Case Reports

Dietary and Lifestyle Changes in the Treatment of a 23-Year-Old Female Patient With Migraine

Brett R. Martin DC, MSAc^{a,*}, David R. Seaman DC, MS^b

^a Instructor, Departments of Basic and Clinical Science, National University of Health Sciences, Seminole, FL

^b Professor, Department of Clinical Science, National University of Health Sciences, Seminole, FL

Received 11 August 2014; received in revised form 9 September 2015; accepted 12 September 2015

Key indexing terms:

Migraine disorders;
Gastroesophageal
reflux;
Diet;
Dietary supplements

Abstract

Objective: The purpose of this case report is to describe the chiropractic management of a patient with atypical migraine headache.

Clinical Features: A 23-year-old woman experienced migraines for 3 months. She had no previous history of migraines and was unresponsive to pharmaceutical and musculoskeletal therapies. The migraine headaches could not be classified according to the common categories associated with migraines. She had a change in diet due to severe gastroesophageal reflux causing her to reduce or avoid consuming foods. She also had a history of smoking and alcohol consumption.

Intervention and Outcome: Dietary and lifestyle changes were recommended in conjunction with the administration of a multivitamin, magnesium oxide, and *Ulmus rubra*. Her migraine headaches improved with the resolution of her gastroesophageal reflux symptoms.

Conclusion: This patient with atypical migraines and a history of poor dietary and lifestyle choices improved using nutritional changes and supplementing with a multivitamin and magnesium oxide.

© 2015 National University of Health Sciences.

Introduction

Migraine headaches (HA) are a major health problem in the United States affecting between 11.7–16.6% of the population.¹ This type of HA can be extremely debilitating causing a significant amount of personal pain and discomfort. The severe nature of

nociceptive pain experienced by migraineurs is demonstrated by the number of visits to the emergency department in 2009. In 2009, 12 million people presented to the emergency department complaining of a migraine HA, which was the fifth most common condition treated in an emergency setting.¹

Although the exact etiology of migraines is not understood, the condition is believed to be influenced by a multitude of different factors. A hereditary component of migraines has been observed in 65–90% of cases.² Women have an 18% risk of having a

* Corresponding author at: 6698 68th Ave. N., Pinellas Park, FL 33781. Tel.: +1 727 623 0146; fax: +1 727 954 3361.

E-mail address: bmartin@nuhs.edu (B. R. Martin).

migraine compared to a 6% chance in men.³ The higher prevalence in women is typically attributed to hormonal fluctuations especially estrogen.⁴ Migraines typically begin during puberty or between the ages of 35 and 45 years.⁵ Alcohol and caffeine can contribute to dehydration initiating a migraine.² Migraines may also occur as a side effect from certain medications. The onset of the migraine may be insidious or can be precipitated by an aura, which lasts a few minutes and includes diplopia or bright spots in the vision; a feeling of fatigue or anxiety, confusion, or disorientation; or unilateral paresthesias in the extremities.⁶

Migraine headaches are classified as being common, classic, complicated, or variant.⁶ Common migraines account for 80% of all migraine HA.⁵ This type of HA manifests as an unusual aura with frontal, unilateral, or bilateral pain for 1 to 3 days.⁵ Classic migraines are responsible for an estimated 10% of cases. They occur with an aura 30 minutes prior to the onset of a unilateral HA, and vomiting is often present. Complicated migraines are unpredictable, last for a variable duration of time and the individual usually experiences a neurologic aura such as vertigo, syncope, diplopia and hemiparesis.⁶ Migraines that do not manifest as any of the previously discussed categories are variant.⁶

The treatment for typical migraine HA ranges from the administration of medications, herbal remedies, and supplements to the utilization of massage, acupuncture, and chiropractic manipulation.⁷⁻¹⁰ The effectiveness of these different therapeutic methods has been well evaluated for the relief of migraine HAs.⁷⁻¹⁰

At present, there are very few case reports that describe the chiropractic treatment of patients with migraine. Therefore, the purpose of this case report is to describe the chiropractic management of a patient with atypical migraine headache.

