

Enzyme Replacement as an Effective Treatment for the Common Symptoms of Complex Carbohydrate Intolerance

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Complex carbohydrates are an essential part of a healthy diet. However, many people suffer from varying degrees of carbohydrate intolerance, resulting in embarrassing gastrointestinal symptoms and avoidance of some components of a healthy diet. To facilitate awareness and discussion, we propose the phrase Complex Carbohydrate Intolerance (CCI) as a broad term to encompass the range of symptoms associated with carbohydrate intolerance. While various treatments offer symptomatic relief, enzyme replacement therapy targets the cause of the problem, an enzyme deficiency. The enzyme, alpha-galactosidase, currently only found in the over-the-counter product, Beano[®], may be an effective preventative treatment for CCI.

Key words: complex carbohydrate intolerance, CCI, *alpha*-galactosidase, gastrointestinal discomfort, flatulence

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Introduction

Complex carbohydrates are an excellent energy source rich in vitamins, minerals, and fiber. The United States Department of Agriculture (USDA) recommends that between 40% and 60% of our total calories come from carbohydrates, preferably from complex carbohydrates (starches) and naturally occurring sugars (Table 1).

Although complex carbohydrates are a healthy addition to the daily diet, many people are intolerant to such foods, including fruits and vegetables, whole grains, rice, breads, cereals, beans, lentils, and dried peas. This intolerance can lead to uncomfortable and embarrassing symptoms such as flatulence, abdominal pain, cramping, diarrhea, and/or constipation.

Many people are unsure if their gastrointestinal symptoms are within normal limits and often hesitate to seek treatment. There is a need to facilitate awareness and discussion about bowel gas and gastrointestinal distress caused by carbohydrate intolerance. As such, we propose the use of the phrase Complex Carbohydrate Intolerance (CCI) as a broad term to encompass the range of symptoms associated with carbohydrate intolerance. By linking common symptoms of carbohydrate intolerance with the term CCI, patients will be able to more easily open discussion with physicians, pharmacists, and other healthcare professionals about the embarrassing symptoms associated with this condition and make appropriate choices to treat rather than merely mask symptoms.

With an understanding of complex carbohydrates that may cause varying degrees of gastrointestinal distress and available treatment alternatives for CCI, people will be able to better tolerate healthy, balanced diets rich in complex carbohydrates. This paper reviews carbohydrate digestion and treatment alternatives that may help patients prevent and/or relieve discomfort associated with complex carbohydrate intolerance.

Carbohydrate Digestion

Complex carbohydrates consist of oligosaccharides, long chains of monosaccharides (small sugar units that cannot be further broken down) held together by *alpha*-galactosidic linkages. Oligosaccharide digestion is necessary because the gastrointestinal tract can only absorb monosaccharides. Complex carbohydrates are generally broken down into monosaccharides, including glucose and galactose, in the small intestine. Following this digestion, the glucose,

galactose, and other simple sugars are transported by an enzyme to specialized cells in the small intestine where they are absorbed and transferred to other cells and used by the body for energy.

The inability of the small intestine to adequately transport and absorb glucose, galactose, and other monosaccharides is caused by a lack of a sufficient number of enzymes required to digest oligosaccharide bonds. In particular, all humans lack the intestinal enzyme *alpha*-galactosidase, which is required to hydrolyze *alpha*-galactosidic linkages present in complex carbohydrates.¹ Such a deficiency of enzymes results in incomplete digestion of complex carbohydrates, allowing unabsorbed undigested sugars to move into the large intestine. As a result of fermentation by native microbial flora in the large intestines, the undigested carbohydrates produce hydrogen, carbon dioxide, and short chain fatty acids,¹ resulting in bloating, pain, and gastrointestinal discomfort.

The Carbohydrate Limit

Many people experience symptoms of incomplete digestion, or impaired glucose/galactose tolerance. Because complex carbohydrate metabolism is dependant on enzyme levels, the range of tolerance to carbohydrates is extremely wide. One person could eat a serving of complex carbohydrates and experience no symptoms of intolerance. However, the same person might experience symptoms following ingestion of a larger serving of complex carbohydrates if the body does not have an adequate supply of enzymes for digestion. As a result, the person may experience uncomfortable bloating and cramping.

