

Comparison of the effects of dietary factors in the management and prophylaxis of migraine

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Abstract: Migraine is defined as a disorder characterized by intermittent headache episodes, accompanied with nausea, photophobia and/or phonophobia. Pharmacological therapy is in accordance with the severity of pain and may include acute, prophylactic and most commonly both approaches. The aim of the acute therapy is stopping or alleviating the attack or progression of the pain and, in case of a migraine attack that has started, lessening the pain. Preventive therapy aims to reduce attack frequency and severity. This study was designed to evaluate the effect of dietary factors in the management and prophylaxis of migraine in cases diagnosed as having migraine disorder according to the 2003-IHS criteria. Fifty consecutive Turkish patients (13 men, 37 women) with diagnosis of migraine were randomly divided into two groups for treatment protocols with the written approval of the ethics committee. The cases in the first group (K) were treated with metoprolol, vitamin B₂ (riboflavin), and naproxen sodium just at the aura or at the beginning of the attacks. The cases in the second group (D) were also supplied with a comprehensive dietary list arranged by our algology clinic in addition to the same medication protocol. There were no demographic differences between the cases ($P > 0.05$). VAS scores were lower in group D than group K ($P < 0.01$), and also the migraine attack frequencies and monthly amounts of analgesic consumed amounts were also statistically significantly less. It was concluded that beta-blocker and riboflavin therapy supplemented with a convenient diet with appropriate alternatives in patients with migraine disorder was associated with statistically significant decreases in headache frequency, intensity, duration and medication intake.

Keywords: migraine, food intake, trigger

Introduction

Migraine is defined as a disorder characterized by intermittent headache episodes, accompanied with nausea, photophobia and/or phonophobia.¹ Migraine attacks seem to result from pathophysiological mechanisms activated by specific trigger factors. The recurrence of migraine attacks may depend either on a reduced threshold or on particularly strong or frequent trigger factors or both.² Biochemical research has provided evidence for certain physiologic characteristics in migraineurs, which have been proposed as predisposing factors for migraine. These include platelet serotonin (5-HT) metabolism, platelet activation, increased sensitivity to nitric oxide (NO) donors, reduced levels of metabolic enzymes, abnormal opiate receptor function, and electro-encephalographic (EEG) abnormalities.³

Pharmacological therapy, in accordance with the severity of pain, may include acute or prophylactic and most commonly both approaches. Acute therapy is stopping or alleviating the attack or progression of the pain and, in case of a migraine

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attack that has started, attempts to lessen the pain. Preventive treatment is indicated when the attacks are long lasting, severe and disabling and do not respond to acute treatments.⁴ Preventive therapy aims to reduce attack frequency and severity.⁵ The preventive treatment for migraine includes beta-blockers, antidepressants, calcium channel antagonists, serotonin antagonists, non-steroid anti-inflammatory drugs (NSAIDs), riboflavin (vitamin B₂) at high doses and anticonvulsant drugs.⁶

An understanding of the aura and headache components of migraine provide a basis for the potential mechanisms of action of dietary triggers. Dietary migraine triggers may influence the pathophysiology of migraine at one or more phases of the migraine attack. They could affect the cerebral cortex, trigeminal nerve, brainstem trigeminal nuclei, thalamus, and brainstem or limbic pathways. The chemical trigger may stimulate neuroreceptors, cause release of neurotransmitters, or have a direct effect on neurons within the trigeminovascular migraine pathways.⁷

We conducted our study on 50 patients who were diagnosed with migraine [according to the 2003-International Headache Society (IHS) criteria⁸ (Table 1)]. In our research, we could not find any studies previously conducted with an extended diet list covering foodstuffs that are acknowledged to trigger migraine attacks. Thus, by completely removing some foodstuffs that we listed as triggering migraine headaches in various studies (having regard to dietary habits of Turkish society) from the daily diet lists of patients, we wanted to observe the effect on the consumption of analgesic medicines used for migraine headaches (recurrence and severity).

Method

With the written approval of the ethics committee, we started our study with 56 patients. However, 6 patients left the study or were ineligible for various reasons. Therefore 50 consecutive Turkish patients (13 men, 37 women) with diagnosis of migraine were randomly divided into 2 groups for treatment protocols. Cases with menstrual migraine were excluded from the study. Patients in each group were well informed about their diseases and the treatment modalities were applied.

Patients in the first group (Group K) were treated with metoprolol (120 mg/day), vitamin B₂ (riboflavin 600 mg, 3 times a day), and naproxen sodium (550 mg) just at the aura or at the beginning of the attacks.