Case Report

A 23-year-old Hispanic woman sought treatment for atypical migraine HAs that did not respond to musculoskeletal (acupuncture and chiropractic) or pharmaceutical (Ibuprofen and Excedrin) therapies. She had been experiencing migraines for 3 months, but had no previous medical history of migraines. The migraine HAs were precipitated by visual and auditory stimuli, which initiated paresthesias in her temples that radiated posteriorly toward the occiput bilaterally and caused debilitating pulsating pain with diplopia. Upon the onset of the migraine, she would go into a dark

room and lie down until the episode dissipated, which could take several hours. She suffered from multiple migraines per week, almost every day at any time of the day and the intensity was a 10-10 according to a numeric pain scale with 1 being the least intense and 10 being most intense. The patient was considerably stressed due to the large number of days that she had to take off from work.

History, Examination, and Laboratory Findings

The patient had neither a family history nor previous personal history of migraines and was unresponsive to over-the-counter ibuprofen and excedrin and musculoskeletal therapies.

During the history taking process, the patient revealed that she had a previous past medical history of severe gastroesophageal reflux (GERD) that started 6 months earlier but was not diagnosed until 4 months ago.

Her GERD caused an erosion of part of her esophagus and the formation of a polyp, which was observed during an endoscopic exam. According to her medical doctor, the GERD was a result of the consumption of fast food, Ramen noodles and toaster strudels for a majority of her meals, since around age 13. She also admitted to drinking 4 to 5 bottles of Coke a week; drinking alcohol 3 to 4 nights a week, consisting of 5 to 6 bottles of beer with 4 to 5 shots; and smoking 1 1/2 packs of cigarettes on the weekend and half pack during the week for 5 years. However, upon the diagnosis of her GERD, she ceased all of these activities except smoking.

For the treatment of her GERD, she made dietary changes and began taking Nexium (Esomeprazole). However, she had adverse effects and began taking Dexilant (Dexlansoprazole). Her migraines began 1 month after she began taking antacids and making the following dietary changes. Her new diet consisted of a fruit smoothie in the morning with breakfast, a sandwich for lunch usually turkey, and usually nothing for dinner. Not only did her GERD symptoms continue but she also began to feel dizzy and light headed and would less frequently experience palpitations and dyspnea with minimal exertion. In addition, when she brushed her hair or showered, some of her hair fell out. She also lost 30 lb over the past 6 months.

An examination exhibited no abnormalities in her vitals, orthopedic tests, reflexes, muscle strength tests, or on abdominal examination. Hypertonicity of the suboccipitals and upper trapezius muscles was evident. Cranial nerve examination was unremarkable. Complete blood count, fecal occult blood test, and urinalysis

were normal. The comprehensive metabolic profile demonstrated no abnormalities except for 105 mg/dL of fasting blood glucose. Normal parameters are below 100 mg/dL fasting. A lactose intolerance was established via an allergy testing panel. Cranial magnetic resonance imaging was performed and found unremarkable.

Working Diagnosis and Treatment Plan

The patient appeared to have been experiencing a migraine variant; since the onset was after puberty, there was no family history or past medical history of migraines and it was not the distinctive unilateral, frontal, or bilateral distribution observed with classic or common migraines.^{2,5,6} It was determined that the patient most likely had multiple nutritional deficiencies and the most appropriate course of action was dietary and lifestyle changes in conjunction with supplementation.

Methods Used to Treat and Outcomes

The patient adhered to several dietary recommendations. She was encouraged to ingest small portion sizes of food multiple times a day as opposed to large meals twice a day. Multiple calorie sources were avoided including fast foods, simple carbohydrates, dairy products, and carbonated beverages such as soda and alcohol. Her dietary focus was the consumption of well-rounded meals from healthy calorie sources such as fish, chicken, vegetables, and fruit. She was also encouraged to consume low glycemic index carbohydrates such as sweet potatoes, beans, and yams.

Several nutritional supplements were recommended. Prior to each meal she took two digestive enzymes, which included protease, amylase, lactase, lipase, and HCl. Two hours after breakfast she took 400 mg of *Ulmus rubra*. Additional recommended supplements included a once-per-day multivitamin and 500 mg of magnesium oxide twice daily.

End Results of Treatment

After 1 week of treatment, a reduction in migraine frequency was observed, yet she still experienced GERD after almost every meal. Within the first month of treatment, the patient suffered from 3 migraine HAs and stated that she had a lower frequency and intensity of GERD. After 1 year, the patient is still supplementing with magnesium oxide and has not had a migraine. The patient still has occasional symptoms and incidents of GERD, but the intensity has greatly declined.

