The Gut and Autoimmunity

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No conflicts here
Overview

- Thought process for assessing patients related to diet, inflammation and the gut
- Three pathways of inflammation related to diet
  1. Gluten, dairy and food sensitivity
  2. Histamines and inflammation
  3. Bacterial overgrowth/dysbiosis and gut inflammation
- Case Study
Pathway #1

Food Sensitivities: Gluten

- Elimination of potentially antigenic foods important in reducing GI inflammation
- Wheat and dairy most problematic, most consumed
- “Intestinal cell damage and systemic immune activation in individuals reporting sensitivity to wheat in absence of Celiac Disease” (1)
- Increase in soluble CD14 and lipopolysaccharide-binding protein (1)
- Increase antibody reactivity to microbial antigens, indicating systemic immune activation (1)
- Elevated levels of fatty acid-binding protein that correlates with the markers of systemic immune activation, suggesting compromised intestinal epithelial barrier integrity. (1)
- Gliadin in wheat can increase intestinal permeability (2)
Pathway #1
Food Sensitivities: Dairy

- Lactose intolerance? Casein sensitivity?
- There is research indicating that certain dairy proteins can be inflammatory to the digestive tract
- Research on A1 vs A2 beta proteins (3-4)
- A1 protein derived from hybridization of Holstein and other cows
- A1 has potential to be most inflammatory to the intestinal lining
- A2 beta protein from Jersey, Guerney and other cows and others has been shown to be less reactive in those with dairy sensitivities
- Goat and sheep are all A2 which may be why we see less reactivity to this dairy
Pathway #2
Histamines

- Via H1-H4 receptors, histamines impact numerous systems (5-6)
Summary of histamine-mediated symptoms

Laura Maintz, and Natalija Novak Am J Clin Nutr 2007;85:1185-1196
Assessing for Histamines

Common Symptoms

- Year round allergy symptoms (rhinitis, itchy eyes)
- Worsening of symptoms with stress
- Urticaria
- Anxiety
- Insomnia
- GI issues common
- Episodes of tachycardia
- **Perimenopause**: Increase in hot flashes, insomnia, painful menses
- Worsening of pain with seasonal change
- Hypotension
- Headache/migraine
Cause and impact of histamines in RA

- Onset of symptoms typically during long period of stress, illness/infection, trauma. Often combined with perimenopause.

- Boiling pot effect, multiple situations occur at once

- Excessive histamine production can lead to multiple symptoms including swelling in joints, pain

- Research linking histamine (H4 receptors) to RA. \((7-8)\)

- H4 antagonist has reduced arthritic pain via reduction IL-17 in vitro. \((9)\)

- Studies have shown increase in H4R in synovial fluid cells. \((10)\)

- No reliable serum markers \((24\) hr urinary methylhistamine, tryptase, histamine, etc.)
Low histamine diet
Foods to remove

- Aged, fermented foods especially high in histamine
- Wine, cider, beer
- Aged meats/cheese/vinegar/pickled foods
- Tomatoes, eggplant, spicy peppers, spinach, pumpkin
- Citrus fruit, banana, avocado, strawberries, raspberries
- Most nuts
- Chocolate, more
Case Study: Histamine

- 36 yo female
- RA dx, seroneg.  Onset post partum.
- Joint pain in thumb, wrist, shoulder; flares random lasting 3-4 day in duration
- GI: Daily diarrhea (watery, urgent).  11 year history of “sensitive stomach” after travel to Panama.  GI workups normal.
- Sx worsen with menstruation, stress.
- Chronic allergy sx including itchy eyes, rhinitis
- HCQ reduced the intensity of pain. Declined Humira.
Case Study: 4-Week F/U

- After one day on low histamine diet, significant reduction in joint pain
- Diarrhea reduced in intensity, now soft stools mixed with episodes of diarrhea
- Introduced both histamines and wheat into the diet and found reactivity to both, so has kept out/low
- About 80% improvement in symptoms with joint flares less often, less intense. Still present.
Reducing histamine production

- Determine personal tolerance threshold to dietary histamines
- Reduction in stress, counseling, meditation
- For some women in perimenopause, progesterone replacement
- Medication? H1/H2 may not be effective
- Home environment, reducing potential allergens, chemical sensitivities
Reducing histamine production

- Filtered water critical
- Supplementation: Vitamin C, quercitin, stinging nettle, DAO
- Assessing for small intestinal bacterial overgrowth or dysbiosis
- Leading to Pathway #3…
Microbiome of the Small Intestine

- Average amount of bacteria in the small intestine in the 100,000’s

- Average amount of bacteria in the large intestine average is 100,000,000,000

- Bacteria in the small intestine present as part of immune system, help with nutrient digestion

- Keep balance of the small intestine through peristaltic waves and pH balance
Small Intestinal Bacterial Overgrowth

- When bacterial concentration increases above normal amounts

- Typical causes include post infectious gastroenteritis (food poisoning), c. Dif infection, long term use of PPI’s, antibiotics, long term stress, thyroid, IC valve disruption, adhesions

- Symptoms include severe flatulence/belch, abdominal bloat, constipation or diarrhea, heartburn.

