The relationship between different fatty acids intake and frequency of migraine attacks

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Abstract

Background: Migraine is a primary headache disorder that affects the neurovascular system. Recent studies have shown that consumption of some fatty acids such as omega-3 fatty acids improves migraine symptoms. The aim of the present study is to assess the association between usual intake of fatty acids such as eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and saturated fatty acids (SFA) with the frequency of migraine attacks.

Materials and Methods: 105 migraine patients with age ranging from 15 to 50 years participated in this cross-sectional study. Usual dietary consumption was assessed by using a semi-quantitative food frequency questionnaire (FFQ). Moreover, frequency of migraine attacks during 1 month period was determined in all participants. Data had been analyzed using independent sample *t*-test and linear regression test with adjustment of confounding variables.

Results: In this study, we found that lower intake of EPA ($\beta = -335.07$, $P = 0.006$) and DHA ($\beta = -142.51$, $P = 0.001$) was associated with higher frequency of migraine attacks. In addition, we observed similar relationship either in men or women. No significant association was found between dietary intake of SFA and the frequency of migraine attacks ($\beta = -0.032$, $P = 0.85$).

Conclusions: Frequency of migraine attacks was negatively associated with dietary intake of omega-3 polyunsaturated fatty acids. No significant relationship was found between SFA intake and migraine frequency. Further studies are required to shed light on our findings.

Key words: Docosahexaenoic acid, eicosapentaenoic acid, fatty acids, migraine

Introduction

Migraine disorder, in addition to being tension-type headache, is known as a progressive and prevalent paroxysmal neurological disorder that can affect nearly 80% of people all over the world.[1] Migraine risk is three times more prevalent in women than men.[2] Its common symptoms are severe headache which accompany with neck pain, muscle tension, and nausea; in several migraine attacks, patients may experience photophobia and phonophobia symptoms.[3,4] The clinical and subclinical symptoms of migraine as a neurovascular disorder occur following the production of producing pro-inflammatory factors around the nerves and in the blood vessels of the head.[2] This disturbance can lead to twofold higher risk for ischemic stroke.[5] Studies reflect that individuals with migraine attacks are more prone to epilepsy, atopic diseases, inflammatory and degenerative disorders, and cardiovascular diseases.[6] Migraine attack is a multi-factorial disorder which can be affected by several genetic, acquired, and environmental factors.[7] It seems managing individuals' lifestyle, such as physical activity, dietary intake, and environmental stress, can be useful to control migraine attacks.[8-12] Very long-chain n-3 polyunsaturated fatty acids

Migraine is an inflammatory disease and we can use the anti-inflammatory roles of micronutrients for its treatment.[3] Long-chain n-3 polyunsaturated fatty acids (PUFAs) including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the major anti-inflammatory micronutrients that seem to reduce the effects of migraine.[13-15] The balance between these pro- and anti-inflammatory nutrients can be related with various symptoms and outcomes of migraine attacks such as severity, frequency, and other related indices.[15,16] Due to the growing recommendation in usage of omega-3 fatty acids in recent years, confirming the useful effects of these nutrients in managing migraine outcomes can be a proper strategy in nursing care. Some studies reported that intake of long-chain n-3 PUFAs has beneficial

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effects on migraine attacks frequency,[15,16] but one study did not show any significant effect.[17] Therefore, findings in this regard are inconsistent and studies are mainly focused on the effects of long-chain n-3 PUFA supplements. The present study was conducted with the aim of assessing the association between various types of fatty acids including dietary EPA, DHA, and saturated fatty acids (SFA) with the frequency of migraine attacks.

Materials and Methods

Study population

This cross-sectional study was conducted on 117 individuals (25 men and 92 women) with age ranging from 15 to 50 years. Migraine was diagnosed by a neurologist according to the International Headache Society (IHS) criteria.[18] Inclusion criteria were having a history of migraine for a long time (>5 years) and having 1 year history of severe, recurrent, and long-lasting migraine attacks (at least one attack per month lasting 4 h). Frequency of migraine attacks during 1 month period was determined in all participants by the neurologist. Patients should answer this question, "How many migraine attacks do you have per month?" High frequency of migraine attacks is defined as having more than 10 attacks per month.[19] Patients with tension-type headache and chronic pain were excluded from the study. After explaining the process and aims of the study, participants were asked to sign a written consent. The ethical committee of Isfahan University of Medical Sciences (IUMS), Isfahan, Iran approved our study.

