Rhythmic and Spatial Abnormalities of Gastric Slow Waves in Patients With Functional Dyspepsia

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Objective: The objectives of this study were to assess differences in gastric slow waves measured by a newly approved multichannel electrogastrogram (EGG) device between patients with functional dyspepsia (FD) and healthy controls.

Materials and Methods: Gastric myoelectrical activity was measured by multichannel EGG for 1 hour preprandially and for 2 hours postprandially in 72 FD patients and 16 healthy volunteers. Computerized spectral analysis methods were used to compute various EGG parameters.

Results: (1) Multichannel EGG was abnormal in 83.3% of patients. (2) The regularity of the gastric slow wave was significantly lower in the FD patients in both fasting and fed states; the lowest regularity was seen in channel 3. (3) There was a significantly higher incidence of arrhythmia and tachygastria in FD patients. The highest percentage of arrhythmia and tachygastria were both seen in channel 3. (4) The FD patients showed a significantly lower percentage of slow wave coupling among the 4-channel EGGs in the fed state. (5) The postprandial-preprandial power ratio was significantly less in FD patients. (6) These patients had high symptom scores particularly to nausea, upper abdominal pain, and bloating. However, no significant correlation was noted between the EGG parameters and the symptoms.

Conclusions: Gastric myoelectrical activity is impaired in most patients with FD. The impairment is reflected as a decreased percentage of normal slow waves and an excessive amount of arrhythmia as well as an abnormal spatial distribution of EGG parameters among the 4 channels, suggesting an impaired coordination of gastric slow waves.

Key Words: electrogastrography, functional dyspepsia, gastrointestinal symptoms, gastric slow waves, gastric motility

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Functional dyspepsia (FD) is a common clinical syndrome defined by pain or discomfort centered in the upper abdomen, which is not explained by any identifiable structural or biochemical abnormality.[1,2] It occurs in 14% to 20% of the population.[3,4] The patients often complain of symptoms in relation to meals. These symptoms include vague epigastric or periumbilical discomfort, early satiety, postprandial fullness, bloating, regurgitation, nausea, and/or vomiting.[5,6] On the basis of the combination of these symptoms, a number of investigators have attempted to subdivide FD into 3 categories: dysmotilitylike, ulcerlike, and refluxlike dyspepsia.[6]

The pathogenesis of FD remains unclear. Gastrointestinal motor disorders have been found in patients with FD, reflected as gastric hypomotility and uncoordinated antral duodenal contractions.[7–10] Gastric antral contractions occur through electromechanical coupling.[11] Electrical slow waves originate in the gastric pacemaker area at a frequency of 3 cycles per minute (cpm) and propagate distally through the antrum toward the pylorus. These electrical slow waves determine the frequency and peristaltic nature of gastric contractions.[11] Abnormal myoelectrical activities were seen in adult and children with FD,[12–14] as well as patients with gastroparesis[15] and patients with chronic idiopathic nausea and vomiting.[16] It has been implied that gastric motor disorders in patients with FD may be pathophysiologically attributed to gastric myoelectrical dysrhythmias.[17,18]

Electrogastrogram (EGG) is the recording of gastric myoelectric activity performed with cutaneous abdominal electrodes.[19] Although some investigators have suggested that some of the cutaneously acquired dysrhythmias may be artifactual in nature,[20,21] other studies have shown good correlation between the frequency of cutaneous EGG recordings and the myoelectrical signals recorded from gastric serosal leads.[22,23] The amplitude of the EGG signal represents a summation of gastric myoelectrical activity. Spike activity, which is associated with gastric contractions, is reflected by an increase in EGG signal amplitude.

Cutaneous EGG is usually performed using a single recording channel.[18] Multichannel electrogastrography has recently been proposed to derive more information about gastric slow waves, especially spatial information.[24–26] In this technique, gastric myoelectrical activity is recorded from several different locations on the abdomen along the antral axis. The multichannel recording and analysis can potentially allow for the detection of slow wave propagation and coupling of the gastric slow wave.[24] At the present time, the results of multichannel EGG have been reported in only a small number of subjects.[24,25]

The aim of this study was to assess differences in gastric slow waves measured by a newly approved multichannel EGG device between patients with FD and healthy controls, and the correlation between the gastrointestinal symptoms and the parameters of multichannel EGG in FD patients.

MATERIALS AND METHODS

Study Subjects

The study was performed on 72 patients with FD (23 men, 49 women; mean age, 46.1 y; range, 14 to 79) based on clinical and laboratory diagnoses. All patients had a

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minimum 3-month history of chronic, persistent, or recurrent upper abdominal discomfort or pain after meals, and had endoscopy that was negative for any focal lesions, including esophagitis, gastric, or duodenal ulcers or erosions, or esophageal or gastric malignancy within 3 months before the study. None of the patients had been diagnosed for gastroesophageal reflux disease, irritable bowel syndrome, chronic intestinal pseudo-obstruction, or diabetes. Also, these patients had the absence of clinical biochemical and ultrasonographic evidence of any known organic disease. Patients with a history of gastrointestinal surgery or taking any drugs that may significantly alter gastric motility and who could not stop the medication were also excluded from the study. The selection of these patients was based on the Rome 2 criteria and a symptom score with a history of the symptoms of $\geq$6-month duration (continuous and intermittent). Common gastrointestinal symptoms of epigastric pain, postprandial bloating, nausea, vomiting, early satiety, anorexia, belch, diarrhea, heart burn, chest pain, regurgitation, and acid reflex were assessed for symptom severity and graded by the patient as none (0), mild (1), moderate (2), severe (3), or very severe (4).

