RECOMMENDING AND ACCURATELY COMMUNICATING INFORMATION ON PROBIOTICS TO PATIENTS

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A BIT ABOUT ME…

- MS2 at Wright State University Boonshoft School of Medicine in Dayton, OH
- Student-initiated elective on probiotics over the summer
- Interest in patient-physician communication and integrative medicine
RELEVANT FINANCIAL DISCLOSURES

Lilian White

I have nothing to disclose
TODAY’S FACILITATED DISCUSSION

- Goals:
  - Gain an improved understanding of probiotics
  - Enhanced ability to communicate the benefits/risks of probiotics to patients and other physicians
  - Improved ability to advise patients on how to incorporate probiotics into their diet safely when recommended
GROUPS AND INTRODUCTIONS

- Groups of 3
- Quick introductions:
  - Name
  - Occupation
  - What piqued your interest to come to this discussion group?
  - What do you like to do for fun? (or insert your own Q/A here)
1. On your own - 30 seconds
2. With your group – 3 minutes
3. With the room – 5 minutes
WHAT ARE PROBIOTICS?

- Several definitions:
  - Substances secreted by one microorganism that stimulate another microorganism – Lilly and Stillwell, 1965
  - Viable bacteria, in a single or mixed culture, that have a beneficial effect on the health of the host – Donohue and Salminen, 1996
  - Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host – Hill et al., 2014
HOW SAFE ARE PROBIOTICS?

- In theory, worry about: infection, toxic/metabolic effects, and transfer of resistance genes (David 2008; Watson 2016)
- Lactic acid bacteria found in <0.1% samples from severe infections (Gasser, 1994)
- FDA and GRAS status for lactic acid bacteria and bifidobacteria (Watson and Victor, 2016)
  - QPS in the EU
Studies:

- Sepsis with Lactobacillus associated with probiotic therapy (DaLand, 2005)
- Lactic acid bacteria and bifidobacteria demonstrated in bacteremia and endocarditis cases (David, 2008)
  - 30% mortality rate for Lactobacillus infections (Cannon et al., 2005)
- Absence of increase in bacteremia with rise in consumption of probiotics in Finland (Salminen, 2002)
  - 1L to 6L over 5 years with increase Lactobacillus bacteremia of 0.3/100,000/inhabitants/year
- Treatment with Lactobacillus for short gut syndrome (with concurrent cholestasis, chronic intestinal inflammation) (Kunz & Fairchok, 2004)
  - Consider state of intact mucosal barrier prior to treatment (Vanderhoof et al., 1998)
### WHAT DOES THE RESEARCH SAY ABOUT THE BENEFITS?

#### “Core Benefits”
- Effects common to probiotics
- Compete with pathogens
- Produce short-chain fatty acids
- Regularize dysbiosis
- Resist colonization
- Regulate transit of the intestine
- Enterocyte turnover

#### “Specific Benefits”
- Effects unique to specific strains or species
- Synthesis of vitamins
- Metabolize bile salt
- Enzymatic activity
- Neutralize carcinogens
- Reinforce barrier of the gut
- Neuro/immuno/endodrinological effects
- Produce bioactives

(Hill, et al., 2014; Scourboutakos, 2017; IPA, 2017)
WHAT ARE THE DISEASES OF THE UNDERSERVED?

“Diseases of Poverty” (Win, 2015)

- Cardiovascular disease
- Hypertension
- Diabetes
- Chronic kidney disease
- Obesity
- Poor dental health
- Asthma
- Arthritis
- Infections of bacterial, parasitic, or congenital origin
- Mental illnesses (E.g. major depressive disorder, etc.)
“Probiotics and blood pressure: current insights” (Upadrasta, et al, 2016)


Cavallini DC, Manzoni MS, Bedani R, Roselino MN, Celiberto LS, Vendramini RC, de Valdez G, Abdalla DS, Pinto RA, Rosetto D, Valentini SR, Rossi EA. Probiotic Soy Product Supplemented with Isoflavones Improves the Lipid Profile of Moderately Hypercholesterolemic Men: A Randomized Controlled Trial. Nutrients.January 19, 2016; 8 (1);


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Michael DR, Moss JW, Calvente DL, Garaiova I, Plummer SF, Ramji DP.. Lactobacillus plantarum CUL66 can impact cholesterol homeostasis in Caco-2 enterocytes Benef Microbes - June 1, 2016; 7 (3); 443-51


“Obesity pandemic: causes, consequences, and solutions—but do we have the will?” (Meldrum, 2017)

- Increased diversity of microbiota associated with greater anti-inflammatory responses and less oxidative stress
- Effect of probiotics on short- and long-term diversity still under study (Qiao et al., 2016)
ADDITIONAL REFERENCES FOR DIABETES, METABOLIC SYNDROME AND PROBIOTICS