In addition to being provided with the same medication protocol, patients in the second group (Group D) were also supplied with a comprehensive dietary list (Table 2) arranged by our algology clinic. Furthermore, patients were also informed about the visual analog scale (VAS) and keeping a daily pain diary (DPD). They were asked to record their headache VAS scores, attack frequencies and severities and also naproxen sodium consumption starting from the beginning of the therapy.

Patients were recalled for control examinations every 15 days and their data (with special attention to their DPD) were recorded throughout a year.

All data were collected in an Excel[®] spread sheet for documentation. For statistical analysis, SPSS 13.0[®] for Windows (LEAD Technologies Inc, USA, 2004) was used. The Mann-Whitney U test was used to compare the differences between demographic data of patients such as age, length and weight; and Chi square test was used to compare the

Table 1 IHS criteria for the diagnosis of migraine

Migraine without aura	Migraine with aura
A 5 attacks fulfilling criteria B – D, and not attributed to another disorder	A 2 attacks fulfilling criteria B and C and not attributed to another disorder
B Attacks lasting 4–72 hours (untreated or unsuccessfully treated)	B Aura consisting of ≥ 1 of the following fully reversible symptoms but no motor weakness: B ₁ Visual symptoms (flickering lights, spots/lines, and/or loss of vision) B ₂ Sensory symptoms (ie, "pins and needles" and/or numbness) B ₃ Dysphasic speech disturbance
C Headache has ≥ 2 of the following characteristics: C ₁ Unilateral location C ₂ Pulsating quality C ₃ Moderate or severe intensity (inhibits or prohibits daily activities) C ₄ Aggravation by, or causing avoidance of, routine physical activity	C ≥ 2 of the following: C ₁ Homonymous visual symptoms and/or unilateral sensory symptoms C ₂ Aura develops gradually over ≥ 5 min and/or different aura symptoms occur in succession over ≥ 5 min C ₃ Each symptom lasts ≥ 5 min and ≤ 60 min
D During headache ≥ 1 of the following: D ₁ Nausea and/or vomiting D ₂ Photophobia and phonophobia	

Adapted from Cephalalgia.⁸

Table 2 Dietary list used for the patients in our algology clinic

Foods to avoid/limit	Alternatives
Beverages	
Cola	Non-cola soft drinks
Coffee	No more than 1 cup
Tea	No more than 2 cups
Chocolate drinks or cocoa	Non-chocolate drinks
Alcoholic beverages, red wine in particular	Vodka, Sauterne or Riesling wines
Fruit juices, decaffeinated drinks, flavored waters should be preferred	
Dairy products	
Milk	Low-fat or skim milk
Buttermilk and cream	
Cream	Butter/margarine
Cheddar, Brie, processed cheeses, aged cheeses (Parmesan, Romano), fats, lard	Vegetable oils
Meats/poultry/seafood	
Ham, bacon, offal – chicken livers	Fresh and non-processed meats
Aged, cured, canned, or marinated meats – pepperoni, salami	Eggs when limited to no more than 3 per week
Salted, smoked, and dried fish	Fresh or frozen fish, canned tuna or salmon
Processed meats – hot dogs, bologna	
Pickled herring	
Vegetables	
Certain navy beans, pinto beans, pole beans, lentils, garbanzo beans, broad beans	String beans
Most peas	Onion when used only for flavoring
Sauerkraut, olives, and pickles	Asparagus, beets, carrots, spinach, tomatoes, squash, corn, zucchini, broccoli, lettuce, potatoes
Grains, breads, cereals	
Yeast breads – most white breads	Whole wheat, rye, English muffins, Melba toast, bagels
Doughnuts	Most cereals
Sourdough	Rice, pasta
Crackers with cheese and pastries containing chocolate or nuts	
Soups	
Canned soups	Soups without MSG or yeast
Soup cubes and bouillon cubes with MSG	
Fruits	
Figs, raisins, plums, papaya, pineapple, avocados, kiwifruit	Apples, prunes, cherries, grapes, apricots, peaches, pears
Citrus fruits, bananas	Limit citrus fruits and bananas to 1/2 to 1 serving per day
Desserts/snack foods	
Chocolate, ice cream	Fruits as above, sherbets, ices, sorbets
Cookies and cakes made with yeast	cakes/cookies made without yeast
Potato chip products	Pretzels
Nuts/seeds, puddings	
Additives	
MSG	Wine vinegar
Seasonings and spices	Limited use of soy sauce
Artificial sweeteners	Small amounts of salad dressing

difference between gender and migraine type. The Mann-Whitney U test was also used to compare the differences between monthly VAS, monthly number of attacks and monthly analgesic consumption of the two groups. Statistical significance was defined as $P < 0.05$.

