Gluten-Free Diet: Imprudent Dietary Advice for the General Population?

Glenn A. Gaesser, PhD; Siddhartha S. Angadi, PhD

ARTICLE INFORMATION

Article history:
Accepted 29 May 2012

Keywords:
Wheat
Gluten
Gut microbiota
Fructan-type resistant starch

2212-2672/$36.00
doi: 10.1016/j.jand.2012.06.009

GLUTEN-FREE DIETING HAS GAINED CONSIDERABLE popularity in the general population.[1-3] Between 2004 and 2011 the market for gluten-free products grew at a compound annual growth rate of 28%, with annual sales expected to reach approximately $2.6 billion in 2012.[2] As of April 20, 2012, Amazon.com listed 4,765 entries for the topic "gluten-free." A Google search at the same time for "gluten-free diet" produced more than 4.2 million results. The number-one reason consumers cite for buying gluten-free products is that they are perceived to be healthier than their gluten-containing counterparts.[3] Endorsements from celebrities have undoubtedly contributed to the increased awareness of possible health benefits of gluten avoidance, including weight loss.[4,5]

Despite the health claims for gluten-free eating, there is no published experimental evidence to support such claims for the general population. In fact, there are data to suggest that gluten itself may provide some health benefits, and that gluten avoidance may not be justified for otherwise healthy individuals. Our primary purpose is to briefly describe this evidence and raise awareness of the potential pitfalls of adopting a gluten-free diet in persons without diagnosed gluten-related disorders.

INDICATIONS FOR A GLUTEN-FREE DIET

Gluten is a protein composite consisting of gliadins and glutenins, and is found in foods processed from wheat and related grains such as barley and rye. There is a spectrum of gluten-related disorders, including celiac disease, gluten sensitivity, and wheat allergy.[1,2] Wheat allergy is an adverse immunologic reaction specific to wheat proteins.[1,2] Prevalence of documented wheat allergy is quite low, estimated at only about 0.1% of individuals in Westernized countries.[1] Because wheat allergy can be treated with wheat avoidance, a wheat-free diet may be more permissive than a strict gluten-free diet.[1] Gluten sensitivity (also referred to as nonceliac gluten intolerance), is characterized by a heightened immunologic reaction to gluten in genetically susceptible people.[6] Clinical diagnosis is generally based on responses to a gluten-free diet.[1] Common symptoms of gluten sensitivity, such as fatigue and headaches, and gastrointestinal distress, including gas, bloating, and diarrhea, frequently improve with the adoption of a gluten-free diet. The inherent subjectivity in diagnosis and resolution of these symptoms likely contributes to the popularity of gluten-free diets.

Celiac disease is a complex autoimmune enteropathy that affects the small bowel after ingestion of gluten-containing grains, including wheat, rye, and barley, in genetically susceptible people.[7] Estimated prevalence of celiac disease is approximately 1%.[8,9] The disease can manifest itself in a range of clinical presentations, including malabsorption syndrome and a spectrum of symptoms affecting multiple target organs.[10] A strict gluten-free diet is an established remedy for individuals with celiac disease because it has been shown to lower incidence of related diseases, such as gastrointestinal cancers.[7-9,11] Lifelong adherence to a strict gluten-free diet, devoid of proteins from wheat, rye, barley, and related cereals, remains the gold standard of treatment in celiac disease.[7-9]

There are some data to suggest that following a gluten-free diet may ameliorate gastrointestinal and/or systemic symptoms in individuals with systemic lupus erythematosus, dermatitis herpetiformis, irritable bowel syndrome, rheumatoid arthritis, type 1 diabetes, thyroiditis, and psoriasis.[12,13] Gluten-free diets have also been used by patients with autism spectrum disorders (ASD).[2,14] However, there are no definitive data to support the use of gluten-free diets in ASD,[15] and the American Academy of Pediatrics does not support the use of gluten-free diets as a primary treatment for individuals with ASD.[16]

Apart from the demonstrated effectiveness of a gluten-free diet for treating the spectrum of gluten-related disorders and the conditions mentioned above, evidence-based research supporting the merits of a gluten-free diet as a healthier option for the general population is lacking.

