The Association of Dietary Phytochemical Index and Migraine Headaches

Moein Askarpour, Habib Yarizadeh, Faezeh Khorsha, Khadijeh Mirzaei* and Mansoureh Togha

Department of Community Nutrition, Faculty of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

Abstract

Background: Migraine is a neurological disorder which can threaten public health and cause socio-economic burdens. Dietary factors are proposed to be associated with migraine pain. The aim of this study was to examine the association between Dietary Phytochemical Index (DPI) and headache severity and duration among migraine patients.

Methods: A sample of two hundred and sixty-six women (18-50 years) took part in the study. Dietary data was collected using a validated and reliable food-frequency questionnaire. DPI was estimated by a formula (Daily energy derived from phytochemical-rich foods (kcal)/total daily energy intake (kcal)×100), based on dietary intake. Anthropometric measurements, headache duration, and visual analog scale for pain questionnaire were assessed for all cases.

Results: An inverse association was found between high-DPI score and severe headaches (OR=0.67; 95% CI: 0.61, 0.98; p=0.011). However, headache duration showed no significant association with DPI score (β= -0.10, 95% CI: -0.51, 0.27, p=0.25).

Conclusion: The present study showed that adherence to phytochemical-rich diets may be associated with reduced headache in migraine patients.

Keywords: Headache, Migraine disorders, Pain, Phytochemicals, Visual analog scale

*** Corresponding author**

Khadijeh Mirzaei, PhD
Department of Community Nutrition, Faculty of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran
Email: mirzaei_kh@tums.ac.ir
mina_mirzaei101@yahoo.com

Received: Jan 24 2020
Accepted: Mar 16 2020

Citation to this article:
Askarpour M, Yarizadeh H, Khorsha F, Mirzaei Kh, Togha M. The Association of Dietary Phytochemical Index and Migraine Headaches. *J Iran Med Counc*. 2020; 3(2):99-105.

Introduction

Migraine is a neurologic disease characterized by severe headaches which could last to 72 *hr* (1). Migraine, affecting 12% of the world population (2), is considered as the first cause of disability in people under 50 *yrs* (3). It could impose economic burden and affect the quality of life (4). Therefore, finding the best approach to manage and control this disease is of utmost importance.

Certain drugs have been proposed to control and manage this disease (5), but due to the major side effects that they could create (6), proper dietary intervention could be a supplementary approach with fewer side effects towards migraine. It was reported that dietary intake especially with high antioxidants and phytochemical content related to reduced headache duration and intensity (7).

The Dietary Phytochemical Index (DPI), is a simple and practical method for the evaluation of diet quality and phytochemical intake (8). Phytochemicals are plant-based bioactive compounds including phenolic, isoperenoids, organosulfor compounds (9). Dietary intake with high phytochemical compounds has gained significant attention due to its effect on control and management of chronic diseases (10-12).

It seems that the risk of migraine headaches and DPI has not been studied before. Therefore, this cross-sectional observational study was conducted to examine a hypothesized association between DPI and intensity and duration of migraine headaches.

Materials and Methods

Participants

In the current study, 266 women aged 18-50 years with migraine headaches were chosen from two neurology clinics in Tehran. Inclusion criteria in the present study were voluntary participation in the study, women with history of migraine headache diagnosed by a professional neurologist and Body Mass Index (BMI) between 18.5 and 30. Participants were excluded from the study if they were on specific diets, lactating or pregnant or their daily energy intakes were lower than 800 *kcal/day* or higher than 4,200 *kcal/day* (n=28). Moreover, women with chronic diseases such as diabetes, cardiovascular diseases, and cancer were excluded.

Ethical considerations: The present study protocol was approved by the research committee of the School of Nutritional Sciences and Dietetics of Tehran University of Medical Sciences (TUMS). All of the participants were asked to sign consent forms.

Assessment of dietary intakes and phytochemical index

Dietary intake was evaluated using a 147-items semi-quantitative Food Frequency Questionnaire (FFQ), and its reliability and validity had been already approved in Iran (13). Nutritionists filled participants FFQ's during a face- to- face interview. The US Department of Agriculture (USDA) Food Composition Tables (FCT) were applied to assess participant's dietary intake due to limited data on Iranian FCT. Then, nutrients intakes were analyzed using Nutritionist IV software (Version 7.0; N-Squared Computing, Salem, OR, USA).

