Role of Bile Acid Diarrhea in Chronic Functional Diarrhea

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Chronic diarrhea is estimated to affect about 5% of the population. This is about 16 million people in the United States alone. Diarrhea is defined as increased frequency of bowel movements (more than 3 bowel movements per day). These bowel movements have a looser consistency (runny to watery). Diarrhea that is considered chronic lasts more than 4 weeks. Normal diagnostic testing such as imaging studies, endoscopy (possibly with biopsies) or other tests are often done to determine the cause. Unfortunately, these tests may identify the underlying cause of the diarrhea in less than 10% of patients. For those where the underlying cause is not identified, many are diagnosed with a form of functional diarrhea. The most well-known include diarrhea predominant irritable bowel syndrome (IBS-D) or chronic functional diarrhea. However, recent research studies have shown that up to a third of patients diagnosed with chronic functional diarrhea may instead have bile acid diarrhea.

What do Bile Acids do in the body?

Bile acids are created by the liver and are used in the small intestine to help with the absorption of fat. Our bodies create two primary bile acids: cholic acid and chenodeoxycholic acid. Most of the bile acids are reabsorbed at the end of the small intestine. This leaves a small proportion (< 5%) that enters the colon.

What is Bile Acid Diarrhea?

Bile acid diarrhea occurs when excess bile acids enter the colon, also known as the large intestine. This causes both increased colonic motility and increased water and electrolyte secretion in the colon. *Colonic motility* refers to the movement of contents through the gastrointestinal (GI) tract. *Electrolytes* are minerals in the body that have an electric charge when they are dissolved in the body's fluids. Electrolytes help the body balance fluid and pH levels. These minerals also provide nutrients and remove waste from the body's cells. Sodium, calcium, potassium, chloride, phosphate, and magnesium are all electrolytes the body receives through foods and fluids you take in. Diarrhea results from these changes in the colon.

How common is Bile Acid Diarrhea?

Most research studies show up to 25-33% of patients who have previously been diagnosed with chronic functional diarrhea may instead have bile acid diarrhea. Recently a review was done of over 1,000 patient medical records in a large teaching hospital. In this research study, up to 50% of the patients diagnosed with chronic functional diarrhea may have bile acid diarrhea. While there is still much to learn about the different causes for diarrhea, improvements in research and testing options now allow healthcare providers to diagnose several different types of diarrhea such as bile acid diarrhea.

What are the symptoms of Bile Acid Diarrhea?

Patients with bile acid diarrhea have the same symptoms as those with chronic functional diarrhea. They have an increased number of bowel movements (more than 3 per day). These bowel movements have a looser consistency (runny to watery). They do not have **rectal** bleeding or undigested food in bowel movements. Some people may experience upper gastrointestinal symptoms such as nausea and vomiting. The severity of these symptoms are similar to those with chronic functional diarrhea. Therefore, there is no way to differentiate bile acid diarrhea from chronic functional diarrhea based on symptoms alone.

> The **rectum** is the final section of the large intestine where bowel movements are stored before being emptied. Bleeding in the rectum can typically be seen as red blood on the outside of bowel movements.

If patients with chronic functional diarrhea do not respond to first line treatments, they should be assessed for bile acid diarrhea. First line treatments for chronic functional diarrhea can include dietary changes and antidiarrheal drugs such as loperamide or diphenoxylate.

How is Bile Acid Diarrhea diagnosed?

There are multiple methods to diagnose bile acid diarrhea. The availability of diagnostic tests depends on location and local regulatory approval. Each country has its own regulations and guidelines for what tests and options are available for diagnosis. Regulatory approval is put into place to ensure that testing options are safe, effective, and provide accurate results.

- *^{75}Selenium HomoCholic Acid Taurine (^{75}SeHCAT)* – Internationally this is the current gold standard testing option; however, it is currently not available in the United States. This is a 7-day test that involves the use of radiation to track bile acid movement. A CT scan is done, and a small dose of the radioactive bile acid is taken by the patient. Seven days later, a repeat CT scan is done. This determines how much radiation containing bile acid is still in the body. People with bile acid diarrhea lose more bile acids through the colon. They have lower retention (<15% bile acid retention) at 7 days.
- *48-hour stool collection* – This is the current best testing option in the United States. This test directly measures both the total number of bile acids as well as the number of individual bile acids (cholic acid and chenodeoxycholic acid) in the stool. There is no radiation exposure with this test. Those taking the test eat a high fat diet (100-grams of fat per day) for 4 days. During the last 2 days of the high fat diet, patients take stool samples with each bowel movement.
- *Serum 7α-Hydroxy-4-cholesten-3-one (C4)* – This test is a simple fasting blood sample and is available in the United States. The sample is taken early in the morning and is often used to rule out bile acid diarrhea. However, those with a positive test may need to undergo additional testing to confirm the diagnosis of bile acid diarrhea.
- *Combined fecal bile acids and serum C4* – Currently, this test is only available in the research setting. This is a single, random bowel movement sample taken in addition to performing the fasting blood test described above (Serum 7α-Hydroxy-4-cholesten-3-one (C4)). The single stool sample, while more convenient than the 48-hour sample, will only measure individual fecal bile acids (but not total bile acids). However, initial data from the research studies show that this testing combination may predict bile acid diarrhea as well as the 48-hour stool collection test (described above).

Is there a treatment for Bile Acid Diarrhea?

There are medications available for those with bile acid diarrhea. They are called bile acid sequestrants (a group of resins or sticky organic substances used to bind certain components of bile in the GI tract). Originally, these medications were used to lower cholesterol. They work by blocking bile acids from being absorbed by the blood. The most common side effects for these medications are nausea and constipation. Currently there are three available: Cholestyramine (available in powder form), Colesevelam (available in tablet or powder form), and Colestipol (available in tablet form). These medications may interfere with absorption of other medications. It is important to take other medications at least 2 hours from the time bile acid sequestrants are taken.

Bile acid sequestrants are good options for people diagnosed with bile acid diarrhea. However, it is important to be accurately diagnosed with bile acid diarrhea before trying a bile acid sequestrant. In one research study, approximately 70-80% of people diagnosed with bile acid diarrhea reported improved diarrhea with these drugs. However, only 26% of patients with chronic functional diarrhea had improvement in diarrhea with bile acid sequestrants.

Summary

Bile acid diarrhea is the true cause of diarrhea in up to 50% of people originally diagnosed with chronic functional diarrhea. Accurate diagnosis is critical to guide treatment. Additional research is being conducted to simplify the diagnosis of bile acid diarrhea and new targeted therapies are being studied. It is vitally important to thoroughly discuss all symptoms with a healthcare provider. Doing so helps your provider determine the best testing options, your diagnosis, and how to treat your condition.

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