Results

There were no demographic differences between the cases ($P > 0.05$) (Table 3). VAS scores were lower in Group D than

in Group K ($P < 0.01$), and the migraine attack frequencies and monthly analgesic consumption amounts were also significantly lower ($P < 0.01$) (Table 4).

Discussion

The pharmacological treatment of migraine may be acute or preventive, and patients who experience frequent severe headache attacks often require both approaches. The contemporary guidelines include few prophylactic drugs under

Table 3 Demographic values of the patients

Group	Age (Year)	Sex (M/W)	Height (cm)	Weight (kg)	Type* of migraine (1/2)
Group K	44.61 ± 12.39	5/20	165.79 ± 7.15	72.49 ± 12.43	8/17
Group D	42.02 ± 10.15	8/17	167.35 ± 9.72	77.41 ± 14.85	10/15
P values	0.87	>0.05	0.86	0.44	>0.05

*Type 1, migraine without aura; Type 2, migraine with aura.

the recommendations of Group I on the basis of evidence, scientific effect and clinical assessment. They are: amitriptyline, atenolol, propranolol, flunarizine, and valproate sodium. Group II includes: nonsteroidal anti-inflammatory drugs, specifically naproxen and naproxen sodium as well as lornoxicam; antiepileptic drugs gabapentin, lamotrigine, topiramate; calcium channel blockers verapamil and cinnarizine; selective serotonin reuptake inhibitor fluoxetine; beta-blockers (metoprolol and nadolol); dihydroergotamine and vitamin B₂.⁹

How beta-blockers reduce attack frequency in migraineurs is not clear, although it is probably by acting on the central monoaminergic system and serotonin receptors. Not all of these drugs are effective, and those used in migraine prophylaxis include atenolol, metoprolol, nadolol and propranolol.^{10–15}

Vitamin B₂ is a water-soluble essential precursor to flavin mononucleotides necessary for electron transport within the Krebs cycle. It is essential to normal production of ATP and thus for maintaining membrane stability and for all energy-related cellular functions.¹⁶ A mitochondrial dysfunction causing impaired oxygen metabolism may play a role in migraine pathogenesis. Riboflavin at high doses (up to 400 mg) showed good effectiveness in preventing migraine attacks with a low rate of unwanted side effects, such as mild abdominal pain and diarrhea.¹⁷

The role of dietary factors in provoking migraine attacks is of increased interest.^{18–21} The role of serotonin (5-HT) in migraine has intrigued investigators observing that the migraine attack is associated with an increased excretion of serotonin metabolites.²² Serotonin released from hypersensitive platelets has been suggested as one of the precipitators of the vasoconstrictor phase of migraine. A reduction in platelet serotonin might thus have a beneficial effect.

Such a reduction could theoretically be achieved by a reduced dietary intake of serotonin and the serotonin precursor tryptophan (TRP).^{23,24} A carbohydrate-rich meal, with subsequent insulin secretion, increases the availability of TRP to the brain and thereby also the serotonin synthesis in the brain.²⁵ TRP is the scarcest of the amino acids and constitutes on average only about 1/100th of the total amino acid content of proteins. The dietary intake of TRP and protein is usually considerably higher than the required amount. However, an increased serotonin level in the brain is probably helpful in alleviating migraine headache, since serotonin is known to be involved in the anti-nociceptive system.²⁶

A variety of amines have been implicated in the development of headache, most commonly tyramine (TYR), histamine (HIS), and beta-phenylethylamine (PEA).^{27–28} Cheeses, peanuts, meats, and alcohol are known to contain TYR, HIS, and PEA. Citrus fruits contain octopamine and synephrine. All of these foods has been implicated clinically to be causally related to headache activity.