While many people may suffer from varying degrees of incomplete digestion, some individuals have a rare genetic disorder that causes impaired tolerance. Glucose-galactose malabsorption, known also as carbohydrate intolerance of glucose-galactose, is an inherited recessive genetic trait characterized by an inability of the small intestine to adequately transport and absorb glucose and galactose. The defective gene responsible for this disorder (the sodium-glucose cotransporter [SGLT1]) is located on the long arm of chromosome 22 (22q13.1).²

Impact of Carbohydrate Intolerance

Individuals with CCI may avoid complex carbohydrate foods due to their intolerance, despite the protective health benefits of such foods. Diets high in fruits, vegetables, nuts, and whole grains rich in phytochemicals and fiber, for example, have been shown to offer significant protection

against coronary heart disease.³ Studies also suggest that the whole grains or other high-fiber foods may help control both insulin production and blood sugar levels to help control type 2 diabetes.⁴ In addition, a diet rich in fiber, such as one containing whole grains, beans, and other complex carbohydrates, may help protect against colon cancer.⁵ As the potential benefits of beans, whole grains, and other complex carbohydrates are realized, more importance is placed on including these foods in the daily diet. However, consumer intake of whole grains and complex carbohydrates is low,⁶ perhaps due to lack of consumer awareness of health benefits and the prevalence of carbohydrate intolerance (CCI).

Symptoms of CCI, including gas, pain/discomfort, burping, and bloating, are similar to symptoms of more serious conditions, including cardiac events. Therefore, it may be common that individuals with CCI seek medical attention for presumed, more serious conditions. This mistaken symptom association could lead to costly medical procedures, including stress tests, cardiovascular exams, and lower/upper GI work ups. In addition, misdiagnosis of symptoms may result in patients taking drugs that are not treating the underlying cause of the condition. To avoid unnecessary treatment measures there is a need for increased awareness of CCI, its symptoms, prevention, and treatment options.

Treatment Options

Due to the prevalence of CCI symptoms, many people would benefit from treatment of carbohydrate intolerance. Diet and lifestyle changes may help some people manage CCI symptoms, while other people may benefit from various pharmacologic approaches. A review of common treatments is provided below.

Diet and Lifestyle

People who are carbohydrate intolerant should follow a low-carbohydrate diet with low intake of legumes, starches, sorbitol, fructose, fiber and lactose. This type of diet will help reduce the amount of substrate for bacterial fermentation during digestion that results in uncomfortable bloating.⁷ Avoiding or limiting intake of particular substances that cause discomfort may also reduce or prevent symptoms.⁸ Unfortunately, many of these high-carbohydrate foods provide important health benefits, including reducing the incidence of coronary artery disease, some cancers, and a variety of bowel problems.

Gas may also be reduced by a variety of simple lifestyle changes. Throughout the day, small quantities of air are swallowed. This air is propelled through the gut, where the oxygen and carbon dioxide are absorbed but the nitrogen is passed on as flatus. To decrease excessive air swallowing and the associated flatulence, patients may benefit from various techniques, including chewing food rather than gulping it, eating and drinking slowly, and avoidance of gum, hard candy, and tobacco products.⁷

Exercise may help gas move more quickly through one's digestive tract, thus reducing the discomfort associated with CCI.

Drug Products

There are a variety of prescription and over-the-counter medications available to address various symptoms associated with carbohydrate intolerance.

Prescription drugs. Tetracycline, an antibiotic, is often recommended for patients with bacterial overgrowth of the small intestine.⁷ Metoclopramide, a gastrointestinal stimulant, is also used for treatment of gastrointestinal discomfort; however, there are limited data to support its use in decreasing distention and bloating.⁷ While these drugs may target specific symptoms associated with CCI, they do not allow the body to more easily digest complex carbohydrates, thus preventing occurrence of CCI symptoms.

