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Physical activity and supplementation as alternative methods in migraine prophylaxis - literature review

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Abstract

Migraine is a common and debilitating neurological disorder. It is crucial to realize that migraines are distinguished from other types of headaches. People suffering from migraine are often unable to function normally, neglecting work and daily duties. The associated costs burden not only the patients but also their family and social life. What is more, many psychiatric comorbidities are common in migraine patients. Because of all these factors, preventive treatment is essential because it can decrease migraine frequency and improve quality of life. There are many preventative medications but satisfactory improvement in reducing the frequency of migraine attacks may not be achieved without modification of lifestyle including taking care of physical activity and supplementation. Many studies have shown that moderate physical activity and supplementation of vitamins B2, D, coenzyme Q10 and magnesium has a positive effect on reducing duration and frequency of the migraine attack.

Purpose of work: The aim of this review is to analyse current research on the effectiveness of supplements and physical activity as a prevention of migraine.

Materials and methods

This article is based on the available literature found in the PubMed database with the use of key words such as migraine, riboflavin, coenzyme Q10, magnesium, vitamin D, migraine prevention, physical activity

Keywords: “migraine”, “riboflavin”, “coenzyme Q10”, “magnesium” “vitamin D” “migraine prevention”, “physical activity”

Introduction

Migraine is a common neurological disease and a leading cause of disability in people under 50 years of age. [1] According to epidemiological studies, it affects both men and women, but women suffer from migraine even three times more often than men. [2] Migraine is significantly different from other types of headaches. It is typical for migraine to last from 4 to 72 hours, a headache is located unilaterally, has a throbbing character, moderate to severe intensity and it is aggravated by physical activity. What is more, a migraine is often associated with nausea, vomiting, sensitivity to light and sounds. [3] Furthermore, many psychiatric comorbidities are common in migraine patients. According to different studies, people with migraines are 2.5 times more likely to develop depression than people who do not suffer from migraine headaches. A meta-analysis of data from 12 studies on migraine and depression found that the incidence of depression in migraineurs is highly variable, ranging from 8.6% to 47.9%. [4] Psychiatric comorbidities are really important risk factors for the progression from episodic to chronic migraine that is defined as a very frequent headache (more than 15 times per month for at least 3 months). [5]

The pathogenesis of migraine is not fully understood but there are many concepts. One of the mechanisms that is involved in pathogenesis of migraine is extracranial arterial vasodilation. The other one is neurogenic inflammation during which as a result of the dilation of the extracranial arteries, the activation of nerve fibers that are involved in the perception of pain is observed, and chemical substances such as substance P or neurokinin A are released. [6] Another important theory suggests that attenuated metabolism of oxygen due to the malfunctioning mitochondria may also have impact on migraine pathophysiology. That is why supplements that improve mitochondrial function might be useful in migraine prophylaxis. [7]

This article presents the benefits of supplementation and physical activity in the prevention of migraine.

Riboflavin

Riboflavin, also known as vitamin B2, is a water-soluble precursor to flavin mononucleotides used to transport electrons in the Krebs cycle. This is required to produce the right amount of energy, maintaining energy-related cellular functions and maintaining cell membrane stability. [8] What is more, riboflavin reduces the intensity of mechanisms such as oxidative stress, neuroinflammation and mitochondrial dysfunction that play a role in the pathogenesis of neurological diseases, including migraine. [9] According to research, vitamin B2 supplementation has a significant effect on duration and frequency of migraine attacks. [10] There were 5 clinical studies investigating the efficacy of riboflavin in the prevention of migraine headaches and they have been rated in a systematic review with positive results. In a randomized double-blind group-controlled trial using 400 mg/day of riboflavin, 59% reduction in migraine attack frequency has been observed. [11] Two other open-label studies also used riboflavin 400 mg daily and showed a reduction in migraine attack frequency from 4 attacks to 2 attacks per month. Four randomized studies compared the effectiveness of vitamin B2 in preventing migraine attacks with other pharmaceuticals used to prevent migraine. In the study of Rahimdel et al. from 2015, 90 patients were included in the study, and they were randomly divided into two equal groups. The first was treated with riboflavin and the other one was treated with valproic acid. It was shown that there is no significant difference in the effects of these substances when it comes to migraine prevention. [12] A similar conclusion was made in the study of Schoenen, where aspirin was compared to vitamin B2. [13] On the other hand, in the study of Natashu and in the study of Sándor where one group was given vitamin B2 and the other group was treated with propranolol or bisoprolol a difference in the intensity of migraine pain was observed, as riboflavin did not reduce it. However, there was no difference in the reduction of migraine attack frequency. [14,15] What is very important, taking riboflavin is associated with a much lower risk of side effects compared to drugs used in the prevention of migraine. [10] Possible side effect that has been observed with riboflavin was diarrhea. [16]