Discussion

A migraine HA is believed to be caused by prolonged emotional stress or other noxious visual, auditory, or olfactory stimuli and initiates a vasospasm resulting in vasoconstriction of the arteries supplying blood to the head and brain.² Vasoconstriction reduces blood flow to the brain resulting in ischemia, which prompts a reflex mechanism within the smooth muscle of the vascular walls causing them to become flaccid and reducing vascular tone for 24 to 48 hours.² The flaccidity and loss of vascular tone of the arteries results in excessive stretching that induces vasodilation and an intense pulsating pain. Since the onset of the migraine is vascular in origin, an intense throbbing headache ensues.

Evidence to support this theory has been demonstrated. Studies have shown that there is a reduction of cerebral blood flow during the prodromal period.⁶ The patient may appear pale or have a lower skin temperature on the affected side of the face during a migraine, which could indicate vasoconstriction prior to vasodilation.⁶ Other possible mechanisms of migraines are platelet disorders, neuronal disorders, and serotonin deficiency.

Individuals with a platelet disorder are prone to spontaneous platelet aggregation, abnormalities in serotonin release, and alterations of the components within platelets.¹¹ Migraines associated with a platelet disorder are caused by emotional stress, which elevate catecholamine levels in the blood stimulating the release of serotonin.⁶ Serotonin acts as a vasoconstrictor and enhances platelet aggregation. Platelets harbor serotonin and release it during aggregation. The concentration of serotonin within platelets is normal at the initial incident. However, the amount of serotonin secreted by platelets progressively increases until the next episode. The platelet aggregation stimulates the release of proinflammatory cytokines, interleukins and tumor necrosis factor- α , which may facilitate nociceptive signaling and hypersensitize the nociceptive system.¹¹

Another possible mechanism is caused by neuronal irregularities affecting the trigeminovascular system.¹² The event is believed to be initiated by a powerful depolarizing wave that begins in the occipital lobe and dissipates through the brain resulting in a subsequent period of down-regulated activity. The trigeminovascular system when activated promotes the trigeminal nerve terminals to secrete neuropeptides such as substance P.¹³ Substance P acts as a mediator to induce vasodilation, mast cell degranulation, and increased vascular permeability. Substance P is also

thought to stimulate the release of arachidonic acid from vascular endothelial cells activating the inflammatory cascade.¹⁴ The combination of these events propagates hypersensitivity in the peripheral and central sections of the brain,⁴ resulting in an excruciating HA.

There is an abundance of evidence that supports the theory that a deficiency of serotonin levels causes a migraine HA.¹⁵ The primary factor in this process is the hyperactivity of monoamine oxidase, which explains how increased levels of 5-hydroxyindoleacetic acid, a component of serotonin metabolism, is found in the urine and why there are low levels of serotonin in the blood.⁶ Low levels of serotonin suppress the nociceptive threshold with the outcome being chronic HAs.

Other theories hypothesize that mitochondrial dysfunction may be responsible for migraines. Impairment of the mitochondrial plasma membrane alters its permeability disrupting calcium channel regulation resulting in elevated calcium influx into the mitochondrial matrix as well as propagation of excessive amounts of free radicals and defective oxidative phosphorylation.¹⁶ Diminished mitochondrial function drastically reduces the production of ATP in neurons preventing the spreading of the depolarization generating a migraine.¹⁶

The precipitating factor for the onset of the patient's migraines is not known. Migraines due to musculoskeletal abnormalities typically respond well to chiropractic and acupuncture. This can be explained by the dysfunction of the mitochondria of the trigeminal nucleus caudalis,¹⁷ which extends from the brain into the cervical spine around C3-4¹⁸ and is associated with the development of chronic cervicogenic migraines.¹⁹ Several studies have demonstrated the efficacy of chiropractic manipulation for the relief of cervicogenic migraines.¹⁰ However, based upon the presentation and the non-responsiveness of this patient to cervical adjusting, it is acceptable to presume that the etiology is attributed to nutritional irregularities and is not musculoskeletal in origin.

An important consideration for this patient was her diet. Before the diagnosis of GERD she avoided meals due to epigastric pain and consumed fast foods that lacked essential nutrients, vitamins, and minerals. Her diet after diagnosis of GERD had more nutrients, vitamins, and minerals. However, due to the symptoms of her GERD she was consuming an antacid, which has been shown to interfere with the absorption of vitamins and minerals. It should be noted that after she changed her diet, her intake of nutrient-dense foods was increased. However, she was still not eating enough

due to her fear avoidance behavior created by the intense epigastric pain experienced during her episodes of GERD resulting in her reducing the amount of food ingested and skipping meals. Therefore, it can be postulated that she was still not achieving the daily requirements for nutrients.

