Nutritional Considerations of Neurology

Presented by Dr. Ron Grabowski, R.D., D.C.
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Thinking Outside the Box
Epidemiological research has shown that in the United States, 18% of women and 6% of men suffer from migraines.

- 18 million females
- 5.6 million males over the age of 12 with this disorder.

30% of migraine sufferers report their first attack before the age of 10, and the condition is most common in adolescents and young adults.
Medical Costs Related to Migraines

• Annual cost of the disease estimated at 18 billion dollars.

• Migraine associated with moderate to severe disability afflicts more than 87 million women and 26 million men in the United States.

• Direct and indirect costs are estimated to be $5.6 to $17.2 billion in time lost from work and loss of productivity.

• Compared with patients without migraines, patients with migraines have greater morbidity in general and greater costs in health care resources.
Migraine Headaches and Children

• Migraine headaches are common in children and occur with increasing frequency through adolescence.

• An estimated 8 to 23 percent of children aged 11 to 15 years experience migraine headaches.

AAFP - 3/2005
2004 International Headache Society Classification of Headache Disorders: Criteria for Pediatric Migraine Without Aura

- Five or more attacks fulfilling features B through D
- Headache attack lasting 1 to 72 hours
- Headache has at least two of the following four features:
  1. Either bilateral or unilateral (frontal/temporal) location
  2. Pulsating quality
  3. Moderate to severe intensity
  4. Aggravated by routine physical exercise
- At least 1 of the following accompanies headache:
  1. Nausea and/or vomiting
  2. Photophobia and phonophobia (may be inferred from their behavior)
Medications & Migraines

- Ibuprofen is effective and acetaminophen is probably effective for treating migraine headaches in children and adolescents.

- Among adolescents, sumatriptan nasal spray is a safe and effective method for migraine treatment.

However, none of the oral triptans (rizatriptan, zolmitriptan) were found to be effective in treating migraines in children and adolescents.
Etiology

The basic cause of migraines are still unknown.

Although genetics may play a role, with 50% to 70% of migraine sufferers reporting a familial occurrence.
Pathophysiological Theories

- Vascular
- Central
- Platelet
- Neurogenic inflammation hypotheses
- Neurochemical
- Mitochondrial Dysfunction
Vascular

Has been a dominant concept in migraine pathophysiology, several difficulties arising from this theory, have been noted.

**FACT**

– During a common migraine attack, only minor changes in cerebral blood flow have been noted.
• Consequence of spreading neuronal depression, which begins as a result of decreased neuronal function in the occipital poles of the brain. It progresses forward at a rate of two to three millimeters per minute.

• Spreading depression involves the depolarization of neurons and has associated with it marked cellular ionic abnormalities.

• Lowered levels of cellular magnesium increase the likelihood of spreading neuronal depression occurring.

• Depression of neural function results in a spreading oligemia that can last up to four to six hours.

• The aura of migraine may be the result of spreading depression, "a phenomenon originating within brain neurons and involving cerebral blood vessels only secondarily."
Inflammation

• Migraine head pain may be the result of inflammation in the trigeminovascular system (TVS).

• Inflammatory neurotransmitters such as substance P, calcitonin gene-related peptide (CGRP) and neurokinin A are released by the fifth cranial nerve signaling adjacent meningeal blood vessels to dilate.

• Neurogenic inflammation sensitizes the neurons and this induces head pain.

• It is interesting to note that stimulation of the presynaptic serotonin receptor (5HT) blocks the release of Substance P, thus preventing inflammation and pain.
Neurochemical

- Platelets contain all of the 5HT normally present in blood, and, after they aggregate, 5HT is released, resulting in a potent vasoconstricting effect.

- During a migraine attack, platelet 5HT increases in the aura phase and diminishes in the headache phase.

- Following a migraine attack, this leads to an increase in Urinary 5-hydroxyindolacetic acid (5-HIAA), the main metabolite of serotonin.

- Many researchers have felt that serotonin (5HT) is the specific neurochemical, fuel for migraine.

- **Serotonergic circuits** are believed to be involved in modulation of sleep cycles, pain perception, and mood, all important factors in the pathogenesis of migraine.
A decrease in the firing rate of serotonergic neurons of the midbrain dorsal raphe nucleus occurs with sleep, correlating with the observation that sleep often aborts a migraine attack.

Serotonin may not be the only vasoactive chemical invoked in the pathogenesis of migraine.

