Novel Treatments May Help Alleviate Constipation, IBS in Women

Second Study Shows Benefits of Hypnotherapy for Bowel Issues in Children

Three new therapy options, including two novel medications, showed promise in the treatment of irritable bowel syndrome (IBS), according to research. Participants in the studies who received one of the two investigational medications experienced significant relief in constipation, while a third study demonstrated the benefits of hypnotherapy in treating bowel and abdominal complications in children.

“With few successful treatment options currently available for IBS sufferers, these studies represent promising progress in the treatment of this and other bowel disorders,” said Maria Abreu, M.D., Director, Inflammatory Bowel Disease Center, Associate Professor of Medicine, Mount Sinai School of Medicine.

Lubiprostone Significantly Improves Symptom Relief Rates in Adults with Irritable Bowel Syndrome and Constipation (IBS-C): Data from Two, Twelve-week, Randomized, Placebo-Controlled, Double-blind Trials

Lubiprostone is a novel therapy indicated for treatment of chronic idiopathic constipation in adults. Two twelve-week, independent studies showed patients who received lubiprostone were nearly twice as likely as those who did not receive the treatment to report moderate or significant relief of IBS symptoms. Endpoints included abdominal discomfort, stool consistency, straining and others. Lubiprostone was also well-tolerated, with only one percent of patients experiencing serious adverse events and only 22 percent of patients experiencing related adverse events, compared with 21 percent of patients on placebo.

The studies included more than 1,100 patients, most of whom were female (91.6 percent) and aged 18–65 years (91.7 percent). Participants were given either lubiprostone or placebo for 12 weeks and asked to rate their IBS symptoms. To be considered a monthly responder, patients had to report moderate relief four out of four weeks or significant relief two out of four weeks. Overall responders were defined as those who had been monthly responders two out of three months.

“The lubiprostone study demonstrates the continuing need for new and emerging therapies for IBS, especially for women,” said Douglas A. Drossman, M.D., Co-Director, University of North Carolina Center for Functional Gastrointestinal and Motility Disorders in Chapel Hill, N.C., and lead author of the study. “We believe more research needs to be done to better determine lubiprostone’s benefits and tolerability, but this study suggests people suffering from IBS and constipation may soon have another option for relief.”

Effects of Novel, First-in-Class Guanylate Cyclase-C Activator, Linaclotide Acetate (MD-1100), on Gastrointestinal and Colonic Transit and Bowel Habits in Patients with Constipation-Predominant Irritable Bowel Syndrome (C-IBS)

Researchers are continually looking for unique pathways to treat digestive diseases, such as constipation and irritable bowel syndrome. Linaclotide is a novel therapy that works on a transmembrane protein in the lining of the gut called guanylate cyclase-C (GC-C). Specific gut hormones utilize GC-C to regulate intestinal fluid secretion. Linaclotide is unique in that it exerts its effect locally in the intestine while having minimal systemic exposure.

Thirty-six women suffering from IBS with constipation (IBS-C) were examined in a double-blind, placebo-controlled study, which consisted of a five-day baseline and a five-day treatment period. The endpoints were gastrointestinal transit and bowel function. Patients who received linaclotide experienced a significant acceleration of ascending colon emptying and overall colonic transit as well as a significant improvement in stool consistency, stool frequency, ease of passage and time to first bowel movement. The degree to which stool was loosened was strongly dependent on the dosage of linaclotide administered.

“Among the study participants, linaclotide was able to improve a range of bowel functions, which are typically impaired in patients with IBS-C,” said Viola Andresen, M.D., of Mayo Clinic in Rochester, Minn., and lead author of this study. “Clearly additional studies are warranted, but we remain optimistic that this treatment may hold promise for people with constipation-predominant IBS.”

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Hypnotherapy for Children with Functional Abdominal Pain or Irritable Bowel Syndrome: a Randomized Controlled Trial

As hypnotherapy has demonstrated effectiveness in adults with IBS, researchers sought to compare its effects in children to standard medical therapy commonly used for the condition as an alternative to drug therapy.

The study involved 53 patients between eight and 18 years old with FAP or IBS, who were administered six half-hour hypnotherapy sessions over a three-month period. Endpoints were pain intensity, pain frequency and other symptoms, such as nausea, headache and appetite, which were recorded at baseline, one, two, and three months after randomization and six and 12 months after therapy. Researchers defined “cure” as those who experienced greater than 80 percent improvement in pain.

The study revealed that hypnotherapy was superior to conventional therapy for children with long-standing functional abdominal pain (FAP) or IBS, curing 59 percent of the patients, versus just 12 percent of patients who received conventional therapy. After one year, the figures were 85 percent and 25 percent, respectively. Patients who received hypnotherapy also experienced less pain after treatment compared to the group that received conventional therapy.

“Our team was pleased to learn that the demonstrated benefits of hypnotherapy on IBS complications appear to be translatable to children,” said Arine M. Vlieger, M.D., Ph.D., of St. Antonius Hospital in Nieuwegein, Netherlands, and lead author of the study. “Hopefully, these findings will be confirmed with additional research so that more children can experience relief from the symptoms of IBS without adherence to a medication regimen.”

Studies Assess Effectiveness of Serotonin and Nerve Stimulants on Irritable Bowel Syndromes

Studies have shown that gastrointestinal (GI) tract function is often influenced by specific stimulants or reactors, which sometimes cause irritable bowel syndrome (IBS) or constipation. Two studies take a closer look at GI stimulation, including one examining the role of serotonin and reactions to certain types of foods and another looking at the potential therapeutic value of nerve stimulation for constipation.