The DPI was determined based on the method developed by McCarty [DPI=(Daily energy derived from phytochemical-rich foods (*kcal*)/total daily energy intake (*kcal*))×100] (8). Vegetables, fruits, whole grains, legumes, nuts, seeds, fruit and vegetable juices, tomato sauces, soy products and olive oil were considered as phytochemical-rich foods. Potatoes were not calculated because of their poor source of phytochemicals.

Migraine severity and duration

In the current study, neurologists diagnosed migraine according to International Classification of Headache Disorders, 3rd edition (ICHD-3) (14).

VAS (Visual analog scale) questionnaire was applied to evaluate headache severity (Categorical variable). The VAS had a 10 *cm* horizontal line and migraine patients pointed to the line to represent their pain. The VAS score ranged from 1 to 10 and categorized pain in three levels of 1 to 3 (Mild pain), 4 to 7 (Moderate pain) and 8 to 10 (Severe pain) (15). A headache diary was given to participants to obtain headache duration (Numerical variable) and record how many hours they had suffered from each migraine attack.

Assessment of other variables

Weight was assessed by a digital scale (SECA, Hamburg, Germany) to the nearest 0.1 *kg*. Height was measured to the nearest 0.5 *cm* by a wall-mounted

stadiometer. BMI was calculated based on following formula "weight (*kg*)/height^2 (m^2)". Characteristics including age, family history of migraine (Yes/no), specific diet, education status (≤Diploma or >Diploma), supplement use (Yes/no), and chronic disease history (Yes/no) were assessed by giving all participants a questionnaire.

International Physical Activity Questionnaire (IPAC) was used to assess Physical Activity (PA). Activity level was classified into low, moderate and high levels as described by the IPAQ scoring protocol (16).

Statistical analyses

The chi-square test was applied to determine the association between DPI and qualitative variables. One-way analysis of variance (ANOVA) was used to determine the relationship between DPI and quantitative variables.

In addition, to compare the dietary intakes of participants among tertile of DPI, covariance analysis (ANCOVA) was applied. To assess the association between DPI scores and the headache severity, multinomial logistic regression was used in crude and adjusted models by adjusting the effect of energy intake, age, BMI, PA, smoking status, menstruation, headaches, water intake, and medication usage.

In addition, to determine the association between DPI (Independent variables) and headache duration (Dependent variable), linear regression was applied in crude and adjusted models. SPSS version 24 (SPSS Inc., Chicago, IL, USA) was used to perform statistical analysis. The level of statistical significance was considered as $p<0.05$.

Results

Characteristics of study population

The baseline characteristics of the participants among tertiles of DPI are presented in table 1. The

Table 1. Characteristics of study population among tertiles (T) of dietary phytochemical index

	Dietary phytochemical index				
	Total (N=266)	T_1 (n=88)	T_2 (n=88)	T_3 (n=90)	*p-value
Age (years)	34.32±7.86	34.65±8.65	34.27±8.05	34.98±6.73	0.471
Height (*m*)	1.61±0.05	1.61±0.05	1.61±0.04	1.62±0.04	0.742
Weight (*kg*)	69.41±13.02	67.5611.23±	68.23±12.62	69.47±13.09	0.141
BMI (kg/m^2)	26.50±4.88	25.28±4.84	26.64±2.30	25.07±3.87	0.347
PA (MET-h/wk)	407.73±519.13	417.24745.78±	354.41±434.83	445.31±431.39	0.218
Headache duration (*hr*)	10.03 (10.78)	12.74 (10.73)	11.35 (9.65)	9.74 (11.32)	0.009
Current smoker n (%)					**0.544**
Yes	21 (4.9)	4 (1.5)	0 (0)	17 (6.4)	
No	245 (95.1)	84 (31.1)	88 (36)	73 (28)	
Marital status n (%)					**0.120**
Single	74 (28)	34 (13)	24 (9)	16 (6)	
Married	192 (72)	75 (28)	57 (21)	60 (23)	
Education status n (%)					**0.573**
≤Diploma	107 (42)	35 (13)	41 (18)	31 (11)	
>Diploma	159 (58)	50 (18)	61 (24)	48 (16)	
Medication use n (%)					**0.251**
Yes	127 (48)	40 (13)	41 (14)	50 (21)	
No	139 (52)	50 (21)	44 (15)	45 (16)	
Family history of migraine n (%)					**0.471**
Yes	173 (65)	62 (28)	56 (19)	55 (18)	
No	93 (35)	29 (12)	31 (10)	33 (13)	

BMI, body mass index; PA, physical activity.