GLUTEN-FREE DIET AND WEIGHT LOSS: WHERE IS THE EVIDENCE?

Despite the growing popularity of gluten-free diets and celebrity endorsements of the merits of a gluten-free diet for weight loss,[4,5] there are no published reports showing that a gluten-free diet produces weight loss in persons without celiac disease or gluten sensitivity. There are a number of studies of patients with celiac disease that reported weight change as an outcome measure following a gluten-free diet.[17-19]

Strict adherence to a gluten-free diet in celiac disease generally improves body mass index (BMI) status.[17] However, normalization of BMI while following a gluten-free diet is not always observed. In a study of 369 adults with celiac disease who followed a gluten-free diet for an average of 2.8 years, 22 of 81 (27%) initially overweight or obese patients gained weight.[17] In a study of 371 adults with celiac disease who followed a gluten-free diet for 2 years, 55 of 67 (82%) initially overweight patients gained weight.[18] Among 149 children with celiac disease who followed a gluten-free diet for at least 12 months, the percentage of overweight children almost doubled (11% to 21%).[19]

These reports indicate that for a significant percentage of overweight or obese patients with celiac disease, body weight may actually increase on a gluten-free diet. This may be due in part to enhanced absorption of nutrients associated with healing of intestinal lining while following a gluten-free diet. Whether weight gain would be observed in persons without celiac disease or gluten sensitivity remains to be established. In this regard it is important to note that gluten-free does not necessarily mean low-energy, and some gluten-free products actually have a greater energy value than corresponding gluten-containing foods.[3] Furthermore, a gluten-free diet may be deficient in whole grains and fiber,[3] both of which have been shown to be inversely associated with BMI.[20]

WHEAT AND GASTROINTESTINAL HEALTH

Naturally occurring fructan-type resistant starches in wheat, such as oligofructose and inulin, are beneficial for creating a healthy composition of gut bacteria,[21-28] and these diet–microbe interactions in the colon may protect the gut from some cancers, inflammatory conditions, and cardiovascular disease.[27,28] Wheat is the most widely consumed grain in the United States, and contributes approximately 70% to 78% of the oligofructose and inulin in typical North American diets.[29,30] Wheat-derived nondigestible carbohydrates have been reported to decrease postprandial glycemia and insulinemia, reduce fasting triglycerides, and reduce body weight.[21] Oligofructose has been shown to improve immune status, lipid metabolism, and vitamin and mineral absorption.[25] By removing the major source (wheat) of fructan-type resistant starches in American diets, strict adherence to a gluten-free diet could have adverse consequences.

In fact, recent evidence suggests that a gluten-free diet may lead to reductions in beneficial gut bacteria.[31] Ten healthy subjects followed a gluten-free diet for 1 month by replacing gluten-containing foods with equivalent products certified as gluten-free.[31] The gluten-free diet significantly reduced a number of beneficial bacteria in fecal samples of the subjects, including *Bifidobacterium*, *Lactobacillus*, *Clostridium litusеburense*, and *Faecalibacterium prausnitzii*, and increased levels of pathogenic *Enterobacteriaceae* and *Escherichia coli*.

Immunostimulatory properties of fecal samples were also reduced after 1 month following a gluten-free diet. For example, the gluten-free diet reduced production of the potent neutrophil chemoattractant tumor necrosis-α. Three-day food diaries (2 weekdays and 1 weekend day) at the beginning and end of the 1-month diet period indicated that total energy and macronutrient intake were not changed, with the exception of a lower polysaccharide intake while following the gluten-free diet. A reduction in polysaccharide intake on a gluten-free diet is not unexpected.[32] Thus, a gluten-free diet produced potentially adverse changes in gut health as a result of reduced intake of naturally occurring fructans in wheat products that have a prebiotic action.