Coenzyme Q10

Coenzyme Q10 is an enzyme cofactor produced endogenously in all cells in the body, whose main function is to promote mitochondrial proton-electron translocation. [7] As a lipid-

soluble nutrient its adsorption of supplemental form can be enhanced by combining it with a meal rich in fat. [17] The studies report that CoQ10 is characterized by its safety and is well tolerated without causing important side effects even in high doses, however some gastrointestinal symptoms can be observed when the dose is higher than 1200mg/day. [18,19]

CoQ10 administration has a wide range of applications. It may be useful as supplemental therapy in various metabolic and cardiac conditions but more studies should be performed. [20] Its supplementation was also studied in neurological diseases such as migraine, Parkinson's disease, Huntington's disease, Alzheimer's disease and several others. [21]

When it comes to migraine, some studies reported that migraine may be caused by the mitochondrial impairment, whereas CoQ10 has been shown to improve mitochondrial oxidative phosphorylation in humans, therefore it could be utilized as a migraine preventive to reduce the severity and frequency of the headaches. [22] Furthermore, oxidative stress also takes place in migraine pathophysiology, which could explain the reduction of antioxidant levels in migraine patients in comparison to controls. [23] Additionally, in a study conducted by Dahri et al. CoQ10 presented ability to decrease inflammatory mediators like TNF- α and its supplementation had significant prophylactic effect on migraine attacks. [24] It could be explained by the fact that migraine in previous studies was associated with higher levels of inflammation. [25] A recent meta-analysis conducted by Sazali et al. (2021) of coenzyme Q10 supplementation for prophylaxis in adult patients with migraine, based only on randomised control trials, that consisted of a total of 371 participants showed that supplementation of CoQ10 can reduce the frequency of migraine headache in comparison to the control group, however, there was no statistically notable decrease in intensity of migraine headache. Daily oral dose of Coenzyme Q10 in included studies varied from 30 to 800mg. [26] Results of different meta-analysis from Parohan et al. (2019) based on four randomized clinical trials with 221 participants included (two of the included clinical trials were the same as in the meta-analysis described before) also suggest that coenzyme Q10 supplementation may be useful in reducing the frequency of migraine attacks per month but without an effect on the severity or length of migraine attacks. The oral dose per day of CoQ10 in those studies varied from 100 to 400 mg. [27] On the other hand, Zeng et al. (2019) presented in meta-analysis that ubiquinone was able to reduce migraine attacks length and frequency but not its severity. [28] Despite different conclusions, due to the promising results of CoQ10 supplementation

presented in those studies further research should be proceeded to clarify the role of ubiquinone use in the management of migraine.

Magnesium

Magnesium is a very important intracellular cation that is necessary for many physiological functions in the human body and essential reactions that lead to energy production. [29] What is more, magnesium plays a role in many mechanisms that could be engaged in migraine pathogenesis such as stabilizing membrane, preventing vasoconstriction and inhibiting platelet aggregation. [30] Insufficient magnesium level in the body will cause these mechanisms to not work properly and migraine pain will arise. Besides, it has been proven that magnesium deficiency causes the formation and secretion of the P substance which acts on sensory fibers, causing neurogenic inflammation and, consequently, headaches. [31] Systemic deficiency of magnesium is observed in many neurological diseases, including migraine. [32] Furthermore, a study has been conducted that patients have reduced levels of magnesium in the brain during the migraine attack. [33] According to research, supplementation with high doses of magnesium can be effective in migraine prevention. [34] A randomized, double-blind study was conducted in which 81 patients suffering from migraine participated. Patients were given 600 mg of oral trimagnesium dicitrate for 12 weeks. The study showed a reduction in the frequency of migraine attacks at week 9-12 compared to placebo. In the group that received 600 mg of magnesium, the reduction was 41.6%, in the placebo group 15.8%. [35] In the magnesium group, the number of migraine days also decreased. The duration of migraine attack and the severity of the pain also lessened but not as much as frequency of migraine. The study of Tarighat that was a single-blind clinical trial, found that magnesium supplementation increased magnesium levels in the blood, leading to a reduction in migraine pain. [36] The research conducted by Facchinetti et al. showed that magnesium supplementation is also effective in the prevention of menstrual migraine. [37] It is very important because as studies reported, about 50% women are suffering from menstrual migraines. [38] It is also possible to administer magnesium to patients intravenously. A study has shown that magnesium, similarly to riboflavin and coenzyme Q10, is associated with a lower risk of side effects than drugs used to prevent migraine. The most common side effect during magnesium supplementation is diarrhea. [39]