Her frequent meal skipping may have also contributed to her headaches. Skipping meals results in hypoglycemia, which is positively correlated with the development of migraines in some individuals.²⁰ Hypoglycemia initiates the release of blood glucose modulators such as epinephrine and norepinephrine. Epinephrine and norepinephrine are vasoconstricting agents and promote the release of serotonin, which may be responsible for the precipitation of her migraines.

In conjunction with her poor dietary habits, her previous excessive alcohol intake and cigarette smoking may have exacerbated her nutritional deficiencies and could potentially be correlated with her migraines. Alcohol impairs absorption of several nutrients especially magnesium²¹ and B vitamins such as B1 (Thiamin) and B₁₂ (Cobalamin).²² Cigarette smoking can also hinder nutrient levels within the body. Several studies have shown that higher nutritional demands are necessary to compensate for the increased levels of oxidative stress associated with cigarette smoking.²²

However, when considering the patient's history and the onset of her migraines, it seems unlikely that these activities are the direct etiologic agents. This is due to the fact that she stopped drinking alcohol when her GERD was diagnosed and the onset of her migraines occurred later on. As for her cigarette smoking, she did continue to smoke after being diagnosed with GERD and while she was experiencing the migraines. However, she has been smoking for many years and does not have a past medical history of migraines. Yet, although her past medical history of alcohol consumption and cigarette smoking may not have been the direct etiologic factor, they potentially contributed to the nutritional deficits that the patient is experiencing.

Another factor that may have been implicated in the development of her migraines was that she was consuming a proton pump inhibitor (Dexilant) with every meal. Despite maintaining a poor diet, consuming excessive alcohol and smoking for many years, her migraine symptoms did not begin until one month after she began to take Dexilant, an antacid proton pump inhibitor, with every meal. Proton pump inhibitors are capable of reducing magnesium levels within the body.²³ It is possible that antacid use magnified her nutritional deficiencies, especially magnesium.

It is also important to note that evidence suggests that 48%²⁴ of the US population is magnesium deficient, that low levels of magnesium are positively correlated with migraines²⁵ and that 50% of individuals that suffer from migraines have inadequate magnesium consumption.²⁶ The fear avoidance behavior in combination with a diet low in magnesium rich foods such as spinach, legumes, or seafood allowed for the speculation that the patient would benefit from the administration of magnesium oxide.

A complicating aspect of the administration of magnesium was that she required the proton pump inhibitor due to her severe GERD, so if she did have a magnesium deficiency, it would not be attenuated until cessation of use of the proton pump inhibitor. Therefore, the necessity to control the patient's GERD became a central point of the treatment. As opposed to using an antacid to neutralize gastric acid impeding digestion, it was proposed for the patient to consume digestive enzymes prior to each meal to enhance the degradation of nutrients, which would theoretically diminish the requirement for the antacid.

Supplementation with *Ulmus rubra* was also recommended. This herb is used as a demulcent, which produces a soothing film that extends over mucous membranes, as well as acting as an anti-inflammatory agent. The demulcent effect is generated from its high mucilage content.²⁷ It is primarily utilized to alleviate pain from irritated and inflamed mucosa lining the esophagus and gastrointestinal tract.²⁷ Reducing the chronic inflammatory response of the tissue should help to reduce the hypersensitivity of her esophageal tissue preventing further episodes of GERD.

The third supplement utilized in the treatment was magnesium oxide due to the fact that it is often used as a prophylactic for migraines and is bioavailable.²⁸ Magnesium oxide is the ideal form of the vitamin for administration. When compared to magnesium citrate, magnesium oxide has a greater bioavailability reducing the risk of adverse effects such as diarrhea or nausea.²⁹ In addition, a recent study emphasized the effectiveness of magnesium as a prophylactic agent. There were 133 patients supplemented with 500 mg/d of magnesium oxide for 12 weeks. After the treatment period, the severity, frequency and duration of migraines was significantly reduced.³⁰

The application of magnesium for treatment of her migraines is multifaceted, which is beneficial in this case since the exact etiologic factor associated with the onset of her migraines is unknown. One of the basic considerations for the use of magnesium in this case was its ability to act as a calcium channel regulator promoting vasodilation.