- Histamine
- Tyramine
- Catecholamines (norepinephrine and dopamine)
- Prostaglandin E, and
- Free fatty acids may all have important roles to play in migraine pathogenesis.
Pathophysiology of Pain

• Release of vasoactive substances (e.g., substance P, calcitonin-gene related peptides and neurokinin A) from trigeminal nerve fibers induces a sterile inflammatory reaction around the blood vessels at the base of the brain and in the blood vessels of the aura and pia.
• This "neurogenic inflammation" may be accompanied by vasodilation and is triggered by nerve impulses originating in the caudal trigeminal nucleus.
• This effect is probably mediated by interaction with specific serotonin receptors ($5-HT_{1D}$).
• Stimulation of inhibitory ($5-HT_{1}$) serotonin receptors is thought to turn off neurogenic inflammation, whereas activation of the excitatory ($5-HT_{2}$) serotonin receptors can lead to migraine.
• Many medications used for migraine prophylaxis work by blocking $5-HT_{2}$ receptors.
Migraine Pathogenesis

Trigeminal ganglion

A trigger activates trigeminovascular fibers

5-HT_{1B/D}

Release of CGRP and SP

Neurogenic inflammation

5-HT_{1F}

Trigeminal nucleus caudalis

Cortex

Thalamus

Pain

Bianchi et al
Mitochondrial Dysfunction Hypothesis and Migraine Headaches

Sangiorgi et al. – 1994
- Defect of reduced NADH, citrate synthase and cytochrome c-oxidase platelet activities.

Okada et al – 1998
- Increase in lactic and pyruvic acid levels.

Sarkela – 2001
- NO radicals can be produced in this structure.
Magnesium and Migraines

- Current evidence suggests that up to 50% of migraine patients have lowered levels of ionized magnesium during acute attacks.
- Inhibits platelet aggregation.
- Serotonin receptors are altered.
- Nitric oxide synthesis and release are affected by magnesium status.
- Reduce the inflammatory eicosanoids.
- Calcium channel blocker.
Magnesium

**Deficiency increased with:**

- High CHO intake
- Stress
- Diabetes
- Alcohol
- Caffeine
- Diuretic therapy
Coenzyme Q10

Mitochondrial Relationship

- Proton-electron translocation in mitochondria.
- Protects mitochondria from oxidation.
- Plays a role in permeability transition of the inner mitochondrial membrane.
- Lowers serum lactate and pyruvate levels.
- > 50% reduction post 3 months
  ✓ Dosage 150 mg/day
Riboflavin

FMN and FAD
  – Electron transport chain
  – Synergistic with NAD and NADP

Amitriptyline
  – Increases the renal excretion of riboflavin.

(Pinto & Rivlin-1987)
Vitamin B12

Exerts a scavenging action against nitric oxide (NO).
- NO has been shown to inhibit respiratory chain by binding to complex I & III, and cytochrome c oxidase.

Homocysteine
- Homocysteic acid
  - Excitotoxin
Serum Vitamin B12

- Approximately 50 percent of patients with subclinical disease have normal serum $B_{12}$ levels.

AAFP – 2003
Homocysteine Metabolism
Choline
Homocysteic Acid

• **Endogenous agonist of N-methyl-D-aspartate (NMDA) receptors.**
  • Play a role in the initiation, propagation, and duration of cortical spreading depression.

• **Effect trigeminovascular system**
  • Sensitize the dura mater and cerebral arteries.
Nutritional Treatment

- **Magnesium**
  - 350 - 600 mg/day

- **CoQ10**
  - 150 mg/day

- **Riboflavin**
  - 400 mg/day

- **Vitamin B12**
  - 1000 mcg/day

- **Pantothenic acid**
  - 1500 mg/day
OMEGA-3 FATTY ACIDS

- May modulate prostaglandins & Leukotrienes
- GERD – caution
- Anti-inflammatory medications – caution
CHOLINE

- Deficient in cluster headaches
- Component of acetylcholine
- Lowers Homocysteine levels
- Found in lecithin
- Liver disorders – may be prone to deficiency.
COPPER

- Has been shown to induce migraine headaches.
- Citrus foods increase the uptake of this mineral.
Tyramine

- Vasopressor amine
- < 5 mg/day
- Foods: (6 mg – mild & 10 to 25mg – severe)
  - Cheeses, aged
    - Camembert
    - Cheddar
    - Stilton
  - Bologna
  - Pepperoni
  - Salami
  - Yeast extracts
Monosodium Glutamate

- Sodium + Glutamate
- Glutamate is the salt of the amino acid glutamic acid.
- Glutamate acts as an excitatory neurotransmitter.
- After ~ 90 seconds of contact, it causes swelling of nerves.
- Glutamate affects blood vessels in the brain.
Nitrites

- Associated with migraine headaches
- Sensitivity
- Foods:
  - Hot dogs
  - Bacon
  - Processed meats
Tension Type Headaches

Most common type of primary headaches.

Wheeler reported vitamin D deficiency in 40% of patients with migraines.

Approximately 40-50% of patients with TTH have low serum Mg levels.

Absorption of dietary Mg through the intestine depends upon vitamin D.

Headache – 2008 and 2009
Principles of Internal Medicine – 2006
Nutritional Neuropathies

• Optimal functioning of the central and peripheral nervous system is dependent on a constant supply of appropriate nutrients.

• Neurologic signs occur late in malnutrition.

