Prucalopride in Gastroparesis

Prucalopride, a selective, 5-hydroxytryptamine 4 receptor agonist used in the treatment of constipation, is able to enhance the gastric emptying rate. A double-blind, placebo-controlled, crossover study evaluated the efficacy of this drug to improve the gastric emptying rate and symptoms in patients with gastroparesis.

A total of 34 patients with gastroparesis (28 idiopathic, 7 men, mean age 42), were evaluated in a double-blind, crossover trial of 4-week treatment periods with placebo or prucalopride 2 mg daily, separated by 2 weeks of washout. The primary end point was a change in symptom severity, assessed by the Gastroparesis Cardinal Symptom Index; secondary end points comprised the Patient Assessment of Upper Gastrointestinal Disorders – Symptom Severity Index, the patient assessment of upper gastrointestinal disorders – Quality of Life and daily diaries, and the gastric emptying rate was assessed by the C-octanoic acid breath test.

Three patients were lost to follow-up. One serious adverse event occurred (small bowel volvulus), and three patients dropped out because of adverse events of nausea and headache. All of the complications were related to prucalopride cases. For the entire patient group compared with placebo, prucalopride significantly improved the GCSI (1.65 vs. 2.28), and the subscales of fullness/satiety, nausea/vomiting and bloating/distention.

Prucalopride significantly improved the overall patient assessment of upper gastrointestinal disorders/quality of life score (1.15 vs. 1.44) under domains of clothing and diet. The gastric half-emptying time was significantly enhanced by prucalopride, compared with placebo and baseline (98 and 126, respectively). These significant improvements are also found when considering only the idiopathic gastroparesis subgroup.

It was interpreted that in a cohort of patients with predominantly idiopathic gastroparesis, 4 weeks of prucalopride treatment significantly improved symptoms and quality of life and enhanced gastric emptying, compared with placebo.

Carbone, F., Van den Houte, K., Clevers, E., et al. "Prucalopride in Gastroparesis: A Randomized, Placebo-Controlled Crossover Study." American Journal of Gastroenterology, 2019; Vol. 114, pp. 1265-1274.

Modified Dual Therapy Compared with Quadruple Therapy in First Line Treatment of H. Pylori

To assess the effectiveness, adverse events, patient adherence and cost of modified dual therapy compared with Bismuth-containing quadruple therapy for treating Helicobacter pylori infection in Chinese patients, an attempt was made to evaluate same and use dual therapy as an alternative first line treatment.

A total of 232 H. pylori-infected, treatment-naïve patients were enrolled in an open-label, randomized clinical trial. Patients were randomly allocated in the two groups: the 14-day dual therapy group and the Bismuth-containing quadruple therapy group. Eradication rates, drug-related adverse effects, patient compliance and drug cost were compared between the two groups.

The modified dual therapy group achieved eradication rates of 87.9%, 91.1%, and 91.1% as determined by the intention-to-treat, per-protocol, and modified intention-to-treat analyses, respectively. The eradication rates were similar, compared with the Bismuth-containing quadruple therapy group: 89.7%, 91.2%, and 90.4%.

In addition, modified dual therapy ameliorated variations in the CYP2C19, IL-1B-511, and H. pylori VacA genotypes.

There were no significant differences in compliance rates between the two groups. The modified dual group exhibited significantly less overall side effects compared with the quadruple therapy group and the cost of medications was lower.

It was concluded that modified dual therapy as high dose and administered frequently is equally effective, safer, and less costly compared with Bismuth-containing quadruple therapy.

Yang, J., Zhang, Y., Fan, L., et al. "Eradication Efficacy of Modified Dual Therapy Compared with Bismuth-Containing Quadruple Therapy as a First-Line Treatment of Helicobacter Pylori." American Journal of Gastroenterology, 2019; Vol. 114, pp. 437-445.

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Atypical Food Allergies in Irritable Bowel Syndrome

Confocal laser endomicroscopy (CLE) permits real-time detection and quantification of changes in intestinal tissues and cells. In a prospective study, 155 patients with IBS received 4 challenges with each of 4 common food components by way of the endoscope, followed by CLE at a tertiary medical center. Classical food allergies were excluded by negative results from immunoglobulin-E serology analysis and skin tests for common food antigens. Duodenal biopsy samples and fluid were collected 2 weeks before and immediately after CLE and were analyzed by histology, immunochemistry, reverse transcription polymerase chain reaction and immunoblots.

Results of patients who had a response to food during CLE (CLE-positive), were compared with results from patients who did not have a reaction during CLE or healthy individuals (controls).