Nutritional assessment

Usual dietary consumption was assessed by using a 168-item semi-quantitative food frequency questionnaire (FFQ).[20,21] This questionnaire consisted of 17 food groups and every food group contained several food items in addition to standard portion size for each food (Willett format)[22] [Table 1]. This

Table 1: Food groups, food items, and standard portion size of each food in FFQ

Food groups	Food items (*n*=168)	Portion size
Whole grains	All whole and dark breads (barbari, sangak, taftoon, and toasted bread (whole grain)) Popcorn Cooked barley, bulgur Corn Biscuits prepared with whole grains	Slice Cup Tablespoon One medium Number
Refined grains	White bread (Lavash) Baguette Cooked rice and pasta Cooked angel hair pasta, reshteh, and wheat flour	Slice Number Plate Cup
Potatoes	French fries, baked potatoes	Number
Dairy products	All kinds of milk (whole, low fat, skim, cocoa and chocolate), doogh (yogurt drink), yogurt (plain and whole) Yogurt (concentrated and creamy), cream, kashk Cheese (plain and creamy) Ice cream (plain and traditional (high fat))	Cup Tablespoon Half of a cup
Vegetables	Raw and cooked leafy vegetables, shredded lettuce, celery, green pea, spinach, mushroom Raw and cooked tomato, cucumber, squash, eggplant, carrot, garlic, onion, green pepper, turnip, green chilies Cooked green bean, fried onion, cruciferous vegetables (cauliflower, red and white cabbage), pumpkin	Cup Number Tablespoon Slice
Fruits	Cantaloupe, Persian melon, watermelon Pear, apricot, apple, cherry, peach, nectarine, green plum, fig, grapes, kiwi, grapefruit, orange, persimmon, tangerine, pomegranate, dates, prune (yellow and red), sour cherry, strawberry, banana, sweet lemon, lime lemon, mulberry, dried fruits (fig, mulberry, peach, and apricot) Cranberry, pineapple (raw and canned) Lime juice Raisins Canned fruits	Slice Number Cup Teaspoon Tablespoon Can
Legumes	Cooked lentil, bean, chickpea, cooked broad bean, soy bean, mung bean, split peas	Tablespoon
Meats	Tuna Egg (all preparations) Hamburger, sausage, organ meat (brain, tongue, feet, and head) poultry, organ meat (liver, kidney, and heart), tripe Bologna (beef), fish (all fishes except tuna) Ground meat Red meats (beef, lamb)	Half of a can Number Slice Piece Tablespoon Slice (ounce)
Nuts and seeds	Peanut, almond, walnut, pistachio, hazelnut, seeds	Number

Contd...

Table 1: Continue

Food groups	Food items (n=168)	Portion size
Solid fats	Hydrogenated fats, animal fats Tallow (fat) Butter, hydrogenated margarine	Tablespoon Piece Teaspoon
Liquid oils	All vegetable oils and olive oil, mayonnaise Olives	Tablespoon Number
Tea and coffee	Tea and coffee	Cup
Salty snacks	Pickles in vinegar and salted vegetables Salted pickles	Tablespoon Number
Simple sugars	Sugar Cube sugar, noghl, and candy	Teaspoon Number
Honey and jams	Honey, Jams	Teaspoon
Soft drinks	All soft and sweet drinks, beer (non-alcoholic), syrup; fruit juices (grapefruit, orange, apple, and cantaloupe)	Cup
17. Snacks and desserts	Sponge cake, other cakes Yazdi cake (plain cake with raisins), chocolates, pastries (non-creamy and creamy), all biscuits other than those made from whole grain, crackers, patties, gaz, sohan Cream caramel, halvah (homemade) Puffs, potato chips, and halvah (non-homemade)	Slice Number Tablespoon Pocket

FFQ: Food frequency questionnaire

questionnaire had almost all the fat-containing foods in Iranian dietary pattern. The questionnaires were completed in a face-to-face interview by an educated dietitian with at least 3 years of experience in the food consumption survey. Participants were asked to reporttheir dietary intake of foods based on questions with nine choices as follows: never or less than once per month, 1-3 times per month, 1 time per week, 2-4 times per week, 5-6 times per week, 1 time per day, 2-3 times per day, 4-5 times per day, 6 or more times per day." We computed daily intake of all food items and then converted it to grams per day using household measures. Each food and beverage was analyzed for the content of energy and fatty acids using NUTRITIONIST III software (version 7.0; N-Squared Computing, Salem, OR, USA), which was designed for evaluation of Iranian foods.[23,24] Reliability and validation of the mentioned FFQ were checked in a previous study.[20]

Statistical analysis

All quantitative variables are presented as mean and standard deviation [Table 1]. Data were compared between men and women by using independent sample t-test. To assess the association between dietary intake of fatty acids and the frequency of migraine attacks, we used linear regression in crude and three adjusted models for dietary intake, age, and body mass index (BMI). All data analysis was performed using SPSS software (version 18.0; SPSS, Inc., Chicago, IL, USA). Significant levels were set as P value less than 0.05.

