

Researchers want to know how newest IBS drug helps stomach pain

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Dr. Satish S.C. Rao is Chief of the Section of Gastroenterology and Hepatology at the Medical College of Georgia at Georgia Regents University and founding Director of the GRU Digestive Health Center. Credit: Phil Jones

The newest drug for irritable bowel syndrome has the welcome benefit of relieving the excruciating stomach pain affecting about a third of patients, and researchers want to know how.

"These [patients](#) seem to have a magnification and misfiring of signals from their gut to their brain," said Dr. Satish S.C. Rao, Chief of the Section of Gastroenterology and Hepatology at the Medical College of

Georgia at Georgia Regents University and founding Director of the GRU Digestive Health Center. "Our hypothesis is that linaclotide dampens and essentially normalizes that communication."

In fact, physicians don't fully understand why belly pain occurs in some patients with IBS, a condition affecting about 15 percent of the population, primarily women age 30-50, and characterized by altered bowel habits, either diarrhea, constipation, or bouts of both.

Interestingly, individuals can have normal bowel habits and be pain-free for years before trouble starts, and then problems can subside as mysteriously as they began.

Rao has documented how long it takes the brain to communicate with the gut and vice versa and the size of the signals normally received. He also knows the two-way communication is much faster and bigger in IBS patients. Sophisticated brain imagery has documented increased activity in IBS patients.

"We know that these basic mechanics seemed to be disturbed in IBS based on our [previous work](#)," Rao said. "Let's see whether the drug truly works by changing how the gut and brain interact with each other."

Linaclotide, or Linzess, is only the second drug approved by the Food and Drug Administration for IBS. It eases constipation by latching onto a receptor on the surface of gastrointestinal cells that line the gut, triggering release of secretions that relieve constipation. The drug, a guanylate cyclase agonist, mimics the work of two hormones normally secreted after eating to activate the receptor, Rao said.

Animal studies, which show a decreased firing of nerves after taking the drug, supports Rao's hypothesis about how it also eases [stomach pain](#). To find whether it holds in humans, Rao is using his safe, well-established

model for studying gut-to-brain and brain-to-gut communication. He uses a magnet to stimulate the portion of the brain that controls gut activity, then measures resulting nerve activity in the gut. He then stimulates the anus and rectum and measures the brain's response.

He'll assess this two-way communication in 45 IBS patients, half of whom will get linaclotide and the remainder a placebo, for 10 weeks.

Previous work has shown that IBS patients also have a heightened sensitivity in the gut. By slowly inflating balloons in the rectum, Rao has found significantly lower pain thresholds in IBS patients compared to healthy individuals. "They feel the balloon at thresholds healthy individuals don't even feel, so they are hypersensitive inside the gut," he said. To the eye and using standard tests, the gut lining looks normal, but with ultramicroscopy and special stains, the inflammation becomes apparent, Rao said.

"As soon as we eat, there is tremendous activity going on in the gut, there are secretions; the stomach is churning and smashing up food; the bowel is contracting, things are moving; nerves are firing; but we don't feel any of that," Rao said. However the noisy mundane becomes clear to IBS patients. "They start feeling normal things as painful and abnormal," Rao said. "We all feel a little bloated, a little gassy sometimes, but these people experience the same things with excruciating pain." He notes that gas and constipation do not always cause pain.

One theory of what triggers IBS is some sort of acute gastrointestinal event, such as food poisoning or a viral or bacterial infection. "They get sick; they get better; then three to six months later, they start getting this grumbling sensation that is IBS," Rao said. He suspects a virus changes the sensitivity of the nerves that sit just behind endothelial cells in the [gut](#) and manage its communication with the brain.

Provided by Medical College of Georgia

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