

Complementary and Integrative Medicine

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Disclosures

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- Non-prescription nutraceuticals, vitamins, and devices do not receive FDA indications in the same way that prescription medications do, but any discussion of off-label medications will be disclosed if presented during the talk.
- Consultant - GLG consulting, Lilly, Allergan
- Speaker - Lilly, Amgen

Goals for Talk

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- To discuss the role of Complementary and Integrative medicine (CIM) in the headache world.
- To describe what CIM means to patients.
- To highlight which CIM approaches are evidence based
- To discuss useful methods when discussing CIM with patients

Case Presentation

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- 44 year old female with past medical history of irritable bowel syndrome and anxiety presents with a thirty-year history of headaches. She reports the headaches occur 15 or more days monthly. Headaches are associated with photophobia, phonophobia, nausea, vomiting and worsening on exertion.
- She has had three brain MRIs with and without gadolinium which have been normal.



Case Presentation

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She repeatedly states that she has tried everything *under the sun* to treat migraine and is skeptical on anything helping her. She reports having intolerable side effects on all prescription medications tried so far. She is currently receiving botulinum toxin injections, from which she has 50% relief in headache frequency and severity.

She would like to discuss complementary and integrative medicine approaches to her treatment regimen.



Treatments tried so far...

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- | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> • Topiramate • Nortriptyline • Amitriptyline • Propranolol • Venlafaxine • Peripheral nerve blockade • Triptans • NSAIDS | <ul style="list-style-type: none"> • Cefaly device • Biofeedback • Cognitive behavioral therapy • Massage • Yoga • Unknown nutraceuticals from naturopath • Butterbur |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



What is CIM?

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- According to the National Center for Complementary and Integrative Health, more than 30% of adults and 12% of children use health care approaches developed outside of conventional medicine to add to mainstream treatments.
- The term "alternative medicine" alludes to replacing mainstream treatments with alternative treatments -- This term is not recommended, and should not be used interchangeably with "complementary medicine" or "integrative medicine".



CIM Limitations

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- There are no scientifically accepted criteria for inclusion or exclusion of specific modalities within CIM.
- Standards for inclusion or exclusion of a given modality as either conventional or CIM is by cultural fiat.
- Measures of efficacy and safety are often measured by qualitative standards that are culture-bound.



US News: 5 Red Flags Your Non-Conventional Medical Provider is Doing Harm

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5 Red Flags Your Non-Conventional Medical Provider is Doing Harm

An infographic on ways your public and family health could be harmed by dangerous practitioners and flags.

By Tracy Reardon-Webster, MPH, Director of Public Health, University of Michigan



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US News: 5 Red Flags Your Non-Conventional Medical Provider is Doing Harm

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- 1. They are conventional medicine-bashers
- 2. Their promises are too good to be true
- 3. They are product, test and technology-happy
- 4. They require a serious commitment
- 5. They have hazy credentials



Resource for Finding Credible CIM Practitioners

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- National Center for Complementary and Integrative health
- <https://nccih.nih.gov/health/integrative-health>



Overview of CIM Usage

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- Title: "Complementary and Alternative Medicine Use among US Adults With Headache or Migraine" by Zhang et. al. (Headache 2017)
- A secondary analysis of 2012 U.S National health interview survey data
- Objectives
 - To describe the CIM modalities that are used most frequently among migraine/headache sufferers
 - To explore the self-reported reasons for CIM use for migraine/headache sufferers
- 34,525 U.S. adults were included of which 6,558 were headache or migraine sufferers (18.7%, est. 43.9 million)
- Every 5 years, the survey includes questions about CIM use.



Overview of CIM Usage

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Study Results:

- CIM use highest in patients aged 30-64
- CIM use greatest in female Caucasians and Asian Americans
- CIM use greatest in college-educated, employed individuals with a higher yearly income
- CIM use greatest in Midwest / Western United States
 - Southern United states has the lowest prevalence of CIM use
- CIM use greatest in patients with a normal Body Mass Index (BMI)
- Half of the cohort also used conventional medications for headache/migraine (prescription drugs 47.7%, OTC drugs 55.1%)



Overview of CIM Usage

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CIM Modality	Number of Respondents	Percentage
Manipulative therapy	1,317	22%
Herbal Supplementation	1,389	21.7%
Mind-Body Therapy	1,100	17.9%



Why do patients turn to CIM?

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- Side effects or a "bad experience" with mainstream treatments such as prescription drugs
- A misconception that CIM is all natural and will cause less harm than mainstream treatments
- Mainstream treatments have been ineffective
- Patient has not been evaluated by a provider and prefers to treat "naturally" first



Patient perspective on social media

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"The saddest part for me is that I'm not to take any pain medication as most of them contain caffeine and paracetamol..... I take Inderal or Purbloka as prophylaxis for migraine.....but if for example...I wake up with a headache....taking prophylaxis doesn't help because all it does is prevent the headache...not make the pain go away if it's there already.....so I sometimes take pain meds though I know I shouldn't take it.....plus I was addicted to pain meds.....I was shaking like a leaf for a week when the neurologist told me to stop using pain meds...."