By contrast, increasing whole-grain wheat intake has been reported to increase beneficial gut bacteria.[33] In a double-blind, randomized, crossover study consisting of two 3-week dietary periods with a 2-week washout in between, 31 healthy women and men added to their diet either 48 g/day 100% whole-grain wheat breakfast cereal or 48 g/day wheat-bran cereal. Fecal samples were collected before and after the 3-week dietary period. After 3 weeks following the diet supplemented with 48 g/day 100% whole-grain wheat breakfast cereal, numbers of fecal *Bifidobacterium* were increased by approximately 10%. Addition of wheat bran to subjects' habitual diets had no effect. Both 100% whole-grain wheat and wheat-bran conditions increased the numbers of lactobacilli in fecal samples, but the 7.4% increase after the 100% whole-grain wheat condition was significantly greater than the 5.0% increase observed after the wheat–bran condition. The results indicate a prebiotic effect of whole-grain wheat breakfast cereal. It has been proposed that one of the mechanisms by which whole-grain foods confer health benefits is via their beneficial effect on gut bacteria.[21-28] These findings may help explain the well-established inverse relationship between whole-grain food intake and risk of cardiovascular diseases.[25,26]

GLUTEN AND HEALTH

Gluten itself may actually be beneficial to the diets of individuals with dyslipidemia without celiac disease or gluten sensitivity. In 24 adults with hyperlipdemia, increased consumption of wheat gluten for 2 weeks on a weight-maintenance diet reduced serum triglycerides by 13%.[34] In this randomized crossover study, subjects consumed diets that differed with respect to gluten, wheat fiber, and bran content. The higher gluten content of the diet was achieved by having subjects consume bread that contained 53.1% protein. This increased gluten intake by 60 g/day, which accounted for 10% of total energy. High levels of wheat fiber and bran did not reduce triglyceride levels when gluten levels were the same in each diet. Only under the high-gluten condition, regardless of wheat fiber content, were triglyceride levels reduced. Therefore, it appeared that the reduction in serum triglyceride levels was attributable to the gluten itself rather than the wheat fiber.

In a randomized crossover study of men and women with hyperlipidemia,[35] subjects consumed either a control diet or a diet in which 11% of the carbohydrate in the control diet was replaced with vegetable protein (as wheat gluten) for 1 month. This resulted in a 78 g/day increase in gluten intake. Total energy, dietary fiber, and fat intake were the same during each diet period. Increasing daily gluten intake for 1 month reduced serum triglycerides by 19.2%, uric acid by 12.7%, and creatinine by 2.5%. In addition, low-density lipoprotein oxidation was reduced by 10.6% in the high-gluten diet. The authors concluded that high intake of vegetable protein in the form of added wheat gluten could have beneficial effects on triglyceride levels and oxidized low-density lipoprotein similar to those of monounsaturated fat and soy protein.

In addition to the potential benefits of gluten for improving blood lipid levels,[34,35] gluten may play a role in blood pressure control. For example, wheat gliadin hydrolysates have been reported to inhibit angiotensin I-converting enzyme (ACE).[36] Thewissen and colleagues[36] extracted gliadin from commercial wheat gluten and demonstrated that several of the resulting peptide fractions from the gliadin hydrolysates exhibited ACE-inhibitory activity. Because ACE converts angiotensin I into angiotensin II (vasoconstrictor) and degrades bradykinin (vasodilator), inhibition of ACE could facilitate reduction in blood pressure. Whole-grain consumption has been shown to reduce blood pressure,[37] with wheat itself having a demonstrated effect.[38] Although the dietary fiber component of whole grains is thought to play a role,[39] it is also possible that gluten, via one of its constituent proteins gliadin, may contribute to the blood-pressure–lowering effect of whole grains.[36]

Gluten may also boost the immune system in humans. This may be due in part to the very high glutamine content of gluten ($\sim$40% of total amino acids). Glutamine supplementation, for example, has been reported to reduce incidence of infectious complications in patients following surgery.[40] In a small study of nine healthy volunteers, five subjects received 3 g/day wheat gluten hydrolysate for 6 days (41). After 6 days, natural killer cell activity was increased significantly (by approximately 6% to 57%; $P<0.05$) in all five subjects who received the wheat gluten hydrolysate. No change was observed in the four control subjects.[41] There were no reported side effects. An increase in natural killer cell activity could be expected to enhance immune monitoring against tumor development and viral infections.[42] Epidemiologic evidence supports a protective role for whole-grain consumption to reduce cancer risk,[43] with specific effects attributable to wheat.[44,45]

