The use of a broad-spectrum plant-based blend of omega-3 and omega-6 essential fatty acids in the treatment of headaches: a case report

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Abstract

Migraines continue to impact an estimated 8.3% of the Canadian population. Although a variety of medications may help subside symptoms and frequency, complete resolve remains difficult to achieve in a clinical setting. In the following case study, a plant-based blend of omega 3 and omega 6 essential fatty acids (EFA) was used as an adjunct to migraine therapy. A formula composed of EFA, including Linoleic Acid (LA), Gamma Linoleic Acid (GLA) and Alpha Linoleic Acid (ALA) with a ratio of 2.5 to 1 omega-6 to omega-3. The omega-6 EFAs were sourced from evening primrose oil, sunflower oil, pumpkin oil, and extra virgin coconut oil, and the omega-3 EFAs from organic flax oil, to make up 755mg of EFAs dosed at six capsules per day.

Settings: Headache, Migraine and Pain Treatment Centre, 555 Kingston Rd W, Ajax, Ontario.

Subjects: Patients with migraines referred from family physicians were pre-screened with a Migraine Disability Score (MIDAS) questionnaire.

Outcome measures: MIDAS questionnaire, functional blood tests, imaging and physical examination including neurological and orthopedic assessment.

Interventions: The first case was treated with the Omega fatty acid formula, Cranial-Electrical Stimulation with daily Audiovisual Entrainment and botox therapy. The second patient received the Omega formula exclusively. Concomitant medications and therapies were also adjusted or discontinued. Duration of treatment varied from 1 to 6 months.

Results: Both patients improved significantly in most outcome measures. In all cases drug use was eliminated or substantially reduced. No major adverse reaction, habituation or tolerance developed. Quality of life was also improved subjectively as per patient report.

Conclusion: A blend of omega-3 and omega-6 essential fatty acids may prove as a successful adjunct treatment for those with migraine headaches.

Introduction

Between 2010 and 2011, an estimated 8.3% of Canadians (2.7 million) reported being diagnosed with a migraine. Studies using the International Classification of Headache Disorders criteria estimates between 2.4% to 27.5% in some American and European reports.[i] Migraine affects 17.6% of women and 5.7% of men a year, with approximately 70% of patients positive for familial history.[ii] Many potential causes of migraines have been postulated, including both genetic and environmental mechanisms, which appear to play a role.

Patients suffering from migraine headache experience a myriad of symptoms. Characterized by recurrent episodes of moderate to severe headache, symptoms may consist of throbbing or pulsatile sensations, nausea, vomiting, and in some cases, visual, sensory or motor symptoms, known as an aura. The pain typically presents as unilateral and localized, often within the frontotemporal and ocular area, which typically lasts between 4 to 72 hours. [iii] Dependent on presentation, the migraine may be diagnosed with or without aura. Further variants of migraine exist that are based on symptoms and localization of the headache. Suggested by focal neurological findings, basilar-type, hemiplegic, ophthalmoplegic or retinal migraine are examples of further subclassifications.

Standards of medical treatment for migraines include both acute and prophylactic use of pharmaceuticals.[iv] Acute treatments may use selective serotonin receptor agonists (triptans), ergot alkaloids (dihydroergotamine), NSAIDs, analgesics and antiemetics. These medications are limited to two to three days per week to avoid tolerance and development of rebound headaches and therefore pose a challenge when treatment of recurrent and severe migraines are present.[v] For chronic cases, prophylactic medications may be used, which include; antieleptics, beta blockers, antidepressants (TCA, SSRI), calcium channel blockers, NSAIDs, serotonin antagnoists and botulinum toxins. The individual pharmaceutical agent is chosen based on the severity of the attack, associated symptoms, comorbid problems and patient treatment response through a trial based approach. Effectiveness, tolerability, and symptomatic relief varies among patients, while side-effects pose a significant hurdle in long-term treatment protocols. Many of the pharmaceutical choices target purposed pathophysiology, yet fail to address underlying individual biochemical alterations.

