Part 2

Integrative Approach for Patients with Intracranial Hypotension

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the gap in time…

onset ➔ diagnosis ➔ treatment(s) ➔ better

days… weeks… months… years… decades
... while waiting for "better"

Let's focus on what we CAN do to improve function + quality of life to optimize outcomes
Supplements for patients with intracranial hypotension
Types of supplements

- nutritional supplements
  - vitamins
  - minerals
  - amino acids
  - fatty acids
  - fiber
- botanicals (from plants)
- probiotics
to supplement or not?

- lifestyle interventions (nutrition, physical activity, sleep, etc) in place?
- evaluate need
- evidence of efficacy
- evidence of safety
  - side effects
  - contraindications
  - interactions with other supplements or medications
- discuss supplement use with your physicians
- role for judicious use if all of the above satisfied
- discontinue most supplements before procedures or surgery
Sourcing dietary supplements

- labeling
- quality / purity / potency
- adulteration (drugs or other unlisted ingredients)
- contamination (heavy metals)
- excipients (allergens, chemical sensitivities)
- get to know better supplement suppliers

- testing organization seals
  - manufacturing standards met
  - contains listed ingredients
  - tested for contaminants

NSF
USP
ConsumerLab.com

Approved Quality
3 common nutrient deficiencies

- Magnesium
- Vitamin D
- n-3 fatty acids
Magnesium

- > 60% in bones
- ~ 26% in muscles
- ~ 6-7% in other cells
- < 1% outside cells (fluids, blood)
Magnesium - in chlorophyll
Magnesium – functional roles

- over 325 essential metabolic reactions
  - energy production
  - energy storage – as Mg ATP
  - synthesis - RNA, DNA
    - neurotransmitters
    - proteins
    - glutathione
- active transport of Ca++ and Mg++ across cell membranes
  - nerve conduction
  - muscle contraction
  - peripheral vascular resistance
  - heart rhythm
  - cellular signaling
  - cellular migration
Symptoms of magnesium deficiency

- nausea, vomiting
- loss of appetite
- anxiety or depression
- insomnia
- headaches
- seizures

- fatigue
- generalized weakness
- muscle cramps
- muscle twitching
- palpitations (arrhythmias)
- constipation
Causes of magnesium deficiency

- inadequate intake
- inadequate absorption from gut or losses from diarrhea (IBD, celiac)
- urinary losses (alcohol, diabetes, diuretics)
- losses from exercise
- depletion from stress
- associated with medication use (PPIs)
Magnesium – role in patient care including brain + pain

- hypertension
- preeclampsia
- diabetes, insulin resistance
- anxiety disorders
- depressive disorders
- sleep
- osteoporosis
- constipation
- chronic fatigue
- fibromyalgia
- dysmenorrhea
- migraine, other headaches
- post-operative pain
- other pain
- medications that deplete magnesium
Testing for magnesium deficiency

- Serum magnesium
  - < 1% of body magnesium in serum
  - Serum magnesium tightly regulated
  - Insensitive test
- RBC (red blood cell) magnesium
  - More helpful but still misses many cases
- 24-hour urinary magnesium
- Ionic magnesium
  - Research labs only
foods rich in magnesium
Magnesium supplementation

Caution:
- impaired kidney function
- cardiac conduction abnormalities
- avoid with some meds (gabapentin)

Remember that nutrients work in networks
- Calcium / Magnesium / Vit D / Vit K

Oral tabs + caps
- Poorly absorbed: oxide, citrate
- Better absorbed: glycinate, taurate, malate

Transdermal
- Epsom salt = magnesium sulfate
- 1 – 2 cups in bathtub, soak for 15 minutes
Vitamin D is a pro-hormone…
- converted to calcitriol (a hormone)
- most cells have Vitamin D receptors
- > 2000 genes affected by Vitamin D
- widespread regulatory effects
- at least as important as insulin
Vitamin D deficiency

