

Effect of Cisapride on Gastric Emptying in Patients with Gastro-oesophageal Reflux Disease

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To investigate the effect of cisapride in gastro-oesophageal reflux disease (GERD), gastric emptying time, measured using scintigraphy, and reflux symptoms were compared before and after cisapride therapy in 30 patients with endoscopically proven GERD. Gastric emptying time was also measured in 20 age-matched controls. Patients with GERD were treated with 30 mg cisapride orally three times daily for 7 days. Gastric emptying time was

significantly reduced following cisapride therapy in 28 of these patients (71.6 ± 18.1 min versus 57.9 ± 13.9 min), although it was still longer than the gastric emptying time of the control group (i.e. 46.2 ± 8.1 min). In addition, cisapride relieved heartburn, which is a representative symptom of GERD. These findings suggest that cisapride may be useful in treating reflux symptoms and oesophagitis in patients with GERD.

KEY WORDS: CISAPRIDE; GASTRO-OESOPHAGEAL REFLUX DISEASE; GASTRIC EMPTYING; SCINTIGRAPHY

Introduction

The causality of gastro-oesophageal reflux disease (GERD) is multifactorial, as is the case with many other diseases, although GERD is primarily a motility disorder. Heartburn is a typical symptom of GERD, which is experienced by people of all ages.¹ The prevalence of heartburn has been reported to be around 30% in western countries^{2,3} and 25.7% in Turkey.⁴ Despite its prevalence, GERD is a common but generally mild disease.

Maintenance therapy is essential for the treatment of GERD and may include sucralfate, various H₂-blockers, cisapride and

proton pump inhibitors. The currently available gastrointestinal motility prokinetic drug, cisapride, has proved effective in gastrointestinal motility disorders.¹ Motor abnormalities of the oesophagus and stomach have been identified in patients with GERD using radionuclide and manometric techniques.⁵⁻⁷

Studies of gastric function have shown delayed gastric emptying and decreased antral motility in some patients with GERD.^{8,9} In this study, we investigated whether or not cisapride therapy has any effect on gastric emptying and reflux symptoms in patients with GERD.

Patients and methods

PATIENTS

To confirm the diagnosis of GERD, patients complaining of reflux symptoms underwent endoscopic examination (Olympus GIF Q20; Olympus, Japan). Patients in whom GERD was thus confirmed were included in this study together with age-matched healthy volunteers as controls. Patients were excluded from the study if they had organic digestive disorders (i.e. biliary tract, pancreas and liver diseases) and irritable bowel syndrome. Also excluded were patients who had undergone abdominal surgery, those with neurological and psychiatric disorders and those with diabetes mellitus. Pregnant women and children were excluded also. All patients and controls taking part in the study were asked not to use antacids, anti-ulcer drugs, steroids, non-steroidal anti-inflammatory drugs and bismuth salts in the 4 weeks prior to the study. The study was approved by the local review board and all participants gave written, informed consent.

TREATMENT

Patients were treated with 10 mg cisapride orally three times daily for 7 days.

ASSESSMENTS

Scintigraphic recordings were performed in the healthy volunteers and before and after cisapride therapy in the patients with GERD. After being deprived of food for at least 8 h, patients and control subjects were given 0.5 – 1 mCi of technetium 99m-sulphur colloid that had been mixed with scrambled eggs and sandwiched between two slices of bread. A γ -camera (General Electric 3200 XR/T and 4000 XC/T; General Electric, USA) was used to take 15 dynamic and seven static images in anterior projection (one every 15 min from 30 to 120 min) in each individual. Gastric emptying time was computed by the

standard software program within the γ -camera, using the region of interest method.

Patients with GERD were assigned a clinical reflux score before and after cisapride therapy according to their symptoms, which included vomiting, pneumonia or asthma, heartburn, haematemesis, dysphagia, regurgitation, belching, non-cardiac angina pectoris and consumption of alcohol and cigarette smoking.

STATISTICAL ANALYSIS

Wilcoxon's signed-rank analysis was used to compare gastric emptying times between patients with GERD and control subjects, whereas the Mann-Whitney *U*-test was used to compare gastric emptying times and clinical reflux scores before and after treatment in the patient group. Correlation between gastric emptying times and symptoms of GERD was determined using Spearman's Rank Correlation Coefficient. Data are expressed as means \pm SD.

Results

PATIENTS

Thirty patients with endoscopically proven GERD (14 females, 16 males; mean age, 41.1 \pm 14.2; age range, 22 – 72 years) and 20 healthy volunteers (eight females, 12 males; mean age, 41.1 \pm 12.0; range 25 – 67 years) were included in this study.

ASSESSMENTS

At baseline, gastric emptying time was significantly longer in the patients with GERD compared with that in the controls (71.6 \pm 18.1 min versus 46.2 \pm 8.1 min; P = 0.0001). Gastric emptying time was reduced significantly after 7 days of cisapride therapy in 28 patients with GERD to 57.9 \pm 13.9 min (P = 0.0001), although it was still significantly longer than that of the control group (P = 0.0014). Increased gastric

emptying times were observed in only two patients after therapy (63.2 min and 51.6 min before and 79.7 min and 58.7 min after treatment).

The clinical reflux score in the 28 patients in whom gastric emptying time had decreased was significantly lower after therapy (6.0 ± 2.6 versus 4.0 ± 1.6 ; $P = 0.0001$). Heartburn was the only symptom of GERD with which there was a correlation with gastric emptying times ($r = 0.4$; $P = 0.01$).

Discussion

It is widely recognized that hypomotility of smooth muscle in the upper gastrointestinal tract is a dominant factor in many patients with GERD. It is not the only factor, however; impaired motility and acid reflux both play important roles in GERD.⁹ It has been shown that gastric emptying times are longer in patients with ulcers than in control subjects

and that these times are reduced to almost normal levels following *Helicobacter pylori* eradication therapy.¹⁰

Cisapride is a prokinetic agent that stimulates gastrointestinal motility by facilitating the release of acetylcholine at the myenteric plexus.¹¹ It has been shown to accelerate gastric emptying of solids and liquids in patients with gastroparesis and non-ulcer dyspepsia.¹² This prompted us to investigate the effect of oral cisapride on gastric emptying in patients with GERD. Our results show that 7 days' treatment with 10 mg cisapride orally, three times daily, significantly accelerated gastric emptying time in these patients. In addition, the symptoms of GERD, heartburn in particular, were relieved. This suggests that cisapride may be useful in treating reflux symptoms and oesophagitis in patients with GERD.

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