Sabine Hazan, MD, Series Editor

Probiotics: What Do We Know So Far?

Skylar Steinberg

Sabine Hazan

Probiotics have grown in popularity in recent years, marketed as a healthy dietary supplement and placed in popular foods such as yogurt, kombucha, kimchi and more. In 2014, Sales of probiotics in the United States exceeded more than $1 billion, constituting a $25 billion market worldwide.[1] The media and proclaimed health magazines have been quick to push the consumption of these products into our everyday lifestyle and diet. However, there is some confusion on the background and potential risks involved with an increased intake of probiotics that needs to be addressed. Furthermore, "probiotic," has become increasingly misused, with many companies exploiting the term's popularity without meeting the requisite criteria.

Probiotic is a general term for live, nonpathogenic microorganisms, many of which exist in a symbiotic relationship within the normal human gut flora.[1] They have been used to treat Gastrointestinal (GI) and non-GI medical conditions, but data demonstrating their effectiveness has been conflicting. The Federal Drug Administration also views probiotics as a health food, not a drug, and does not regulate these products.[1] One major issue is the fact that selection and dosing vary among products and the specific, beneficial effects of each probiotic strain cannot be generalized.[1] Not all species of probiotics are a part of the normal human gut bacteria and the benefits associated with one strand cannot be generalized to others.[1] Therefore, not all brands should promise equal effectivity and choosing a probiotic can be incredibly confusing and potentially harmful,[1] especially in immunosuppressed individuals or critically ill patients. For example, two cases of Lactobacillus Bacteremia during probiotic treatment of short gut syndrome have been discovered demonstrating that probiotics may not be as benign a treatment as generally thought.[2] Yet, as a result of media and marketing, most consumers now believe that probiotics are key to helping remedy a variety of health issues, keeping the demand for these products high.[1]

Evidence has shown, however, that probiotics have been beneficial for the treatment of acute diarrhea, pouchitis, atopic eczema, and some genitourinary infections.[1] A 2010 analysis of 63 studies, totaling 8014 participants, concluded that probiotics helped decrease the duration and severity of acute infectious diarrhea.[3] In fact, Irritable Bowel Syndrome (IBS) is one of the most

Skylar Steinberg, BS, Health Promotion and Disease Prevention, Research Assistant, Ventura Clinical Trials Sabine Hazan, MD, Gastroenterology/Hepatology/Internal Medicine Physician, CEO, Ventura Clinical Trials, CEO, Malibu Specialty Center, Ventura, CA

common reasons that probiotics are consumed in clinical practice and also one of the most commonly studied with over 80 clinical trials of probiotics for IBS. The main reason for use of probiotics for both IBS constipation or IBS diarrhea is lack of pharmacologic treatment options.[4]

There has been no evidence or even weak evidence that probiotics help in conditions of Crohn's disease or ulcerative colitis.[5,6,7] In fact, Rolfe et. al. in 2006 showed that out of 160 participants with Crohn's disease, probiotics were not superior to a placebo or aminosalicylates for the maintenance of remission in patients.[8] In 2007, Lirussi et al. conducted further studies on liver disease that showed no benefit or harm from probiotics in patients with end-stage liver disease.[9] However, Xu and al. showed probiotics "significantly reduced the development of overt hepatic encephalopathy" in patients with liver cirrhosis.[10]

With regards to metabolic diseases, probiotics have shown to significantly decrease plasma glucose and glycosylated hemoglobin. However, there is no agreement that they reduce blood insulin levels in diabetes patients.[11,12,13,14,15] For patients with cardiovascular and cholesterol conditions, studies found that probiotics decreased LDL, but did not raise HDL. Although Cho and Kim, like several others, emphasized, "both the efficacy of probiotics for cholesterol lowering and safety should be investigated further in well-designed clinical trials."[16,17,118,19]

When looking at the role of probiotics in GI infections like Helicobacter pylori and Clostridium difficile, the data has been controversial. Chao et al. in 2016 showed that probiotics, plus standard therapy, did not improve the eradication rate of H.pylori compared to placebo, however, probiotics did improve the side effects of diarrhea and nausea from the antibiotics.[20] When given with antibiotics, probiotics did decrease the risk of developing CDAD by 64%.[21]

There is also inadequate evidence recommending probiotics for respiratory tract infection,[22] Bacterial vaginosis,[23,24] UTI,[25] or chronic periodontitis.[26]