Vitamin D

Vitamin D is a fat-soluble vitamin that is essential for many physiological processes including calcium absorption, bones mineralization and proper functioning of the musculoskeletal system. Additionally, vitamin D has an anti-inflammatory effect. [40,41] A source of vitamin D can be foods such as fatty fishes, but most is synthesized in the skin after exposure to sunlight. Factors that increase the risk of vitamin D deficiency in the body include dark skin, insufficient exposure to the sun, some endocrine disorders such as diabetes mellitus, chronic renal or liver diseases. Insufficient level of vitamin D in the body may be a cause of many disorders including osteoporosis, depression or also migraine. [42]

The pathogenesis of migraine as a result of vitamin D deficiency in the body is not fully understood, but it is believed to be related to the inflammation, which causes pain development. Vitamin D affects the immune system, reducing inflammation. [41] According to studies, vitamin D deficiency causes an increase in the frequency of migraine attacks per month. [43] A randomized, double-blind, placebo-controlled study was conducted involving 36 women and 12 men suffering from migraines that were divided into two groups. The participants were aged 18-65. After 4 weeks of baseline, the first group received vitamin D at a dose of 100 µg/day D3-Vitamin for 24 weeks, the second group received a placebo. At the end of the study, a reduction in the number of headache days was observed in the group that took vitamin D to a greater extent than the placebo group. What's more, patients receiving vitamin D had a reduced incidence of migraine attacks. Patients did not complain of any side effects of treatment. [44] Some studies have shown that patients that suffer from chronic migraine are more likely to have insufficient vitamin D level. [45]

Physical activity

Although physical activity exacerbates pre-existing migraine pain, it is proven that regular exercise can be effective in migraine prevention by reducing the frequency of migraine and also a reduction in the severity of pain and duration of a migraine attack. What is more, low physical activity is associated with a higher risk of headaches and an increase in the frequency of migraines. [46] A study by Molarius et al. which was conducted on a Swedish population of 43,770 women and men aged 18 to 79, found that physically inactive people were more likely to have migraine attacks than physically active people. [47] It has been investigated in several studies that aerobic exercises are the best option for migraine

prevention. When it comes to other-non-aerobic exercises for migraine prophylaxis, scientific evidence is limited. [46] However, randomized controlled study has shown that also yoga can have a positive effect on reducing the frequency of migraine pain, reducing the severity of pain and the duration of the attack, thus contributing to the quality of life of migraineurs. In other study that was conducted, 42 women suffering from migraine were randomly divided into two groups, where one group was a control group and received only medication for 12 weeks, while in other group participates took part in a yoga exercise program and were treated with the same medications as the control group. The aim of this study was to investigate if yoga could be helpful in improving vascular function in migraine sufferers. As far as we know, vascular dysfunction is one of the mechanisms responsible for migraine. Study participants had their blood drawn to measure plasma concentrations of the intercellular adhesion molecule (ICAM) and the vascular cell adhesion molecule (VCAM) after yoga exercise. The results of the study showed that in the group that was included in the yoga exercise program, plasma levels of VCAM decreased compared to the control group but plasma ICAM levels did not differ considerably between the two groups. Therefore, we can conclude that regular yoga exercises in combination with pharmacological treatment can have a beneficial effect on reducing migraine attacks by improving endothelial function. [48]

Conclusions

Migraine is a common neurological disorder that causes disability among young people, especially women. It is very important to prevent migraine attacks that significantly reduce the quality of life and can lead to mental problems such as depression. Although there are many medications that are used in migraine prevention, they often have many side effects. Supplements can be helpful, as studies have shown, they are burdened with a lower risk of side effects and are effective in migraine prevention. It has been proven that riboflavin, coenzyme Q10, magnesium and vitamin D used daily can reduce the frequency of migraine attacks and the duration of pain but to varying degrees. Regular, moderate physical activity is also very important. Studies have proven that people who do not engage in physical activity are more likely to suffer from migraine attacks. It has been investigated that aerobic exercise and yoga are the most effective in preventing migraines.

