Acıbadem Univ. Sağlık Bilim. Derg. 2025; 16 (2)
https://doi.org/10.31067/acusaglik.1486442

Investigation of The Relationship Between Primary Headache Severity and Daily Food Preferences in Young Adults not yet Diagnosed with Migraine

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Received: 19.05.2024
Accepted: 30.10.2024

ABSTRACT

Purpose: Migraine is a complex neurological disease. The aim of our study is to provide sustainable food-mediated benefit in migraine prophylaxis to people with severe symptoms who have not yet been diagnosed with migraine.

Methods: The study included 197 people between the ages of 18-45 who had not yet been diagnosed with migraine had strong symptoms, had no metabolic disease, psychiatric disease or disability. In the first stage of the study the internationally used "Headache Disability Index" scale was applied to the participants. After 4 weeks of consuming the recommended reference foods, the Headache Disability Index test was repeated and the score difference was accepted as data. Evaluation of the data SPSS 26 statistical program was used and $p<0.05$ was considered significant.

Results: The inclusion of beef liver as a reference food in the diet resulted in a significant improvement in the Headache Disability Index F19 ($p<0.003$) recommendation, and the inclusion of broccoli provided statistically significant improvements in the E9 ($p<0.039$) and F13 ($p<0.025$) recommendations.

Conclusion: In people with severe migraine symptoms; Providing only the daily recommended amounts of vitamins A, B12, K1 and C to their diet through broccoli and beef liver foods; It provided improvement in emotional and functional disabilities.

Keywords: Migraine, Beef liver, Broccoli, Headache Disability Index, Sustainable health

ÖZET

Amaç: Migren kompleks nörolojik bir hastalıktır. Çalışmamızın amacı henüz migren tanısı almamış kuvvetli semptomları olan kişilere, migren proflaksisinde besin aracılı sürdürülebilir fayda sağlamaktır.

Yöntemler: Çalışmaya henüz migren tanısı almayan kuvvetli semptomları olan, herhangibir metabolik psikiyatrik hastalığı ve engeli bulunmayan 18-45 yaş arası 197 kişi dahil edildi. Araştırmanın ilk aşamasında katılımcılara uluslararası alanda kullanılan "Headache Disability Index" ölçeği uygulandı. Önerilen referan besinler 4 hafta tüketildikten sonra "Headache Disability Index" ölçeği tekrarlanarak, oluşan skor farkı veri olarak kabul edildi. Verilerin değerlendirilmesinde SPSS 26 istatistik programı kullanıldı ve $p<0.05$ anlamlı kabul edildi.

Bulgular: Diyete referans besin olarak karaciğerin dahil edilmesi Headache Disability Index F19 ($p<0,003$) önermesinde anlamlı iyileşme, brokolinin dahil edilmesi ise E9 ($p<0,039$) F13 ($p<0,025$) önermelerinde istatistiksel olarak anlamlı iyileştirmeler sağlamıştır.

Sonuç: Kuvvetli migren semptomları taşıyan kişilerde; brokoli ve karaciğer besinleri aracılığı ile, diyetlerine sadece günlük önerilen miktarlarda A, B12, K1 ve C vitaminlerinin sağlaması; emosyonel ve fonksiyonel engeliliklerde iyileşme sağlamıştır.

Anahtar Kelimeler: Migren, Karaciğer, Brokoli, Baş ağrısı engellilik indeksi, Sürüdürülebilir sağlık

Migraine is a recurrent neurological disease that causes deterioration in the person's quality of life with its symptoms. It mostly affects patients during their most productive years. It is known as the second leading cause of disability in the world (1).

Migraine affects 12-17% of the population annually, and its lifetime incidence is 43% in women and 18% in men (2,3).

According to the latest updated data, while the prevalence of migraine in the general population was 2.89% in 2008, it has been stated that this value increased to 14% in 2022, and the pathophysiology of migraine has not been fully elucidated yet (4).