Quantitative variables (Age, height, weight, BMI, PA, headache duration) reported as Mean±SD.

Qualitative variables (Current smoker, education, medication use, marital and history of migraine) reported as number (%).

* Chi-square test and ANOVA were applied for qualitative and quantitative variables, respectively.

mean (SD) age, height, weight, BMI, and headache duration of patients were 34.32 (7.86) *years*, 161.87 (5.14) *cm*, 69.41 (13.02) *kg*, 26.50 (4.88) kg/m^2, 10.03 (10.78) *hr*, respectively. Quantitative and qualitative variables did not show any significant differences across DPI tertiles. However, headache duration showed a statistically significant difference across DPI, with an ascending trend from highest to lowest tertile of DPI. Moreover, 84% of our participants reported that some dietary intakes could aggravate their headache severity and they eliminated those dietary factors from their diet.

Dietary intake and DPI

Dietary intakes of the participants among DPI tertiles are shown in table 2. Participants with higher scores of DPI had more consumption of vegetables, fruits, legumes and nuts, while having lower intake of refined grain and meat compared to the lower scores of DPI. Moreover, the dairy and water intake across tertiles of DPI did not present any significant differences.

DPI score and migraine headache severity and duration

The association between severity and duration of migraine headache and DPI score, in crude model and adjusted model are presented in table 3. A significant inverse association was observed between DPI score and odds of severe headaches in crude and adjusted models.

Participants with higher score of DPI were less likely to have severe headache compared with those with lower score in crude (OR= 0.74; 95% CI: 0.42, 0.87; p<0.001) and adjusted models (OR= 0.67; 95% CI: 0.61, 0.98; p=0.011).

Linear Regression Models (LRM) presented no statistically significant relation between DPI score and headache duration in crude (β= -0.12, 95% CI: -0.57, 0.18; p=0.19), and adjusted models (β= -0.10, 95% CI: -0.51, 0.27, p=0.25).

Table 2. Dietary intake of study population among tertiles (T) of dietary phytochemical index

	Dietary phytochemical index			
	T_1 (n=88)	T_2 (n=88)	T_3 (n=90)	*p-value
Vegetables (*g/d*)	135.91±41.35	197.16±120.16	279.37±90.79	<0.001
Fruits (*g/d*)	309.65±184.32	330.41±239.55	424.93±245.91	<0.001
Dairy (*g/d*)	304.70±91.99	279.07±129.56	307.97±98.68	0.071
Legumes and nuts (*g/d*)	34.53±25.48	45.24±21.16	71.04±23.64	<0.001
Refined grain (*g/d*)	390.99±156.44	324.05±123.57	301.81±157.70	<0.001
Meat (*g/d*)	57.83±20.95	56.24±29.90	47.71±32.25	<0.001
Water intake (*L/d*)	1.20±0.78	1.17±0.68	1.28±0.68	0.352

* Based on ANCOVA, adjusted for total energy except total energy.
Mean±SD (All such values).

Table 3. Crude and adjusted odds ratios for severity and duration of migraine headaches across DPI scores

	Crude models		p-value	Adjusted models		[a] p-value
	OR	(0.95% CI)		OR	(0.95% CI)	
	VAS					
Mild pain[∞]	-	-	-	-	-	-
Moderate pain	0.87	(0.45, 1.07)	0.131	0.94	(0.65, 1.25)	0.360
Severe pain	0.74	(0.42, 0.87)	<0.001	0.67	(0.61, 0.98)	0.011
Headache duration of each attack	*-0.12	(-0.57, 0.18)	0.19	*-0.10	(-0.51, 0.27)	0.25

DPI, dietary phytochemical index.
VAS, visual analog scale.
* The β coefficient has been shown.
a Adjusted for confounders.
∞ Considered as reference group.

Discussion

Our main analyses showed that there was no significant association between DPI scores and headache duration. However, it was found that higher DPI scores were significantly associated with reduced headache intensity. To the best of our knowledge, the present study is the first study to examine the association between the DPI score and migraine headaches.

There are possible mechanisms through which the hypothesis of the effect of phytochemicals on migraine could be justified. Migraine is a neurovascular disease, trigged by a set of actions starting within the brain and then involving the blood vessels (17). Fluctuation of blood flow in the brain may contribute to the pain (18). Calcitonin Gene-Related Peptide (CGRP) is a neuropeptide that acts as a vasodilator and could cause neurogenic inflammation (19). Some studies proposed the role of CGRP in migraine (20,21). CGRP antagonist drugs were shown to reduce the average number of migraine frequency in migraine sufferers (22). Several studies indicated that food intake could also be capable of altering CGRP levels (23,24).

