SIBO and Skin Diseases

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Gut Microbiome and Skin Diseases

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Microbiome, SIBO, and Skin Disorders

- Acne
- Atopic dermatitis
- Psoriasis
- Urticaria
- Systemic sclerosis
- Skin cancer
- Rosacea – Dr. Weinstock

Disclosures: Traub

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Potential Pathways of the Gut-Brain-Skin Axis in Acne
'everything has been thought of before, but the difficulty is to think of it again'

Goethe

Hygiene Hypothesis

A lack of early childhood exposure to infectious agents, symbiotic microorganisms (decreased diversity of intestinal microbes and probiotics), and parasites increases susceptibility to allergic diseases by suppressing the natural development of the immune system

Strachan 1989
**Acne and hypochlorhydria**

- 13,000 adolescents with acne: increased prevalence of halitosis, GERD, bloating and constipation
- Hypochlorhydria as risk factor for SIBO
- SIBO detected on HBT in 50% of patients on long term PPI

**Probiotics for Acne**

- 45 females randomized to 1 of 3 arms in open-label study
  - Grp B minocycline
  - Grp C probiotic + minocycline
- At 8- and 12-week follow-up, grp C had significant decrease in total lesion count versus grp A (p < .001) and B (p < .01)
### Probiotics for Acne


### Probiotics for Acne

- RDBCT 20 adults given L. rhamnosus SP1 or placebo x 12 wk
- Bx at baseline and at 12 wk
- Probiotic group had 32% (P<0.001) reduction, and 65% increase (P<0.001) in IGF1 and FOXO1 gene expression in the skin, respectively, and an adjusted odds ratio of 28.4 (95% confidence interval = 2.2-411.1, P<0.05) to be rated by physicians as improved/markedly improved.
- No changes in placebo group
  - Fabbrocini G et al. Supplementation with Lactobacillus rhamnosus SP1 normalises skin expression of genes implicated in insulin signalling and improves adult acne. Benef Microbes. 2016 30;625-630

### SIBO and Psoriasis

- 60% psoriasis pts (33/55) had malabsorption vs. 3% controls based on D-xylose screening test
- 21% had SIBO based on LBT
- Rx with metronidazole or rifaximin successfully eradicated SIBO, normalized absorption and improved skin lesions of these pts
- Celiac disease was diagnosed in 3% of the pts in this study. GF diet improved their skin lesions


### Urticaria

- 48 pts with chronic spontaneous urticaria (CSU)
- Scored for urticaria activity and QOL
- H. p. in 11 and SIBO in 13; SIBO pts had worse CSU
- Rx x 1 wk and evaluated before and 4 wks after the eradication Rx
- Rx of H.p. led to improvement in CSU (p< 0.002)
- Rx of SIBO – no improvement in CSU

- What else could explain this – worse CSU to start, 1 wk not enough gut lesions of SIBO (incomplete resolution of leaky gut), mast cells continue in gut and skin, memory T cells continue to circulate and activate skin mast cells

Urticaria
Role of allergy and mast cells

- Food allergies – lead to IgE elevation
- Mast cell activation syndrome: 700 MCAS patients had 36 sx: fatigue, muscle pain, near syncope, headache, itching, urticaria, and nausea occurred in the top 57%

Systemic Sclerosis (SSc)

- Malabsorption and pseudo-obstruction can occur in 44-88% of those affected leading to malnutrition
- Nutritional deficiencies - common cause of morbity and mortality
- Malabsorption: 50% mortality rate at 8.5 yrs
- SIBO in SSc: 30% - 63% of pts w GI Sx

SIBO in SSc

- Eradication of SIBO achieved in 52% of 22 pts with significant improvement of intestinal Sx
- Enteral and parenteral nutrition may be used to reverse severe nutritional deficiencies
- Consider new elemental diet formulation