Epidemiology

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- 28-82% of headache sufferers use CIM approaches
- 50% of CIM users do not discuss their CIM treatments with their health care provider
- Most common practices in the US are meditation, breathing exercises and yoga



Classification of CIM Modalities

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- **Natural Products**
 - Riboflavin, Magnesium, CoQ10, Butterbur, Feverfew, Omega 3
- **Mind-Body Medicine**
 - Cognitive-Behavioral Therapy, Acceptance-Commitment Therapy, Meditation, Biofeedback, Exercise, Hypnotism
- **Manipulative and Body-Based Practices**
 - Massage, Chiropractic, Acupuncture, Cranio-Sacral



Complementary and integrative medicine
in the management of headache

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- By Denise Millstine, Christina Y Chen, Brent Bauer
- A literature review which searched English language papers published 2011-2016
- 608 clinical trials, systematic reviews or meta-analyses that focused on integrative medicine
- Randomized controlled trials (RCTs) and systematic reviews were prioritized



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Moderate evidence - Magnesium

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- cofactor in over 325 different intracellular reactions including protein synthesis, glucose metabolism, polynucleotide synthesis, cellular energy production and storage, stabilization of mitochondrial membranes, and in muscle function
- Involvement in cortical spreading depression - underlying mechanism in migraine with aura and possibly without aura.
- Mg deficiency more common in migraineurs, esp. menstrual migraineurs.
- 5 RCTs of magnesium for prevention of migraine
- one out of two Class I clinical trials—Peikert et al, showed a significant effect compared to placebo, while two out of three Class III studies showed such an effect.
- The best evidence is for prevention is at 600 mg



Moderate evidence - Riboflavin

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- Cofactor in electron transport chain of the Krebs cycle
- Riboflavin catalyzes the activity of flavoenzymes in the mitochondrial respiratory chain and its deficiency can result in mitochondrial dysfunction
- As mitochondrial dysfunction has been speculated in migraine, riboflavin has been studied for migraine prevention
- 11 clinical trials completed of which 5 showed a consistent positive effect
- A dose of 400 mg showed 50% improvement in 60% of pts (compared with 15% in placebo)



Limited evidence - Coenzyme Q10

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- coQ10 is an essential cofactor of the electron transport chain helps maintain mitochondrial integrity.
- Blocks endothelial dysfunction by stimulating endothelial release of nitric oxide
- Anti Inflammatory effects
- Magnetic resonance spectroscopy has shown evidence of interictal mitochondrial dysfunction in the occipital lobes of migraineurs
- One randomized control trial for migraine prevention in 43 patients
- -1.19 migraine attacks per month versus -0.09 in the placebo group



Mixed evidence - Feverfew

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- Daisy-like perennial plant
- Used in the 1st century by the Greeks for "all hot inflammations."
- Bioactive ingredient is parthenolide, which is thought to prevent migraine through antiplatelet, vascular smooth muscle relaxation and antiinflammatory properties.
- 4 studies total, 1 negative study (although a subanalysis showed benefit for people with at least 4 migraine attacks a month), 1 equivocal study and two studies showed some benefit



Limited evidence - Omega-3 Polyunsaturated Fatty Acids

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- Thought to have role in decreased platelet aggregation, vasodilation, anti-inflammatory effects and endothelial function.
- One RCT which showed no difference in the mean number of migraine attacks
- No adverse effects noted



Butterbur controversy

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- Butterbur / "Petasites hybridus"
- RCTs have shown a reduction in headache frequency
- Use is LIMITED due to safety
- Can be hepatotoxic due to naturally occurring pyrrolizidine alkaloids
- Can induce hepatic failure serious enough to require a liver transplant
- A 2012 evidence based guideline from the American Academy of Neurology was completely retired and considered invalid because of the group's desire to withdraw its endorsement of butterbur in the management of migraine



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Horizontal lines for notes

Moderate evidence - Acupuncture

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- 3 systematic reviews, 1 meta-analysis and 6 RCTs



Horizontal lines for notes

Limited evidence - Manual Therapy (chiropractors, massage therapists, osteopathic physicians)

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- two systematic reviews, one meta-analysis, and nine RCTs on the use of manual medicine in headache
 - BEWARE! Systematic review with lower quality studies due to inadequate control groups!
- Meta-analysis of 5 RCTs of 206 patients with Tension-type headache compared manual therapy with prescription drug therapy for 4-6 weeks
 - Immediately after intervention, headache frequency and severity improved
 - 20 week follow-up showed no significant improvement



Horizontal lines for notes

Limited evidence - Manual Therapy (chiropractors, massage therapists, osteopathic physicians) - migraine specific

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- RCT - 44 patients with migraine and active trigger points in the upper back and neck muscle groups compared positional release therapy (PRT) with routine medical care to routine medical care alone for two weeks.
 - four months' follow-up the PRT group had reduced headache frequency (reduction by 2 days over 2 weeks), severity and duration.
- RCT - 105 patients with chronic migraine compared osteopathic manipulative therapy (OMT) plus drugs, sham OMT plus drugs, and drugs alone over six months. It reported improved HIT-6 scores in the OMT group, sham and control.



Side effects of spinal manipulation

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- Occur 33-60.9% of the time
- Dizziness
- Neck pain
- Stiffness
- Local discomfort
- Stroke, artery dissection (5 per 100,000 manipulations)



How to discuss CIM with patients

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- Conventional therapy experiences
- Avoid judgement
- Review integrative approaches and their limitations
- Enquire why



Thank you for listening!

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Resources

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