

Relationship of polyunsaturated fatty acids (PUFA) intake to peripheral neuropathy (PN) among adults with diabetes in National Health and Nutrition Examination Survey (NHANES) 1999-2004

Min Tao¹, MD, PhD; Margaret A. McDowell², MPH, RD; Sharon H. Saydah³, PhD;
Mark S. Eberhardt³, PhD

¹Epidemic Intelligence Service Program, Centers for Disease Control and Prevention,
Hyattsville, Maryland

²Division of Health and Nutrition Examination Surveys,
National Center for Health Statistics, Hyattsville, Maryland

³Office of Analysis and Epidemiology, National Center for Health Statistics,
Hyattsville, Maryland

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Corresponding author:
Mark Eberhardt
Email: mse1@cdc.gov.

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Abstract:

Objective: This study investigated the association between dietary intake of PUFAs and PN in the U.S. population.

Research Design and Methods: We analyzed data from NHANES 1999-2004 for adults ≥ 40 years with diagnosed diabetes, an assessment of PN and reliable 24-hour dietary recall. The dietary intake of PUFAs was analyzed by PN status. Multivariate logistic regression models were used to estimate the odds of having PN 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 PN, significantly lower than 1.45 ± 0.02 g among those without PN. After controlling for potential confounding variables, adults whose linolenic acid intake in the highest quintile had lower odds of PN compared with 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 PN.

The prevalence of PN is 28.5% among adults ≥ 40 years with diabetes in the U.S. population [1]. Besides improving glycemic control, few of available therapeutic choices for PN can influence its natural history [2]. Identification of additional modifiable factors that may be related with the progression of PN is important. This study was to investigate whether dietary PUFA intake is associated with measured PN.

Research design and methods

This study used data from NHANES 1999-2004. The sample includes 1062 adults ≥ 40 years with self-reported diagnosed diabetes, PN measurement and complete and reliable 24-hour dietary recall data.

Measurements of PN

PN was assessed by testing foot sensation using a 5.07-gauge Semmes-Weinstein nylon monofilament [3]. Three plantar metatarsal sites (hallux, first and fifth metatarsal head) were tested on each foot in a random order. PN was defined as having ≥ 1 insensate sites [1].

Assessment of PUFA intake

Dietary nutrient intake estimates were obtained from a single in-person interview of 24-hour 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, 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 $\geq 7\%$ [10].

Statistics

Descriptive statistics on the dietary intake of PUFAs and other characteristics were calculated. The student's t-test or Chi-square test was used separately for continuous or categorical variables.

The percentages of adults with PN in each quintile of PUFA intake were reported. Chi-square test was used to test whether the percentage of persons with PN differs by quintiles of PUFA intake. Logistic regression model was used to estimate the odds of having PN among adults in higher PUFA intake quintiles relative to adults in the lowest PUFA intake quintile (Q1), first adjusting for energy intake, then further adjusting for previously identified covariates. Analyses were conducted using SUDAAN 9.0 [11].

Results:

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

Among adults with PN, 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 16.82 ± 0.59 g and 1.45 ± 0.05 g among adults without PN. Intake of other

PUFAs was not statistically different by PN status.

Relative to adults in Q1 of total PUFA intake, the odds of having PN 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 PN was 0.54 (95%CI: 0.30-0.99) for adults in Q4 and 0.40 (95%CI: 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 and PN.

Only 4.04% of adults reported taking supplements containing PUFAs. The association between taking supplements containing PUFAs and the risk of PN 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 PN.

Conclusions:

This is the first study to explore whether the high dietary PUFA intake is associated with lower risk of PN. We found that dietary intake of linolenic acid C18:3 (undifferentiated) is negatively associated with the odds of PN among adults with diabetes. Studies shown that γ -linolenic acid (C18:3 n-6, GLA) supplements have a protective effect on diabetic PN [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). So it is reasonable to expect that the negative association between C18:3 and PN in this study is due to ALA.

No study has looked at the association between ALA and diabetic PN. 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 PN [2,19]. The protective effect of ALA on macrovascular diseases and its association with diabetic PN may due to similar biological mechanisms.

One limitation of this study is that the PUFA intake was classified based on a single 24-hour 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 PN is measured and the association of PUFAs to other sensory functions, such as temperature sensitivity can not be considered. However, monofilament is an inexpensive and well-accepted tool for measuring PN. It has a sensitivity of 85-100% and specificity of 76% in predicting foot ulcer [20].

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

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Table 1. Percent with Peripheral Neuropathy (PN) and the Odds of Having PN by Quintile of Total Polyunsaturated Fatty Acids (PUFA) Intake and Linolenic Acid (C18:3) Intake in Adults with Diagnosed Diabetes Aged ≥ 40 Years, National Health and Nutrition Examinations Survey (NHANES), 1999-2004

	Quintiles of PUFA intake					P value
	Q1	Q2	Q3	Q4	Q5	
Total PUFA*						
With PN (%, SE)	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 PN (%, SE)	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)	

* The quintiles of total PUFA intake were defined as Q1 (<7.72g), Q2 (7.72-11.44g), Q3 (11.45-16.14g), Q4 (16.15-24.74g) and Q5 (≥24.75g). The quintiles of linolenic acid intake were defined as Q1 (<0.61g), Q2 (0.61-0.91g), Q3 (0.92-1.34g), Q4 (1.35-2.10g) and Q5 (≥2.11g).

[†]Chi-square test

[‡] Adjusted for age, gender, race/ethnicity, education, height quintile, weight quintile, duration of diabetes, glycemic control, high blood pressure, smoking status and total energy intake. Numbers in the tables are point estimates and 95% confidence intervals.