



RhAPP

RHEUMATOLOGY ADVANCED
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Integrative Medicine

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Faculty Disclosures

- Amanda Mixon – I have no relevant disclosures pertinent to this presentation
- Dr. Lisa Butler – I have no relevant disclosures pertinent to this presentation

Case Presentation

- 40 year old female being seen for routine follow up regarding her psoriatic arthritis and Sjogren's syndrome.
- PMH notable for CVID (gets monthly IVIG).
- Not on any medications. Manages symptoms with diet, exercise, and OTC remedies. Has been reluctant to take more meds given CVID.

Case Study Cont...

- Chronic GI issues
 - Has chronic dysphagia, bloating, nausea, diarrhea
 - Has seen GI – told she has GERD and IBS – told to take a PPI daily, which she has not wanted to do
 - Continues to struggle daily. Has lost weight. Diet is extremely limited

Case Study Cont...

- Physical exam
 - Vitals normal – wt 124, BP 120/80
 - Looks tired. Very thin
 - Joint exam unremarkable – no synovitis
 - Raynaud's changes to fingers, toes – no ulcers
 - Diffuse abdominal tenderness, BS normal, no masses
 - Heart, lungs unremarkable
 - Minimal psoriasis to scalp

Case Study Cont....

- Conversation about tx options – does not want DMARD therapy because of CVID which is reasonable as disease is mild
- She is very concerned about ongoing GI issues. Feels blown off by GI. Feels desperate and that no one wants to help her
- Has seen a naturopath and brought some studies for me to review

Case Study Continued...

- **Results:**

- CBC – WBC 4.3, HGB 13.9. PLT 188, **Lymphs 0.3, Monocytes 0.2**, Neuts abs 3.71
- Sed rate 6
- CRP 1.9
- **Tpo Ab 79**, Reverse T3 16.8 , TSH 2.37, Free T3 2.4
- CMP – Na 135, BUN 9, Creat .76, Calcium 8.2, Alb 3.1, Glob 4.3, Tot prot 7.4, AST 27, ALT 24
- Zinc 112, CU 123, Ceruloplasmin 22.9

Case Study Cont...

- No clue what to do... so I call Lisa to help!

Integrative Medicine Perspective

- Gut health is strongly linked to autoimmune diseases. Increased intestinal permeability and disruptions of the intestinal microbiome are considered to be two risk factors for development and exacerbation of autoimmune conditions
- Gut health influence on immune system
 - Absorption of nutrients in proper ratios
 - Inflammation within the gut
 - Systemic inflammation stimulated by increased gut permeability
- All three are interrelated and influence each other
- **Patient in case describes GI issues diagnosed as IBS and GERD**

Irritable Bowel Syndrome (IBS)

Symptoms

- Abdominal pain – hypersensitivity
- Diarrhea
- Constipation
- Bloating and gas

Pathogenesis

- Onset typically after a viral gastroenteritis or food poisoning
- Development of antibodies to a human cell migration and adherence protein called vinculin (antibody test available)
- Migrating Motor Complexes (“housekeeping” peristaltic waves) in the small intestines are reduced causing abnormal movement of substances through the small intestine

IBS Treatment

FODMAP Diet

- Reduces fermentable foods to reduce bloating and discomfort but does not treat the underlying problem of dysbiosis
- Monash University is the authority on what is included

