Relationship of Polyunsaturated Fatty Acid Intake to Peripheral Neuropathy Among Adults With Diabetes in the National Health and Nutrition Examination Survey (NHANES) 1999–2004

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OBJECTIVE — This study investigated the association between dietary intake of polyunsaturated fatty acids (PUFAs) and peripheral neuropathy in the U.S. population.

RESEARCH DESIGN AND METHODS — We analyzed data from the National Health and Nutrition Examination Survey (NHANES) 1999–2004 for adults ≥40 years of age with diagnosed diabetes, an assessment of peripheral neuropathy, and reliable 24-h dietary recall. The dietary intake of PUFAs was analyzed by peripheral neuropathy status. Multivariate logistic regression models were used to estimate the odds of having peripheral neuropathy in higher quintiles of PUFA intake compared with the lowest quintile.

RESULTS — The mean dietary intake of linolenic acid was 1.25 ± 0.07 g among adults with peripheral neuropathy, significantly lower than the 1.45 ± 0.05 g intake among those without peripheral neuropathy. After controlling for potential confounding variables, adults whose linolenic acid intake was in the highest quintile had lower odds of peripheral neuropathy than adults in the lowest quintile (adjusted odds ratio 0.40 [95% CI 0.21–0.77]).

CONCLUSIONS — Among adults with diagnosed diabetes, dietary intake of linolenic acid is positively associated with lower odds of peripheral neuropathy.

Diabetes Care **31:93–95, 2008**

The prevalence of peripheral neuropathy is 28.5% among adults aged ≥40 years with diabetes in the U.S. population (1). Besides improving glycemic control, few available therapeutic choices for peripheral neuropathy can influence its natural history (2). Identification of additional modifiable factors that may be related to the progression of peripheral neuropathy is important. This study investigated whether dietary polyunsaturated fatty acid (PUFA) intake is associated with measured peripheral neuropathy.

RESEARCH DESIGN AND METHODS

This study used data from the National Health and Nutrition Examination Survey (NHANES) 1999–2004. The sample includes 1,062 adults ≥40 years of age with self-reported diagnosed diabetes, peripheral neuropathy measurement, and complete and reliable 24-h dietary recall data.

Measurements of peripheral neuropathy

Peripheral neuropathy was assessed by testing foot sensation using a 5.07-gauge Semmes-Weinstein nylon monofilament (3). Three plantar metatarsal sites (hallux and first and fifth metatarsal heads) were tested on each foot in random order. Peripheral neuropathy was defined as having one or more insensate sites (1).

Assessment of PUFA intake

Dietary nutrient intake estimates were obtained from a single in-person interview of 24-h dietary intake. The NHANES data files include energy intake, total PUFA intake, and intake of seven specific fatty acids (C18:2, C18:3, C18:4, C20:4, C20:5, C22:5, and C22:6). Total long-chain PUFA intake was calculated by summing intake of PUFAs with ≥20 carbon atoms. Use of dietary supplements containing PUFA in the past 30 days was ascertained during the household interview (4).

Covariates

The analysis controlled for previously reported risk factors (5–7), namely self-reported age, sex, race/ethnicity, education, smoking status, duration of diabetes, and measured weight, height, blood pressure, and glycohemoglobin (A1C) (8,9). High blood pressure was defined as average systolic blood pressure ≥140 mmHg or average diastolic blood pressure ≥90 mmHg. Poor glycemic control was defined as A1C ≥7% (10).

Statistics

Descriptive statistics on the dietary intake of PUFAs and other characteristics were calculated. Student's t test or χ^2 test was used separately for continuous or categorical variables.

The percentages of adults with peripheral neuropathy in each quintile of

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Received for publication 2 June 2007 and accepted in revised form 1 October 2007.

Published ahead of print at http//:care.diabetesjournals.org on 3 October 2007. DOI: 10.2337/dc07-0931.

Abbreviations: ALA, α-linolenic acid; GLA, γ-linolenic acid; NHANES, National Health and Nutrition Examination Survey; PUFA, polyunsaturated fatty acid.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Percent with peripheral neuropathy and the odds of having peripheral neuropathy by quintile of total PUFA intake and linolenic acid (C18:3) intake in adults with diagnosed diabetes aged ≥40 years, NHANES 1999–2004*

	Quintiles of PUFA intake					
	Q1	Q2	Q3	Q4	Q5	*P*
Total PUFA*						
With peripheral neuropathy	33.11 (3.69)	28.80 (3.63)	29.06 (3.06)	29.80 (3.67)	19.67 (4.03)	0.20†
Energy-adjusted odds ratio	1.0 (ref.)	0.76 (0.43–1.32)	0.73 (0.45–1.20)	0.71 (0.38–1.34)	0.36 (0.16–0.82)	
Multivariate-adjusted odds ratio‡	1.0 (ref.)	0.83 (0.44–1.52)	0.85 (0.49–1.47)	0.63 (0.31–1.27)	0.43 (0.19–1.00)	
Linolenic acid (C18:3)*						
With peripheral neuropathy	33.10 (3.84)	23.90 (4.18)	35.47 (3.78)	27.17 (3.75)	20.68 (3.81)	0.12†
Energy-adjusted odds ratio	1.0 (ref.)	0.61 (0.33–1.15)	1.04 (0.63–1.72)	0.69 (0.40–1.19)	0.46 (0.24–0.90)	
Multivariate-adjusted odds ratio‡	1.0 (ref.)	0.57 (0.29–1.11)	0.71 (0.45–1.23)	0.54 (0.30–0.99)	0.40 (0.21–0.77)	