Author's Contribution

Conceptualization: Daria Aleksandrowicz; Methodology: Daria Aleksandrowicz, Olga Wieczorek; Software: Marta Głąbień, Paweł Miłkowski; Check: Anna Kuśnierz, Zofia Jakubczak; Formal analysis: Daria Aleksandrowicz, Karolina Kusiak, Investigation: Daria Aleksandrowicz, Patryk Śliwiak; Resources: Aneta Kondratowicz, Maria Weronika Zimniak; Data curation: Marta Głąbień, Paweł Miłkowski; Writing - rough preparation: Daria Aleksandrowicz; Writing- review and editing: Daria Aleksandrowicz, Olga Wieczorek; Visualisation: Daria Aleksandrowicz, Anna Kuśnierz, Karolina Kusiak; Supervision: Zofia Jakubczak, Maria Weronika Zimniak; Project administration: Daria Aleksandrowicz, Agata Kondratowicz, Patryk Śliwiak

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Bibliography:

1. 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? *Journal of Headache and Pain*. 2018;19(1). <https://doi.org/10.1186/s10194-018-0846-2>
2. Lempert T, Neuhauser H. Epidemiology of vertigo, migraine and vestibular migraine. *J Neurol*. 2009;256(3):333-338. <https://doi.org/10.1007/s00415-009-0149-2>

3. Olesen J. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38(1):1-211. <https://doi.org/10.1177/0333102417738202>
4. Minen MT, De Dhaem OB, Van Diest AK, et al. Migraine and its psychiatric comorbidities. *J Neurol Neurosurg Psychiatry*. 2016;87(7):741-749. <https://doi.org/10.1136/jnnp-2015-312233>
5. Buse DC, Silberstein SD, Manack AN, Papapetropoulos S, Lipton RB. Psychiatric comorbidities of episodic and chronic migraine. *J Neurol*. 2013;260(8):1960-1969. <https://doi.org/10.1007/s00415-012-6725-x>
6. Spierings1995. <https://doi.org/10.1046/j.1468-2982.1994.1405328.x>
7. Sun-Edelstein C, Mauskop A. Foods and Supplements in the Management of Migraine Headaches.; 2009. <https://doi.org/10.1097/AJP.0b013e31819a6f65>
8. Evans RW, Taylor FR. “Natural” or alternative medications for migraine prevention. *Headache*. 2006;46(6):1012-1018. <https://doi.org/10.1111/j.1526-4610.2006.00473.x>
9. Marashly ET, Bohlega SA. Riboflavin has neuroprotective potential: Focus on Parkinson’s disease and migraine. *Front Neurol*. 2017;8(JUL). <https://doi.org/10.3389/fneur.2017.00333>
10. Chen YS, Lee HF, Tsai CH, et al. Effect of Vitamin B2 supplementation on migraine prophylaxis: a systematic review and meta-analysis. *Nutr Neurosci*. 2022;25(9):1801-1812. <https://doi.org/10.1080/1028415X.2021.1904542>
11. Thompson DF, Saluja HS. Prophylaxis of migraine headaches with riboflavin: A systematic review. *J Clin Pharm Ther*. 2017;42(4):394-403. <https://doi.org/10.1111/jcpt.12548>
12. Yazdian-Anari P, Rahimdel A, Zeinali A, et al. Effectiveness of Vitamin B2 versus Sodium Valproate in Migraine Prophylaxis: a randomized clinical trial. 2015;(6):1344-1348. <https://doi.org/10.14661/1344>
13. Schoenen J, Lenaerts M, Bastings E. High-dose riboflavin as a prophylactic treatment of migraine: results of an open pilot study. <https://doi.org/10.1046/j.1468-2982.1994.1405328.x>
14. Nambiar NJ, Aiyappa C, Srinivasa R. Oral Riboflavin versus Oral Propranolol in Migraine Prophylaxis: An Open Label Randomized Controlled Trial. *Neurol. Asia*. 2011;16:223–229. [[Google Scholar](#)]
15. Sándor PS, Áfra J, Ambrosini A, Schoenen J. Prophylactic Treatment of Migraine With-Blockers and Riboflavin: Differential Effects on the Intensity Dependence of

