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VARIATION IN L-ARGININE INTAKE ACCORDING TO DEMOGRAPHIC CHARACTERISTICS AND CARDIOVASCULAR RISK

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Abstract

Little is known regarding the patterns of dietary intake of the amino acid L-arginine in the general population, and particularly whether intake varies according to race or the presence of cardiovascular risk factors. This study is an analysis of adults 18 years and older who participated in the Third National Health and Nutrition Examination Survey (NHANES III), a national public-use nutrition survey of non-institutionalized persons. Mean arginine intake for the US adult population was 4.40 g/day, with 25% of people consuming <2.6 g/day. Minorities, obese individuals, and people with diabetes consumed more arginine per 1000 calories than people without those characteristics. Whites had consistently lower intake than African Americans and Hispanics. Smokers had lower intake than non-smokers. After adjustment for demographic factors and caloric intake, women and smokers remained more likely to be in the lowest quartile of arginine consumption. Hypertension status was not significantly related to arginine consumption. In conclusion, L-arginine intake varies according to demographic and cardiovascular risk factors in the population. These results may have implications for cardiovascular risk.

Keywords

dietary patterns; l-arginine; cardiovascular risk; smoking; NHANES; human

1. Introduction

L-arginine is a conditionally essential amino acid in the human diet. L-arginine deficiency is linked to a variety of inflammatory and oxidative processes in the vascular endothelium, and may be crucial in the development of atherosclerosis [1]. The normal function of the vascular system depends on nitric oxide (NO) production by vascular endothelial cells. However, under conditions associated with oxidative vascular injury, such as obesity or hypertension, excess formation of reactive oxygen species (ROS) can lead to an accumulation of asymmetric dimethyl arginine (ADMA) [2,3]. This accumulation of ADMA competitively inhibits NO synthase (NOS), which decreases NO production. With limited L-arginine, NOS forms superoxide (O-), which causes vascular endothelial injury and further inflammation. The deleterious effects of low L-arginine availability may lead to a pro-atherosclerotic environment and subsequent cardiovascular disease [4].

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Thus, dietary intake of L-arginine may be critically important in the context of how the human body responds to inflammation and oxidative stress. Lower intake of dietary L-arginine has recently been associated with higher levels of C-reactive protein, an inflammatory biomarker [5]. Recent studies suggest that supplemental L-arginine may be helpful in preventing harmful oxidation and reversing endothelial dysfunction [6]. In addition, supplementation with L-arginine may reverse the endothelial dysfunction associated with hypercholesterolemia, smoking, and hypertension [7-14]. Some of L-arginine's antioxidant and anti-inflammatory effects are independent of NO production [15,16].

The current study examines the intake of L-arginine in a nationally representative sample of non-institutionalized U.S. adults to determine patterns of use in people at higher cardiovascular risk. Because of the important role of L-arginine in oxidative and inflammatory processes, knowledge of L-arginine intake patterns in the population is important. Our hypothesis is that L-arginine intake will vary according to the presence of demographic and cardiovascular risk factors.

2. Methods

This study was an analysis of adults 18 years and older who participated in the Third National Health and Nutrition Examination Survey (NHANES III), a national public-use dataset collected between 1988 and 1994. The NHANES III collected multistage, stratified, clustered samples from the civilian, non-institutionalized population. The National Center for Health Statistics administered the survey to a randomly selected group of approximately 40,000 residents in 89 communities across the United States. [17] Most (86%, 33,994) of the surveyed residents were interviewed in their homes and all were invited to examination centers for additional data collection including physical examination and laboratory measurements. Approximately 79% (31,311) of those surveyed completed all or some of the physical examination and laboratory data collection. During the 6 years of NHANES III data collection, 20,050 adults completed the household survey. Further details on the methodology of the NHANES III, including examination and laboratory assessment, can be found at http://www.cdc.gov/nchs/about/major/nhanes/NHANESIII_Reference_Manuals.htm (accessed November 9, 2007).

To examine the patterns of L-arginine intake in the population, data from four of the NHANES III data files were used: the household-adult data file, the examination data file, the laboratory data file, and the individual-foods data file from the 24-h dietary recall. All NHANES III public-use data files are linked by a common survey-participant variable. The current study was limited to participants 18 years and older who had complete data (n =17,158).

Arginine consumed during the 24-h dietary recall period was calculated with the nutrition data system database of the University of Minnesota. There are no established nutritional guidelines for daily arginine intake. Interventional studies with L-arginine have used widely divergent dose levels. Therefore, quartiles of intake were used to stratify and describe the dietary intake of the population.

The following factors were included in the analyses: age, gender, race, smoking status, body mass index (BMI – kg/m^2), diabetes status, and hypertension. Race included four categories: non-Hispanic white, non-Hispanic black, Hispanic, and other. Each participant's height and weight were measured. Smoking status was determined by self-report as to whether the respondent was a current smoker. Diabetes was identified from a subject's response to the question "Has a doctor ever told you that you have diabetes?" The diagnosis of hypertension was determined by a positive response to the question, "Have you ever been told by a doctor that you have hypertension, also called high blood pressure?"

