New class of drugs shows promise in treating chronic diarrhea

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A pilot study testing a new type of drug in patients with chronic diarrhoea has shown promising effects on reducing their symptoms.

Bile acid diarrhoea (BAD) is a common cause of chronic diarrhoea that is estimated to affect one in 100 adults in western countries, but is often mistaken for irritable bowel syndrome (IBS) by doctors. Many patients

are not diagnosed correctly and undergo repeated unnecessary tests.

The study at Imperial College London found that the drug obeticholic acid (OCA) could provide relief for patients with BAD. OCA is the first in a new class of drugs, farnesoid X receptor (FXR) agonists, and the response of the patients to OCA shows that abnormalities in the system it targets may be critical for this condition. The research is published today in the journal *Alimentary Pharmacology and Therapeutics*.

Professor Julian Walters, from the Department of Medicine at Imperial College London, who led the study, said: "Many doctors are totally unaware of bile acid diarrhoea, but it's more common than Crohn's disease and ulcerative colitis. When patients are correctly diagnosed, there are specific treatments that can help them, but many people find these current drugs are unpalatable.

"The condition often has a serious impact on patients' work and social lives, causing people to have up to ten watery bowel movements a day, often for many months, with an urgent need to go to avoid accidental incontinence."

BAD is caused by excessive secretion of bile acids, a component of bile that aids digestion. After bile is secreted into the intestine from the gall bladder, the bile acids are normally absorbed in the ileum, a part of the small intestine. But in BAD, excess bile passes into the colon and causes watery diarrhoea.

A hormone produced in the ileum, FGF19, regulates the production of bile acids in the liver, and previous studies found that patients with BAD have low levels of FGF19. OCA targets the receptors in the ileum that stimulate the production of FGF19.

The researchers tested OCA in three groups of patients: 10 with primary

BAD, where the intestine is otherwise healthy; 10 with secondary BAD, where malabsorption can occur as a result of another disease such as Crohn's; and eight with other causes of chronic diarrhoea, who served as a control group. The patients, who were treated at Imperial College Healthcare NHS Trust, recorded their symptoms in a diary for two weeks before starting OCA treatment, for two weeks taking the drug daily, and two weeks afterwards. They also had blood tests at the start and end of the OCA treatment period.

Symptoms improved with OCA treatment in the primary BAD patients and some secondary BAD patients, but not in those with other causes of chronic diarrhoea. The treatment was generally well tolerated.

Professor Walters added: "This drug represents a new potential approach to treating BAD by restoring the levels of the FGF19 hormone and so controlling bile acid production in the liver. These early findings suggest that FXR agonists could be effective for treating patients with chronic diarrhoea. This is exciting and we need larger studies to confirm this."

More information: J.R.F. Walters et al. 'The response of patients with bile acid diarrhoea to the farnesoid X receptor agonist obeticholic acid.' *Aliment Pharmacol Ther*, 20 October 2014. DOI: 10.1111/apt.12999

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