- Auditory Evoked Cortical Potentials. <https://doi.org/10.1046/j.1526-4610.2000.00005.x>
16. Schoenen J, Jacquy J, Lenaerts M. Effectiveness of High-Dose Riboflavin in Migraine Prophylaxis A Randomized Controlled Trial.; 1998. <https://doi.org/10.1212/wnl.50.2.466>
 17. Bhagavan HN, Chopra RK. Coenzyme Q10: Absorption, tissue uptake, metabolism and pharmacokinetics. *Free Radic Res.* 2006;40(5):445-453. <https://doi.org/10.1080/10715760600617843>
 18. Hidaka T, Fujii K, Funahashi I, Fukutomi N, Hosoe K. Safety Assessment of Coenzyme Q 10 (CoQ 10). Vol 32. IOS Press Review Article; 2008. <https://doi.org/10.1002/biof.5520320124>
 19. Villalba JM, Parrado C, Santos-Gonzalez M, Alcain FJ. Therapeutic use of coenzyme Q10 and coenzyme Q10-related compounds and formulations. *Expert Opin Investig Drugs.* 2010;19(4):535-554. <https://doi.org/10.1517/13543781003727495>
 20. Zozina VI, Covantev S, Goroshko OA, Krasnykh LM, Kukes VG. Coenzyme Q10 in Cardiovascular and Metabolic Diseases: Current State of the Problem. *Curr Cardiol Rev.* 2018;14(3):164-174. <https://doi.org/10.2174/1573403x14666180416115428>
 21. Rauchová H. Coenzyme Q10 Effects in Neurological Diseases. *Physiol Res.* 2021;70:683-714. <https://doi.org/10.33549/physiolres.934712>
 22. Rozen T, Oshinsky M, Gebeline C, et al. Open label trial of coenzyme Q10 as a migraine preventive. <https://doi.org/10.1046/j.1468-2982.2002.00335.x>
 23. Tripathi GM, Kalita J, Misra UK. A study of oxidative stress in migraine with special reference to prophylactic therapy. *International Journal of Neuroscience.* 2018;128(4):318-324. <https://doi.org/10.1080/00207454.2017.1374959>
 24. Dahri M, Tarighat-Esfanjani A, Asghari-Jafarabadi M, Hashemilar M. Oral coenzyme Q10 supplementation in patients with migraine: Effects on clinical features and inflammatory markers. *Nutr Neurosci.* 2019;22(9):607-615. <https://doi.org/10.1080/1028415X.2017.1421039>
 25. Tietjen GE, Khubchandani J. Vascular biomarkers in migraine. *Cephalalgia.* 2015;35(2):95-117. <https://doi.org/10.1177/0333102414544976>
 26. Sazali S, Badrin S, Norhayati MN, Idris NS. Coenzyme Q10 supplementation for prophylaxis in adult patients with migraine - A meta-analysis. *BMJ Open.* 2021;11(1). <https://doi.org/10.1136/bmjopen-2020-039358>