Antibiotics

Herbals

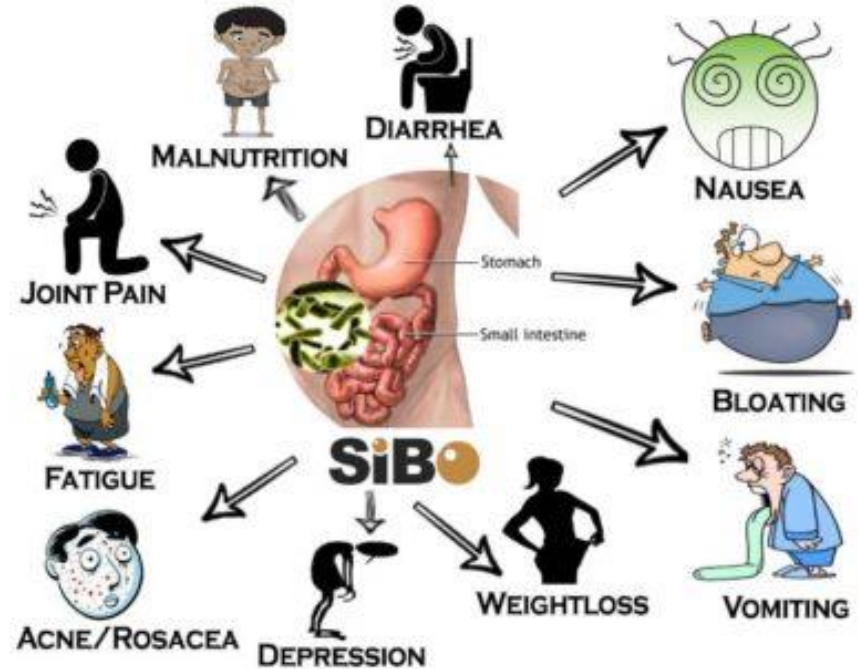
Medications

- Numerous medications for control of symptoms including diarrhea, constipation, and pain

Is It Really SIBO?

Small Intestinal Bacterial Overgrowth

- Rule out life-threatening disease first (GI consultation)
 - EGD with biopsy Celiac and H Pylori
 - Colonoscopy
- SIBO is a functional problem, not a “disease”



Pathogenesis in SIBO

SIBO is a direct consequence of IBS – Irritable Bowel Syndrome

IBS



SIBO

- Onset typically after a viral gastroenteritis or food poisoning
 - Development of antibodies to a human cell migration and adherence protein called vinculin (antibody test available)
 - Migrating Motor Complexes (“Housekeeping” peristaltic waves) in the small intestines are reduced causing abnormal movement of substances through the small intestine
- Bacteria are allowed to proliferate and some colonic bacteria may cross into the terminal ileum
 - Proliferation of the wrong microbial mix causes dysbiosis (abnormal composition of flora) or bacterial overgrowth (SIBO)

SIBO Diagnosis

Diagnosis:

- Lactulose Breath Testing \$\$\$
 - Patient drinks lactulose then supplies at least three hourly breath samples which are assessed for Hydrogen and methane production increase of > 20 ppm of either gas is a positive test.
- Clinical Diagnosis
 - Bloating
 - Nausea
 - Diarrhea or Constipation
 - Dysphagia
 - Weight loss or Stable weight

Figure 6: Late Double Peak

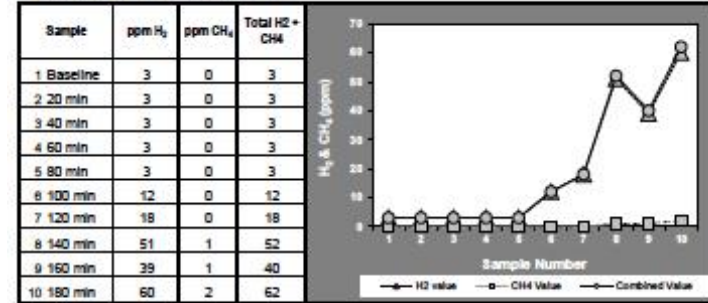
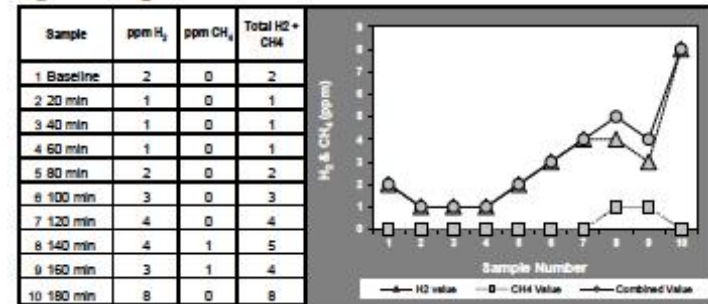


Figure 7: Negative Test



SIBO Treatment

Rifaximin

- Antibiotic specific to small intestine
- No systemic absorption and no effect on large intestinal flora
- Immune modulating properties which impact gut inflammation
- Can be used repeatedly for “IBS” and SIBO. Indication is for IBS-D.
 - 550 mg three times daily x 2 weeks
 - Cost: \$1500-2000
 - No generic currently on the market

Herbal protocols

- Effective per studies
- 4 week of treatment
- Several options of supplements (*see attached references*)

Response to Treatment

Improvement or resolution of symptoms

- Decreased pain
- Decreased bloating
- Improved stool consistency

Improvement of gut health

- Decreased gut permeability
- Decreased inflammation
- Modulation of gut microbiome
- Modulation of gut immune signaling

Anti-vinculin antibodies persist which means symptoms can return, often after another trigger.