Findings detected during migraine attacks can be listed as cerebral vasoconstriction, increased glutamate levels, magnesium deficiencies, monoaminergic pathway dysfunctions, mitochondrial damage, calcitonin gene-related peptide retention, and neuroinflamation. Numerous studies support the role of neuroinflamation in the initiation and progression of migraine through different pathways (5).

Diagnostic criteria for migraine in the International Headache Classification (beta version; ICHD-3beta) published in 2013; recurrent headache characterized by a history of at least five years, headache attacks lasting 4-72 hours, and these two main symptoms; pain is defined as being accompanied by at least two of the following: predominance of pain on a certain side of the head, persistent throbbing, causing avoidance or abandonment of routine activities, and finally nausea/vomiting and/or hypersensitivity to light/sound (6).

Studies on ICHD-4 are ongoing and the aim is to work on revisions and collect data for approximately another 5 years (7).

The International Headache Society has been making revisions to the classification of headache disorders since 1988. The last evaluations were made for migraine classification and diagnostic criteria in 2004, and symptoms lasting at least 3 months and lasting 15 days were defined as chronic migraine, while migraine that did not meet these criteria was classified as episodic migraine. However, it is claimed that this classification is insufficient to understand the migraine burden and the patient's treatment needs (8).

Despite its prevalence and impact, 50% of migraine patients are not yet diagnosed as having migraine by a clinician, and only 26% of those diagnosed receive minimal care. It is possible to say that there are still insufficient diagnostic and treatment practices to reach these rates. (9,10).

Current pharmacological and neuromodulation treatments for migraine prevention show low acceptability due to their limited effectiveness and adverse effects. Therefore, it is very important to identify the determinants of migraine headache and develop effective management strategies based on its pathophysiology (11,12).

Among non-pharmacological preventive treatments of migraine, nutritional interventions have been studied to offer innovative treatment strategies for primary headaches to avoid adverse effects and drug interactions (13,14).

There is a strong need to create practical approaches and reduce the burden of this disease with migraine preventive treatments.

The reasons that trigger attacks in migraine patients may not be specific to migraine, and may not be experienced by every migraine patient for example, many factors such as women's menstrual period, stress, differences in sleeping and eating patterns, loud noise, strong odors and bright light can trigger an attack. Approximately one quarter of the patients; ıt has been stated that many packaged products containing monosodium glutamate, meats and delicatessen products containing nitrites, drinks and cheeses containing tyramine, shelled cookies and chocolate containing phenylethylamine trigger migraine attacks citrus fruits, pickles and vinegar are among the possible causes. These foods do not need to be approved by all patients, and removing these products from the diet does not mean that there will be no migraine attacks (15).

While dehydration and starvation make migraines worse, it is recommended that daily caffeine consumption should not exceed 200 mg and aspartame content should be avoided (16).

Various studies have attempted to demonstrate the effectiveness of some alternative treatments. These include magnesium (400-600 mg/day) and riboflavin (400 mg/day). These are the ones that have just been discovered (17).

Prevention of nutrition-mediated migraine attacks; It is very important as it is a sustainable process in which the patient personally accompanies both the individual identification of root causes and prophylaxis/treatment/patient follow-up.

For this reason, a study was conducted with volunteers between the ages of 18 and 45 who had strong symptoms that had not yet been diagnosed with migraine. For this; two different foods of animal and plant origin, which provide macro and micro nutrients in appropriate compositions, were determined as references. The change they make with the reference foods recommended in their diets at four-week intervals; it was investigated whether there were differences in the duration and severity of pain and in the emotional and functional areas where they experienced limitations due to pain, taking into account the Headache Disability Index scores and its components.

Material and Methods

The study included 197 people between the ages of 18-45 who had not yet been diagnosed with migraine, had strong symptoms, had no metabolic disease psychiatric disease or disability. Participants who did not meet these criteria were not included in the study.

The research is a prospective descriptive-comparative study and the data of the participants were collected in digital environment between June 2021 –July 2021. To increase the possibility of accurate and reliable data collection; the minimum sample size was determined with the G*Power (v3.1.9.7) program. In the power analysis, $\alpha = 0.05$, effect size = 0.2 and 95% power were selected and a total of 197 participants was calculated.

