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Utility of Electrogastrography in Differentiating Parkinson's Disease with or without Gastrointestinal Symptoms: A Prospective Controlled Study

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Key Words
Electrogastrography · Parkinson's disease · Gastric myoelectrical activity

Abstract
Background/Aims: Parkinson's disease (PD) may be associated with various gastrointestinal symptoms. This study was designed to assess the gastric myoelectrical functioning in patients with PD and in healthy controls by using electrogastrography (EGG) with the water load test and to determine the clinical utility of EGG in differentiating PD patients with or without upper gastrointestinal symptoms. ***Methods:*** Twenty patients (13 men, mean age 63 years) with PD and 11 healthy controls (5 men, mean age 55 years) were studied. The PD patients were stratified into two subgroups: 9 were assessed as PD without upper gastrointestinal symptoms (group A) and 11 as PD with upper gastrointestinal symptoms (group B). The gastric myoelectrical activity was assessed using cutaneous electrodes to record EGG before and after the subjects ingested water until full. ***Results:*** The PD patients drank significantly less water until full as compared with the controls (303 ± 45 vs. 627 ± 67 ml, $p < 0.05$). At baseline, the PD patients had a significantly higher 1.0- to 2.5-cpm activity as compared with the controls (44 ± 3 vs. 33 ± 3%, $p < 0.05$). These differences persisted after ingestion of the water load. The PD patients had a significantly lower 2.5- to 3.75-cpm activity late after ingestion of the water load as compared with the controls (33 ± 4 vs. 49 ± 5%, $p < 0.05$). No statistically significant differences were found in any EGG variables or the water load between the two groups of PD patients. ***Conclusions:*** This study has shown that the gastric myoelectrical activity is impaired in both groups of PD patients. EGG appears to have a limited, if any, clinical utility in the differentiation of PD patients with or without upper gastrointestinal symptoms.

Introduction

The primary defect in Parkinson's disease (PD) is the degeneration of the neurons of the substantia nigra in the central nervous system. The pathophysiological basis for gastrointestinal symptoms associated with PD remains poorly understood [1]. The gastrointestinal symptoms are shown to be correlated with the disease severity and reflect the primary disease process affecting the gastrointestinal tract [1]. Recent studies [2] have found that the gastric motility is impaired in patients with advanced PD. Another study [3] has demonstrated an abnormal gastric myoelectrical activity not only in untreated but also treat-

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ed PD patients. These findings suggest a direct involvement of the gastrointestinal tract in addition to symptomatic central lesions. It remains unclear whether all PD patients or only those with gastrointestinal symptoms have an impaired gastric myoelectrical activity.

Electrogastrography (EGG) enables the cutaneous measurement of the gastric myoelectrical activity and provides information on frequency and relative amplitude of antral contractions [4, 5]. These activities originate from the gastric pacemaker located in the midportion of the stomach which fires at three cycles per minute (cpm) with aboral propagation of spike burst to the pylorus [6]. Since its first application in the 1920s [6], numerous studies have demonstrated a close association of electric abnormalities with gastrointestinal motility disorders [7]. The water load test is a standardized test to induce gastric distension and to evoke gastric motility responses without the complex hormonal responses of a caloric test meal. EGG with the water load test has been validated to be reliable and reproducible [8].

In this study, we aimed at assessing the gastric myoelectrical functioning in PD patients and in healthy controls by using EGG and to determine the value of EGG in differentiating PD patients with or without upper gastrointestinal symptoms.

