15]. Countless studies provided evidence of links between vitamin D deficiency in pregnant and lactating women and neonatal hypocalcemia, early onset of rickets and long-term consequences for bone development in offspring, which prompted the World Health Organization (WHO) to hold a symposium to prioritize vitamin D research globally [16]. One study reported prenatal vitamin D status contributed to a diminished intrauterine linear growth, such that lower cord blood vitamin D concentration, as an indicator of last trimester maternal vitamin D status, is associated with shorter infant body length [17]. Other researchers showed vitamin D deficiency during pregnancy was correlated with an immune challenge and fetal sex-specific dysregulated placental inflammatory response, which all may have negative effects on the health and viability of offspring [18].

Numerous studies have shown that higher BMI, age, and race are associated with developing hypertension throughout the lifespan [2, 19-20]. However, this study shows that vitamin D intake may also be associated with developing hypertension and needing treatment. There have been studies that have looked at vitamin D supplementation and risk of cardiovascular disease, and have found that supplementation is not associated with a decrease in risk of developing hypertension or cardiovascular disease [6, 21-22]. Further, research is showing that higher concentrations of vitamin D may not prevent disease from occurring, but that lower levels may be a consequence of ill health [8]. Therefore, it is important for future studies to examine ways to increase the prevalence of vitamin D in the diet. Future research should also investigate whether screening for vitamin D deficiency is effective at identifying high-risk individuals for cardiovascular disease.

Our study confirms other studies that have found associations between vitamin D intake and risk of hypertension [3-4, 7, 9-10]. Medical providers should discuss the importance of lifestyle interventions, such as increased exposure to sunlight, low-fat dairy products and fatty fish in the diet to help control blood pressure with every patient, considering the prevalence of low vitamin D levels throughout the world.

The study's generalizability is limited by several factors. First, the CARDIA study did not use serum levels of vitamin D, only self-report of food intake and vitamin supplementation. Therefore, the risk of recall bias may significantly affect our findings. Additionally, we do not know how much time each subject spent out in the sun, which could also affect our findings. The CARDIA study also used self-report of antihypertensive medication use, which may be vulnerable to recall bias because some patients may not know why they are taking certain medications, leading to an over-estimation or under-estimation of those who

were actually taking an antihypertensive medication at baseline and at year 20.

Despite the study's limitations, this study is one of the first that examines the association between long-term vitamin D dietary intake and taking an antihypertensive medication. Our study found that those subjects with low vitamin D intake at baseline and whose vitamin D intake decreased over 20 years were associated with taking an antihypertensive medication. Providers need to discuss the importance of diet modifications with patients who are at high-risk of developing hypertension and those who have hypertension.

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