CONCLUSIONS

Gluten-free diets are clearly indicated for patients with celiac disease or for persons with gluten sensitivity, and may be beneficial for individuals with other chronic autoimmune disease conditions such as psoriasis, rheumatoid arthritis, and type 1 diabetes.[12,13] With the substantial growth in the gluten-free products market,[2] a greater number of food choices are now available to individuals for whom gluten avoidance is essential. There are many gluten-free grains available to help consumers obtain the benefits of whole grains and overcome some of the nutritional deficiencies (eg, inadequate intakes of thiamin, riboflavin, niacin, folate, and iron) reported to be associated with gluten-free diets.[9,46] A gluten-free diet can be a well-balanced diet if care is taken in choosing whole-grain products, including more legumes, and selecting foods with lower energy density. This does not imply that a gluten-free diet, per se, is a healthier diet.

Despite numerous health claims and the exploding popularity of gluten-free products, there are no published data to support a weight loss claim for a gluten-free diet.[3] Results of several studies of patients with celiac disease suggest that a gluten-free diet may actually worsen BMI status in some overweight and obese individuals. Gluten-free baked goods can be high in fat and total energy.[9] Moreover, whole-grain intake is inversely associated with BMI, and wheat is the most widely consumed grain in America. Thus, going gluten-free for purposes of weight loss may have unintended consequences. Randomized-control trials are necessary to establish the effect of a gluten-free diet on weight loss in overweight or obese individuals for whom a gluten-free diet is not medically indicated.

Gluten-rich grains, especially wheat, may have health benefits attributable to naturally occurring fructan-type resistant starches as well as gluten itself. By creating a healthy composition of colon bacteria, whole-grain wheat products may protect the gut from some cancers, inflammatory conditions, and cardiovascular disease. Gluten, and one of its component proteins gliadin, may contribute to blood pressure control and immune function. Because wheat is the main source of gluten in the American diet,[29,30] these studies may help explain the consistent findings of health benefits of whole-grain consumption.[25,26,43,44]

There is no evidence to suggest that following a gluten-free diet has any significant benefits in the general population. Indeed, there is some evidence to suggest that a gluten-free diet may adversely affect gut health in those without celiac disease or gluten sensitivity.[31] Additional research is needed to clarify the health effects of gluten, and potential consequences of avoiding gluten-containing grains.

References

1. Piezak M. Celiac disease, wheat allergy, and gluten sensitivity: When gluten free is not a fad. *JPEN J Parental Enterol Nutr*. 2012;36(suppl 1):68S-75S.
2. Sapone A, Bai JC, Ciacci C, et al. Spectrum of gluten-related disorders: Consensus on new nomenclature and classification. *BMC Med*. 2012; 10:13.
3. Marcason W. Is there evidence to support the claim that a gluten-free diet should be used for weight loss? *J Am Diet Assoc*. 2011;111(11): 1786.
4. Hasselbeck E. *The G-Free Diet: a Gluten-Free Survival Guide*. New York, NY: Center Street Books; 2009.
5. Miley Cyrus: Gluten-free diet is responsible for weight loss. Huffington Post website. http://www.huffingtonpost.com/2012/04/10/miley-cyrus-gluten-free-diet-weight-loss_n_1414641.html. Accessed April 20, 2012.
6. Hadjivassiliou M, Grunewald RA, Davies-Jones GAB. Gluten sensitivity as a neurological illness. *J Neurol Neurosurg Psychiatry*. 2002;72(5): 560-563.
7. Briani C, Samaroo D, Alardini A. Celiac disease: From gluten to autoimmunity. *Autoimmunity Rev*. 2008;7(8):644-650.
8. Catassi C, Fassano A. Celiac disease. *Curr Opin Gastroenterol*. 2008; 24(6):687-691.
9. Niewinski MM. Advances in celiac disease and gluten-free diet. *J Am Diet Assoc*. 2008;108(4):661-672.
10. Cascella NG, Kryszak D, Bhatti B, et al. Prevalence of celiac disease and gluten sensitivity in the United States Clinical Antipsychotic Trials of Intervention Effectiveness study population. *Schizophrenia Bull*. 2011;37(1):94-100.
11. Haines ML, Anderson RP, Gibson PR. Systematic review: The evidence base for long-term management of celiac disease. *Aliment Pharmacol Ther*. 2008;28(9):1042-1066.
12. Green PH. Mortality in celiac disease, intestinal inflammation, and gluten sensitivity. *JAMA*. 2009;302(11):1225-1226.
13. El-Chammas K, Danner E. Gluten-free diet in nonceliac disease. *Nutr Clin Pract*. 2011;26(3):294-299.
14. de Magistris L, Familiari V, Pascotto A, et al. Alterations of the intestinal barrier in patients with autism spectrum disorders and in their first-degree relatives. *J Pediatr Gastroenterol Nutr*. 2010;51(4):418-424.
15. Mulloy A, Lang R, O'Reilly M, Sigafoos J, Lancioni G, Rispoli M. Gluten-free and casein-free diets in the treatment of autism spectrum disorders; a systematic review. *Res Autism Spectrum Disord*. 2010;4(3):328-339.
16. Buie T, Campbell DB, Fuchs GJ 3rd, et al. Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: A consensus report. *Pediatrics*. 2010;125 (suppl 1):S1-S18.