Overlooking the literature, it is evident that some effects of probiotics are well-documented, and their use alone or in combination with other therapies can be considered "evidence-based," such as antibiotic-associated diarrhea, and C. diff-associated diarrhea, and yield positive results. In other conditions, however, further studies are crucial to determine the benefits of probiotics, because the available evidence is insufficient to show the efficacy of probiotics themselves and the studies included a wide swath of participants with varying degrees of ailments. Careful trials are needed to validate the effects of particular strains of probiotics given at specific dosages and for specific durations[27] but more importantly, probiotics need to be specific to the individual because, clearly, microbiome profiling has demonstrated species-specific patterns.[28,29] ■

References

1. Saif Ul Islam, MD, RPh. Clinical Uses of Probiotics. Medicine: Volume 95, Number 5, February 2016. 1-5
2. Kunz, Anjali N., Noel , James M., Fairchok, Mary P. Two cases of Lactobacillus Bacteremia during Probiotic Treatment of Short Gut Syndrome. J of Pediatric Gastroenterology and Nutrition: April 2004-Volume 38- Issue 4.457-458.
3. Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. Cochrane Database Syst Rev; 2010:CD003048.
4. Elizabeth A Parker Ph.D.,RD, Tina Roy B.S.,Christopher R. D'Adamo Phd., L.Susan Wieland Ph.D. Probiotics and Gastrointestinal conditions: An overview of evidence from the Cochrane Collaboration: Nutrition 45 (2018) 125-134.
5. Doherty G, Bennett G, Patil S, Cheifetz A, Moss AC. Interventions for prevention of post-operative recurrence of Crohn's disease. Cochrane Database Syst Rev; 2009:CD006873.
6. Naidoo K, Gordon M, Fagbemi AO, Thomas AG, Akobeng AK. Probiotics for maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev; Dec. 7, 2011:CD007443.
7. Mallon P, McKay D, Kirk S, Gardiner K. Probiotics for induction of remission in ulcerative colitis. Cochrane Database Syst Rev; Oct. 17, 2007:CD005573.
8. Rolfe VE, Fortun PJ, Hawkey CJ, Bath-Hextall F. Probiotics for maintenance of remission in Crohn's disease. Cochrane Database Syst Rev; Oct. 18, 2006:CD004826.
9. Lirussi F, Mastropasqua E, Orando S, Orlando R. Probiotics for non-alcoholic fatty liver disease and/or steatohepatitis. Cochrane Database Syst Rev; Jan. 24, 2007:CD005165.
10. Xu J, Ma R, Chen LF, Zhao LJ, Chen K, Zhang RB. Effects of probiotic therapy on hepatic encephalopathy in patients with liver cirrhosis: An updated meta-analysis of six randomized controlled trials. Hepatobiliary Pancreat Dis Int Aug. 13, 2014; 13:354-60
11. Zhang Q, Wu Y, Fei X. Effect of probiotics on glucose metabolism in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. Medicina (Kaunas) 2016; 52:28-34; PMID:26987497
12. Samah S, Ramasamy K, Lim SM, Neoh CF. Probiotics for the management of type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes Res Clin Pract August