Migraine and the Functional Medicine Model

Functional Medicine is a personalized, systems-oriented model that empowers patients and practitioners to achieve the highest expression of health by working in collaboration to address the underlying causes of disease.[vi] It is an emerging medical model that focuses on personalized medicine and seeks to understand the unique underlying biological process leading to the overt diagnosed condition, in this case, a migraine. Although, the clinical presentation for migraines (downstream effect) may appear to be similar, the origin (upstream cause) is different for each case and therefore resolution of the disease requires a focus on the underlying process, rather than simply emphasizing therapeutics aimed at the resulting symptoms and control thereof.

In addition to genetic and environmental factors, studies have identified alterations in; CNS function, neurotransmitter status (serotonin and

glutamate levels), vascular and vasomotor dysfunction, hormonal fluctuations and influence of biogenic vasoneuroactive substances such as histamine, catecholamines and prostaglandins.[vii] [viii] [ix] In addition, epigenetics suggest that these biological substances are under the regulatory influences of environment and lifestyle factors, such as: diet, food additives, stress response, barometric change, sleep and circadian rhythm, exercise and activity level and social habits such as alcohol consumption.[x] A functional medicine approach seeks to understand each patient's unique story and empowers them to understand how these environmental, social and dietary factors influence their condition and seeks to restore balance and achieve optimal health.[xi]

Essential Fatty Acids

EFAs are biologically active fatty acids that consist of several different derivatives, which the body cannot synthesize and thus, must come from either plant or animal sources. Longer-chain polyunsaturated fatty acids (LC-PUFAs) are metabolites of omega-3 alpha-linolenic acid (ALA) and omega-6 linoleic acid (LA) (Figure 1). Of these derivatives, LC-PUFA such as eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3), are made as needed by the body. In humans, LC-PUFAs are synthesized via desaturase and elongase enzyme activity (Figure 1). Due to genetic variances in desaturase enzymes (FADS1, FADS2) and low conversion efficiency in humans, it has been recommended to obtain EPA and DHA directly;[xii] [xiii] However, omega-3, omega-6 and their derived PUFAs are key mediators of various physiological processes that require an appropriate balance.

Phospholipids are shown to exert a wide-range of neurochemical and cellular effects and influence inflammation, vascular tone and hemostasis. The most commonly known impact involve their anti-inflammatory pathway, where cyclooxygenase and lipoxygenase enzymes covert LC-PUFA into prostaglandins, leukotrienes and thromboxane[xiv].(Figure 2) LA may be converted into PGE1 and PGI2 (prostacyclin). While PGE1 is a potent anti-inflammatory, these metabolites are also significant vasodilators. If functional LA bioavailability is deficient, the potential for inflammation will rise. Furthermore, the body will substitute these EFA with less functional oils, such as nonessential omega-9 oleic acid, which results in a marked decrease of cellular oxygen transport and cellular metabolism.[xv] Each of a human's 100 trillion cells consists of a phopholipid membrane in which EFA's comprise 25% - 33% of their polyunsaturated lipids and thus affect cell membrane properties, such as fluidity, flexibility, permeability, and the activity of membrane-bound enzymes.[xvi] [xvii] Membrane fluidity increases when more functional (undamaged) polyunsaturated fatty acids such as, linoleic acid, are available to incorporate into the membrane lipid bilayer. In addition to important structural components of cell membranes, EFAs serve as precursors to bioactive lipid mediators, and provide a source of energy. Dietary lipids not only influence the biophysical state of the cell membranes but, via direct and indirect routes, they also act on multiple pathways including, intracellular signaling, gene expression, protein modifications and aggregation.[xviii] EFAs can be considered the "brick and

mortar" of every cell, tissue, and organ, including mitochondria. [xix] [xx]

It is postulated that headaches, being an expression of underlying inflammation, are ameliorated by providing the brain and other tissues with proper, unadulterated LA and ALA, improve cell membrane and mitochondrial function and promote the production of PGE1, leading to resolution of the chronic, underlying inflammatory state and resolution of the patients headaches.