SSc: Fecal Calprotectin (FC) and SIBO

- 125 consecutive pts tested for FC and SIBO
- 93 pts had abnl levels of FC (>50 μg/g); 68 of these pts had high levels of FC (>200 μg/g)
- Global Sx score of digestive Sx: esophageal and gastric dysfx correlated w elevated FC
- Strong assoc between elevated FC and presence of SIBO on LBT
  - Higher significant correlation when level ≥275 μg/g
SSc, FC, and SIBO

- FC level $\geq 275$ $\mu$g/g and risk of SIBO: sensitivity 0.93, specificity 0.95
- Eradication of SIBO was obtained in 52% pts, yielding sig improvement of intestinal Sx
- 3 mo rotating antibiotics: norfloxacin and metronidazole, eradication of SIBO was associated with sig decrease of FC

Marie et al. Autoimmun Rev. 2015;14:547-54

SSc pt with Rosacea

4 wks after 2 wks Xifaxan and metronidazole (failed doxycyline)

Rosacea: nose and cheeks much better RLS: completely better

Pruritis in SSc: role for LDN

- SSc = autoimmune disease causes fibrosis and vasculopathy in skin, lung, and GI tract
- Pilot trials of low-dose naltrexone hydrochloride (LDN) for pruritus, pain, and quality of life (QOL) in other GIT diseases have been successful
- 3 pt case series - sig improvement in pruritus and total GIT Sx by 10-pt faces scale and UCLA SCTC GIT 2.0 questionnaire

The Take Away

- Test for SIBO in acne, atopic dermatitis, psoriasis, and scleroderma
- SIBO is not the whole answer
- Altered immunity is critical – Rx all possible (not just the SIBO)
- Publish your case series

Dr. Weinstock says:

Political statement – agree

Next: The Gut and Rosacea

Rosacea – Modern Day Anti-Trump Affliction?

The Gut and Rosacea

Leonard Weinstock, MD

Associate Professor of Clinical Medicine
Washington University in St. Louis
Specialists in Gastroenterology
Rosacea and Risk of GI disorders

Nationwide Denmark Cohort Study

Rosacea      N = 49,475
Controls      N = 4,312,213

Cox regression analysis to obtain hazard ratios of the risk of **new-onset** Celiac, CD, UC, HP, SIBO and IBS in rosacea pts

**Rosacea and Risk of GI disorders**

Significant assoc developing:

- CeD (HR 1.46)
- CD (HR 1.45)
- UC (HR 1.19)
- IBS (HR 1.34)

Not H.p. (HR 1.04) or SIBO (HR 0.71)

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**CONCLUSIONS**

GI complaints in pts with rosacea warrant clinical suspicion of diseases

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• Opposite not studied – did GI disease cause rosacea
• SIBO and H.p. testing not performed

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**Crohn’s disease and Rosacea**

Incidence of 5/60 consecutive CD clinic pts

– 3 active rosacea: treated with rifaximin:
  1 partial and 2 complete response
– 2 not currently active (for both)

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**Response to therapy in active cases**

• 60 y.o. WF w 40 yr ileitis on no Rx
  CD flares assoc w nasal rosacea
  – Rifaximin Rx – cleared both

• 46 y.o. WM 26 yr CD s/p IC resection on 6-MP; CD flares assoc w facial rosacea
  – Rifaximin Rx – cleared both

• 32 y.o. WF severe CD colitis and rosacea
  – See next

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32 y.o. WF with CD and Rosacea

32 y.o. WF with CD failing Rx. Off all meds.