Results

We had complete data about a total of 105 subjects (23 men and 82 women) with a mean age of 32.30 ± 9.66 years, and 12 individuals refused to participate. Mean dietary intake of energy, SFA, EPA, and DHA, in addition to age, BMI, and frequency of migraine attacks in the entire study population as well as in men and women separately are shown in Table 2. Table 3 reveals the differences between patients with moderate and high frequency of migraine attacks in their dietary intake of fatty acids. Migraine patients with high frequency of migraine attacks had lower dietary intake of EPA and DHA in crude or energy-adjusted form and higher BMI, compared to patients with moderate frequency of migraine attacks. No significant differences were found between patients with moderate and high frequency of attacks in age, dietary intake of energy and SFA, either in crude or energy-adjusted form.

Table 4 presents the results of multiple linear regression analysis for the association between dietary intake of SFA, EPA, and DHA with the frequency of migraine attacks. There was a significant negative association between EPA and DHA intake with migraine attack frequency. This relationship remained significant even after adjustment of energy, age, and BMI. No significant relationship was found between dietary intake of SFA and frequency of migraine attacks, either in crude or confounding variable adjusted models.

Results of sex-stratified analysis for the association between dietary intake of fatty acids and frequency of migraine attacks are shown in Table 5. Among men, a significant negative association was found between EPA and DHA consumption with the frequency of migraine attacks. However, this relationship attenuated

Table 2: Demographic characteristics of participants

Variables	Men	Women	Total
Age (years)	30.95±10.61	32.68±9.42	32.3±9.66
BMI (kg/m^2)	23.45±4.23	25.73±5.09	25.24±4.98
Energy (kcal)	2582.85±1002.37	2229.87±806.66	2307.19±860.73
SFA (g)	22.84±11.68	19.24±9.93	20.03±10.39
EPA (mg)	8.7±6.2	10.5±10.4	10.1±9.6
DHA (mg)	27.4±19.8	33.4±29.3	32.1±27.5
Energy-adjusted SFA (g)	19.92±4.69	19.68±5.86	19.73±5.61
Energy-adjusted EPA (mg)	8.0±6.1	10.1±10.4	9.6±9.6
Energy-adjusted DHA (mg)	25.9±19.0	33.4±29.1	31.7±27.3
Frequency (per month)	10.04±8.59	10.86±9.57	10.67±9.32

Data are presented as mean and standard deviation. BMI: Body mass index, SFA: Saturated fatty acids, EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid

Table 3: Dietary intake of fatty acids in patients with moderate and high frequency of migraine attacks†

Variables	Moderate frequency	High frequency	*P* value
Age (years)	31.97±9.11	33.29±10.45	0.53
BMI (kg/m^2)	24.7±4.6	26.92±5.55	0.04*
Energy (kcal)	2330.06±858.0	2182.57±685.37	0.42
SFA (g)	20.33±10.01	18.28±8.67	0.34
EPA (mg)	11.8±10	5.6±6.9	0.003*
DHA (mg)	37.5±29.2	17.8±15	<0.001*
Energy-adjusted SFA (g)	19.81±4.83	19.17±7.24	0.67
Energy-adjusted EPA (mg)	11.4±10	5.2±7	0.004*
Energy-adjusted DHA (mg)	37±29.2	17.9±15	<0.001*

Data are presented as mean and standard deviation. †High frequency of migraine attacks is defined as more than 10 attacks per month. BMI: Body mass index, SFA: Saturated fatty acids, EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid. *P <0.05 considered as significant level

after adjustment of potential confounding variables. Among women, dietary intake of EPA and DHA was negatively associated with the frequency of migraine attacks. Controlling for confounders showed no changes in this relationship. No significant association was found between dietary intake of SFA and frequency of migraine attacks, either in men or women.

Discussion

In this study, we aimed to assess the association between usual intake of fatty acids including SFA, EPA, and DPA and the frequency of migraine attacks. We found that lower intake of EPA and DHA was associated with higher frequency of migraine attacks. This relationship remained significant even after adjustment of potential confounding variables. In addition, such relationship was observed either in men or women. No significant association was found between dietary intake of SFA and frequency of migraine attacks either in crude and adjusted model. This is one of the few studies that examined the association between usual consumption of fatty acids and migraine symptoms.

Although some studies have demonstrated that fatty acids may affect migraine symptoms, data on the association between usual consumption of fatty acids and migraine are scarce. Earlier studies have mostly focused on the use of high doses of fatty acids, especially PUFAs.[16] These studies have shown that high doses of omega-3 PUFAs have beneficial effects on migraine symptoms, especially the frequency of migraine attacks.[16]

In this study, higher consumption of omega-3 PUFAs such as DHA and EPA was associated with lower frequency of migraine attacks. In line with our findings, Harel *et al*. reported that administration of fish oil rich in very long-chain n-3 PUFAs reduced the frequency of migraine attacks.[16] In an open-label uncontrolled study, consumption of gamma-linolenic and alpha-linolenic acids decreased the frequency of migraine attacks.[15] In contrast, Pradalier *et al*. reported that consumption of omega-3 PUFAs had no effect on the frequency of migraine attacks.[17] Inconsistent results obtained in different studies may be due to the differences in subjects' genetic polymorphism, physical activity level, and their health status.