Neurol Clin (2007)
Nutritional Deficiencies and Peripheral Neuropathies

- Thiamin
- Riboflavin
- Niacin
- Pyridoxine
- Pantothenic acid
- Vitamin B12
- Selenium
- Chromium
- Serine
- Copper
- Vitamin E
- Biotin
- Alpha Lipoic acid
- Acetyl L-Carnitine
Mirror Images

**Multiple Sclerosis**
- Optic neuritis
- Demyelination
- Peripheral neuropathy
- Myopathy
- Spastic gait
- Sensory ataxia
- Fatigue
- MRI changes

**Copper Deficiency**
- Optic neuritis
- Demyelination
- Peripheral neuropathy
- Myopathy
- Spastic gait
- Sensory ataxia
- Fatigue
- MRI changes

Clinical Manifestations of Vitamin B\textsubscript{12} Deficiency

**Hematologic**
- Megaloblastic anemia
- Pancytopenia (leukopenia, thrombocytopenia)

**Neurologic**
- Paresthesias
- Peripheral neuropathy
- Combined systems disease (demyelination of dorsal columns and corticospinal tract)

**Psychiatric**
- Irritability, personality change
- Mild memory impairment, dementia
- Depression
- Psychosis

**Cardiovascular**
- Possible increased risk of myocardial infarction and stroke.
Proton Pump Inhibitors

- **Medications**
  - Nexium
  - Aciphex
  - Prevacid
  - Prilosec
  - Protonix

- **Nutrients**
  - Vitamin B12
  - Calcium
  - Iron
  - Copper
Framingham Heart Study

Subjects aged 67–93 years

- High prevalence of inadequate B vitamin status.

- The percentages of subjects with inadequate B vitamin status were 30% for folate, 20–25% for vitamin B-12, and 20% for vitamin B-6.
Statins and CoQ10

CoQ10-lowering effect of statins and its compensation by administration of CoQ10 was described approximately 15 y ago and since then has been confirmed in numerous studies of animals and humans. 

AJCN (1/2000)

Long-term statin treatment may be associated with chronic peripheral neuropathy.

Adverse reactions—myalgia; myopathies; rhabdomyolysis; gastrointestinal symptoms, including hepatic injury; and the initiation or accelerated progression of cataracts and neoplasia—could be a direct or indirect consequence of the CoQ10-deficiency state associated with statin treatment.

AJCN (1/2000)
Chemotherapy Induced Neuropathy

- Peripheral neurotoxicity is a major complication associated with the use of chemotherapeutic agents such as platinum compounds, taxanes and vinca alkaloids.

- Some of the properties exhibited by Acetyl-L-Carnitine (ALC) include neuroprotective and neurotrophic actions, antioxidant activity, positive actions on mitochondrial metabolism, and stabilisation of intracellular membranes.

- The present studies support the use of ALC in cancer patients with persisting neurotoxicity induced by paclitaxel or cisplatin treatment. CNS Drugs – 2007;21

European J of Cancer – 2005,
Neurosci Lett. 2006, Apr 24
Diabetic Neuropathy

- Metformin – has been shown to decrease Vitamin B12 and folate levels.
- Acetyl-L-Carnitine (Diabetes Care – 1/2005)
  - Decreases symptoms
  - Improves nerve fiber regeneration
  - Improves vibratory sense.
- Biotin
- Alpha lipoic acid
- Chromium
Case Study #1

53 year old male
Initial visit: May 17, 2006
Previous diagnosis: Plantar fascitis
  – History: Burning feet bilaterally x7 years
  – Surgery: Calcaneal spurs removed seven years ago.
  – Examination: Negative for plantar fascitis and Tarsal tunnel syndrome
Medications: Nortriptyline – 25mg/bedtime, Tylenol arthritic pain – 1 tablet every 4 hours.
Supplementation with 1000mg pantothenic acid and within 4 weeks burning sensation was resolved.
Dosage is presently 500mg/day
Case Study #2

20 year old female

Initial visit: January 2, 2008

Chief Complaint: Migraine headaches and chronic sinusitis

- **History**: PMS, three to four sinus infections per year, migraines for the past four to five years, depression and anxiety.
- **Surgery**: Fractured fifth digit of right hand.
- **Examination**: Cheilosis, dry skin. Neurological and orthopedic examination was WNL.

Medications: **Yaz (OCA) and OTC analgesics and anti-inflammatories**

**SpectraCell**: Vitamin B12, Pantothenate and Vitamin D.

**Spectrox** - 57.5%

- **Marginal Values**: Riboflavin, folate, choline, serine, CoQ10 and vitamin E
Case Study #3

39 year old female

Initial visit: April 24, 2007

Chief Complaint: Migraine headaches and PMS

- **PM Hx.**: Depression and hypertension
- **Family Hx.**: Mother: Scleroderma and HTN, Sister: Depression
- **Examination**: Positive for chondromalacia patella and bilateral osteoarthritis of the knees.

Medications: Wellbutrin, and Prozac. Tylenol - prn

SpectraCell Results: Vitamin B12 and vitamin E deficiencies. Spectrox of 51.9%.

- **Marginal values**: Pyridoxine, folate, pantothenate, inositol, glutathione and magnesium.
Questions and Answers
Please join us next month, Thursday April 15\textsuperscript{th}, for our webinar on, “Nutritional Considerations of Endocrinology Part 1: Women’s Health.”

To register log on to \url{www.spectracell.com/webinars}