2016; 118:172-82;
13. Kasinska MA, Drzewoski J. Effectiveness of probiotics in type 2 diabetes: A meta-analysis. Pol Arch Med Wewn 2015; 125:803-13; PMID:26431318
14. Ruan Y, Sun J, He J, Chen F, Chen R, Chen H. Effect of probiotics on glycemic control: A systematic review and meta-analysis of randomized, controlled trials. PLoS One Jul. 10, 2015; 10:e0132121; PMID:26161741
15. Sun J, Buys NJ. Glucose- and glycaemic factor-lowering effects of probiotics on diabetes: A meta-analysis of randomised placebo-controlled trials. Br J Nutr April 14, 2016; 115:1167- 77
16. Shimizu M, Hashiguchi M, Shiga T, Tamura HO, Mochizuki M. Meta-analysis: Effects of probiotic supplementation on lipid profiles in normal to mildly hypercholesterolemic individuals. PLoS One Oct. 16, 2015; 10: e0139795; PMID:26473340
17. Sun J, Buys N. Effects of probiotics consumption on lowering lipids and CVD risk factors: A systematic review and meta-analysis of randomized controlled trials. Ann Med 2015; 47:430-40
18. Guo Z, Liu XM, Zhang QX, Shen Z, Tian FW, Zhang H, Sun ZH, Zhang HP, Chen W. Influence of consumption of probiotics on the plasma lipid profile: A meta-analysis of randomised controlled trials. Nutr Metab Cardiovasc Dis Nov. 21, 2011; 21:844-50
19. Cho YA, Kim J. Effect of probiotics on blood lipid concentrations: A meta-analysis of randomized controlled trials. Medicine (Baltimore) Oct. 2015; 94:e1714; PMID:26512560
20. Chao L, Jianzhong S, Haijian H, Xingyong W, Yiming L, Lan L, Youming L, Chaohui Y. Probiotic supplementation does not improve eradication rate of Helicobacter pylori infection compared to placebo based on standard therapy: A meta-analysis. Sci Rep 2016; 6:23522; PMID:26997149
21. Goldenberg JZ, Ma SS, Saxton JD, Martzen MR, Vandvik PO, Thorlund K, Guyatt GH, Johnston BC. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. Cochrane Database Syst Rev May 31, 2013; CD006095; PMID:23728658
22. Gu WJ, Wei CY, Yin RX. Lack of efficacy of probiotics in preventing ventilator-associated pneumonia probiotics for ventilator-associated pneumonia: A systematic review and meta-analysis of randomized controlled trials. Chest 2012; 142:859-68; PMID:22797719
23. Huang H, Song L, Zhao W. Effects of probiotics for the treatment of bacterial vaginosis in adult women: A meta- analysis of randomized clinical trials. Arch Gynecol Obstet June 2014; 289:1225-34
24. Senok AC, Verstraelen H, Temmerman M, Botta GA. Probiotics for the treatment of bacterial vaginosis. Cochrane Database Syst Rev Oct. 7, 2009; CD006289; PMID:19821358
25. Schwenger EM, Tejani AM, Loewen PS Probiotics for preventing urinary tract infections in adults and children. Cochrane Database Syst Rev Dec. 23, 2015; CD008772; PMID:26695595
26. Martin-Cabezas R, Davideau JL, Tenenbaum H, Huck O. Clinical efficacy of probiotics as an adjunctive therapy to non-surgical periodontal treatment of chronic periodontitis: A systematic review and meta-analysis. J Clin Periodontol June 2016; 43:520-30
27. Mariangela Rondanelli, Milena Anna Faliva, Simone Perna, Attilio Giacosa, Gabriella Peroni, and Anna Maria Castellazzi. Using probiotics in clinical practice: Where are we now? A review of existing meta-analyses. Gut Microbes 2017, VOL. 8, NO. 6, 521–543.
28. McCord, A.I. et al. Fecal microbiomes of non-human primates in Western Uganda reveal species-specific communities largely resistant to habitat perturbation. Am. J. Primatol. 76, 347–354 Jul. 15, 2014.
29. Amato, K.R. et al. Variable responses of human and non-human primate gut microbiomes to a Western diet. Microbiome 3, 53 Nov. 2015..

Answers to this month's crossword puzzle:

1 R	E	2 C	U	3 R	R	4 E	N	5 T	■	6 N	O	7 D	A	8 L
N	■	E	■	U	■	U	■	E	■	A	■	E	■	E
9 A	E	R	O	B	I	C	B	A	C	T	E	R	I	A
S	■	V	■	■	■	L	■	C	■	A	■	M	■	N
10 E	P	I	■	11 E	12 P	I	T	H	E	L	I	A	13 L	■
■	■	14 C	15 I	T	E	D	■	■	■	I	■	16 L	A	17 C
18 H	I	A	T	A	L	■	19 G	20 A	U	Z	E	■	21 B	A
O	■	L	■	■	T	■	■	Q	■	U	■	22 N	■	T
23 T	B	■	■	24 G	■	25 S	Q	U	A	M	O	U	26 S	■
■	■	27 G	■	A	■	A	■	E	■	A	■	28 C	E	E
29 T	H	E	R	M	A	L	■	O	■	30 B	I	L	E	■
U	■	N	■	B	■	M	■	U	■	■	■	E	■	31 J
32 B	I	O	L	O	G	I	C	S	■	33 A	C	U	34 T	E
E	■	M	■	G	■	A	■	■	■	M	■	35 S	E	T
■	36 M	E	S	E	N	C	H	Y	M	A	L	■	A	■