Effect after 2 wks
Rifaximin
1200/mg/d/10 d

Subsequent effect of 8 wks biologic Rx w adalimumab

SIBO in Rosacea: Prevalence

- Genoa: 46% 113 pt in Rosacea Clinic
- St. Louis: 51% of 63 my pts
- St. Louis: 66% of 176 my pts (incl. CH4+)

False positive LBT: Controls

- Genoa, Italy: 3/60 age matched controls
- St. Louis, MO: 3/30 healthy controls

(Lactulose gets to colon faster causes FP)

**Rifaximin for rosacea: Italy**

- N=113 pts seen in Rosacea Clinic
  - 83 F, 31 M, age 52
- 52/113 (46%) LBT+
- 24/113 H.p.+ (7 had SIBO)
  - 7 pts Rx for H.p. 1 mo p SIBO Rx (clin. response occurred with SIBO Rx)
- GI sx response analyzed

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**Rifaximin for Rosacea**

- N = 52 LBT+ (H2 excretion)
- Rifaximin 1200 mg/d/10d vs. Placebo
  - Randomized, blinded only to pts
  - IGA scoring
  - 2 dermatologists (Kappa = 0.97)

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**Randomized study results**

- Rifaximin normalized LBT in 28/32
- 71% cleared rosacea (GA score 0)
- 21% marked impr. (GA score 1)
- Placebo 2/20 worsened, rest unchg.
- GI sx sig. decreased with rifaximin

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**Before & 1 mo after 1200 mg/d/10d rifaximin**

Rifaximin for Rosacea: St. Louis

- N=63 pts
- ETR in 50, PP in 9, refract. ocular in 4 (3 E)
  - Most did not have GI sx
- 51% LBT+ vs. 10% controls (RR, 5.0; 95% CI, 1.7-15.1; P<0.001)
- 28/32 given Rx rifaximin 1200 mg/d/10d

Improvement in 28 pts

- 71% marked-moderate responders

42 F s/p Mont. revenge 13 yrs ago followed by:
- E/F/Phyma
- and ocular rosacea
- Nail disorder
- IBS-c
- Cognitive dysfx
- Fatigue
- RLS
- Steatohepatitis
- Type 2 DM

Dx: Bacterial overgrowth

Before & 5 wk after rifaximin 1650/mg/d/14d

Before & 1 mo after rifaximin 1200 mg/d/10d

Before & 1 mo after rifaximin 1200 mg/d/10d

Significant change in nose & pruritic rash over right eyebrow – patient seen 1 year later & both areas were clear
Before & 1 mo after rifaximin 1200 mg/d/10d**

**Pi-IBS and rosacea (worsened after colon cancer resection)

Before & 1 mo after rifaximin 1650/mg/d/14d

Subsequent experience

Higher dose to match IBS studies and additional Rx for complex pts:

- Rifaximin 550 mg TID for 14 days
- Comprehensive post-SIBO Rx for complex patients
- Low dose naltrexone

Ocular Rosacea: SIBO Study

- N=24 (21F/3M), age 59
- Refractory ocular rosacea pts referred by ophthalmologists
- Facial rosacea in 4
- LBT+ in 9/24 (38%)
- GI sx in 63% LBT+ vs. 33% LBT-

Ocular Rosacea SIBO Study

Methods

- Open-label, rifaximin 1650-mg/d/10-14 d in LBT+ pts
- Global assessment 10 d & 20 d after ending rifaximin: marked, moderate, mild improvement, or unchanged


Improvement in 8 pts

75% marked-moderate responders

Rifaximin 1200-mg/day/10d: Day 0 & Day 30

Less edema, redness and foreign body symptoms after Rx
Rifaximin 1650/mg/day/14d: Day 0 & Day 14

Conclusions

- Rifaximin led to improvement in this small open-label study
- Dysregulation of innate immune system d/t GI inflammation could increase systemic cytokines and microbial antigens/antibodies affecting eyelids and meimobian glands

Keep in mind DDx SIBO

Naltrexone & OGFr

Animal studies:

- Decreased T- and B-cell activity and less permeability

(Decreased neovascularity in cornea – rats)

Rosacea and LDN Rx

Stages of truth
Arthur Schopenhauer, 1788-1860

• First it is ridiculed
• Second it is violently opposed
• Third it is accepted as self-evident