Additional treatment to promote migrating motor complexes (housekeeping peristalsis) may be needed if persistent.

Promoters of small intestinal motility include low-dose Erythromycin (50 mg daily) or Ginger 500 mg 1-3 times daily.

Absorption of Nutrients

Nutrient absorption may be altered by:

- Medications
 - Methotrexate
 - Prednisone and NSAIDS
 - Medications Rx by other providers
- IBS or SIBO
- Diet
 - Reduced consumption due to symptoms
 - High processed food diet
- Supplements
 - Patients supplement and sometimes don't really know what they are taking
 - Protein Powders or Smoothies
- Water
 - Filtered water
 - Well water
- Smoking
- Alcohol use
- Lack of digestive enzymes

Digestive Enzymes

Consider adequacy of digestive enzymes in cases of

- Multiple nutrient deficiencies
- Advanced age
- Any sign of pancreatic failure (type I DM, chronic pancreatitis)
- Smoking
- Diets high in sugar, alcohol, processed foods
- Food sensitivity
- Severe emotional or physical stress
- Chronic GI inflammation or symptoms, IBD, celiac disease
- High levels of antibiotic use

Enzymes

- Pancreatic
- Brush Border
- Salivary

Nutrients to Watch

Vitamin D

- Commonly low unless supplemented. Improves outcomes in treatment of rheumatologic diseases.

Calcium

- Often low with PPIs.

Zinc

- Often low with PPIs. Critical in immune response.

B-12

- Testing poor for evaluation. Some studies indicate target level 800 for adequacy because most testing misses deficiency at cellular level. Some recommend using Homocystine as marker for B-12 but not much better.

Nutrients to Watch (Continued)

Folate

- Folic acid vs. Methylfolate debate with integrative/functional medicine. Methylfolate generally recognized as improved response to lower dose especially if MTHFR variant.

Magnesium

Copper

- Free copper vs Serum copper and Ceruloplasmin
- Serum copper – 3x Ceruloplasmin = Free Copper
- Ceruloplasmin is an acute phase reactant and may be elevated in inflammatory diseases (SLE/Lupus), malignancies or in other illnesses that may affect copper metabolism. It may also be raised by excessive levels of phenylalanine and tyrosine.

Selenium

- Especially important for patients with thyroid antibodies for proper function of thyroid. May help reduce antibodies if supplemented 200 mcg daily or 5-7 Brazil Nuts.

Nutrients to Watch (continued)

Omega 3

- Improves outcomes in DMARD treatment according to some studies. Tests are available but given improvement shown with virtually all other chronic diseases (cardiac disease, GI disease, diabetes) reasonable to supplement. 1-4 grams is recommended treatment. Start low and go slow.

Iron/Ferritin

- May be low with chronic NSAIDS or prednisone. Ferritin as acute phase reactant may be artificially elevated but if < 30 indicates iron deficiency. Testing serum iron is not much use.

Case Considerations

Diagnoses

- IBS
- GERD
- Psoriasis
- Raynauds
- Sjogrens

Lab abnormalities

- Lymphocytopenia
- Calcium – actually normal when corrected for low albumin
- Thyroid antibodies
- High-normal Zinc
- Elevated free copper NI < 25

Implications of altered levels of copper:

- Gut disturbance
- Myalgia
- Neuralgia
- Psychiatric disorders including depression and psychosis
- Lymphocytopenia

Copper and Zinc intake antagonize each other

- Zinc low / copper high – supplement Zinc Sulfate or Glycinate 50 mg daily to lower copper levels.
- Zinc high / copper high – check for supplementation and discontinue
- Zinc high / copper low – check for supplementation recommend combination supplement Zinc 25 mg with Copper 2 mg if patient desires to continue

Case Considerations

Given findings, patient's use of a Naturopath, and chronic gut issues priorities include:

Treat Gut issues

- Treat for SIBO
- Address microbiome with probiotics – evidence-based probiotics are available from multiple pharma companies
 - Include beneficial yeast – *Sacchromyces Boulardii* for balance
- Eliminate triggering foods and reintroduce individually, monitoring for increased symptoms. With some exceptions, most foods can be reintroduced within 3-6 months without issue.
 - Exceptions:
 - Celiac disease
 - True allergies (IgE mediated)
 - Food sensitivity testing (IgG) is generally not helpful. IgG testing will yield different results day to day. It may provide a starting point for elimination but is an expensive way to do so. I do not use IgG testing.
- Test for digestive enzymes if you feel it is warranted
 - Pancreatic – Fecal Fat and Elastase – supplement if deficient
 - Brush Border – Breath testing is available for lactase and sucrase/isomaltase deficiency
 - – Other brush border enzymes no available testing or supplementation
 - Salivary – In cases of Sjogrens, salivary enzymes may also be deficient

Case Considerations

Review all supplements, remove any unnecessary supplements and add needed supplements

- Targeted supplementation for nutrients with verified deficiency or those affected by medications
- Exceptions include Vitamin D and Omega 3 fatty acids which benefit most patients with Rheumatologic Diseases
 - Vitamin D to achieve a serum level of 60-80
 - Omega 3 fatty acids 1-4 gm daily (start low and go slow to avoid diarrhea)
- I have seen cases of supplement-induced lupus with positive labs which resolved upon cessation of supplements

It is essential to educate patients regarding what they take and whether it is necessary.

Case Considerations

Assess diet and lifestyle for exacerbating factors – not necessarily in detail but look for big red flags

- Many people with health issues may try exotic diets. These diets may not only be unnecessary, in some cases they may be harmful
 - Restricted eating
 - Timed-restricted feeding / intermittent fasting
- Alcohol and drug intake may affect nutrient status and response to medications
- Extreme intake of artificial sweeteners like Nutrasweet could affect Ceruloplasmin
- Filtered water or water in potentially contaminated areas
 - Demineralized water may affect the status of multiple minerals negatively impacting the efficacy of medications, altering bone density, and increasing the risk of heavy metal toxicity if exposed through other sources

Case Considerations – Disease Specific

Disease specific considerations

- Psoriasis and psoriatic arthritis in integrative care studies has been shown to respond to the use of Ox Bile. For patients who desire to not use DMARDs, it could be a consideration once underlying gut issues are addressed.
- Sjogren's is known to affect glandular structures of the head/neck – salivary glands, lacrimal glands. Some studies do indicate that there are gut effects in addition to the oral effects.
 - Lack of salivary enzymes, oral flora, and other substances in saliva affect digestion. Food breakdown and the introduction of flora from the mouth begin the digestive process.
 - Chewable probiotics at least nightly after brushing teeth to provide flora to keep pathologic bacteria in check.
 - Xylitol to improve moisture – available as lozenges, rinses, in gum and mints, some products adhere to the gums providing a slow “drip” of xylitol over hours which improves moisture and has beneficial effects on flora.
 - Chewable digestive enzymes with meals to aid in early digestion.

A Few Words About Yeast

Many patients with GI issues worry about yeast overgrowth because it is a common target of nutritionists, naturopaths, and other natural healers

- Candida is part of normal flora
- Candida is rarely as far out of balance as would be believed by diets and treatments recommended
- Candida diets are difficult to follow and rarely improve symptoms
- Long-term antifungals are rarely indicated

Beneficial Yeast

- *Saccharomyces Boulardii* or *Cerevesiae* will often resolve yeast imbalance
- Beneficial yeasts also prevent antibiotic induced diarrhea including *C. Diff* and should be considered with ALL antibiotic prescriptions.
- Beneficial yeasts help prevent travelers' diarrhea.
- *Saccharomyces Cerevesiae* (Brewers Yeast) is the source from which brush border enzyme supplements are derived

Anti-saccharomyces antibodies are not uncommon in rheumatologic diseases and are very common (70%) in Crohn's disease patients. However the use of saccharomyces and exposure to brewers yeast (*saccharomyces cerevisiae*) has not been found to exacerbate these inflammatory conditions.