Plant foods as phytochemical rich sources were also found to combat migraine with an antagonistic ability against CGRP (25). Previous studies have shown the value of high-DPI diet that is inversely related to oxidative stress, hypercholesterolemia, insulin resistance, hypertension, and prediabetes (26-28). Phytochemicals also have been shown to have neuroprotective activity.

Inflammation plays an important role in migraine pain, with sensitization of nerve endings in meninges. High-DPI diets have anti-inflammatory activity by decreasing biomarkers of inflammation via inhibiting neuronal growth especially in the hippocampus, altering gut microflora, and suppressing the production of inflammatory cytokines (29,30). In addition, nutritional antioxidants protect the body cells from the free radicals and act in favor of anti-inflammatory balance (31).

Several studies are suggesting a positive association between hypertension and migraine (32-34). On other hand, many experimental studies in rats have shown that phytochemicals may reduce the arterial pressure and enhance the vasorelaxant process (35).

Limitations

The study population was relatively low. If men also had been recruited, better insights could have been achieved. In addition, questionnaires are based on participants' feeling of pain and their memory. Our results are associational and do not prove causality. It is better to confirm a hypothesized association by using evidence from multiple epidemiological studies, especially in different populations and/or countries.

Conclusion

In conclusion, our findings showed that higher adherence to phytochemical-rich diets may be associated with reduced headache.

Conflict of Interest

Not declared.

Acknowledgments

The authors thank the participants and the neurology clinics of Sina and Khatam Alanbia hospitals. This study was extracted from a dissertation that was confirmed by Tehran University of Medical Sciences (Grants ID: 95-01- 103-31348). The authors report no conflict of interest. The ethical code number of the ethics committee of Tehran University of Medical Science (TUMS) was IR.TUMS.REC.2141.1394.

References

1. Dodick DW, Silberstein SD, Bigal ME, Yeung PP, Goadsby PJ, Blankenbiller T, et al. Effect of fremanezumab compared with placebo for prevention of episodic migraine: a randomized clinical trial. JAMA 2018;319(19):1999-2008.

2. Woldeamanuel YW, Cowan RP. Migraine affects 1 in 10 people worldwide featuring recent rise: a systematic review and meta-analysis of community-based studies involving 6 million participants. J Neurol Sci 2017;372:307-15.

3. Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: will health politicians now take notice? J Headache Pain 2018;19(1):17.

4. Leonardi M, Raggi A. Burden of migraine: international perspectives. Neurol Sci 2013;34(Suppl 1:)S117-8.

5. Pardutz A, Schoenen J. NSAIDs in the Acute Treatment of Migraine: A Review of Clinical and Experimental Data. Pharmaceuticals (Basel) 2010;3(6):1966-87.

6. Harirforoosh S, Asghar W, Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications. J Pharm Pharm Sci 2013;16(5):821-47.

7. Amer M, Woodward M, Appel LJ. Effects of dietary sodium and the DASH diet on the occurrence of headaches: results from randomised multicentre DASH-Sodium clinical trial. BMJ Open 2014;4(12):e006671.

8. McCarty MF. Proposal for a dietary “phytochemical index”. Med Hypotheses 2004;63(5):813-7.

9. Han X, Shen T, Lou H. Dietary polyphenols and their biological significance. Int J Mol Sci 2007;8(9):950-88.

10. McMacken M, Shah S. A plant-based diet for the prevention and treatment of type 2 diabetes. J Geriatr Cardiol 2017;14(5):342-54.

11. Satija A, Bhupathiraju SN, Spiegelman D, Chiuve SE, Manson JE, Willett W, et al. Healthful and unhealthful plant-based diets and the risk of coronary heart disease in U.S. adults. J Am Coll Cardiol 2017;70(4):411-22.

12. Lanou AJ, Svenson B. Reduced cancer risk in vegetarians: an analysis of recent reports. Cancer Manag Res 2010;3:1-8.

13. Mirmiran P, Hosseini-Esfahani F, Jessri M, Mahan LK, Shiva N, Azizi F. Does dietary intake by Tehranian adults align with the 2005 dietary guidelines for Americans? Observations from the Tehran lipid and glucose study. J Health Popul Nutr 2011;29(1):39-52.