17. Cheng J, Brar PS, Lee AR, Green PHR. Body mass index in celiac disease. Beneficial effect of a gluten-free diet. *J Clin Gastroenterol*. 2010;44(4):267-271.

18. Dickey W, Kearney N. Overweight in celiac disease: Prevalence, clinical characteristics, and effect of a gluten-free diet. *Am J Gastroenterol*. 2006;101(10):2356-2359.

19. Valletta E, Fornaro M, Cipolli M, Conte S, Bissolo F, Danchielli C. Celiac disease and obesity: Need for nutritional follow-up after diagnosis. *Eur J Clin Nutr*. 2010;64(11):1371-1372.

20. Gaesser GA. Carbohydrate quantity and quality in relation to body mass index. *J Am Diet Assoc*. 2007;107(10):1768-1780.

21. Neyrinck AM, Delzene NM. Potential interest of gut microbial changes induced by nondigestible carbohydrates of wheat in the management of obesity and related disorders. *Curr Opin Clin Nutr Metab Care*. 2010;13(6):722-728.

22. Gibson GR. Prebiotics as gut microflora management tools. *J Clin Gastroenterol*. 2008;42(suppl 2):S75-S79.

23. Delzenne NM, Cani PD. Gut microbiota and the pathogenesis of insulin resistance. *Curr Diab Rep*. 2011;11(3):154-159.

24. Jonnalagadda SS, Harnack L, Liu RH, et al. Putting the whole grain puzzle together: Health benefits associated with whole grains—Summary of American Society for Nutrition 2010 Satellite Symposium. *J Nutr*. 2011;141(5):1011S-1022S.

25. Harris KA, Kris-Etherton PM. Effects of whole grains on coronary heart disease risk. *Curr Atheroscler Rep*. 2010;12(6):368-376.

26. Slavin J. Why whole grains are protective: Biological mechanisms. *Proc Nutr Soc*. 2003;62(1):129-134.

27. Fava F, Gitau R, Lovegrove J, Tuohy KM. The gut microflora and lipid metabolism: Implications for human health. *Curr Med Chem*. 2006;13(25):3005-3021.

28. Rastall RA, Gibson GR, Gill HS, et al. Modulation of the microbial ecology of the human colon by probiotics, prebiotics and synbiotics to enhance human health: An overview of enabling science and potential applications. *FEMS Microbiol Ecol*. 2005;52(2):145-152.

29. van Loo J, Coussement P, de Leenheer L, Hoebregs H, Smits G. On the presence of inulin and oligofructose as natural ingredients in the Western diet. *Crit Rev Food Sci Nutr*. 1995;35(6):525-552.

30. Moshfegh AJ, Friday JE, Goldman JP, Ahuja JKC. Presence of inulin and oligofructose in the diets of Americans. *J Nutr*. 1999;129(7 suppl):1407S-1411S.

31. De Palma G, Nadal I, Collado MC, Sanz Y. Effects of a gluten-free diet on gut microbiota and immune function in healthy adult human subjects. *Br J Nutr*. 2009;102(8):1154-1160.

