Original Article

Assessment of pyridoxine and folate intake in migraine patients

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Abstract

Background: Migraine is a highly prevalent disorder worldwide. It affects 10–20% of the population during their lifetime. Recent studies have indicated that supplementation with folate and pyridoxine improves migraine symptoms. This study was undertaken to evaluate dietary intake of folate and pyridoxine in migraine patients and assessed their association with the frequency of migraine attacks.

Materials and Methods: This is a case–control study performed on 124 migraine patients and 130 non-migraine subjects. Individuals' common dietary intake was determined by using a valid semi-quantitative 168-item food frequency questionnaire (FFQ). Data had been analyzed using independent *t*-test using SPSS software (version 18).

Results: In this study, we found that migraine patients had lower intake of dietary folate compared with control group, but energy and pyridoxine intake were not different between the two groups. Further analysis among men and women revealed no statistically significant changes in these relationships. In addition, we found no significant association between dietary intake of pyridoxine and folate with the frequency of migraine attacks.

Conclusion: Migraine patients had lower dietary intake of folate, compared with non-migraine group subjects. There was no significant association between folate and pyridoxine intake with the frequency of migraine attacks. Further studies are needed to confirm our findings.

Key Words: Folate, frequency, migraine, pyridoxine

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INTRODUCTION

Migraine is a recurrent and troublesome neurovascular disorder. Statistics show that nearly one-fifth of people are suffering from its clinical and subclinical vascular brain lesions worldwide.[1-3] Lowered quality of life and working-day loss are the common outcomes of this progressive disease. Severe head pain, in addition to the symptoms of nausea and vomiting, is the most bothersome complaint of these patients. Usually, light and sound can have an effect on the severity and frequency of these symptoms.[4] Middle-aged women are more susceptible to migraine occurrence than men.[5,6] Migraine occurs either with or without visual disturbances, and this criterion is defined to divide migraine disorder into migraine with or migraine without aura, respectively. Also, 25% of individuals

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can be categorized in the first division (defined as migraine with aura).[7] The risk of ischemic stroke is 2 times higher in migraine patients.[8-10] The major etiology of migraine occurrence is not clear; however, several basic causes have been explored. Genetic defects and environmental risk factors play effective roles.[11] Smoking, inactivity, and nutritional deficiencies, besides psychological distress can worsen migraine symptoms.[12-16] One of the items of dietary intake which seem to play an effective role in migraine attacks is B group vitamins such as pyridoxine and folic acid.[17] The chief relationship is based on their effects on the level of homocysteine. Folic acid and B6 consumption shows an inverse association with plasma homocysteine concentration.[18] Higher homocysteine level is one of the major risk factors in several degenerative and inflammatory diseases.[19] The roles of these vitamins in managing its concentration shows that they can be helpful in reducing migraine and its symptoms.[20] This association creates the need to focus deeply on the comparison of B complex intake between migraine and non-migraine subjects and in patients with different degrees of migraine symptoms. Although most studies have evaluated the effects of pyridoxine and folate supplementation on migraine symptoms, few studies have assessed the association between dietary intake of these vitamins and migraine symptoms. The main purpose of this study was to compare pyridoxine and folate consumption in migraine and non-migraine subjects.

MATERIALS AND METHODS

This case–control study was conducted on 29 men and 95 women with migraine with aura (MA). Subjects' age ranged between 15 and 65 years. Migraine disorder was diagnosed based on the standard criteria by a neurologist.[7] Non-migraine individuals were selected in the same age range and sex distribution. An informed consent was obtained from all the participants.

Migraine assessment

Diagnosis of migraine was performed by an expert neurologist according to Headache Classification Committee of the I nternational Headache Society (IHS) criteria. The inclusion criteria were as follows: Having history of migraine for a long time (>5 years), current diagnosis of MA, and 1 year history of severe, recurrent, and long-lasting migraine attacks (at least one attack per month, lasting 4 h). Exclusion criteria included presence of certain disorders such as chronic heart disease, previous stroke, and chronic renal failure. The frequency of migraine attacks during 1 month period was determined in the case group. High frequency of migraine attacks was defined as more than 10 attacks per month.[21]