Case Study 2

- 39 year old female with known history of long standing Sjogren's syndrome and Fibromyalgia.
- Managed on HCQ 200mg BID and Lyrica 75mg BID.
- Overall feeling ok but continues to struggle with fatigue. Has some joint/muscle pain that's constant.
- Physical exam unremarkable and labs are fine.

- Her main question is – is there anything she can “naturally” take to help fatigue and inflammation.
- So I call Lisa!

Integrative Medicine Perspective

Assess GI health

- Ask – many patients won't think about GI health as something to bring up to you
- GI consult if “red flag” symptoms or overdue screening
- Consider gut permeability and immune triggering issues (IBS, SIBO)
- Consider probiotics to normalize flora if mild symptoms
- Consider enzymes, especially with Sjogrens

Normalize nutrients – check for deficiencies

- Magnesium is a common deficiency in Fibromyalgia patients
- B-12/folate
- Copper – myalgia and neuralgia
- Zinc

HCQ – may deplete Vitamin D and Calcium
Pregabalin may exacerbate Sjogren's symptoms of dry mouth

Reducing Inflammation

Reduce foods that promote inflammation

- Sugars
- Processed foods
- What about nightshades...
 - Improvement with a “no nightshade diet” MAY reduce pain
 - Worth a 2-4 week trial
 - Nightshades
 - Tomato
 - Peppers
 - Potatoes
 - Eggplant

Reducing Inflammation

Supplements should be added one at a time with several days between additions to assess for any side effects. Most common side effects are stomach upset. Start with a low dose and increase slowly.

- Turmeric 400-600 tid
- Palmitoyl Ethanolamide (PEA) 600-700 qd-bid
- Green Tea EGCG 500 mg bid-tid
- Omega 3 1-4 gm
- Boswellia 300-500 mg bid
- Resveratrol 50-500 mg daily
- Cats Claw 20-60 mg daily

Herbals MAY have side effects, though for those listed below they are few.

Consideration must be taken for side effects with some medication, specifically Coumadin interacts with MANY supplements.

Other Considerations for Pain and Inflammation

Assess sleep:

Sleep is commonly affected in Fibromyalgia and other illnesses involving pain.

Poor sleep status exacerbates inflammation, pain, and fatigue

Inability to fall asleep vs stay asleep

Sleep Hygiene Factors

- Screens
- Clocks and lights
- Timing of sleep

Sleep Apnea

Stress and busy brain

Sleep

The trouble with Medications

Sedative-hypnotics, Benzos, muscle relaxants, narcotics

- Many medications used for sleep reduce the quality
 - Lights on / Lights off
 - Altered sleep phases

Association with cognitive difficulties

Exception: Trazodone

The trouble with alcohol and MMJ

- Sleep onset
- Altered sleep phases

Supplement alternatives

- Do not negatively impact sleep phases

Melatonin

- Dosing 3-5 mg
- Useful for sleep induction only if deficient
- Timed-release not necessary
- Only use at night

L-theanine – amino acid

- Dosing 200-600 mg
- Reduces busy brain, does not induce sleepiness
- May reduce anxiety

The Case for Melatonin

There is a strong evidence base for a role for Melatonin other than sleep induction

- Melatonin and psoriasis / psoriatic arthritis
- Melatonin and periodontal disease (Sjogrens)
- Melatonin as anti-inflammatory
- Melatonin for skin and alopecia

Available in variety of forms

- Oral 3-5 mg
- Topical skin preparation Melatonin 0.1 – 1% compounded cream or powder
- Topical for gums and periodontal Melatonin 1% in glycerine 1 teaspoon swish and spit 1-3 times daily

Melatonin should only be dosed at night.
Dosing during the daytime may have harmful side effects including increased growth of tumors.

The Case for Low-Dose Naltrexone

Naltrexone is indicated for use in opioid dependence and alcohol dependence dosed at 50 mg orally

Low-Dose Naltrexone is increasingly used in Rheumatology

- Reduction of pain in fibromyalgia and other rheumatologic diseases
- Reduction of inflammation in Crohn's disease
- May have a role in psoriasis (reduces lesions in Hailey Hailey Disease)

Low dose is 4.5 mg or less

- Begin with 1 mg compounded and gradually increase by 1 mg weekly to maximum 4.5 mg
- Side effects are rare but include headache or dizziness and GI upset

Questions



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