**Signs**
- rickets
- bone tenderness (shins)
- low bone mass on X-ray (osteopenia, osteoporosis)

**Symptoms**
- absence of symptoms
- fatigue
- muscle weakness
- muscle aches
- bone pain
Vitamin D and the brain

Roles
- neurodevelopment
- neuroprotection
- neurotransmission
- neuroplasticity
- gene expression

Research
- cognitive decline
- multiple sclerosis
- traumatic brain injury
- depression
- autism

*monotherapy largely ineffective*
Vitamin D and pain

- mechanisms not well-understood
- high prevalence of Vitamin D deficiency in patients with chronic pain
- mixed results with supplementation… several recent meta-analyses found benefit
  - decrease in pain score in people with chronic pain
    2016 Pain Physician, Wu et al
  - improved pain and function in patients with knee osteoarthritis
    2017 International Journal of Surgery, Gao et al
  - lower pain scores in patients with chronic widespread pain
    2017 Clinical Rheumatology, Yong et al
Vitamin D - supplementation

Supplementation
- guided by labs
- caution:
  - hyperparathyroidism
  - liver disease
  - kidney disease
  - kidney stones
  - sarcoidosis
  - tuberculosis

Serum testing
- test = 25 hydroxy vitamin D
- ref range 30 – 100 ng/mL
- rickets prevented at > 20 ng/mL
- bone health requires > 30 ng/mL
- most other diseases optimized at 40 – 60 ng/mL
- toxicity > 150 ng/mL
- conversion: 1 ng/mL = 2.5 nmol/L
n-3 fatty acids

- 2 polyunsaturated fatty acids are “essential”
  - n-3 : alpha linolenic acid
  - n-6 : linoleic acid
- n-3 fatty acids more often deficient
n-6 and n-3 fatty acids

**LA** (linoleic acid) - 18

**GLA** (gamma linolenic acid) - 18

**DGLA** (dihomo-gamma linolenic acid) - 18

**AA** (arachidonic acid) - 20

**ALA** (alpha linolenic acid) - 18

**EPA** (eicosapentanoid acid) - 20

**DHA** (docosahexanoic acid) - 22

ALA “essential” conversion in humans is inefficient levels of EPA + DHA often low “conditionally essential”
n-6 and n-3 fatty acids

Cell membrane

Extracellular space

Intracellular space

Protein channel

Carrier proteins

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n-6 and n-3 fatty acids

- Lipid mediators known as eicosanoids (prostaglandins, leukotrienes, thromboxanes)
  - Critical roles in immune and inflammatory responses
  - Regulation of cell growth and division
  - Blood clotting
  - Regulation of gene expression

Relative balance of fatty acids influences many aspects of health
n-3 fats and brain

Roles
- brain structure + volume
- brain function (mood, cognition)
- neuroendocrine function
- neuroimmune function
- neuroprotection
- neuroinflammation
- neuroplasticity
- gene expression

Research
- depression
- cognitive impairment, dementia
- learning, behavior, ADHD
- traumatic brain injury

combo therapies generally superior
n-3 fats and pain

Positive clinical trials

- pain due to rheumatoid arthritis
- painful periods
- myofascial pain syndrome, fibromyalgia
- chronic daily headache (diet)
- back pain
- diabetic neuropathy, other neuropathic pain
n-3 fatty acid supplements

- **ALA** (alpha linolenic acid) - 18
- **EPA** (eicosapentanoid acid) - 20
- **DHA** (docosahexanoic acid) – 22

**ALA** “essential” conversion in humans is inefficient, levels of EPA + DHA often low “conditionally essential”

- lab testing available -

- **ALA** – abundant in plant foods, flax seed
- **Marine sources of EPA + DHA**
  - Fish oil
  - Marine algae (vegan)
Curcumin

- the most studied botanical, extracted from turmeric root
- curcumin = several curcuminoids
- human clinical trials in many diseases
Curcumin – many molecular pathways

- anti-inflammatory
- anti-oxidant
- anti-nociceptive
- anti-bacterial
- anti-viral
- anti-fungal
- anti-cancer
- anti-atherogenic / cardioprotective
- pulmonary protective
- neuroprotective