Patients and Methods

Patients

Twenty patients (13 men; mean age 63, age range 34–81 years) with PD lasting from 1 to 10 years were referred from the PD Clinical and Research Center at Buddhist Tzu Chi General Hospital. All patients fulfilled the diagnostic criteria for PD (at least 2 of the 3 cardinal symptoms of PD: tremor, rigidity, and bradykinesia) [9], and the presence of neurological disorders other than PD was excluded on the basis of a detailed history and neuroimaging study. Patients were excluded, if they suffered from gastrointestinal disease or were taking medications known or suspected of altering the digestive motility. Patients were also excluded, if they had excessive tremors and skeletal muscle contractions that would introduce artifacts and prevent acquisition of data. All subjects were interviewed at the beginning of the study to define the presence of upper gastrointestinal symptoms experienced, including nausea, abdominal pain, early satiety, abdominal fullness, and vomiting. The PD patients were stratified into two groups on the basis of the presence of at least three of the above symptoms 3 months before the EGG study. Of the 20 patients, 9 were assessed as PD without upper gastrointestinal symptoms (group A; 6 men, mean age 57, age range 34–81 years) and 11 as PD with upper gastrointestinal symptoms (group B; 7 men, mean age 67, age range 54–80 years). All patients had been treated with levodopa for at least 6 months prior to entering the study. All treated patients improved with therapy. All patients were taken off their PD therapy for 48 h to eliminate the effect of levodopa on the EGG results. All patients were asked to stop using medications such as anticholinergics, cholinergics, antispasmodics, and antiemetics 2 days before the EGG tests. Eleven healthy controls (5 men, mean age 55, age range 30–77 years) served as a control group. Written consent was obtained from each subject prior to enrollment.

Electrogastrography

EGG was performed after a 12-hour overnight fast. The EGG signal was recorded using standard Ag/AgCl cutaneous electrodes. One electrode was positioned in the midclavicular line 2 inches below the left costochondral margin. Another electrode was positioned at the midpoint between umbilicus and xiphoid process. The reference electrode was placed 2 inches below the costal margin in the right midclavicular line. The electrode sites were prepared by rubbing with an abrasive paste, followed by application of an electroconductive gel. An EGG recorder and software were utilized to record the EGG signals. Overall power spectra were computed for 15 min at baseline, after which the subjects ingested cool (23°C) water during a period of 5 min, until they felt full. The EGG was recorded for 30 min after ingestion of the water load.

Analysis of the EGG Signals

The recording channel with the clearest electrogastrographic signal was chosen for visual and computer analysis, as previously described [8]. Frequencies of interest recorded in the EGG are 1.0–2.5 cpm (bradygastria), 2.5–3.75 cpm (normal range), 3.75–10 cpm (tachygastria), and 10–15 cpm (duodenal or respiratory frequency). In addition, the digitized file was analyzed using Fourier transformation, running spectral analysis (RSA) with Fourier transformation, and calculation of the percentage distribution of power in the four frequency ranges described above. EGGs were classified as normal or abnormal based on the raw signal, the RSA, and the percentage of EGG signal power in various bandwidths. The study was considered abnormal, if a 2.5- to 3.75-cpm activity was seen for <70% of the study period [10].

Statistics

All results are expressed as mean values ± SEM or percentages. Two-way ANOVA with repeated measures was used to assess significant differences in the percentages of total EGG power in bradygastria, tachygastria, duodenal-respiratory, and normal ranges between the groups. Student t tests were used where appropriate. The α level was set at 0.05 for all statistical analyses.

Results

The PD patients drank significantly less water until they felt full as compared with the controls (303 ± 45 vs. 627 ± 67 ml, $p < 0.05$). For PD subjects, a significant difference existed, with group B drinking less water than group A (209 ± 34 vs. 412 ± 78 ml, $p < 0.05$). The group B patients were older than the group A subjects, though the difference was not statistically significant (p = NS).

The EGG in healthy controls showed no dysrhythmias, but was abnormal in 5 group A patients (56%) and