32. Kinsey L, Burden ST, Bannerman E. A dietary survey to determine if patients with coeliac disease are meeting current healthy guidelines and how their diet compares to that of the British general population. *Eur J Clin Nutr*. 2008;62(11):1333-1342.

33. Costabile A, Klinder A, Fava F, et al. Whole-grain wheat breakfast cereal has a prebiotic effect on the human gut microbiota: A double-blind, placebo-controlled, crossover study. *Brit J Nutr*. 2008;99(1):110-120.

34. Jenkins DJA, Kendall CWC, Vuksan V, et al. Effect of wheat bran on serum lipids: Influence of particle size and wheat protein. *J Am Coll Nutr*. 1999;18(2):159-165.

35. Jenkins DJA, Kendall CWC, Vidgen E, et al. High-protein diets in hyperlipidemia: Effect of wheat gluten on serum lipids, uric acid, and renal function. *Am J Clin Nutr*. 2001;74(1):57-63.

36. Thewissen BG, Pauly A, Celus I, Brijs K, Delcour JA. Inhibition of angiotensin I-converting enzyme by wheat gliadin hydrolysates. *Food Chem*. 2011;127(4):1653-1658.

37. Behall KM, Scholfield DJ, Hallfrisch J. Whole-grain diets reduce blood pressure in mildly hypercholesterolemic men and women. *J Am Diet Assoc*. 2006;106(9):1445-1449.

38. Tighe P, Duthie G, Vaughan N, et al. Effect of increased consumption of whole-grain foods on blood pressure and other cardiovascular risk markers in healthy middle-aged persons: A randomized controlled trial. *Am J Clin Nutr*. 2010;92(4):733-740.

39. Streppel MT, Arends LR, van't Veer P, Grobbee DE, Geleijnse JM. Dietary fiber and blood pressure: A meta-analysis of randomized placebo-controlled trials. *Arch Intern Med*. 2005;165(2):150-156.

40. Novak F, Heyland DK, Avenall A, Drover JW, Su X. Glutamine supplementation in serious illness: A systematic review of the evidence. *Crit Care Med*. 2002;30(9):2022-2029.

41. Horiguchi N, Horiguchi H, Suzuki Y. Effect of wheat gluten hydrolysate on the immune system in healthy human subjects. *Biosci Biotechnol Biochem*. 2005;69(12):2445-2449.

42. Herberman RB, Oltaldo JR. Natural killer cells: Their roles in defenses against disease. *Science*. 1981;214(4516):24-30.

43. Jacobs DR, Marquart L, Slavin J, Kushi LH. Whole-grain intake and cancer: An expanded review and meta-analysis. *Nutr Cancer*. 1998;30(2):85-96.

44. Fardet A. New hypotheses for the health-protective mechanisms of whole-grain cereals: What is beyond fibre? *Nutr Res Rev*. 2010;23(1):65-134.

45. Reddy BS, Hirose Y, Cohen LA, Simi B, Cooma I, Rao CV. Preventive potential of wheat bran fractions against experimental colon carcinogenesis: Implications for human colon cancer prevention. *Cancer Res*. 2000;60(17):4792-4797.

46. Case S. *Gluten-Free Diet: A Comprehensive Resource Guide*. Regina, Saskatchewan, Canada: Case Nutrition Consulting; 2006.

AUTHOR INFORMATION

G. A. Gaesser is a professor, Exercise and Wellness Program, Healthy Lifestyles Research Center, School of Nutrition and Health Promotion, Arizona State University, Phoenix. S. S. Angadi is a postdoctoral scholar, Exercise and Metabolic Disease Research Laboratory, Translational Sciences Section, UCLA School of Nursing, Los Angeles, CA.

Address correspondence to: Glenn A. Gaesser, PhD, Healthy Lifestyles Research Center, School of Nutrition and Health Promotion, Arizona State University, 500 N 3rd St, Phoenix, AZ 85004. E-mail: glenn.gaesser@asu.edu

STATEMENT OF POTENTIAL CONFLICT OF INTEREST

G. A. Gaesser is chairman of the Grain Foods Foundation Scientific Advisory Board.

FUNDING/SUPPORT

Preparation of this article was supported in part by a grant from the Grain Foods Foundation.