“We know that conditions of the bowel, such as constipation, diarrhea and irritable bowel syndrome, are quite troubling for a large number of individuals. These conditions can be highly volatile and unpredictable, but we are still trying to determine how we can manage these variables and what preventive or treatment options may help patients who suffer from these conditions,” said Alan Buchman, M.D., MSPH, AGAF, Feinberg School of Medicine of Northwestern University School of Medicine. “These two studies point to options that may help doctors manage symptoms in their patients and hopefully lead to better treatment options in the future.”

Olfactory Receptors on Human Intestinal Enterochromaffin (EC) Cells Function as Sensors for Spices and Odorants

One primary research focus in GI disorders is how and why the system reacts to certain foods or other stimulants; specifically, researchers are investigating the primary factors responsible for regulating digestion. Enterochromaffin (EC) cells, which are present throughout the digestive system, release serotonin (a chemical associated with the etiology of various diseases such as migraine, diarrhea, respiratory disturbances and hypertension) and are important in regulating gut motility. Researchers from the Technical University of Munich and the Ludwig Maximilian University of Munich in Germany investigated whether EC cells in the intestine express nasal olfactory receptors (ORs, receptors used for smelling) to determine whether odorants present in spices, fragrances, cigarettes, detergents and cosmetics may cause serotonin release, thereby provoking a GI response.

To evaluate this connection, researchers studied human EC cells isolated from mucosal biopsies by laser microdissection and an EC derived cell line. The experiments revealed expression of several ORs in the isolated EC cells, as well as the cell line. Using digital fluorescence imaging, the team found that activation of the cells with odorants caused elevation of intracellular Ca2+, followed by serotonin release up to 10-fold that of the controls. Odorants like thymol (thyme),...
eugenol (cloves), bourgeonal (floral, lily-of-the-valley), helional (brown algae) and substances present in roses, bananas or raspberries, specifically, caused an elevation of Ca2+ levels.

The findings suggest that these types of odorants may cause a serotonin-related GI reaction. The effects could be inhibited by known OR antagonists, such as methyl isoeugenol (a competitive antagonist of eugenol) or by blocking Ca2+ influx (e.g., via Ca2+ channels with nifedipine, a drug used in the treatment of hypertension because it relaxes blood vessels).

“Our results show that odorants present in the gut may stimulate serotonin release via olfactory receptors expressed in human enterochromaffin cells in the gut mucosa,” said Petra Voland, Ph.D., of the Technical University of Munich, and one of the lead investigators of the study. “Serotonin controls peristalsis and is implicated in pathological conditions such as vomiting, diarrhea and irritable bowel syndrome. Thus, olfactory receptors are potential novel targets for the treatment of gastrointestinal diseases and motility disorders.”

**Sacral Nerve Stimulation for Constipation: An International Multi-Centre Study**

In patients with idiopathic constipation, which occurs with no identifiable cause, in whom conservative treatment has failed, surgical procedures (e.g., colectomy) are associated with a high failure rate and substantial morbidity. Researchers from five European sites set out to explore an alternative approach: modulating the extrinsic nerve supply to the bowel. In doing so, investigators evaluated the symptomatic response and physiological effect of sacral nerve stimulation in patients with slow transit constipation and normal transit constipation with impaired evacuation.

In this prospective, multi-center trial, 65 patients (58 female) who failed treatment with laxatives and biofeedback (retraining pelvic floor muscle coordination using exercises and electronic aids that create feedback when successful muscle contraction occur) underwent test stimulation, each serving as their own control. The effect of temporary sacral nerve stimulation was assessed by a 21-day bowel habit diary. Patients with more than 50 percent improvement in symptoms were eligible for permanent stimulation. Long-term results were assessed by: bowel habit diary, symptom questionnaire, Cleveland Clinic constipation score (CCCS), visual analogue score (VAS) and short form-36 (SF-36) quality of life questionnaire. Primary endpoints included an increase in the frequency of defecation, reduction in straining and reduction in the sensation of incomplete evacuation.

After a median follow up of 12 months, subjects with both slow transit and impaired evacuation benefited from therapy and 43 patients (66 percent) proceeded to chronic stimulation. Frequency of defecation increased from 3.4 to 6.1 times per week, while evacuation days per week increased from 2.4 to 4.4. Time spent in facilities decreased from 17.6 to 9.3 minutes, straining decreased from 4.4 to 2.9 episodes per week, abdominal pain decreased from 4.4 to 2.0 days per week, and perception of incomplete evacuation decreased significantly.

In evaluating the results of the various assessment tools set forth at the start of the trial, researchers found that: the CCCS (0 = no constipation, 30 = severe constipation) decreased from 18.0 to 10.2; mean VAS (0 = severe symptoms, 100 = no symptoms) increased from 18 to 66; and SF-36 subsets of physical functioning, general health, vitality, social functioning and mental health significantly improved.

“While constipation is rarely life-threatening, associated symptoms of abdominal pain, bloating and the sensation of incomplete evacuation can severely affect the physical and emotional well-being of patients. There are many treatment options for the condition and the best approach relies on a clear understanding of the underlying cause,” said Thomas Dudding, M.D., of St. Mark’s Hospital in London, England, and lead investigator for the study. “This study found that sacral nerve stimulation is an effective treatment for idiopathic constipation that is resistant to conservative treatment. As a result of this stimulation process, improvement occurs in bowel frequency, associated symptoms and overall quality of life.”

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