Evidence exists that diets low in magnesium have higher levels of circulating catecholamines³¹ as well as elevated blood cortisol.³² This suggests that deficits in magnesium may act as a physiologic stressor on the body increasing cortisol and catecholamines.

In a retrospective analysis performed by Beltramone et al, 8821 patients were selected. The investigators found that the major factors that elicit the onset of a migraine were stress and menstruation. Stress was more commonly associated with a frequency of 68.8% compared to menstruation at 31.3%.³³ Supplementing with magnesium may help dissipate the physiological stress by antagonizing catecholamines release.

Therefore, for this patient, this treatment protocol seems apt. Although the cause of her migraines is unknown, she is experiencing an increased frequency, severity and duration of her migraines. She has no past medical history of migraines and has endured a magnitude of tests, which all indicate that there are no physiological abnormalities. She expressed during the history that her stress is increasing since she has been missing a large amount of work and believes that her employment may be in jeopardy and the etiology of her condition is unknown.

It should be noted that the combination of the reduction in the vasodilating activity of magnesium in conjunction with the increasing levels of catecholamines, which act as vasoconstrictors, has the potential to predispose individuals to the vasospasm precipitating an episode of a migraine. In fact, many therapeutic modalities for the treatment of migraines are aimed at enhancing vasodilatory effects in order to prevent the initial vasospasm, which perpetuates the ischemic event.

Magnesium has been highly touted as an exercise enhancing agent. Various studies have shown that it has the ability to induce both vasodilatory and bronchodilatory effects.³⁴ Both of these mechanisms have the capacity to potentiate oxygen transport and utilization in the tissues. Enhancing oxygen delivery to the tissue may abate ischemia or reduce the intensity.

Ischemia generated by interfering with vasodilation creates a pro-inflammatory state inducing the release of cytokines and other inflammatory markers. As a vasodilatory agent, magnesium possesses the ability to attenuate the inflammatory cascade. Furthermore, a deficiency of magnesium is linked to an increase in nuclear factor- κ B activity, which is the transcription factor involved with the generation of arachidonic acid.³⁵ Up-regulation of the arachidonic acid formation and the subsequent production of pro-inflammatory eicosanoids augments the generation of platelets, which in turn stimulates serotonin release.³⁶

Magnesium has the potential to affect serotonin receptor function directly inhibiting release associated with platelet disorders.²² Therefore, it would be rational to postulate that in addition to helping to lower catecholamines and cortisol generating the physiological stress response magnesium may also assist by preventing the inflammatory precursors to the migraine impeding or ameliorating the severity of a migraine. This seems to be a possible cause. Although Ibuprofen and Excedrin were prescribed, these agents are cyclooxygenase inhibitors, but are ineffective for reducing 5-lipoxygenase activity and thus have no effect on leukotrienes. Leukotrienes produce vasoconstricting and chemotactic effects. The use of leukotriene antagonists is associated with a reduction in migraines.³⁷ Therefore, if the entire arachidonic acid cascade is not diminished, the migraine may still ensue unhindered.

Another possible mechanism for the onset of her migraines could be hyperactivity of the sympathetic nervous system potentiating the release of catecholamines stimulating the release of serotonin initiating vasoconstriction and platelet aggregation. Since the patient is stressed, she most likely has higher levels of catecholamines, which may be amplifying sympathetic activity. However, magnesium in studies have been shown to act a vasodilator capable of inhibiting sympathetic nervous system activity and thus catecholamine release as well as attenuating platelet aggregation, which has been correlated with the alleviation of migraines.³⁸

The stress that she is experiencing may also interfere with mitochondrial function, which is believed to be a major cause of migraines. As demonstrated in many experiments, stress creates higher levels of reactive oxygen species within the body or increasing oxidative stress. Oxidative stress is positively correlated with mitochondrial dysfunction.

In addition, magnesium deficiency can hinder mitochondrial function reducing ATP production, which has been theorized to interfere with the propagation of action potentials of neurons possibly inducing a migraine. Magnesium has been shown to promote energy production by fortifying mitochondrial function. As an energy enhancing agent, magnesium has been shown to maintain the integrity of the mitochondrial membrane and prohibit dysfunction of the electron transport chain.³⁹ It also precludes the elevation in calcium that is observed in the mitochondrial matrix due to dysfunction. Enhancing mitochondrial function may sustain the output of ATP and attenuate migraines.