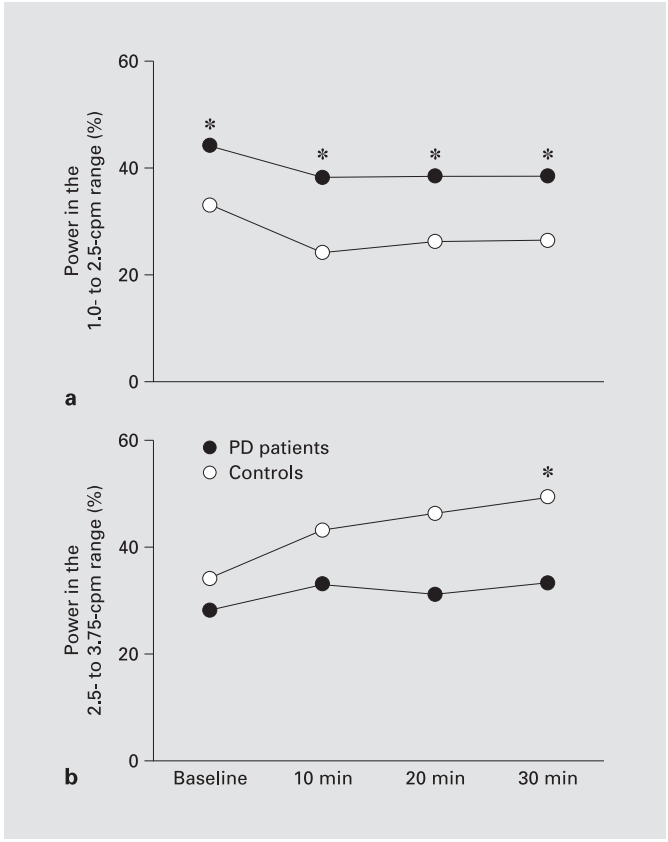

Fig. 1. EGG power in PD patients and in healthy controls. **a** At baseline, the PD patients had a significantly higher 1.0- to 2.5-cpm activity as compared with the healthy controls (* $p < 0.05$). These differences persisted after ingestion of the water load. **b** The PD patients had a significantly lower 2.5- to 3.75-cpm activity by 21–30 min after ingestion of the water load as compared with the healthy controls (* $p < 0.05$).

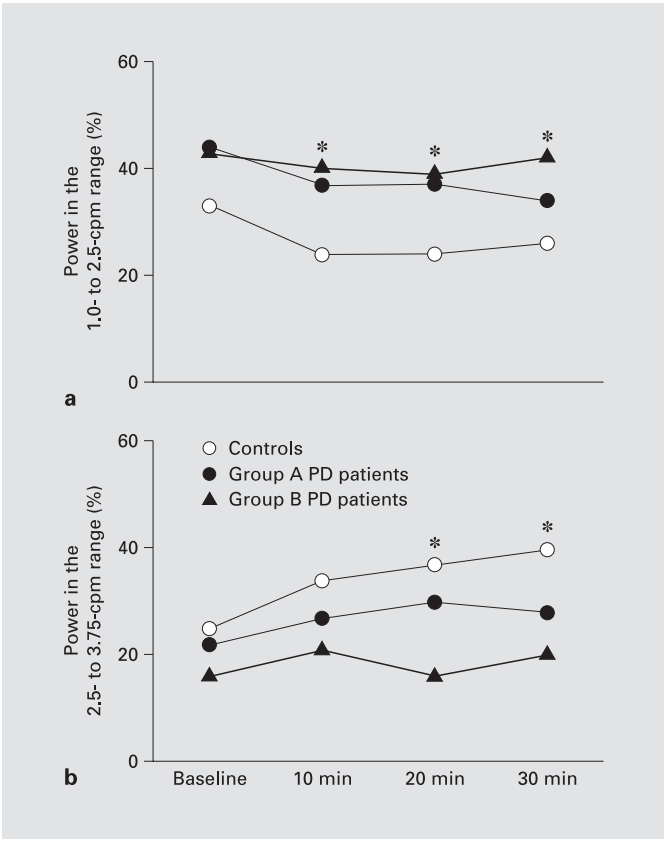

Fig. 2. EGG power in the two groups of PD patients and in the healthy controls. **a** Group B patients had a significantly higher 1.0- to 2.5-cpm activity as compared with the healthy controls after the water load (* $p < 0.05$). No differences were found between group A and group B. **b** Group B patients had a significantly lower 2.5- to 3.75-cpm activity as compared with the healthy controls after the water load (* $p < 0.05$). No differences were found between group A and group B.

in 8 group B patients (73%). The abnormalities seen consisted of bradygastrias in both groups of the PD patients. At baseline, the PD patients had a significantly higher 1.0- to 2.5-cpm activity as compared with the controls (44 ± 3 vs. 33 ± 3%, $p < 0.05$). These differences persisted after ingestion of the water load (fig. 1a). The PD patients had a significantly lower 2.5- to 3.75-cpm activity by 21–30 min after ingestion of the water load as compared with the controls (33 ± 4 vs. 49 ± 5%, $p < 0.05$; fig. 1b). The percentages of power in the tachygastric and duodenal-respiratory ranges were similar in each group of subjects throughout the study. Although the group B patients had a significantly higher 1.0- to 2.5-cpm activity ($p < 0.05$) and a significantly lower 2.5- to 3.75-cpm activity ($p < 0.05$) than the controls after the water load (fig. 2), there was no statistically significant difference in the EGG variables between the two groups of PD patients.