- GI diagnostics typically negative. Dx: “IBS”
SIBO: Link to Autoimmunity

- Bacterial infection of c. Jejunii, Salmonella, e. Coli, c. Diff, Shigella can lead to increase in CdtB toxin (12)
- Triggers immune response to CdtB toxin → GI inflammation (12)
- CdtB toxins are structurally similar to vinculin, a protein that helps to manage the MMC (migrating motor complex) which helps to maintain motility (12)
- Molecular mimicry leads to creation of anti-Vinculin antibodies (12)
- Reduced motility leads to reduced peristaltic/cleansing waves, constipation, increase in bacterial concentration in SI (12,13)
Symptoms and effects

- Overgrowth increases hydrogen/methane gas and endotoxin in the GI causing intestinal bloat, inflammation (11)

- Those with IBS have been found to have intestinal intestinal permeability. Unclear relationship between SIBO and permeability. (14)

- Permeability can lead to translocation of bacteria and endotoxin (14)
Studies

Studies and published case studies linking SIBO to systemic inflammation.

- Rosacea (15)
- PMR (16)
- Sleep apnea (17)
- Hepatic encephalopathy and NAFLD (18)
- IBS (19)
- Parkinson’s Disease (20)
- Diabetes (21)
- Fibromyalgia (22)
- IBD (23)
- Pancreatitis (24)
- Prostatitis (25)
Hydrogen breath testing

- Current best way to diagnose bacterial overgrowth is through lactulose hydrogen breath testing (26)

- Available through UW Gastro, VM Gastro, Seattle Children’s (for peds only), Puget Sound Gastro Eastside, external clinics who specialize

- Test involves a special prep diet, fast and 3 hour breath collection after drinking lactulose solution

- Measures concentration of hydrogen and methane production in the small intestine

- Not perfect but best we currently have
Treatment options

- Antibiotics: Rifaximin (H2) Neomycin Sulfate (CH4) (11, 27, 28)
- Herbal antibiotics
- Medical food fast x 2 weeks (starve them out)
- f/u treatment with prokinetic (Erythromycin) 29
- Diet modification: Low FODMAP diet (30)
Diet for SIBO

- Low FODMAP/starch/sugar diet \(^{(30)}\)
- Reduces fuel for bacteria
- Similar to Paleo/AIP approach but low in fermentable fruits and vegetables
- Broccoli, cauliflower, brussels sprouts, cabbage, garlic, onion, apples, pears, stone fruits, lactose
- Diet consists of high animal protein, vegetable, fruit, nut, lactose-free dairy
The histamine connection

• Some species of bacteria have been shown to increase histamine production: (L. casei and L. bulgaricus) 31

• Others have shown to decrease histamines: L. rhamnosus, B. infantis, L. plantarum 32

• SIBO can contribute to histamine production and contribute to the boiling pot effect
Case Study Continued

- Patient’s RA pain improved on low histamine diet.
- Ordered hydrogen breath test
- Positive for hydrogen producing bacteria (37 ppm at 60 mins increasing to 92 ppm at 120 mins)
- Rifaximin: 550 mg tid x 14d
- f/u tx: Erythromycin 250 mg qhs ongoing
- Omit fodmaps, starches, limit histamines
# First Hydrogen Breath Test

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<tr>
<th>Time</th>
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<th>#3 H2 ppm</th>
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Complete cessation of joint pain, diarrhea during the antibiotics

2 weeks post tx: Return of diarrhea, joint pain completely abated

Tx: Rifaximin 550 mg tid x 14 d

2 weeks post tx: Stools firm, with only occasional diarrhea, joint pain abated

Ordered follow up HBT
Second Hydrogen Breath Test

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Ongoing Treatment

- Garlic/oil of oregano, probiotics (lactobacillus GG)
- Erythromycin 250 mg ¼ cap qhs ongoing. Will likely maintain long term.
- f/u HBT still positive, but continues to improve
- Rotational herbals (garlic/oo).
- Patient continues to do well with no joint pain or diarrhea
- Dc’d HCQ without return of joint pain
- Slight joint flares with menstruation, which she keeps under control with reduced dietary histamines
- Back to grains and FODMAP’s without issue
- Self-managed currently
# Third Hydrogen Breath Test

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Observations and Patterns

- Clinically, I have observed prevalence of bacterial overgrowth in patients with EDS, Scleroderma, Crohns, Rheumatoid Arthritis, Ankylosing Spondylitis, reactive arthritis and undetermined inflammatory arthritis.

- Treating bacterial overgrowth doesn’t always reduce symptoms of joint pain/inflammation but can improve quality of life by improving intestinal function especially in those debilitated by chronic diarrhea or constipation.

- Severe constipation can increase lower back pain.

- Those with histamine issues don’t always have bacterial overgrowth and vice versa.
Conclusion

- There is a correlation between diet and inflammation. Food sensitivities, histamines in foods, or the nutrients that feed bacteria can all impact inflammation in the gut.

- Histamines may impact inflammation that leads to inflamed joints and other allergy symptoms. Low histamine diet and stress reduction can help.

- Bacterial overgrowth or dysbiosis can increase gases, histamines and endotoxin production that can increase gut permeability, food sensitivities and may increase systemic inflammation.

- If patient not responding to Rx treatment, look at other symptoms related to allergy or GI that could help you consider another pathway of inflammation.

- If patient has excessive IBS sx, refer to GI doc who specializes in SIBO for treatment or RDN in private practice to help make dietary change
Thank you!

- Heidi Turner, MS, RDN
- The Seattle Arthritis Clinic @ Northwest Hospital/UW Medicine
- www.theseattlearthritisclinik.com
References

Gluten and gut/systemic inflammation


Dairy and gut inflammation

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Overview on histamine intolerance


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SIBO overview

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SIBO/GI and Autoimmunity


SIBO and intestinal permeability

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SIBO and other inflammatory conditions


SIBO and breath testing

References

SIBO and Antibiotics


SIBO and low FODMAP diet

References

Bacteria that increase/decrease histamines


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Histamines and Autoimmunity (cont)


Herbal remedies to reduce mast cell activation, histamine production


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