Essential Fatty Acids in the Treatment of Migraine

The literature of the past 20 years contains numerous studies and clinical investigations that highlight the critical role played by omega-3 PUFAs in human health and disease. To date, the majority of research on the benefits of EFA has been placed on the LC-PUFA compounds, particularly EPA and DHA, which show benefit in migraines, depression, cardiovascular disease, inflammation, pain and cognitive function.[xxi] [xxii] [xxiii] [xxiv] [xxv] However, other essential fatty acids show potential benefit. In a small randomized, placebo controlled, cross-over study, olive oil was used as a placebo control against EPA and DHA. Olive oil, which contains monounsaturated omega-9 and omega-6 fatty acids, oleic acid and linoleic acid respectively, showed a 70% reduction in headaches over 60 days, while the EPA and DHA mixture gave a statistically similar response rate of 74%.[xxvi] The use of EFAs have been used successfully in the treatment of chronic headaches. The proper dietary and supplemental intake of EFAs and omega formulas are shown to positively influence underlying neurological, vascular, immunological, inflammatory and prostaglandins abnormalities associated with the biochemistry of migraine. [xxvii]

Mechanistic and biochemical data also suggests a role for a more comprehensive and use of a wider variety of oils in supplementation. Omega-3 fatty acids are known to play a role in; nervous system activity, cognitive development, memory-related learning, neuroplasticity of nerve membranes, synaptogenesis and synaptic transmission.[xxviii] The discovery of essential fatty acids omega-6 and omega-3 have shown that deficiencies and imbalances result in visual and cognitive impairment and disturbances in cognitive function, as fatty acids are beneficial to vascular health and may forestall cerebrovascular disease and thus dementia.[xxix]

Significant advances have been made in understanding the relation between dietary factors and pro-inflammatory prostaglandins as a central component of many chronic diseases. More specifically, omega-3 PUFAs have been shown to inhibit eicosanoid production in glial cells, block voltage-gated sodium channels (VGSCs), inhibit neuronal protein kinases and modulate gene expression. They also appear to have mood-stabilizing and sympatholytic effects (anti-stress effects). Perhaps these known and potentially some unknown modulatory effects on biological function and gene expression may impact the course and symptoms of migraine headaches. Based on what is known about the neural and non-neural effects of omegas, EFAs may directly attenuate the neuronal and glial processes that underlie neuropathic and inflammatory pain, and possibly migraines.[xxx]

In the case studies below, favourable effects on migraines were shown with the use of a balanced ratio of

omega-3 and omega-6 EFAs. A formula composed of EFAs, including Linoleic Acid (LA), Gamma Linoleic Acid (GLA) and Alpha Linoleic Acid (ALA) with a ratio of 2.5 to 1 omega-6 to omega-3. The omega-6 EFAs were obtained from a standardized extract of evening primrose oil, sunflower oil, pumpkin oil, and extra virgin coconut oil, and the omega-3 EFAs from organic flax oil, to make up 755mg of EFAs dosed at six capsules per day.

Migraine Case study using standardized blend of omega-3 and omega-6

Case 1 is a 17yo female, onset of migraines age 12. At initial assessment, she experienced 6 to 8 migraines per month, which required visitation to the emergency room for either intravenous or intramuscular treatment. Migraines were generally right-sided, located frontally and last 8 to 10 hours. Associated symptoms included, aura, nausea, vomiting and photophobia. Headache frequency and severity were affected by periods and weather. Chiropractic and massage therapies aggravated the pain. Medications included; Elavil 37.5mg QHS, venlafaxine 75mg 2 tabs QAM, stemetil 10mg PRN, ES Tylenol PRN, ES Advil PRN and Gravol 50mg PRN. Past medical history revealed possible head injury age 11. Allergies were Imitrex, Penicillin and pollen. Work history included, McDonalds 2 days a week. Sleep 12-14 hours a night without feeling rested. Diet was noted as "unhealthy", with perpetual weight gain. Family history was positive for migraines. Her Memory and Concentration shows the headaches caused her to miss final exams. Her psychological background shows she is diagnosed with behavioral disorder and is estranged from her mother. Review of systems is positive for bloating and reflux and stiffness in the neck.