14. Levin M. The international classification of headache disorders, (ICHD III)–changes and challenges. Headache: The Journal of Head and Face Pain 2013;53(8):1383-95.

15. Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983;17(1):45-56.

16. Wanner M, Probst-Hensch N, Kriemler S, Meier F, Autenrieth C, Martin BW. Validation of the long international physical activity questionnaire: Influence of age and language region. Prev Med Rep 2016;3:250-6.

17. Buse DC, Greisman JD, Baigi K, Lipton RB. Migraine orogression: A systematic review. Headache 2019;59(3):306-38.

18. Bahra A, Matharu M, Buchel C, Frackowiak R, Goadsby P. Brainstem activation specific to migraine headache. Lancet 2001;357(9261):1016-7.

19. Durham PL. CGRP-receptor antagonists--a fresh approach to migraine therapy? N Engl J Med 2004;350(11):1073-5.

20. Goadsby PJ, Edvinsson L. The trigeminovascular system and migraine: studies characterizing cerebrovascular and neuropeptide changes seen in humans and cats. Ann Neurol 1993;33(1):48-56.

21. Lassen LH, Haderslev PA, Jacobsen VB, Iversen HK, Sperling B, Olesen J. CGRP may play a causative role in migraine. Cephalalgia 2002;22(1):54-61.

22. Urits I, Jones MR, Gress K, Charipova K, Fiocchi J, Kaye AD, et al. CGRP antagonists for the treatment of chronic migraines: a comprehensive review. Curr Pain Headache Rep 2019;23(5):29.

23. Katz DL, Doughty K, Ali A. Cocoa and chocolate in human health and disease. Antioxid Redox Signal 2011;15(10):2779-811.

24. Slavin M, Bourguignon J, Jackson K, Orciga MA. Impact of food components on in vitro calcitonin gene-related peptide secretion-a potential mechanism for dietary influence on migraine. Nutrients 2016;8(7):406.

25. Jain MM, Kumari N, Rai G. A novel formulation of veggies with potent anti–migraine activity. Int J Comput Biol Drug

Des 2015;8(1):54-61.

26. Carnauba RA, Chaves DF, Baptistella AB, Paschoal V, Naves A, Buehler AM. Association between high consumption of phytochemical-rich foods and anthropometric measures: a systematic review. Int J Food Sci Nutr 2017;68(2):158-66.

27. Abshirini M, Mahaki B, Bagheri F, Siassi F, Koohdani F, Sotoudeh G. Higher intake of phytochemical-rich foods is inversely related to prediabetes: A case-control study. Int J Prev Med 2018;9:64.

28. Golzarand M, Mirmiran P, Bahadoran Z, Alamdari S, Azizi F. Dietary phytochemical index and subsequent changes of lipid profile: A 3-year follow-up in Tehran Lipid and Glucose Study in Iran. ARYA Atheroscler 2014;10(4):203-10.

29. Estruch R, Martinez-Gonzalez MA, Corella D, Basora-Gallisa J, Ruiz-Gutierrez V, Covas MI, et al. Effects of dietary fibre intake on risk factors for cardiovascular disease in subjects at high risk. J Epidemiol Community Health 2009;63(7):582-8.

30. Dash S, Clarke G, Berk M, Jacka FN. The gut microbiome and diet in psychiatry: focus on depression. Curr Opin Psychiatry 2015;28(1):1-6.

31. Grimble RF. Nutritional antioxidants and the modulation of inflammation: theory and practice. New Horiz 1994;2(2):175-85.

32. Cirillo M, Stellato D, Lombardi C, De Santo NG, Covelli V. Headache and cardiovascular risk factors: positive association with hypertension. Headache 1999;39(6):409-16.

33. Gudmundsson LS, Thorgeirsson G, Sigfusson N, Sigvaldason H, Johannsson M. Migraine patients have lower systolic but higher diastolic blood pressure compared with controls in a population-based study of 21,537 subjects. The Reykjavik Study. Cephalalgia 2006;26(4):436-44.

34. Franceschi M, Colombo B, Rossi P, Canal N. Headache in a population-based elderly cohort. An ancillary study to the Italian Longitudinal Study of Aging (ILSA). Headache 1997;37(2):79-82.

35. Harnafi H, Amrani S. Flavonoids as potent phytochemicals in cardiovascular diseases prevention. Pharmacogn Rev 2007;1(2):193-202.