27. Parohan M, Sarraf P, Javanbakht MH, Ranji-Burachaloo S, Djalali M. Effect of coenzyme Q10 supplementation on clinical features of migraine: a systematic review and dose–response meta-analysis of randomized controlled trials. *Nutr Neurosci.* 2020;23(11):868-875. <https://doi.org/10.1080/1028415X.2019.1572940>
28. Zeng ZY, Li YP, Lu SY, Huang WS, Di W. Efficacy of CoQ10 as supplementation for migraine: A meta-analysis. *Acta Neurol Scand.* 2019;139(3):284-293. <https://doi.org/10.1111/ane.13051>
29. Taylor2011. <https://doi.org/10.1111/j.1526-4610.2011.01847.x>
30. Bianchi A, Salomone S, Caraci F, et al. And Vitamin B 12 in Migraine Prophylaxis.; 2004. [https://doi.org/10.1016/S0083-6729\(04\)69011-X](https://doi.org/10.1016/S0083-6729(04)69011-X)
31. Sun-Edelstein C, Mauskop A. Role of magnesium in the pathogenesis and treatment of migraine. *Expert Rev Neurother.* 2009;9(3):369-379. <https://doi.org/10.1586/14737175.9.3.369>
32. Xue W, You J, Su Y, Wang Q. The Effect of Magnesium Deficiency on Neurological Disorders: A Narrative Review Article. Vol 48.; 2019. <http://ijph.tums.ac.ir>
33. Address Correspondence To: K MA, Welch MD. Department of Neurology, K-11. W. Grand Blvd; 2799. <https://doi.org/10.1111/j.1526-4610.1989.hed2909590.x>
34. Cohen JS. High-Dose Oral Magnesium Treatment of Chronic, Intractable Erythromelalgia. Vol 36.; 2002. <https://doi.org/10.1345/aph.1A186>
35. Peikert1996. <https://doi.org/10.1046/j.1468-2982.1996.1604257.x>
36. Tarighat Esfanjani A, Mahdavi R, Ebrahimi Mameghani M, Talebi M, Nikniaz Z, Safaiyan A. The effects of magnesium, L-carnitine, and concurrent magnesium-L-carnitine supplementation in migraine prophylaxis. *Biol Trace Elem Res.* 2012;150(1-3):42-48. <https://doi.org/10.1007/s12011-012-9487-5>
37. Maasumi K, Tepper SJ, Kriegler JS. Menstrual Migraine and Treatment Options: Review. *Headache.* 2017;57(2):194-208. <https://doi.org/10.1111/head.12978>
38. Parazzini F, Di Martino M, Pellegrino P. Magnesium in the gynaecological practice: A literature review. *Magnes Res.* 2017;30(1):1-7. <https://doi.org/10.1684/mrh.2017.0419>
39. Dolati S, Rikhtegar R, Mehdizadeh A, Yousefi M. The Role of Magnesium in Pathophysiology and Migraine Treatment. *Biol Trace Elem Res.* 2020;196(2):375-383. <https://doi.org/10.1007/s12011-019-01931-z>
40. Uwitonze AM, Razzaque MS. Role of magnesium in vitamin d activation and function. *Journal of the American Osteopathic Association.* 2018;118(3):181-189. <https://doi.org/10.7556/jaoa.2018.037>

41. Rebecchi V, Gallo D, Princiotta Cariddi L, et al. Vitamin D, Chronic Migraine, and Extracranial Pain: Is There a Link? Data From an Observational Study. *Front Neurol.* 2021;12. <https://doi.org/10.3389/fneur.2021.651750>
42. Chang SW, Lee HC. Vitamin D and health - The missing vitamin in humans. *Pediatr Neonatol.* 2019;60(3):237-244. <https://doi.org/10.1016/j.pedneo.2019.04.007>
43. Song TJ, Chu MK, Sohn JH, Ahn HY, Lee SH, Cho SJ. Effect of vitamin D deficiency on the frequency of headaches in migraine. *Journal of Clinical Neurology (Korea).* 2018;14(3):366-373. <https://doi.org/10.3988/jcn.2018.14.3.366>
44. Gazerani P, Fuglsang R, Pedersen JG, et al. A randomized, double-blinded, placebo-controlled, parallel trial of vitamin D 3 supplementation in adult patients with migraine. *Curr Med Res Opin.* 2019;35(4):715-723. <https://doi.org/10.1080/03007995.2018.1519503>
45. Plantone D, Primiano G, Manco C, Locci S, Servidei S, De Stefano N. Vitamin D in Neurological Diseases. *Int J Mol Sci.* 2023;24(1). <https://doi.org/10.3390/ijms24010087>
46. Amin FM, Aristeidou S, Baraldi C, et al. The association between migraine and physical exercise. *J Headache Pain.* 2018;19(1):83. <https://doi.org/10.1186/s10194-018-0902-y>
47. Molarius A, Tegelberg Å, Öhrvik J. Socio-economic factors, lifestyle, and headache disorders - A population-based study in Sweden. *Headache.* 2008;48(10):1426-1437. <https://doi.org/10.1111/j.1526-4610.2008.01178.x>
48. Naji-Esfahani H, Zamani M, Marandi SM, Shaygannejad V, Javanmard SH. Preventive Effects of a Three-Month Yoga Intervention on Endothelial Function in Patients with Migraine. Vol 5.; 2014 <https://pubmed.ncbi.nlm.nih.gov/24829729/>