Descriptive data and demographics of the sample were compiled using data from the NHANES III. Unadjusted analyses were performed to describe the dietary intake of the population according to the factors of interest. In addition, L-arginine intake was calculated per 1000 dietary Calories to correct for different total energy consumption by each individual. Next, a logistic regression model was used to evaluate which demographic and cardiovascular risk factors were associated with L-arginine intake in the lowest quartile. [18] Control variables included age, gender, race, smoking status, body mass index, diabetes status, and hypertension. Weighting variables were used in SUDAAN (Research Triangle Institute, Research Triangle, NC) to account for the complex sampling design of the NHANES III, which over sampled minority, low-income, and elderly households.[19,20] Standardized β values, *P* values, odds ratios, and 95% confidence intervals were obtained from the logistic regression output.

3. Results

Mean arginine intake for the US adult population was 4.40 ± .05 g/day, with 25% consuming <2.6 g/day (Table 1). When adjusted for daily caloric intake, the mean consumption of arginine was 2.03 ± .01 g/1000 Calories/day, with 25% consuming <1.52 g/1000 Calories/day. Individuals 40 years or older consumed less arginine than individuals under the age of 40 years, but consumed more arginine per 1000 Calories. Men consumed more arginine than women, but this was due to them having greater caloric intakes. The gender difference in arginine consumption per 1000 Calories was statistically significant but small. Compared to non-Hispanic Whites, minorities consumed more arginine both in total grams and grams per 1000 Calories. Non-smokers consumed less arginine than smokers, but more arginine per 1000 Calories. Overweight and obese individuals, while consuming no more arginine than normal weight individuals, consumed more arginine per 1000 Calories. Individuals with diagnosed diabetes consumed slightly (but not significantly) less arginine than non-diabetics, but consumed significantly more arginine per 1000 Calories. Similarly, individuals with diagnosed hypertension consumed less arginine than normotensive individuals, but more arginine per 1000 Calories.

The results from the logistic regression analyses (Table 2) further highlight these results. While older individuals are more likely to be in the lowest quartile of arginine consumption, they are less likely to have low arginine consumption when consumption is adjusted for total caloric intake. Women are more likely to be in the lowest quartile of arginine consumption regardless of whether consumption is adjusted for daily calories. Minorities are less likely than whites to be in the lowest quartile of arginine consumption per 1000 Calories per day. Obese individuals (BMI ≥30), non-smokers, and diabetics are less likely to have low caloric-adjusted arginine consumption. Hypertension status was not significantly related to arginine consumption after adjusting for all the other factors.

4. Discussion

The results of this study show that L-arginine intake varies according to demographic and cardiovascular risk factors in the population. Whites have consistently lower intake than African Americans and Hispanics. Individuals with obesity have higher intake, even after correction for caloric intake. Women and smokers have consistently lower intake. Due to the impact of L-arginine on oxidative processes in human metabolism and its link to the production of ADMA [4], these results may have implications for cardiovascular risk.

Previous research has established an association between lower L-arginine intake and inflammatory markers associated with cardiovascular risk [5,21]. Further, the L-arginine/ADMA pathway is emerging as critical to endothelial function [22] and insulin resistance

[23]. Because of the emerging evidence, interest in L-arginine intake and supplementation is likely to grow.

The most common dietary sources of L-arginine are meat, poultry and fish, dairy products, and nuts [24-26]. Lower intake of L-arginine-rich foods such as fish and nuts has been consistently shown to be associated with future cardiovascular risk [25-28]. The association of lower L-arginine intake with inflammation and subsequent cardiovascular risk is bolstered by the fact that dietary intake of L-arginine is directly related to serum arginine levels [29]. In light of the recent finding that ADMA, a chemical that blocks the proper metabolism of L-arginine, is an independent predictor of cardiovascular risk, it is particularly important to characterize L-arginine intake patterns. Correspondingly, the lower intake of L-arginine in women and smokers documented in the current study may be a possible contributing factor to their cardiovascular risk. Only future research can answer this important question.

The cross-sectional nature of this study limits the ability to establish cause and effect. Further, dietary information was based on 24-hour dietary recall, which may not be a precise estimate of long-term dietary habits. There also is the potential for dietary confounders, due to the fact that foods that are high in L-arginine may also be high in other substances such as antioxidant vitamins or other yet-to-be-identified beneficial nutrients. Because L-arginine intake was not calculated in more recent NHANES studies, the data from the 1988-1994 NHANES III may not reflect current dietary patterns in the U.S. Dietary patterns in groups at higher cardiovascular risk may have changed in the interim.