Limitations

As this is a case study, the positive results of treatment for this patient may not necessarily be relevant to other patients. It is possible that the patient would have improved regardless of treatment. Other factors may have been responsible for her condition. Although based upon the presentation it appears as if the patient had possible vitamin, mineral and nutrient deficiencies from poor dietary and lifestyle choices and was experiencing a great deal of stress, a limiting factor was the absence of vitamin and minerals testing, which was not performed due to financial constraints of the patient. In addition, an evaluation of serotonin levels or thyroid function was not performed, therefore these are possible additional factors in this case that were unaccounted for.

Conclusion

This patient with atypical migraines and a history of poor dietary and lifestyle choices improved using basic nutritional changes and supplementing with a multivitamin and magnesium oxide. However, the exact etiological factor remains unknown.

Funding Sources and Conflicts of Interest

No funding sources or conflicts of interest were reported for this study.

References

1. Smitherman T, Burch R, Sheikh H, Loder E. The prevalence, impact and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies. *Headache* 2013;53:427–36.
2. Guyton A. Guyton and Hall textbook of medical physiology. 12th ed. Jackson, MS: Elsevier Saunders; 2011.
3. Nazari F, Eghbali M. Migraine and its relationship with dietary habits in women. *Iran J Nurs Midwifery Res* 2012;17:65–71.
4. Carolei A, Degan D, Ricci S, Sacco S. Migraine in women: the role of hormones and their impact on vascular diseases. *J Headache Pain* 2012;13:177–89.
5. Shaik M, Gan S. Vitamin supplementation as possible prophylactic treatment against migraine with aura and menstrual migraine. *Biomed Res Int* 2015; 469521.
6. Murray M, Pizzorno J. Textbook of natural medicine. 3rd ed. St. Louis, MO: Churchill Livingstone Elsevier; 2012.