- Palacios T, Vitetta L, Coulson S, Madigan CD, Denyer GS, Caterson ID, The effect of a novel probiotic on metabolic biomarkers in adults with prediabetes and recently diagnosed type 2 diabetes mellitus: study protocol for a randomized controlled trial. Trials. January 9, 2017; 18 (1); 7
Probiotics for the management of type 2 diabetes mellitus: A systematic review and meta-analysis

Samah, S., Ramasamy, K., Lim, S., Neoh, C. Diabetes Research and Clinical Practice, 2016-08-01, Volume 118, Pages 172-182


Yan Q, Li X, Feng B., The efficacy and safety of probiotics intervention in preventing conversion of impaired glucose tolerance to diabetes: study protocol for a randomized, double-blinded, placebo controlled trial of the Probiotics Prevention Diabetes Programme (PPDP). BMC Endocr Disord. December 1, 2015; 15 (); 74
“Association between probiotic and yogurt consumption and kidney disease: insights from NHANES” (Yacoub, 2016)
- Frequent yogurt and probiotic consumption (at least 3x/week) significantly lowered adjusted odds of albuminuria compared to infrequent users
- No significant relationship found with the estimated glomerular filtration rate (study cites sample size and population limitations)

“Influence of prebiotic and probiotic supplementation on the progression of chronic kidney disease” (Pavan, 2016)
- N = 12 prospective observational study. Stable stage III or IV CKD patients not on dialysis
- Assigned either a low-protein or low-protein + prebiotic + probiotic (tablet form) for 6 months
- Significant difference in decline of GFR (-11.6±8.6 vs. -3.4±4.6 mL/min per 1.73 m2 per year, 95% CI -6.45 - -9.86, P<0.001)
ADDITIONAL REFERENCES FOR CHRONIC KIDNEY DISEASE AND PROBIOTICS


The Use of a Kidney Based Probiotic for Chronic Kidney Disease: Recognition of the Importance of the Gut


“Effects of Probiotics and Synbiotics on Obesity, Insulin Resistance Syndrome, Type 2 Diabetes and Non-Alcoholic Fatty Liver Disease: A Review of Human Clinical Trials” (Sáez-Lara, 2016)

- Support for probiotics and synbiotics as part of preventive care
- More research needed to understand the specific mechanisms of action and related effects


- Gut microbiota contributes to the physiology of obesity
- Probiotics may contribute to antibiotic resistance, - area of safety to explore more
- Probiotics result in decreased production of LPS by modulating the gut microbiota, helping to prevent obesity
- Treatment of obesity via synbiotics reduced inflammatory cytokines, serum lipid profile, and altered gut microbiota (Rajkumar, 2015)
da Silva ST, dos Santos CA, Bressan J. Intestinal microbiota; relevance to obesity and modulation by prebiotics and probiotics. Nutr Hosp. July 1, 2013; 28 (4); 1039-48


Halkjaer SI, Nilas L, Carlsen EM, Cortes D, Halldórsson TI, Olsen SF, Pedersen AE, Krogfelt KA, Petersen AM.. Effects of probiotics (Vivomixx®) in obese pregnant women and their newborn: study protocol for a randomized controlled trial. Trials. October 11, 2016; 17 (1); 491


Mekkes MC, Weenen TC, Brummer RJ, Claassen E.. The development of probiotic treatment in obesity: a review. Benef Microbes. March 1, 2014; 5 (1); 19-28

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“The Effect of Iranian Customary Used Probiotic Yogurt on the Children’s Salivary Cariogenic Microflora” (Nozari, 2015)

- Short-term (7-week) study comparing effect of probiotic yogurt with *Bifidobacterium lactis* and normal yogurt
- Normal yogurt consumption resulted in a decrease in *Streptococcus mutans*; probiotic yogurt did not
- Agreed with some other studies, but similar studies with adults showed the reverse

“Antimicrobial Efficacy of Probiotic and Herbal Oral Rinses against Candida albicans in Children: A Randomized Clinical Trial” (Mishra, 2016)

- Double-blind study over the course of one week, rinses used 2x/day
- Probiotic rinse (probiotic mint tablet + water) as effective as 0.2% chlorohexidine digluconate mouth rinse in eradication of C. albicans
Cannon ML. A Review of Probiotic Therapy in Preventive Dental Practice. Probiotics Antimicrob Proteins. June 1, 2011; 3 (2); 63-7


Nozari A, Motamedifar M, Seifi N, Hatamizargaran Z, Ranjbar MA. The Effect of Iranian Customary Used Probiotic Yogurt on the Children's Salivary Cariogenic Microflora. J Dent (Shiraz) - June 1, 2015; 16 (2); 81-6

Probiotics in the dental practice: a review. Laleman I, Teughels W. Quintessence Int. March 1, 2015; 46 (3); 255-64

“Probiotics enhance the effect of allergy immunotherapy on regulating antigen specific B cell activity in asthma patients” (Liu, 2016)