In summary, L-arginine intake varies according to important demographic and cardiovascular risk factors. Future research linking L-arginine intake to subsequent mortality in the NHANES III follow up cohort may be of particular importance in establishing further correlations between L-arginine intake and cardiovascular risk.

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Abbreviations

ADMA, asymmetric dimethyl arginine; BMI, body mass index; NHANES III, Third National Health and Nutrition Examination Survey; NO, nitric oxide; ROS, reactive oxygen species; SUDAAN, statistical software program.

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Table 1

Demographic characteristics of participants according to daily dietary arginine intake.

Variable	Group	Arginine (g) Mean (SE)	Arginine (g) Median (Interquartile Range)	Arginine/1000 Calories Mean (SE)	Arginine/1000 Calories Median (Interquartile Range)
All people		4.40 (0.05)	3.8 (2.6-5.5)	2.03 (0.01)	1.92 (1.52-2.41)
Age Group	18-39	4.79 (0.07)	4.2 (2.8-6.1)	1.96 (0.02)	1.85 (1.46-2.34)
	40-64	4.26* (0.06)	3.8* (2.7-5.3)	2.08* (0.02)	1.98* (1.57-2.46)
	65+	3.50* (0.04)	3.20* (2.2-4.3)	2.12* (0.02)	2.02* (1.59-2.50)
Gender	Male	5.39 (0.07)	4.8 (3.4-6.7)	2.05 (0.02)	1.95 (1.54-2.45)
	Female	3.50* (0.04)	3.2* (2.2-4.4)	2.01* (0.01)	1.90 (1.50-2.37)
Race	White	4.30 (0.06)	3.8 (2.6-5.4)	1.97 (0.01)	1.87 (1.49-2.34)
	Black	4.51* (0.06)	3.9 (2.6-5.7)	2.13* (0.02)	2.02* (1.58-2.53)
	Hispanic	4.66* (0.08)	4.1* (2.7-5.9)	2.17* (0.03)	2.04* (1.66-2.57)
	Other	5.55* (0.32)	4.9* (3.3-7.1)	2.57* (0.09)	2.39* (1.86-3.01)
Current Smoker	Yes	4.66 (0.09)	4.0 (2.7-5.9)	1.96 (0.02)	1.85 (1.45-2.37)
	No	4.29* (0.04)	3.8* (2.6-5.4)	2.06* (0.01)	1.95* (1.55-2.43)
BMI	<25	4.39 (0.07)	3.8 (2.6-5.5)	1.98 (0.01)	1.86 (1.48-2.34)
	25.0-29.9	4.49 (0.06)	4.0 (2.7-5.7)	2.05* (0.02)	1.95* (1.54-2.43)
	30+	4.29 (0.08)	3.8 (2.6-5.3)	2.12* (0.03)	2.01* (1.58-2.52)
Diabetes	Yes	4.10 (0.16)	3.5 (2.6-5.1)	2.39 (0.04)	2.25 (1.80-2.80)
	No	4.42 (0.05)	3.9 (2.6-5.6)	2.01* (0.01)	1.91* (1.51-2.39)
Hypertension	Yes	4.15 (0.06)	3.7 (2.5-5.2)	2.12 (0.02)	2.01 (1.59-2.53)
	No	4.48* (0.06)	3.9* (2.7-5.6)	2.00* (0.01)	1.90* (1.50-2.37)

* Value is significantly different ($p<0.05$) from the first group for each variable, using t-test for comparison of means.

Table 2

Regression modeling of the relative likelihood (Odds Ratio – OR and 95% Confidence Interval) of being in the lowest quartile of arginine consumption.

		Arginine (g)		Arginine/1000 Calories	
Variable	**Group**	**OR**	**95% CI**	**OR**	**95% CI**
Age Group	18-39	1	1	1	1
	40-64	1.16	0.99-1.34	0.72	0.62-0.85
	65+	2.00	1.75-2.28	0.72	0.62-0.85
Gender	Male	1	1	1	1
	Female	3.76	3.40-4.15	1.22	1.10-1.36
Race	White	1	1	1	1
	Black	1.12	1.01-1.24	0.74	0.66-0.84
	Hispanic	0.92	0.81-1.06	0.59	0.50-0.71
	Other	0.64	0.33-1.25	0.37	0.18-0.74
Smoker	Yes	1.11	0.99-1.25	1.23	1.07-1.41
	No	1	1	1	1
BMI	<25	1	1	1	1
	25.0-29.9	0.96	0.83-1.11	0.92	0.79-1.08
	30+	0.88	0.75-1.04	0.81	0.67-0.98
Diabetes	Yes	0.88	0.72-1.06	0.52	0.39-0.70
	No	1	1	1	1
Hypertension	Yes	0.96	0.83-1.10	0.94	0.83-1.06
	No	1	1	1	1

Footnote: Odds ratio (OR) and 95% confidence intervals from logistic regression analysis.