- hepatoprotective
- nephroprotective
- chondroprotective
- radioprotective / radiosensitizer
- chemosensitizer
- anti-diabetic
- wound healing
- immunomodulation
- modulation of transcription factors
- modulation of action of growth factors and cytokines
Curcumin - brain and pain

Human clinical trials and BRAIN
- cognitive decline in elderly
- cognition + mood in healthy pts
- occupational stress
- depression (alone or add-on to meds)
- anxiety

Human clinical trials and PAIN
- osteoarthritis of knee
- rheumatoid arthritis
- post-op pain
- delayed-onset muscle soreness
- recent trial using combo with n-3 fats in migraine

Note: patient numbers small in most trials
Curcumin supplements

- **low bioavailability** - several formulations with enhanced bioavailability

- **generally safe but caution**
  - gallstones
  - blood thinning meds, pre-op
  - iron deficiency
  - potential for drug interactions
  - (turmeric but not curcumin high in oxalate - kidney stones)
Behavioral + Mind-Body Approaches for patients with intracranial hypotension
THE MIND-BODY PROBLEM

Get up.

No.
Mind-Body?

**STRESS response**
(sympathetic activation)
- heart rate ↑
- blood pressure ↑
- respiration rate ↑
- dilated pupils
- slower gut function
- tight muscles
- catabolic

**RELAXATION response**
(parasympathetic activation)
- heart rate ↓
- blood pressure ↓
- respiration rate ↓
- constricted pupils
- digestion
- relaxed muscles
- anabolic
Vagus Nerve Stimulation

- invasive VNS; non-invasive VNS: autonomic neuromodulation of the 10th cranial nerve

- vagus nerve has regulatory roles in
  - neuro-endocrine-immune axis
  - peripheral + central pain mechanisms
  - mood
  - inflammation
  - memory

- research
  - 1º headache disorders: migraine; cluster
  - refractory epilepsy
  - depression; bipolar disorder
  - dementia
  - fibromyalgia
  - pain
  - asthma
  - gastroparesis; irritable bowel syndrome
  - traumatic brain injury; stroke
  - heart failure
Vagus Nerve Stimulation

gammaCORE ®

non-invasive vagus nerve stimulation device
FDA-approved for cluster headache

also approved for use in Europe, Canada, Australia, other countries
EFFECTS of mind body approaches

- pain
- sleep
- mood / anxiety / stress
- nausea / gut function / gut flora
- cognition
- cardiovascular function
- tissue healing
- immune function
- hormone function
Mind-Body therapies

- breathwork
- cognitive-behavioral therapies
- biofeedback
  - heart rate variability biofeedback
- mindfulness
- progressive muscle relaxation
- meditation
- hypnosis, guided imagery
- prayer
- disclosure, journaling
- virtual reality
- creative arts, music therapy

Evidence of safety and effectiveness for several approaches
Mind-Body component

- yoga
- Tai chi
- Qigong
- massage
- ANYTHING you do to relax
  - time in green space
  - adult coloring
  - jigsaw puzzles
  - time with with people, pets

Photo credit Laura Williams
Summary

Multi-modal approaches more effective than single approaches
Lifestyle can impact QoL

**Nutrition / supplements**
- pain
- sleep
- energy
- mood, stress, cognition
- tissue healing
- insulin sensitivity

**Physical activity**
- pain
- sleep
- energy
- mood, stress, cognition
- balance, strength
- insulin sensitivity

**Mind-Body**
- pain
- sleep
- energy
- mood, stress, cognition
- tissue healing
Integrative approaches for patients with intracranial hypotension

- treat underlying problem
  - spinal injections + surgery
- position change
- hydration
- tincture of time
- medications (Rx and OTC)
- assistive devices (compression garments)

- treat co-morbid disorders
- nutrition
- supplements
- physical activity + physical therapy
- mind-body
- sleep
- other therapies (nerve blocks, Botox, acupuncture, etc)
closing the gaps...

onset of symptoms → faster diagnosis → refined imaging → refined treatments → better sooner

prevention → awareness → education → research → research