A voluntary "Informed Consent" form was obtained from all participants in the study. The study was approved by the İstanbul Esenyurt Ethics Committee numbered E-12483425-199-263 dated 12.01.2021

In the first stage of the study. the internationally used "Headache Disability Index" scale was applied to the participants. Four-week usage frequency changes in reference foods were recorded and then Headache Disability Index" scale was applied again. Score differences between test and retest were accepted as data.

Headache Disability Index (HDI) is a scale developed by Dr Jacobson GP, Ramadan NM and colleagues that tries to detect the impact of headache on daily life. The test begins by asking participants to rate the severity of their headache (mild, moderate and severe), frequency (1 per month, more than 1 per month but <4, and more than 1 per week). Subsequently, 25 propositions inspired by case stories are presented. Propositions are scored as 4 points when the participant approves the proposition (Yes), 2 points when he/she partially approves it (Sometimes), and 0 points when he/she rejects it. When the test is repeated, a difference of 29 points or more suggests that the factors causing this change have a therapeutic effect (18).

SPSS 26 program was used for statistical analysis of the data in the study. One-way ANOVA test was used for multiple group comparisons. Bonferroni tests were performed for the correlation of significant groups and $p < 0.05$ was considered statistically significant.

Results

It was recorded how often the participants consumed broccoli and beef liver, which were chosen as reference foods, and then their Headache Disability Index scores were measured. Information about foods was given and diet follow-ups were made.

During this period; while 47.7% of the participants have never consumed broccoli, 53.5% consume it every 2-3 days; while 67.1% had never consumed beef liver, 56.8% started to consume it every other day. At the end of four weeks, a new Headache Disability Index score was created for them.

It was determined that our participants increased the frequency of use of the products at different levels, and the Headache Disability Index test-retest score difference was ≥29 in 46.1%, and the score difference was <29 in 53.9%. The effect of different frequency of food consumption on each proposition in the index was investigated in participants with a score difference of ≥29. According to the validity of the Headache Disability Index, it can be suggested that the change is therapeutically effective only when the test-retest score difference is ≥29 (Table 1).

Although the specified reference foods and their consumption frequencies showed a percentage improvement on headache frequency and severity (Headache frequency 78.6% more than one per week-46.8% 1 per month; headache severity 72.1% severe-46.8% moderate), it did not create a statistically significant difference (Table 2).

Table 1. Statistical significance and p values of referans foods in each index ıtems on test to retest when Headache Disability score ≥29 point

Headache Disability Index Items		Broccoli	Beef liver
F1	Because of my headaches I feel handicapped.	0.358	0.880
F2	Because of my headaches I feel restricted in performing my routine daily activities.	0.998	0.527
E3	No one understands the effect my headaches have on my life	0.608	0.163
F4	I restrict my recreational activities (e.g., sports, hobbies) because of my headaches.	0.273	0.793
E5	My headaches make me angry	0.894	0.692
E6	Sometimes I feel that I am going to lose control because of my headaches.	0.806	0.116
F7	Because of my headaches I am less likely to socialize	0.732	0.886
E8	My spouse (significant other), or family and friends have no idea what I am going through because of my headaches.	0.574	0.244
E9	My headaches are so bad that I feel that I am going to go insane	0.039	0.283
E10	My outlook on the world is affected by my headaches.	0.980	0.134
E11	I am afraid to go outside when I feel that a headache is starting	0.823	0.742
E12	I feel desperate because of my headaches.	0.445	0.234
F13	I am concerned that I am paying penalties at work or at home because of my headaches.	0.025	0.729
E14	My headaches place stress on my relationships with family or friends.	0.727	0.783
F15	I avoid being around people when I have a headache.	0.698	0.909
F16	I believe my headaches are making it difficult for me to achieve my goals in life.	0.175	0.580
F17	I am unable to think clearly because of my headaches.	0.069	0.571
F18	I get tense (e.g., muscle tension) because of my headaches.	0.628	0.654
F19	I do not enjoy social gatherings because of my headaches.	0.738	0.003
E20	I feel irritable because of my headaches.	0.498	0.729
F21	I avoid traveling because of my headaches.	0.267	0.668
E22	My headaches make me feel confused	0.697	0.735
E23	My headaches make me feel frustrated.	0.907	0.350
F24	I find it difficult to read because of my headaches.	0.653	0.213
F25	I find it difficult to focus my attention away from my headaches and on other things	0.059	0.860