On physical exam (Table 1): BP 116/92mmHg, 76bpm, weight 179lbs. Neurological exam revealed; tender supraorbital nerves, zygomatic temporal, auricular temporal, greater occipital nerves all exacerbating headache, spasm of splenius capitis, scalenes, rhomboids and trapezius muscles bilaterally as well as right pectoralis minor muscles, ROM decreased in cervical spine especially with left rotation. All other exams WNL.

Investigations revealed MRI normal, and initial bloodwork if found in Table 1.
Migraine Disability Score (MIDAS) was 33, signifying severe disability.

Diagnostic Impression was:

1) Chronic Daily Headaches with Migraine
2) Mild Cervical Dystonia
3) Non-restorative Sleep
4) Anxiety
5) Obesity
6) Behavioral Disorder

Plan:

1) Cranial-Electrical Stimulation with Audiovisual Entrainment daily
2) Nutritional protocol with Plant-Based Omega supplementation
3) Discontinuation of all medic ations

Results:
One month: the patient reported 1 migraine and 2 minor headaches, lost 10lbs, reduced Elavil to 12.5mg, and discontinued all other medications.
Three Months: Discontinued all medications, reported improvement in

sense of control, less stress, reduction of 20lbs, with no migraines to report
Six Months: No migraines, more weight loss, re-established relationship with mother, doing very well at school, has first boyfriend, Blood Work: vit D level 74, vit B12 299, Hs-CRP 1.21* (now normal), only supplement taken was plant-based Omega, no more follow-up needed
Follow up MIDAS Score was 0

Case 2

Case 2 is a 56-year-old female. In January 2015, she developed right elbow swelling and pain, diagnosed as tendinitis. She was off work 1 week but the next week she developed a right frozen shoulder. She was given cortisone intraarticular in the emergency room and told she had calcium deposit in the joint space. Since then she has much more generalized pain. She now has back pain, recurring "crushing" shoulder and arm pain and intense "migraine" headaches. She has been unable to work and now on long term disability. Autoimmune disease was ruled out by a rheumatologist, she was diagnosed as fibromyalgia. She has pain everyday 8/10, lasting 24 hours a day. Nausea and photophobia were present without aura or vomitus. It is worse with stress, some relief with Cymbalta. Her past history shows chronic anxiety, hiatus hernia, migraines (rare), degenerative disc disease in the lumbar spine, and a whiplash injury x 2 in 2009. Her medication included Celexa 20mg QD, Imovane 7.5mg QHS, Sumatriptan 50mg PRN, Naproxen 275mg BID PRN, Ranitidine 150mg QHS, Ativan 0.5mg BID, ES Tylenol QD, and a multivitamin QD. One interesting fact is she moved into new house just before developing these issues. Work History: Customer Service Rep but now on LTD. She sleeps 2 to 5 hours a night, wakes up multiple times and finds it non-restorative. Diet she rates as average. Family history is negative for migraines or chronic disease. Her memory and concentration she has noted marked deterioration in short term memory and she can no longer read a book. Review of systems shows smell sensitivity, metallic taste, chest pains especially into shoulders and arms, chronically feels SOB, now gets abdominal bloating and cyclical vomiting lasting up to 12 hours requiring ER intervention, stiff muscles all over, anxiety and depression.

Physical Exam shows a BP 130/80, P 107, 160 lbs. She had tender supraorbital, zygomatic temporal, auricular temporal, greater occipital nerves, which exacerbated her headaches. She had spasm of the capitis, scalenes, rhomboids and traps with very restricted ROM of c-spine in all directions. She had 18/18 tender points of fibromyalgia.