One of the most commonly cited food triggers of headache is chocolate. Chocolate is especially rich in a variety of vasoactive amines including PEA, which crosses the blood–brain barrier and effects cerebral blood flow. Headache may therefore be related to a different metabolism. Theobromine, a methylxanthine found in cocoa that is similar in chemical structure to caffeine may act as a headache trigger.²⁹

Many people believe that by avoiding some specific foods it is possible to reduce the frequency of migraine attacks. Putative allergic factors are often considered responsible for migraine attacks, whereas, only in rare cases, a specific food directly causes migraine. By contrast, fasting has been described to be a precipitating factor in 25% of children and in 40% of adults affected. Also, some foods are involved as precipitating factors in percentages varying from 10% to

Table 4 Monthly VAS, number of attacks and analgesic consumption rates of the patients

Group	Monthly VAS	Monthly number of attacks	Monthly analgesic consumption
Group K	0.88 ± 0.53	5.15 ± 1.33	3.64 ± 0.76
Group D	0.44 ± 0.51	2.70 ± 1.59	1.88 ± 0.78
P values	0.006	0.007	0.003

Table 5 Dietary items and chemical migraine triggers⁷

Food item	Chemical trigger
Cheese	Tyramine
Chocolate	Phenylethylamine, theobromine
Citrus fruits	Phenolic amines, octopamine
Hot-dogs, ham, cured meats	Nitrites, nitric oxide
Dairy products, yogurt	Allergenic proteins (casein, etc) ^a
Fatty and fried foods	Linoleic and oleic fatty acids
Asian, frozen, snack foods	Monosodium glutamate
Coffee, tea, cola	Caffeine, caffeine withdrawal
Food dyes, additives	Tartrazine, sulfites
Artificial sweetener	Aspartame
Wine, beer	Histamine, tyramine, sulfites
Fasting	Stress hormone release, hypoglycemia

^aIce cream headache is probably a cold-induced vasoconstrictor reflex response.

45%, namely: chocolate, cheese, some fruits, citrus fruits, fatty foods and fried food.³⁰ Table 5 lists potential food items that have been reported to trigger migraine headaches and the chemical constituent thought to be specifically involved in the mechanism of the attack.⁷

Some dietary restriction studies have reported a decrease in headache after participation in an elimination diet.^{31,32} In contrast some studies have found that dietary restriction does not significantly decrease headache³³ or that placebos are as likely to result in headache as challenge foods.³⁴

Peatfield³⁵ recorded 19% of patients reporting sensitivity to cheese, chocolate, or both, and 11% of patients sensitive to citrus fruits. The exact mechanism of these migraine attacks is unknown, although migraines are believed to be caused by a chemical reaction consisting of the release of serotonin from the intestinal wall, or by an enzymatic defect, and not by allergic reactions.

Peatfield studied 60 patients with migraine – mean duration of migraines was 18 years for women and 22 years for men. When patients were put on an exclusion diet, in most cases, migraines disappeared by the fifth day. The mean number of foods causing symptoms was 10 per patient, the most frequent offenders being wheat, orange, egg, tea and coffee, chocolate and milk, beef, corn, cane sugar, and yeast, mushrooms, and peas. When offending foods were avoided, all patients improved. In fact, the number of headaches fell from 402 to 6 per month, with 85% of the subjects becoming headache free.³⁵

Elimination diets have been shown to be valuable in treating migraine. When 88 children with severe migraines were put on an oligoantigenic diet, 93% improved.³¹ In another study of 17 patients who completed an elimination diet, migraine attacks were found to be most frequently

caused by cow's milk (10 out of the 17). Other culprits included flour, eggs, cheese, pork, and artificial colors and preservatives.^{36,37}

In this study we tried to prepare a detailed and strict dietary program that avoided food that is believed to precipitate migraine attacks. In light of the previous studies on this subject patients can also be offered alternative food choices. We believe that avoiding stress is as effective as diet and prophylactic medications in the prevention of headache episodes. The findings of this study revealed decreased severity and frequency of headache episodes and less analgesic consumption in the group that was treated with the dietary list, verifying our hypothesis.

Conclusions

It was determined that beta-blocker and riboflavin therapy supplied with an appropriate diet (with alternatives) was associated with statistically significant decreases in headache frequency, intensity, duration and medication intake. The prevention of headaches by attention to precipitating factors may be preferable to long-term prophylactic drug treatment with attending adverse reactions.

We once again ascertained in this study that diet is of great importance in migraine treatment. Throughout the course of treatment, we observed many positive effects of an appropriate diet list and its correct application on patients with migraine. We believe more positive results can be achieved if a diet list is attached to prescriptions.

Consent

Written informed consent was obtained from the patients for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Disclosure

The author declares that he has no competing interests. BZ presented the case histories, performed case management, drafted the manuscript. The author read and approved the final manuscript.

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