Data are % (SE) and point estimate (95% CI). *The quintiles of total PUFA intake were defined as Q1, <7.72 g; Q2, 7.72–11.44 g; Q3, 11.45–16.14 g; Q4, 16.15–24.74 g; and Q5, ≥24.75 g. The quintiles of linolenic acid intake were defined as Q1, <0.61 g, Q2, 0.61–0.91 g; Q3, 0.92–1.34 g; Q4, 1.35–2.10 g; and Q5, ≥2.11 g. †χ^2 test. ‡Adjusted for age, sex, race/ethnicity, education, height quintile, weight quintile, duration of diabetes, glycemic control, high blood pressure, smoking status, and total energy intake.

PUFA intake were reported. χ^2 test was used to test whether the percentage of people with peripheral neuropathy differs by quintiles of PUFA intake. A logistic regression model was used to estimate the odds of having peripheral neuropathy among adults in higher PUFA intake quintiles relative to adults in the lowest PUFA intake quintile (Q1), first adjusting for energy intake and then further adjusting for previously identified covariates. Analyses were conducted using SUDAAN 9.0 (11).

RESULTS

Adults with peripheral neuropathy were significantly older, taller, and more likely to be male and had lower education and longer duration of diabetes than adults without peripheral neuropathy.

Among adults with peripheral neuropathy, the mean daily total PUFA intake was 14.60 ± 0.79 g and the mean daily intake of linolenic acid (C18:3) was 1.25 ± 0.07 g, significantly lower than the 16.82 ± 0.59 and 1.45 ± 0.05 g respective values among adults without peripheral neuropathy. Intake of other PUFAs was not statistically different by peripheral neuropathy status.

Relative to adults in Q1 of total PUFA intake, the odds of having peripheral neuropathy was 0.43 (95% CI 0.19–1.00) for adults in Q5 after adjusting for previously identified covariates (Table 1). Relative to adults in Q1 of C18:3 intake, the odds of having peripheral neuropathy was 0.54 (0.30–0.99) for adults in Q4 and 0.40 (0.21–0.77) for adults in Q5. Logistic models including and excluding diabetes duration had virtually identical findings, suggesting that diabetes duration does not change the association between PUFA intake and peripheral neuropathy.

Only 4.04% of adults reported taking supplements containing PUFAs. The association between taking supplements containing PUFAs and the risk of peripheral neuropathy was not estimated because of small sample size. Inclusion of supplement usage in regression models did not affect the association between dietary PUFA intake and peripheral neuropathy.

CONCLUSIONS

This is the first study to explore whether high dietary PUFA intake is associated with lower risk of peripheral neuropathy. We found that dietary intake of linolenic acid C18:3 (undifferentiated) is negatively associated with the odds of peripheral neuropathy among adults with diabetes. Studies have shown that γ-linolenic acid (C18:3 n-6) (GLA) supplements have a protective effect on diabetic peripheral neuropathy (12–14). However, GLA is seldom found in foods. The major form of C18:3 in food is α-linolenic acid (C18:3 n-3) (ALA). Thus, it is reasonable to expect that the negative association between C18:3 and peripheral neuropathy in this study is due to ALA.

No study has examined the association between ALA and diabetic peripheral neuropathy. However, high dietary intake of ALA was found to reduce the risk of coronary heart disease (15–17) and to be associated with lower risk for hypertension (18). Vascular factors are important in the pathogenesis of peripheral neuropathy (2,19). The protective effect of ALA on macrovascular diseases and its association with diabetic peripheral neuropathy may be due to similar biological mechanisms.

One limitation of this study is that the PUFA intake was classified based on a single 24-h dietary recall. Due to daily variation in dietary intake, adults may be misclassified with respect to their usual PUFA intake, but the effect seems to be random across the groups. In NHANES, only tactile peripheral neuropathy is measured, and the association of PUFAs to other sensory functions, such as temperature sensitivity, cannot be considered. However, monofilament is an inexpensive and well-accepted tool for measuring peripheral neuropathy. It has a sensitivity of 85–100% and specificity of 76% in predicting foot ulcer (20).

Identification of prevention methods for peripheral neuropathy can help reduce the prevalence of peripheral neuropathy and its complications. More work is needed to study the association between ALA and peripheral neuropathy reported here and to clarify the biological mechanisms.

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