Nutritional assessment

Individuals' common dietary intake was determined by using a valid semi-quantitative 168-item food frequency questionnaire (FFQ).[22] The questionnaire contained national food items and portion sizes of typical foods. All the food questionnaires were checked carefully by an educated dietitian by conducting a face-to-face interview. Frequency of food consumption during the last year was collected on a daily, weekly, or monthly time period. Then, daily dietary intake of food items was converted to grams per day by using common portion size.[23] Total food intake was estimated by summing up the content of all foods and nutrients. In order to decrease the imbalance in food items number and sample size of participants, various food groups were defined based on the nutrient content of every food item and food pyramid guideline. It should be mentioned that we considered several of the foods as an individual food group and this definition was made according to the similarity of nutrient profiles (i.e., egg) or combined food items [i.e., doogh (as a yogurt and water preparation)]. Moreover, validation of this FFQ reflected a proper correlation between dietary intake estimated by this questionnaire and a multiple-day 24-h dietary recall.[22]

Statistical analysis

Dietary intake and all other quantitative variables are shown as average and standard deviation (SD) in Table 1. Nutrient intake had been adjusted for mean energy content of usual dietary consumption using binary logistic regression. The comparison of quantitative variables between migraine and non-migraine participants was performed by using sample *t*-test. In addition, we applied independent sample *t*-test to compare the dietary intake of pyridoxine and folate between patients with moderate and high frequency of migraine attacks. We used SPSS software (version 18.0) (SPSS, Inc., Chicago, IL, USA) for data analysis. *P* value less than 0.05 was defined as statistically significant level.

Table 1: Dietary intake of folate and pyridoxine in migraine and non-migraine subjects

Variables	Migraine patients	Non-migraine patients	*P* value
Energy (kcal)	2276.35±863.48	2209.40±313.09	0.41
Pyridoxine (mg)	1.33±0.74	1.34±0.24	0.79
Folate (μg)	254.72±146.89	344.07±26.91	<0.001*
Energy-adjusted pyridoxine (mg)	1.29±0.42	1.36±0.11	0.09
Energy-adjusted folate (μg)	250.60±94.21	347.99±20.06	<0.001*

**P* value <0.05 considered as significant level

RESULTS

In this study, 254 subjects (124 migraine patients and 130 non-migraine patients) with age range of 15-65 years participated. Migraine patients included 29 men and 95 women, and there were 31 men and 99 women in the control group. The differences between migraine and non-migraine patients in dietary intake of energy, pyridoxine, folate, and energy-adjusted pyridoxine and folate levels are presented in Table 1. Intake of energy and pyridoxine were not significantly different between migraine patients and patients in the control group. This difference remained non-significant for pyridoxine even after adjustment for energy intake. However, migraine patients had lower intake of folate or energy-adjusted folate, compared with non-migraine patients.

Results of independent sample *t*-test among men or women are shown in Table 2. Among men and women, dietary intakes of energy and pyridoxine were not different between migraine and control groups, but non-migraine patients consumed higher folate in comparison to migraine patients.

Table 3 shows comparison of dietary intake of pyridoxine and folate between patients with moderate and high frequency of migraine attacks. Dietary intake of folate and pyridoxine in migraine patients with frequent attacks was not significantly higher than in patients with moderate attacks. Sex-stratified analysis revealed the same relationship.

Table 2: Dietary intake of folate and pyridoxine in men and women with and without migraine

Variables	Migraine patients	Non-migraine patients	*P*
Men			
Energy (kcal)	2599.05±1013.20	2644.41±234.04	0.81
Pyridoxine (mg)	1.43±0.87	1.63±0.20	0.23
Folate (μg)	268.70±180.44	367.35±24.99	0.007*
Energy-adjusted pyridoxine (mg)	1.17±0.52	1.34±0.10	0.10
Energy-adjusted folate (μg)	225.83±115.16	319.03±11.54	<0.001*
Women			
Energy (kcal)	2177.84±792.40	2073.18±183.47	0.21
Pyridoxine (mg)	1.29±0.70	1.25±0.17	0.59
Folate (μg)	250.46±135.85	336.78±23.18	<0.001*
Energy-adjusted pyridoxine (mg)	1.33±0.37	1.36±0.11	0.84
Energy-adjusted folate (μg)	258.16±86.12	357.05±11.86	<0.001*

