Medical Xpress

# Fecal transplant plus fibre supplements improve insulin sensitivity in severely obese patients, clinical trial shows

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A clinical trial led by medicine professor Karen Madsen showed that a single oral fecal transplant followed by fibre supplements improved insulin sensitivity in severely obese patients. Improved insulin sensitivity allows the body to use glucose more effectively, reducing blood sugar. Credit: Photo: Faculty of Medicine & Dentistry

A transplant of healthy gut microbes followed by fibre supplements

benefits patients with severe obesity and metabolic syndrome, according to University of Alberta clinical trial findings published today in *Nature Medicine*.

Patients who were given a single-dose oral fecal microbial transplant followed by a daily fibre supplement were found to have better insulin sensitivity and higher levels of beneficial microbes in their gut at the end of the six-week trial. Improved insulin sensitivity allows the body to use glucose more effectively, reducing blood sugar.

"They were much more metabolically healthy," said principal investigator Karen Madsen, professor of medicine in the Faculty of Medicine & Dentistry and director of the Centre of Excellence for Gastrointestinal Inflammation and Immunity Research.

"These patients were on the best known medications (for metabolic syndrome) and we could improve them further, which shows us there is an avenue for improvement by targeting these different pathways in the microbiome."

Sixty-one patients with a body mass index of 40 or higher completed the double-blind, randomized trial. Recruited from the bariatric surgery waitlist in Edmonton, all had metabolic syndrome, a condition that includes insulin resistance, high blood glucose, high blood pressure and other complications. It can eventually lead to diabetes.

## The overlooked organ

The microbiome is all of the bugs—micro-organisms, bacteria, viruses, protozoa and fungi—found in the gastrointestinal tract. People with various diseases are known to have altered microbial contents. It is not fully understood whether microbiome changes cause disease or whether disease causes changes in the gut, but it is likely a bit of both, Madsen

said. It is known that replacing unhealthy bacteria with healthy bacteria can lead to improved health.

Fecal transplants, which contain microbes from healthy stool donors, are currently used extensively for treating Clostridium difficile, or C. difficile, bacterial infections, and research is underway to test their usefulness in treating other illnesses such as inflammatory bowel disease, mental health and metabolic disorders.

"We know that the gut microbiome affects all of these processes—inflammation, metabolism, immune function," said Madsen, who is a member of the Women and Children's Health Research Institute and is one of the University of Alberta leads for the national Microbiome Research Core (IMPACTT).

"The potential for improving human health through the microbiome is immense," Madsen said. "We are only scratching the surface at the moment."

## The right kind of fibre

This is the first study to show that oral delivery of fecal transplantation is effective in patients with obesity-related metabolic syndrome.

A previous study done in Europe on a small number of male patients with obesity and metabolic syndrome had shown promising results, but the transplants in that study were given through an invasive endoscopy (a tube down the throat) and the patients had milder disease.

The fecal microbial transplants in this study were from four lean, healthy donors, and were taken by mouth in a single dose of about 20 capsules prepared in a U of A lab. The capsules have no taste or odour.

The fibre supplements following the transplant were key to the success, Madsen said.

"When you transplant beneficial microbes, you need to feed them to keep them around," Madsen explained. "If you give a new microbe and you don't feed it, if you continue to eat a diet of processed foods and no fibre, then that microbe will likely die."

Our bodies do not naturally produce the enzymes needed to break down fibre, but that's what healthy bacteria in the microbiome need to live, thus the supplements. The team experimented with fermentable fibre (the kind found in beans, which produce gas) and non-fermentable fibre (essentially cellulose, found in whole grains).

"Non-fermentable fibre can change gut motility—how fast things move through—as well as acting as a bulking and binding agent that can change levels of bile acids, which could help explain our results," Madsen explained.

## Proof of concept

Madsen said the next step will be to do a longer study with more participants in multiple centres to learn how the transplant/fibre combination works and to monitor for changes in medication requirements, weight loss and other indicators. If results continue to show benefit, she said the pills could be available as a potential therapy within five years.

While scientists continue to narrow down which bacteria are the most beneficial for us, Madsen recommends we support the health of our own gut microbiome by eating fewer processed foods and more foods that contain fibre, such as whole grains, fruits and vegetables.

**More information:** Valentin Mocanu et al, Fecal microbial transplantation and fiber supplementation in patients with severe obesity and metabolic syndrome: a randomized double-blind, placebo-controlled phase 2 trial, *Nature Medicine* (2021). DOI: 10.1038/s41591-021-01399-2

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