- Patients with asthma were given either allergen specific immunotherapy (AIT) and/or probiotics (via Clostridium butyricum (CB))
- While both AIT and AIT+CB resulted in an alleviation of asthma symptoms, the combined therapy resulted in a decrease in serum IL-4, -5, -13, and specific IgE persistent after 12 months (whereas AIT alone did not maintain the decrease beyond 2 months)
- CB heightened the effect of AIT via the generation of B10 cells

“Probiotic administration in early life, atopy, and asthma: a meta-analysis of clinical trials” (Ta, 2014)

- Atopic sensitization and total IgE were significantly reduced in those receiving probiotics both pre- and postnatally (not postnatally alone), but did not significantly reduce asthma or incidence of wheezing
- Trials exploring the relationship between probiotics and atopic sensitization and asthma have been mixed. More clinical trials are needed.
Azad MB., Coneys JG., Kozyrskyj AL., Field CJ., Ramsey CD., Becker AB., Friesen C., Abou-Setta AM., Zarychanski R. Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systematic review and meta-analysis. BMJ. December 4, 2013; 347 (); f6471


Elazab N, Mendy A, Gasana J, Vieira ER, Quizon A, Forno E. Probiotic administration in early life, atopy, and asthma: a meta-analysis of clinical trials. Pediatrics - September 1, 2013; 132 (3); e666-76


ARThRITIS

- Rheumatoid:
  - “Effects of Probiotic Supplementation on Oxidative Stress Indices in Women with Rheumatoid Arthritis: A Randomized Double-Blind Clinical Trial” (Vaghef-Mehrabany et al., 2016)
    - Trial for 8 weeks, experimental group given *Lactobacillus casei* 01 in capsule form
    - Did not show a significant difference in oxidative status between placebo and experimental group

- Juvenile Idiopathic (JIA)
  - “Effect of probiotics on clinical and immune parameters in enthesitis-related arthritis category of juvenile idiopathic arthritis” (Shukla, 2016)
    - Probiotics did not significantly improve the symptoms of enthesitis-related JIA compared to NSAIDS over 12 weeks
ADDITIONAL REFERENCES FOR ARTHRITIS AND PROBIOTICS


MENTAL ILLNESS

- “Probiotic normalization of Candida albicans in schizophrenia: A randomized, placebo-controlled, longitudinal pilot study” (Severence, 2017)
  - Longitudinal, double-blind, placebo-controlled trial over 14 weeks
  - Male patients with schizophrenia were noted to have a significant reduction in C. albicans, positive psychiatric symptoms, and GI discomfort when given probiotics (Lactobacillus rhamnosus and Bifidobacterium animalis) vs placebo

- “The gut microbiota and psychiatric illness” (MacQueen, 2017)
  - Evidence for recommendation of pre-/probiotics gaining ground in animal trials, but not enough human trials to date

- “Clinical and metabolic response to probiotic administration in patients with major depressive disorder: A randomized, double-blind, placebo-controlled trial” (Akkasheh, 2016)
  - Patients with major depressive disorder given probiotic (Lactobacillus acidophilus, Lactobacillus casei and Bifidobacterium bifidum) or placebo for 8 weeks
  - Significant improvement in Beck Depression Inventory
ADDITIONAL REFERENCES FOR MENTAL ILLNESS AND PROBIOTICS


- Latalova K, Hajda M, Prasko J. Can gut microbes play a role in mental disorders and their treatment? Psychiatr Danub. March 1, 2017; 29 (1); 28-30


HOW CAN PROBIOTICS BE ADDED TO A DIET PLAN?

1. Yogurt
2. Kefir
3. Aged cheese*
4. Cottage cheese
5. Fermented cabbage (sauerkraut, kimchi)
6. Pickled Vegetables

NYA seal for CFU
Pasteurization time
Sugar/fat content
Prebiotics: pectin, inulin, FOS, polydextrose

Brine-cured/salt-cured, not preserved with sodium benzoate
TAKE-AWAYS

- Gain an improved understanding of probiotics
- Enhanced ability to communicate the benefits/risks of probiotics to patients and other physicians
- Improved ability to advise patients on how to incorporate probiotics into their diet safely
- Discuss briefly in groups
REFERENCES


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Qiao YQ, Cai CW, Ran ZH. Therapeutic modulation of gut microbiota in inflammatory bowel disease: More questions to be answered. J Dig Dis. December 1, 2016; 17 (12); 800-810


Salminen MK, Tynkkynen S, Rautelin H, et al. Lactobacillus bacteremia during a rapid increase in probiotic use of Lactobacillus rhamnosus GG in Finland, Clin Infect Dis, 2002, vol. 35 (pg. 1155-60)


Win, Aung Zwa. Disease and poverty go hand in hand in America. American Journal of Medicine, The, 2015-12-01, Volume 128, Issue 12, Pages 1380-1381

Thank you for your participation!