**P* value <0.05 considered as significant level

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

Variables	Moderate frequency	High frequency	*P*
Total			
Energy (Kcal)	2314.16±868.67	2172.07±853.40	0.42
Pyridoxine (mg)	1.34±0.73	1.29±0.78	0.75
Folate (μg)	261.91±154.50	234.91±123.49	0.36
Energy-adjusted pyridoxine (mg)	1.28±0.41	1.33±0.43	0.53
Energy-adjusted folate (μg)	253.25±98.50	243.30±82.20	0.60
Men			
Energy (kcal)	2667.61±1082.76	2336.22±697.04	0.48
Pyridoxine (mg)	1.44±0.93	1.42±0.64	0.95
Folate (μg)	273.66±198.51	249.70±91.68	0.77
Energy-adjusted pyridoxine (mg)	1.13±0.57	1.34±0.18	0.37
Energy-adjusted folate (μg)	222.59±128.99	238.38±28.63	0.59
Women			
Energy (kcal)	2194.62±755.83	2135.60±891.81	0.74
Pyridoxine (mg)	1.30±0.65	1.26±0.82	0.79
Folate (μg)	257.94±138.06	231.62±130.73	0.39
Energy-adjusted pyridoxine (mg)	1.33±0.33	1.33±0.47	0.99
Energy-adjusted folate (μg)	263.63±84.48	244.40±90.28	0.32

†High frequency of migraine attacks is defined as more than 10 attacks per month

DISCUSSION

In this study, we found that migraine patients had lower intake of dietary folate compared to the control group, but energy and pyridoxine intake were not different between the two groups. Further analysis among men and women revealed no statistically significant changes in these relationships. In addition, we found no significant association between dietary intake of pyridoxine and folate with the frequency of migraine attacks. This is the first study to investigate the association between dietary intake of pyridoxine and folate with migraine in Iran.

Migraine is highly prevalent in the world, affecting 10–20% of the population during their lifetime.[1,24] It seems that several factors including genetic and environmental factors are involved in the etiology of migraine.[11] Among environmental factors, alcohol consumption, nutritional deficiencies, as well as smoking and low physical activity have been shown to affect the incidence of migraine.[25,26] In addition, some studies have shown that abnormal levels of blood factors such as homocysteine may increase the incidence of migraine, especially migraine with aura, or migraine symptoms such as frequency of migraine attacks.[27] Moreover, several studies reported that supplementation with pyridoxine and folate not only reduces the homocysteine levels but also improves the migraine symptoms.[17,20,28] Although most studies evaluated the effects of pyridoxine and

folate on migraine symptoms, data on the association between dietary intake of these vitamins and migraine symptoms are scarce.

In this study, dietary intake of folate in migraine patients was lower than in control group, but there was no difference in pyridoxine intake between the two groups. In line with our finding, Lea *et al*. reported that the mean folate concentration in migraine patients is lower than average value of general Caucasian population, which represents the low intake of folate in migraine patients. In addition, the average level of pyridoxine intake was in the normal range in this study,[17] while Menon *et al*. reported that the mean level of folate in migraine patients was higher compared to a general Caucasian population.[20] We found no significant association between dietary intake of pyridoxine and folate with the frequency of migraine attacks. Our finding is in line with a clinical trial study which indicates that supplementation with folate and pyridoxine has no effect on the frequency of migraine attacks;[20] but in another similar study, supplementation with these vitamins was found to decrease the frequency of migraine attacks.[17] Conflicting results in previous studies may be due to differences in genetic polymorphisms, common diet consumption, daily physical activity, and health status of the participants.

The main mechanism that explains the effects of folate deficiency on migraine attacks is unknown. The basic role of folate in conversion of homocysteine to methionine and the high risk impact of homocysteine level in increasing inflammatory factors can play a major role.[29] Low intake or low blood levels of folate can decrease the homocysteine metabolism and induce hyperhomocysteinemia.[18] High level of homocysteine is associated with endothelial damages such as atherosclerosis and thrombosis.[19,30] Moreover, hyperhomocysteinemia can affect migraine incidence, because migraine is a vascular disorder.

The strength of this study is that we assessed the association between dietary intake of folate and pyridoxine and migraine attack and its frequency according to the gender for the first time in the Iranian population.

Several limitations could be considered for the present study. Our study had a case–control design and we could not determine any time sequence or cause and effect association between dietary intake of these nutrients and migraine. Moreover, the low sample size in this study may cause insufficient power to detect the mentioned association. More studies should be performed with larger sample size and in prospective design to assess the relationship. We assessed the dietary intake of folate and pyridoxine using an FFQ. Although this valid FFQ has been shown to provide reasonable data of dietary intake, recall bias cannot be excluded.

CONCLUSION

Migraine patients had lower dietary intake of folate, compared to non-migraine group. There was no significant association between folate and pyridoxine intake with the frequency of migraine attacks. Further studies are needed to confirm our findings.

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