Discussion

In this study, we have demonstrated abnormalities in the gastric myoelectrical activity in both groups of PD patients. These findings are similar to those of previous studies [2, 3] that also showed gastric dysrhythmias in patients with PD. The volumes of water ingested by the PD patients were less as compared with those of the controls. Although the PD patients with upper gastrointestinal symptoms ingested significantly less water as compared with those without symptoms, no difference in any

EGG parameters could be observed between the two groups of PD patients.

Gastric myoelectrical disturbances with bradygastrias have been found in a variety of diseases, including intestinal pseudo-obstruction, diabetic gastroparesis, and functional dyspepsia [11]. Moreover, bradygastrias have been recorded from the gastric body after vagotomy and transection of the antrum [12]. Kaneoke et al. [13] found a postprandial reduction in the EGG power in PD patients, concluding that PD patients had deficits of the autonomic systems similar to those present in vagotomized patients [14]. Our study showed predominant bradygastric patterns at baseline and after the water load in PD patients, and these patterns were more marked in those with upper gastrointestinal symptoms. Although we did not assess the vagal nerve function in the current study, our data are in line with results of previous studies [13, 14] indicating that autonomic dysfunction is present in PD patients.

The PD patients drank significantly less volumes of water as compared with the healthy controls, suggesting that altered perceptions of fullness from gastric distension induced by water loads distinguished PD patients and control subjects. Furthermore, differences in water load occurred between subgroups of PD patients. It has been well established [15] that mechanoreceptors in the stomach relay sensory information regarding gastric distension and contractions via vagal afferent nerve activity. Neuronal degeneration and the presence of Lewy bodies in central structures of the autonomic nerve system as well as in gastric myenteric plexuses have been detected in PD [16, 17]. Thus, the presence of an altered perception of fullness due to gastric distension in PD patients might reflect the underlying degenerative process of the disease itself and more gastric neuromuscular disturbances.

Several potential factors may be responsible for the upper gastrointestinal symptoms experienced by PD patients. Dysphagia and constipation are regarded as direct involvement of the PD process, while upper gastrointestinal symptoms such as nausea, vomiting, satiety, bloating, and fullness are thought to be rather related to the dopaminergic medications being utilized as therapy [18]. Previous studies [19] have demonstrated an abnormal gastric emptying in a subset of PD patients with upper gastrointestinal symptoms receiving medical treatment, suggesting that levodopa therapy contributes to the accompanying nausea and dyspepsia. Conversely, more recent studies [3] using EGG have shown gastric dysrhythmias in untreated PD patients with upper gastrointestinal symptoms, indicating direct gastrointestinal involvement by the primary disease process. Our PD patients with upper gastrointestinal symptoms ingested significantly less water and had more frequently bradygastrias as compared with the healthy controls. These patients might represent a subset of PD patients with an advanced stage and a long duration of the disease, in whom an impaired gastric motility has been more frequently demonstrated in previous studies [2]. An altered perception of fullness may also mediate the occurrence of gastrointestinal symptoms experienced in these patients because of the difference in the water load between the two groups of PD patients. Conversely, the coexistence of a visceral afferent neuropathy may attenuate the intensity of gastrointestinal symptoms in asymptomatic PD patients, but having gastric dysrhythmias, since neuronal degeneration has been observed in the enteric nervous system of patients with PD [17]. A visceral afferent neuropathy has also been reported in diabetic subjects with gastric dysrhythmias [20].

In conclusion, we have demonstrated that both groups of PD patients had bradygastrias and an increased sensitivity to gastric distension by the water load. There was no difference in any EGG variable among PD patients with or without upper gastrointestinal symptoms. These findings may reflect the primary degenerative process in the enteric nervous system of the gut. The presence of upper gastrointestinal symptoms appears to have an impact on the water load, but not on the gastric myoelectrical activity. Our study reemphasizes the noninvasive role of EGG in assessing the gastrointestinal motility in neurodegenerative diseases. However, the clinical utility of EGG in differentiating PD patients with or without a variety of digestive symptoms seems to be limited.

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