7. Marmura M, Silberstein S, Schwedt T. The acute treatment of migraine in adults: The American Headache Society Evidence Assessment of migraine pharmacotherapies. *Headache* 2015;55:3–20.
8. Ferro E, Biagini A, da Silva IE, Silva ML, Silva JR. The combined effect of acupuncture and Tanacetum parthenium on quality of life in women with headache: randomised study. *Acupunct Med* 2012;30:252–7.
9. Chatchawan U, Eungpinichpong W, Sooktho S, Tiamkao S, Yamauchi J. Effects of Thai traditional massage on pressure pain threshold and headache intensity in patients with chronic tension-type migraine headaches. *J Altern Complement Med* 2014;20:486–92.
10. Aickin M, Haas M, Peterson D, Spegman A, Vavrek D. Dose response and efficacy of spinal manipulation for chronic cervicogenic headache: a pilot randomized controlled trial. *Spine J* 2010;10:117–28.
11. Dannese E, Lippi G, Montagnana M. Platelets and migraine. *Thromb Res* 2014;134:17–22.
12. Nosedà R, Burstein R. Migraine pathophysiology: anatomy of the trigeminovascular pathway and associated neurological symptoms, CSD, sensitization and modulation of pain. *Pain* 2013;154:1–10.
13. Kojic Z, Stojanovic D. Pathophysiology of migraine—from molecular to personalized medicine. *Med Pregl* 2013;66:53–7.
14. Nicoletti M, Neri G, Maccauro G, et al. Impact of neuropeptide substance P an inflammatory compound on arachidonic acid compound generation. *Int J Immunopathol Pharmacol* 2012;25:849–57.
15. Ayalp S, Benli Aksungar F, Karsidag S, Sahin S. Evaluation of platelet serotonin levels in migraine without aura. *Agri* 2012;24:117–22.
16. Hardison H, Yorns W. Mitochondrial dysfunction in migraine. *Am J Physiol Cell Physiol* 2013;20:188–93.
17. Fried N, Moffat C, Oshinsky M, Seifert E. Functional mitochondrial analysis in acute brain sections from adult rats reveals mitochondrial dysfunction in a rat model of migraine. *Am J Physiol Cell Physiol* 2014;10:1152.
18. Cramer G, Darby S. Basic and clinical anatomy of the spine, spinal cord and ANS. 2nd ed. St. Louis, MO: Elsevier Mosby; 2005.
19. Antonaci F, Bono G, Chimento P. Diagnosing cervicogenic headache. *J Headache Pain* 2006;7:145–8.
20. Finocchi C, Sivori G. Food as trigger and aggravating factor of migraine. *Neurol Sci* 2012;10:10070–2.
21. Godber I, Peake R, Maguire D. The effect of magnesium administration on erythrocyte transketolase activity in alcoholic patients treated with thiamine. *Scott Med J* 2013;58:139–42.
22. Groff J, Gropper S, Smith J. Advanced nutrition and human metabolism. 5th ed. Belmont, CA: Wadsworth Cengage Learning; 2009.
23. Arntzenius A, Kuipers M, Thang H. Hypomagnesaemia due to use of proton pump inhibitors—a review. *Neth J Med* 2009;67:169–72.
24. Rosanoff A, Rude R, Weaver C. Suboptimal magnesium status in the United States: are the health consequences underestimated? *Nutr Rev* 2012;70:153–64.
25. Asghari N, Ghorbani R. Blood magnesium levels in migraineurs within and between the headache attacks: a case control study. *Pan Afr Med J* 2012;11:46.
26. Mauskop A, Varughese J. Why all migraine patients should be treated with magnesium. *J Neural Transm* 2012;119:575–9.
27. PDR for herbal medicines. 4th ed. Montvale, NJ: Thomson; 2007.
28. Aube M, Becker W, Christie S, et al. Canadian Headache Society guideline for migraine prophylaxis. *Can J Neurol Sci* 2012;39:1–59.
29. Coudray C, Feillet-Coudray C, Gueux E, et al. Study of magnesium bioavailability from ten organic and inorganic Mg salts in Mg-depleted rats using a stable isotope approach. *Magnes Res* 2005;18:215–23.
30. Ebrahimi Mameghani M, Mahdavi R, Nikniaz Z, Safaiyan A, Talebi M, Tariqhat Esfajani A. The effects of magnesium, L-carnitine, and concurrent magnesium–L-carnitine supplementation in migraine prophylaxis. *Biol Trace Elem Res* 2012;150:42–8.
31. Bansal D, Garg M, Mehra P. Hormonal imbalance and disturbances in carbohydrate metabolism associated with chronic feeding of high sucrose low magnesium diet in weanling male Wistar rats. *Mol Cell Biochem* 2014;389:35–41.
32. Murck H. Ketamine, Magnesium and major depression—from pharmacology to pathophysiology and back. *J Psychiatr Res* 2013;47:955–65.
33. Beltramone M, Donnet A. Status migrainosus and migraine aura status in a French tertiary-care center: an 11-year retrospective analysis. *Cephalalgia* 2014;34:633–7.
34. Amaral A, Crescencio J, Gallo L, Martinez J, Vannucchi H, Vianna E. The effect of acute magnesium loading on the maximal exercise performance of stable chronic obstructive pulmonary disease patients. *Clinics (Sao Paulo)* 2012;67:615–22.
35. Altura BM, Altura BT, Jiang XC, Li W, Li Z, Perez-Albela JL. Magnesium deficiency upregulates sphingomyelinases in cardiovascular tissues and cells: cross-talk among proto-oncogenes, Mg(2+), NF-κB and ceramide and their potential relationships to resistant hypertension, atherogenesis and cardiac failure. *Int J Clin Exp Med* 2013;6:861–79.
36. Alacam H, Aydin O, Aydin T, Azak E, Ince H, Ozyurek H. Urinary leukotriene E4 and prostaglandin F2a concentrations in children with migraine: a randomized study. *Acta Neurol Scand* 2014:1–5.
37. Bucciarelli T, Di Ilio C, D’Orazio N, Mancini B, Riccioni G. Antileukotriene drugs: clinical application, effectiveness and safety. *Curr Med Chem* 2007;14:1966–77.
38. Awad G, Aviv A, Bogden J, Kemp F, Kimura M, Lu X. Potassium chloride supplementation diminishes platelet reactivity in humans. *Hypertension* 2004;44:969–73.
39. Csont T, Duicu O, Gorbe A, Ferdinandy P, Mirica NS, Privistirescu A. P165 magnesium orotate in high concentrations elicits cardioprotection via modulation of mitochondrial functions. *Cardiovasc Res* 2014;103:29.