The exact mechanism through which omega-3 PUFAs might affect the frequency of migraine remains unknown. However, migraine is affected by inflammatory factors and studies have shown that omega-3 PUFAs can decrease the inflammation status.[13] Omega-3 PUFAs can reduce the production of nitric oxide which is believed to play a role in the occurrence of migraine attacks.[25] Moreover, several studies have shown a possible link between n-3 PUFAs and serotonin, so its effects on serotonin level can explain the etiology of migraine.[26] Confirming the effects of omega-3 PUFAs can be useful in nursing care and in the process of reducing bothersome migraine attacks.

The present study has some limitations. The first one is the cross-sectional nature of our study; hence, we cannot establish a causal link between omega-3 PUFA consumption and the frequency of migraine attacks. Further studies are needed to confirm our findings. Second, the sample size of

Table 4: Association between dietary intake of fatty acids and frequency of migraine attacks†

	SFA		EPA		DHA	
	β (95% CI)	*P* value	β (95% CI)	*P* value	β (95% CI)	*P* value
Crude	−0.108 (−0.44, 0.22)	0.51	−0.245 (−0.42, −0.06)	0.009*	−0.1 (−0.16, −0.03)	0.003*
Model 1	−0.105 (−0.43, 0.22)	0.53	−0.246 (−0.43, −0.06)	0.009*	−0.1 (−0.16, −0.036)	0.003*
Model 2	−0.098 (−0.43, 0.23)	0.56	−0.243 (−0.42, −0.05)	0.011*	−0.99 (−0.16, −0.035)	0.003*
Model 3	−0.032 (−0.37, 0.31)	0.85	20.335 (−0.57, −0.09)	0.006*	−0.142 (−0.22, −0.05)	0.001*

SFA: Saturated fatty acids, EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid. †Fatty acids are energy adjusted. *P <0.05 considered as significant level. Model 1: Adjusted for energy, Model 2: Further adjusted for age, Model 3: Additionally controlled for BMI

Table 5: Association between dietary intake of fatty acids and frequency of migraine attacks among men and women†

	SFA		EPA		DHA	
	β (95% CI)	*P* value	β (95% CI)	*P* value	β (95% CI)	*P* value
Men						
Crude	−0.398 (−1.2, 0.41)	0.31	−0.748 (−1.29, −0.2)	0.009*	−0.202 (−0.38, −0.01)	0.032*
Model 1	−0.439 (−1.3, 0.42)	0.30	−0.771 (−1.33, −0.21)	0.009*	−205 (−0.39, −0.01)	0.035*
Model 2	−0.390 (−1.2, 0.5)	0.37	−0.756 (−1.35, −0.15)	0.016*	−0.197 (−0.39, −0.003)	0.046*
Model 3	−0.312 (−1.23, 0.61)	0.48	−0.688 (−1.38, −0.008)	0.052	−0.175 (−0.42, 0.07)	0.15
Women						
Crude	−0.053 (−0.42, 0.32)	0.77	−0.203 (−0.4, −0.003)	0.047*	−0.091 (−0.16, −0.02)	0.012*
Model 1	−0.058 (−0.43, 0.31)	0.75	−0.207 (−0.4, −0.005)	0.044*	−0.092 (−0.16, −0.02)	0.012*
Model 2	−0.057 (−0.43, 0.32)	0.76	−0.206 (−0.4, −0.003)	0.047*	−0.091 (−0.16, −0.02)	0.013*
Model 3	0.014 (−0.37, 0.4)	0.94	−0.293 (−0.56, −0.02)	0.032*	−0.139 (−0.23, −0.04)	0.004*

SFA: Saturated fatty acids, EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid. †Fatty acids are energy adjusted. *P <0.05 considered as significant level. Model 1: Adjusted for energy, Model 2: Further adjusted for age, Model 3: Additionally controlled for BMI

our study was small and more studies with larger participant number are required. Third, despite several adjustments, further control for confounding variables such as genetic polymorphism and psychosocial factors will be needed to reach an independent association between omega-3 PUFA consumption and migraine frequency.

Conclusion

Frequency of migraine attacks was negatively associated with dietary intake of omega-3 PUFAs. This relationship remained significant even after adjustment of potential confounding variables. No significant relationship was found between SFA intake and migraine frequency either in crude or adjusted model. Further studies are required to shed light on our findings.

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