Over-the-counter drugs. Simethicone, an agent that results in less residual gas to cause uncomfortable cramping, is often used for treatment of excess gas. Simethicone may cause gas bubbles in the stomach to combine, forming larger bubbles thereby allowing the patient to excrete a greater volume of gas at one time. Alternatively, simethicone may facilitate the passage of gas through the bowel lumen.⁸ Simethicone treatment, however, does not reduce the actual amount of gas in the intestinal lumen. In fact, some studies suggest that simethicone does not exhibit any beneficial effect on symptoms of intestinal gas.⁹ Simethicone is available as a single agent or in combination with antacids.

Antacid/anti-diarrhea products, such as bismuth subsalicylate, are often used to help reduce indigestion, nausea, and diarrhea, and to reduce fecal and flatus odor.⁷ However, these products do not prevent the formation of gas.

Dietary Supplements

In addition to antacids, dietary supplements are available for over-the-counter treatment of CCI symptoms. Activated charcoal tablets can be taken after meals or at the first sign of gas discomfort. Although there are limited data to support efficacy,⁷ charcoal may decrease odor from gas in the colon. Importantly, however, charcoal does not prevent gas from forming. In addition, charcoal can be associated with unpleasant side effects, including black, tarry stools.

Research suggests that bacteria may be an effective therapy for prevention or treatment of some gastrointestinal conditions. Probiotics and prebiotics, therefore, may relieve gas, bloating, and other conditions caused by gut flora.¹⁰

Peppermint and other herbs that soothe the digestive tract may also be beneficial in preventing belching and decreasing bloating after large meals. Evidence suggests that enteric-coated peppermint oil capsules may reduce abdominal pain, distention, flatulence, and bowel movements in 70% to 80% of patients 8 years of age and older with irritable bowel syndrome.¹¹⁻¹⁴ Despite its efficacy, it should be noted that peppermint and other herbs do not target the enzyme deficiency responsible for CCI discomfort.

Enzyme Replacement

Nonprescription enzyme replacement/anti-gas products are available to relieve flatulence, burping, bloating, and abdominal discomfort associated with CCI. Unlike lifestyle/diet changes, drug treatments, and dietary supplements, enzyme replacement helps the body break down complex carbohydrates thereby preventing the formation of gas and associated discomfort.

Alpha-galactosidase. The enzyme *alpha*-galactosidase, which is derived from the mold *Aspergillus niger*, has been shown to diminish intestinal gas production by enhancing the breakdown of oligosaccharides before they reach the lower intestine.¹⁵⁻¹⁸ Although further study is warranted, the available data suggest that *alpha*-galactosidase added to high-fiber foods decreases gas, bloating, and flatulence. A variety of studies, summarized in Table 2, demonstrate the efficacy of *alpha*-galactosidase (available under the Beano[®] trade name) in treatment of CCI symptoms. Three crossover studies demonstrate that *alpha*-galactosidase preparations combined with a bean-based meal decreased gastrointestinal symptoms, including flatulence, diarrhea, and belching.¹⁵⁻¹⁷ An additional randomized, double-masked, placebo-controlled crossover study suggested that this enzyme decreased flatulence.¹⁸ Two studies also demonstrated that *alpha*-

galactosidase decreased the concentration of breath hydrogen, a measure of intestinal gas production.^{15,18}

As a valuable therapy for preventing gas formation leading to CCI symptoms, it is important to evaluate the safety of *alpha*-galactosidase therapy. Enzymes from *Aspergillus niger*, including *alpha*-galactosidase, are considered GRAS (Generally Recognized as Safe) by the U.S. Food and Drug Administration (FDA).²⁰ While generally recognized as safe, its use is contraindicated in some patients, including patients with diabetes and people with allergy to molds. The addition of *alpha*-galactosidase to complex carbohydrate foods makes more sugars available, adding an estimated 2 to 6 grams of carbohydrates per 100 grams of food, a factor that patients with diabetes should be aware of.²⁰ In addition, while patients with diabetes taking acarbose (Precose[®]), a drug that increases flatulence, may benefit from *alpha*-galactosidase therapy, it should be noted that long-term *alpha*-galactosidase use may interfere with the glucose-lowering effects of this drug. However, occasional use of *alpha*-galactosidase to relieve symptoms attributable to acarbose may be acceptable.¹⁸ Patients with mold allergies should be cautioned, as gastrointestinal distress, skin rashes, or other allergic symptoms may result from *alpha*-galactosidase therapy.²⁰ Additionally, patients with galactosemia should use *alpha*-galactosidase with caution, as this enzyme produces galactose.²⁰