Investigations: CT head normal, MRI head normal, Bloodwork: 25 Hydroxy vit D 64, Urinary Indican 3+, Magnesium 0.82 mmol/L, Hs-CRP 7.0* (normal <2), vit B12 306 pmol/L, AM Cortisol 441 nmol/L

Migraine Disability Score (MIDAS) was category IV or severe.

Impression:

1) Fibromyalgia-like syndrome with high inflammatory levels NYD
2) Chronic Daily Headaches with Migraines
3) Cervical Dystonia
4) Chronic Anxiety

5) Non-restorative Sleep Disorder
6) Memory and Concentration Impairment

Plan:

1) Nerve Blocks (did not tolerate)
2) Botox
3) Nutritional Supplementation with Plant-Based Omega's
4) Cranial Electrical Stimulation with Audio-Visual Entrainment

Results: After 4 weeks of Plant-Based Omega supplementation, headaches disappeared and have not returned and her other issues have improved but not resolved. Continues to be seen on an irregular basis but headaches have stayed away. MIDAS score not possible due to other chronic problems preventing a return to work.

Discussion

As health care moves from a disease-based model to a more patient-centric approach, a functional approach addresses biochemical individuality to address underlying mechanism that contribute to disease. Migraine is a complex condition with a myriad of underlying processes that contribute to the presentation. As such, an individualized functional approach to address the pathophysiology, genetics and lifestyle components improve clinical outcome and response beyond conventional pharmaceutical approaches is needed. In this case study, two patients suffering from migraine pain improved using a standardized pharmaceutical grade plant based blend of omega-6 and omega-3 fatty acids to address cellular mechanisms of migraine. Prior research has established the efficacy of LC-PUFA, mainly EPA and DHA, and their anti-inflammatory effects. However, their therapeutic influence extends beyond inflammatory pathways. PUFAs serve as precursors to eicosanoids and arachidonic acid to mediate prostaglandin, leukotrienes and thromboxane, which influence not only inflammation but vascular tone and intracellular signaling. In addition, EFAs integrate within the cellular membrane to influence fluidity, membrane bound enzyme activity and protein function. These effects influence neurological function through synaptic transmission, voltage-gated sodium channels and neuronal protein kinase alterations to potentially target underlying biochemical processes that contribute to migraine. With the emerging knowledge of the biochemistry of EFAs, balanced omega supplementation may be considered a successful adjunct to resolve migraines and reduce pharmaceutical administration. Further well designed studies are warranted to assess the role of essential fatty acids on migraines and potential use with other conditions.

Table 1

	Case 1		Case 2	
Values	Baseline	6 months	Baseline	
Weight	179lb	159lb	160lb	
BP	116/92 mmHg		130/80 mmHg	
Pulse	76 bpm		107 bpm	
Vitamin B12	318 pmol/L	299 pmol/L	306 pmol/L	364 pmol/L
25-hydroxy Vitamin D	75 nmol/L	74 nmol/L	64 nmol/L	130 nmol/L
hsCRP	3.6 (<2.0 WNL)	1.21	7.0	7.6
Magnesium	0.83 mmol/L		0.82 mmol/L	0.86 mmol/L
AM cortisol	376 mol/L		441 mol/L	
MIDAS	33 (severe)	0	>21 (severe)	0 for migraine
Urinary indican			3+	2+