Table 2. Headache frequency and severity p values according to use in referans foods when Headache Disability score ≥29 point

Headache characteristics	Referans foods	
	Broccoli	Beef liver
Headache frequency	0.077	0.070
Headache severity	0.533	0.787

Discussion

The macro and micro nutrients and amounts that healthy adults should consume daily for sustainable health are shared by the Food and Drug Administration. Accordingly, reference foods were selected by scanning the national food composition database. These foods; care was taken to ensure that it was from plant and animal sources produced/grown in our country and that it could provide half or one portion of any of the macro/micro nutrients needed daily in nutrition.

Vitamin A, which is recommended to be taken 900 micrograms daily, was presented to the participants with beef liver, one of the reference foods. The fact that beef liver, which contains a minimum of 1691 micrograms of Vitamin A in every 100 grams, was consumed by the participants every other day, met this need containing Vitamin B12, which is well above the daily requirement, and providing 50% of the daily selenium requirement and 42% of the B6 requirement on its own, makes beef liver distinctive from other vitamin A sources.

Considering that migraine is a state of sterile inflammation, it comes to mind that vitamin A plays a role in both immunomodulation and T cell regulation. It is known to reduce the production of pro-inflammatory IL-6 and IFN-8 from T cells and increase the number of anti-inflammatory mediators such as IL-4. The decrease in serum Retinol binding protein amounts in migraine patients compared to control groups is one of the important findings that the amount of vitamin A in circulation decreases in migraine patients (19).

It is known that B12 reduces NO-mediated vasodilation by reducing the amounts of acetylcholine in the vascular area in the nervous system. Biochemically, its use in migraine prophylaxis comes to mind due to its scavenger effect on NO. In a study in which hydroxycobalamin was administered nasally to migraine patients, a decrease in the frequency of migraine attacks was detected in 10 out of every 19 patients. In children diagnosed with tension-type headache, whose etiology is similar to migraine etiology, vitamin B12 levels are deficient to certain degrees (moderately deficient <200 pg/mL; severely deficient <160 pg/mL), and symptoms decrease in the follow-up after B12 serum levels are increased with replacement has been reported.

It can be thought that taking vitamins A and B12, which are the reference nutrients we recommend, which support antioxidant and anti-inflammatory capacity in the liver, together and in sufficient amounts, has an effect by improving the item "I do not enjoy social gatherings because of my headaches" (F19) in the Headache Disability Index.

Broccoli is another reference food, with 100 grams (half a portion) of it covering the entire vitamin C deficiency, which is recommended to be taken as 90 milligrams per day. It is very important that it contains vitamin K1 (104.3 micrograms-minimum), which meets almost the entire daily need (120 micrograms), and that vitamins C and K1 are presented together and in sufficient quantities. 90% of dietary vitamin K consists of the K1 form (20). There are study results showing that anti-inflammatory activity is achieved by taking daily recommended amounts of vitamin K1 from green leafy vegetables, even in different populations/ethnic groups (21). Studies have suggested that this anti-inflammatory effect develops by inhibiting I-kappaB kinase phosphorylation in tissues, preventing the nuclear translocation of NFkB and blocking gene expression. Suppression of the synthesis of the pleiotropic cytokine IL6, which is responsible for the production of other inflammatory factors, and the decrease in its circulating amounts strengthen this hypothesis. It has been stated that serum d-dimer and fibrinogen levels remain at normal levels in the ≤65 age range when KI is used in daily recommended doses (22).

What is noteworthy here is that vitamin K did not exert its anti-inflammatory effect as a cofactor of the carboxylation reaction; a different biochemical pathway of vitamin K is mentioned.