Based on the available safety information, *alpha*-galactosidase should be considered safe for use in adults and children over age 12. Individuals with known medical conditions, including galactosemia (a rare autosomal recessive inborn error of galactose metabolism) and diabetes should use *alpha*-galactosidase under the supervision of a doctor. In addition, pregnant and lactating women should be advised to consult a physician before taking this, or any, dietary supplement.

Other enzyme replacement therapies. As suggested for treatment of CCI, enzymes have proven to be effective in treating other types of food intolerances. Lactose intolerance, a condition with similar etiology and symptoms as CCI, can be treated with enzyme replacement. Lactose-intolerant individuals can take lactase enzymes, which hydrolyze lactose, the primary carbohydrate in dairy products, thus decreasing the flatulence due to lactose intolerance.²¹⁻²³ While conditions of lactose intolerance and CCI and their treatments are similar, it is important to realize that lactose intolerance and CCI are caused by deficiencies of different enzymes.

Therefore, treating a CCI patient with lactase would not be an effective therapy and ultimately would lead to added discomfort and avoidance of healthy, complex carbohydrate foods.

Treating the Cause of the Problem

While there are a variety of measures that can be taken to help patients manage bloating and flatulence, effective treatments for CCI target the root cause of the problem, rather than just the symptoms. Enzyme replacement therapy with *alpha*-galactosidase, such as Beano[®], is the only treatment alternative that treats the deficiency in enzymes necessary to digest complex carbohydrate, thus preventing formation of gas and CCI symptoms. To prevent gas before it starts, *alpha*-galactosidase preparations (one tablet or 5 drops liquid)[†] should be taken at the same time as ingestion of each half-cup serving of complex carbohydrate foods. There is significant scientific agreement that the symptoms associated with CCI are related to insufficient quantities of the *alpha*-galactosidase enzyme. As such, most authoritative bodies and sources of healthcare information recognize enzyme replacement as the only option for preventing symptoms in patients who should not, or choose not, to avoid foods rich in complex carbohydrates.

Confusion regarding the cause of CCI and the available treatment options may result in improper use and added suffering. Accordingly, there is need for increased CCI and treatment awareness.

Conclusions

Patients should be aware that gastrointestinal discomfort following meals containing complex carbohydrates is common and that this discomfort can be alleviated through a variety of over-the-counter treatments. Unlike treatment options that may only relieve symptoms, enzyme replacement with *alpha*-galactosidase is the most effective option because it treats the cause of CCI and thereby prevents the symptoms. CCI is caused by a deficiency in enzymes to break down oligosaccharides, the difficult to digest sugar units in complex carbohydrates. While clinical studies demonstrate the efficacy of *alpha*-galactosidase, it should be noted that most studies utilized a unique preparation available publicly under the trade name Beano[®]. While

[†] Commercial preparations (Beano[®]) contain 150 GALU *Alpha*-galactosidase enzyme (derived from *Aspergillus niger*)

some people may understand that complex carbohydrates such as vegetables, legumes, and breads may cause bloating, burping, or flatulence, treatment options for such discomfort are largely unknown. Many people may perceive that products such as Beano[®], for example, alleviate symptoms associated with bean consumption only. However, *alpha*-galactosidase enzyme replacement therapies can treat by preventing CCI symptoms from a variety of oligosaccharides-containing foodstuffs. As such, it is evident that there is a need for understanding complex carbohydrate intolerance in otherwise healthy individuals, as well as awareness of viable treatment alternatives that target the root cause of the intolerance, a deficiency in enzymes required from complex carbohydrate digestion.

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