Figure 1

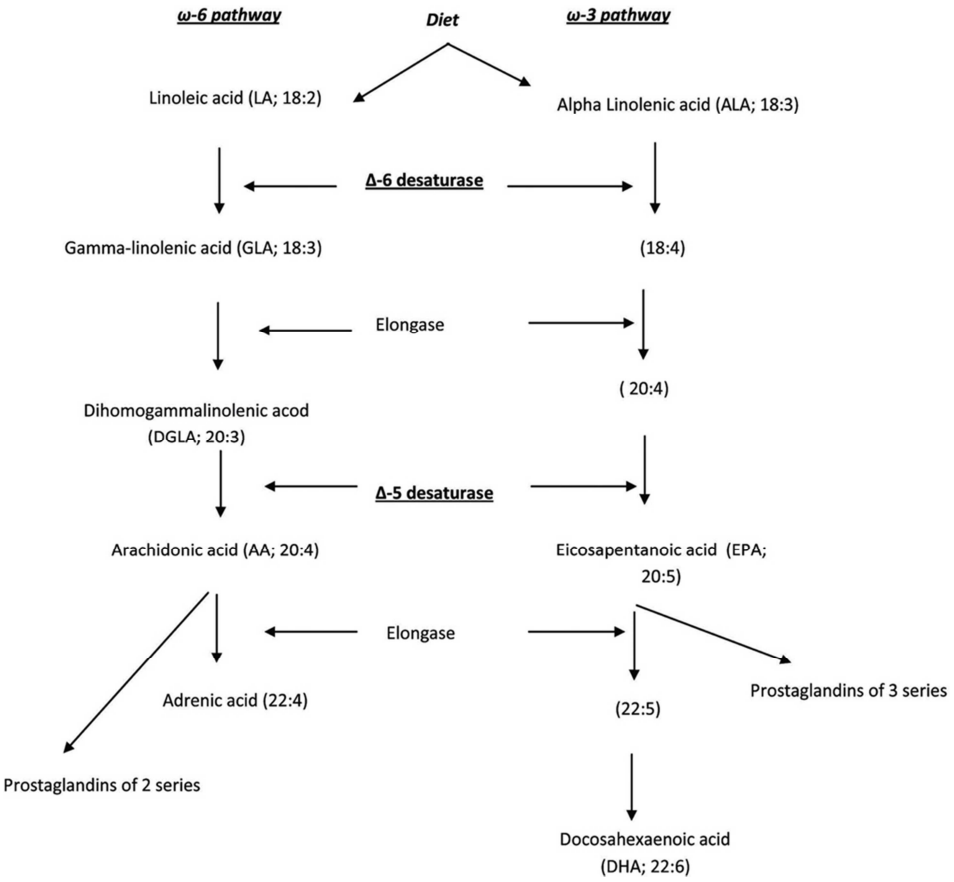
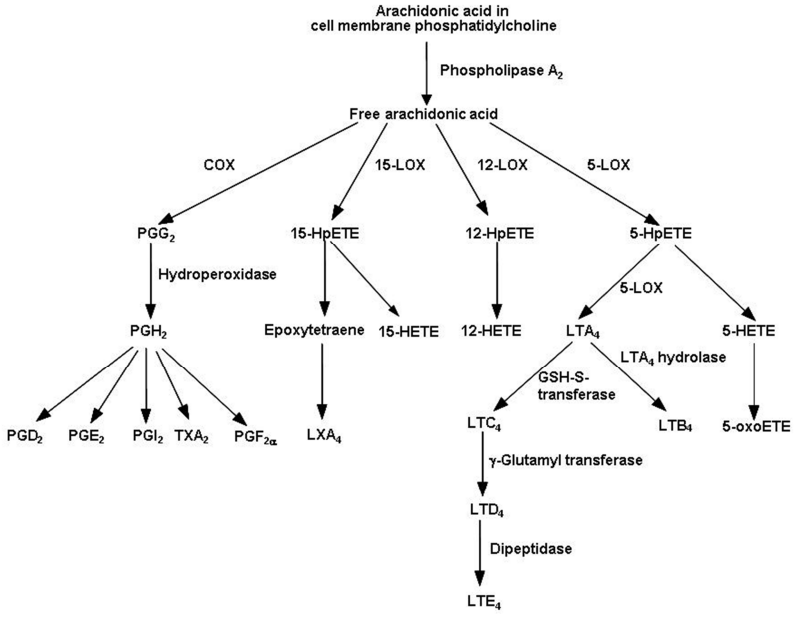


Figure 2 [xxxi]



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