In migraine, where increased oxidative stress and neurogenic inflammation in the brain tissue are thought to be possible pathophysiology, increased oxygen and nitrogen free radicals in the circulation and cerebrospinal fluid and decreased antioxidant capacity are the outcomes of many studies. However, in clinical studies, only pine bark extract has been used to support Vitamin C content by creating pharmaceutical preparations, and no nutritional content has been presented (23).

In our research, broccoli was recommended as a suitable composition that supports antioxidant and anti-inflammatory capacity with the combination of vitamins C and K1. Broccoli causes improvement in the parameters "My headaches are so bad that I feel that I am going to go insane" (E9), and "I am concerned that I am paying penalties at work or at home because of my headaches" (F13) in migraine attacks. It can be suggested that.

Another study shared the incidence and prevalence of migraine in the world between 1990 and 2019 with color codes. According to the color code in Turkey; migraine incidence rate decreased from 1431.61 to <1503.832; the prevalence rate increased from 18813.44 to <20400.82 (24).

Looking at China, which produces and consumes the most broccoli; ıt is remarkable data for our study that migraine incidence (1291.2) and prevalence (17203.82) rates are much lower. The good news is that in 2024, broccoli will be harvested in Bafra, a district of Samsun province, with a harvest of over 12 tons. Increasing the applicability of the Mediterranean diet, which UNESCO declared as a world heritage, in Turkey and, more importantly, benefiting its own geography and the people living in this geography by consuming the products it grows, will be valuable steps for both sustainable agriculture and sustainable health (25,26).

The biochemical pathway we encounter in both recommended reference foods is related to the anti-inflammatory and antioxidant content and the reduction of NO synthesis and its effects. NO changes the molecular structure of serotonin and the changed serotonin is not recognized by its own receptors; It shows us that the serotonin sources to be included in the process will be ineffective unless significant control is achieved in NO levels (27-30).

Moreover, this effect was achieved with minimum concentrations of A, B12, C, K1, which are involved in metabolism, despite individual bioavailability differences.

Conclusion

In our study, attention was paid to recommend reference foods among the products that can be accessed by the participants and then by the whole society and included in their daily diets. We believe that the foods and amounts that can be included in the diet are an important step for sustainable health. Another issue we paid attention to in the design of our study was; what will be recommended is that migraine prophylaxis can be achieved by regulating the daily use of nutrients, primarily macro and micro nutrients. For this reason, patients who have not yet been diagnosed with migraine, who are in the earlier stages of the disease, and who have the highest incidence were preferred. For this reason, those who have not yet been diagnosed with migraine, those in the earlier stages of the disease, and those at the ages with the highest incidence were preferred.

Another important point we want to emphasize in our study is; the point is that in therapeutic processes, it is not the specific macro/micro nutrients but the matches of these molecules needed in the biochemical pathways that are meaningful.

When the biochemical characters of the molecules are evaluated; it is noteworthy that vitamins A and K1 are lipid soluble, while vitamins C and B12 are water soluble. While these pairings require pharmaceutically advanced techniques, the food itself contains the appropriate composition to modulate these conditions.

We hope that with further research, we will encounter such molecular matches and examples of natural compositions found in plant and animal sources that support antioxidant and anti-inflammatory processes.

It should not be forgotten that from time to time, foods not only satisfy our pleasure and desires with their taste, smell, texture and visuals, but also serve as a medicine with their content.

Declarations

Funding

Not applicable

Conflicts of interest/ Competing interests

The authors declare no competing interests related to the subject matter or materials discussed in this article.

Ethics approval

A voluntary "Informed Consent" form was obtained from all participants in the study. The study was approved by the İstanbul Esenyurt University Ethics Committee numbered E-12483425-199-263 dated 12.01.2021.

Availability of data and material

Data can be shared if requested.

Authors' contributions

Conceived and designed the experiments: DV; performed the experiments: DV, ÖO; analyzed the data: DV; contributed reagents/ materials/ analysis tools: DV, ÖO; wrote the manuscript: DV, OÖ; final edit of paper: DV.

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