Of 108 patients who completed the study, 76 were CLE-positive (70%) and 46 of these (61%) reacted to wheat. CLE-positive patients had a 4-fold increase in prevalence of atopic disorders, compared with controls.

In a CLE analysis of patients with IBS, more than 50% of patients could have nonclassical food allergy with immediate disruption of the intestinal barrier upon exposure to food antigens. Duodenal tissues from patients with responses to food components during CLE had immediate increase in expression of claudin-2 and decreases in occludin and had increased eosinophil degranulation, indicating an atypical food allergy characterized by eosinophil activation.

Fritscher-Ravens, A., Phlaum, T., Mosinger, M., et al. "Many Patients With Irritable Bowel Syndrome Have Atypical Food Allergies Not Associated With Immunoglobulin-E." Gastroenterology 2019; Vol. 157, pp. 109-118.

Medical Vs. Surgical Treatment for Refractory GERD

Patients who were referred to Veterans Affairs (VA) gastroenterology clinics for PPI-refractory heartburn received 20 mg of omeprazole twice daily for 2 weeks and those with persistent heartburn underwent endoscopy, esophageal biopsy, esophageal manometry, and multichannel intraluminal impedance pH monitoring in order to evaluate treatment for refractory heartburn. The patients were randomly assigned to receive surgical treatment (laparoscopic Nissen fundoplication), active medical treatment (omeprazole plus baclofen), with desipramine added depending on symptoms or control medical treatment (omeprazole plus placebo).

The primary outcome was treatment success defined as a decrease of 50% or more in the GERD health-related quality of life score (range 0-50), with higher scores indicating worse symptoms at one year.

A total of 366 patients with a mean age of 48.5 years were enrolled. Prerandomization procedures excluded 288 patients; 42 had relief of their heartburn during the 2-week omeprazole trial, 70 did not complete trial procedures, and 54 were excluded for other reasons; 23 had non-GERD esophageal disorders and 99 had functional heartburn (not due to GERD or other histopathologic, motility or structural abnormalities.

The remaining 78 patients underwent randomization. The incidence of treatment success with surgery (18 of 27 patients, 67%), was significantly superior to that with active medical treatment (7 of 25 patients – 28%), or controlled medical treatment (3 of 26 patients – 12%).

The difference in the incidence of treatment success between the active medical group and the controlled medical group was 16 percentage points.

It was concluded that among patients referred to VA Gastroenterology Clinic for PPI-refractory heartburn, systematic workup included truly PPI-refractory and reflux-related heartburn in a minority of patients. For that highly selective subgroup, surgery was superior to medical treatment.

Spechler, S.J., Hunter, J.G., Jones, K.M., et al. "Randomized Trial of Medical Vs Surgical Treatment for Refractory Heartburn." New England Journal of Medicine, 2019; Vol. 381/16, pp. 1513-1523.

Budesonide Vs. Fluticasone in Treatment of Eosinophilic Esophagitis

To compare multi-dose inhaler (MDI) with swallowed fluticasone with oral viscous budesonide (OVB slurry), a double-blind, double-dummy trial was carried out with patients with a new diagnosis of eosinophilic esophagitis (EoE) and groups were randomly assigned to 8 weeks of either treatment twice a day, with a placebo inhaler also utilized.

Primary outcomes were post-treatment maximum eosinophil counts per high-power field (eos/hbf), and a validated dysphagia score by dysphagia questionnaire (DSQ). At week 8, secondary outcomes included endoscopic severity with an endoscopic reference score and histologic response (less than 15 eos/hbf), and safety.

In a modified intention-to-treat analysis, the subjects had baseline peak eosinophil counts of 73 and 77 eos/hbf in the OVB and MDI groups, respectively, and DSQ scores of 11 and 8. Post-treatment eosinophil counts were 15 and 21 in the OBV and MDI groups, respectively, with 71% and 64%, respectively, achieving histologic response. DSQ scores were 5 and 4 in the OBV and MDI groups. Similar trends were noted for post-treatment total EoE endoscopic reference scores.

Esophageal candidiasis developed in 12% of patients receiving OBV and 16% receiving MDI. Oral thrush was observed in 3% and 2%, respectively.

It was concluded in a randomized clinical trial that initial treatment of EoE with either OBV or fluticasone MDI produced a significant decrease in esophageal eosinophil counts and improved dysphagia and endoscopic features. OBV was not superior to MDI and both are acceptable treatments for EoE.

Dellon, E., Woosley, J., Arrington, A., et al. "Efficacy of Budesonide vs. Fluticasone for Initial Treatment of Eosinophilic Esophagitis in a Randomized, Controlled Trial." Gastroenterology 2019; Vol. 157, pp. 65-73.

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