Sixteen healthy volunteers (8 men, 8 women; mean age, 40.9 y; range 20 to 68) were also enrolled in the study as controls. They had no history of gastrointestinal disease and were free of gastrointestinal symptoms. None of the subjects took any medications known to affect gastrointestinal motility during 3 days before the study.

The study protocol was approved by the Human Subjects Committee at the University of Texas Medical Branch at Galveston, and written consent forms were obtained from all subjects before the study.

Study Protocol

After an overnight fast of $\geq$8 hours, the subject was examined at the Division of Gastroenterology Motility Laboratory in the morning. The surface multichannel EGG recording was performed for 1 hour in a supine position in the fasting state. The subject was then allowed to sit for 15 minutes and consumed a solid standard test meal of 500 kcal (Turkey sandwich, 30% fat, 30% protein, and 40% carbohydrate) with 250 mL of noncaffeinated, noncarbonated juice. The subject then resumed the supine position, and the postprandial multichannel EGG recording was made for 2 hours. At the end of the study, the recording device was disconnected and the electrodes were removed.

Recording of Gastric Myoelectrical Activity

Gastric myoelectrical activity of the subjects was measured using surface multichannel EGG with a specially designed multichannel device (Medtronic-Synectics, Shoreview, MN). The multichannel EGG consisted of 4 identical amplifiers with a recording range of 1.0 to 12.0 cpm. An analog to digital converter was installed in the recording device for online digitization of the multichannel EGG. The sample frequency was 4 Hz.

Before the placement of electrodes, the epigastric skin where electrodes were to be positioned was shaved, if necessary, cleaned, and abraded with sandy skin preparation jelly (Omni Prep, Weaver, Aurora, CO) to reduce the impedance. Six silver chloride electrocardiogram electrodes were placed on the abdominal skin. Four active surface electrodes (E1 to E4) were positioned over the stomach, reflecting approximately the corpus (channel 1), proximal antrum (channel 2), distal antrum (channel 3), and pylorus region (channel 4). One reference electrode and a ground electrode were also placed. The placement of the electrodes has been standardized to assure accurate readings.[24] Electrode 3 was placed at the mid point between the xiphoid process and the umbilicus; electrode 4 was placed 4 cm horizontally to the right of electrode 3. Electrodes 2 and 1 were placed 45 degrees superior and to the left of electrode 3, respectively, with a 4 to 6-cm interval, depending on subject size. The common reference electrode was placed at the cross point of 2 lines, 1 horizontal, connecting electrode 1, and 1 vertical, connecting electrode 3. The ground electrode was placed on the left costal margin horizontal to electrode 3. Connection of the 4 active electrodes to the common reference electrode generated 4-channel EGG signals. All recordings were made in a quiet room and the subject was asked not to talk and to remain as still as possible during the recording to avoid motion artifacts.

Data Analysis

Before the computerized analysis of the EGG, segments of the recording with motion artifacts were deleted. The motion artifact was featured with abnormally high amplitude simultaneously occurring in all 4 channels. Previously, validated quantitative analysis software was used to derive the following parameters.[23,24]

Percentage of Slow Wave Coupling

Cross-spectral analysis was developed to compute the percentage of slow wave coupling.[24] The percentage of slow wave coupling was defined as the percent of time during which the slow wave was determined to be coupled. The computation was carried out on a minute-by-minute basis. Each channel of the EGG recording was divided into blocks of 1 minute without overlapping. The power spectrum of each 1-minute EGG was calculated and the slow waves in 2 channels were defined as coupled if the difference in their dominant frequencies was <0.5 cpm. The percentage of coupling between every possible pair among the 4 channels was computed, and the values were then averaged.

EGG Dominant Frequency/Power

The frequency at which the EGG power spectrum had a peak in the range of 0.5 to 9.0 cpm was defined as the EGG dominant frequency. The power at the dominant frequency in the power spectrum was defined as the EGG dominant power. These 2 parameters were calculated by using the smooth power spectral analysis methods. The EGG dominant frequent was defined as abnormal if it was out of the range of 2 to 4 cpm. The EGG dominant power was defined as abnormal if there was a postprandial decreased of dominant power.

Percentage of Normal Gastric Slow Waves

The percentage of normal gastric slow waves was defined as the percentage of time during which regular 2 to 4-cpm slow waves were present over the entire recording period and was computed by using the adaptive spectral analysis method. In this method, each EGG recording was divided into blocks of 1 min without overlapping. The power spectrum of each 1-minute EGG was calculated and examined to see whether the peak power was within the range of 2 to 4 cpm. The 1-minute EGG was called normal if the peak power was within the 2 to 4-cpm range, otherwise it was defined as dysrhythmia. The percentage of normal slow wave frequency was more than 70% was defined as normal.

Percentage of Gastric Dysrhythmia

Gastric dysrhythmia includes tachygastria, bradygastria, and arrhythmia. The calculation of the percentage of gastric dysrhythmia was performed in the same way as the percentage of normal gastric slow waves. The 1-minute EGG was called tachygastria if the peak power was in the range of 4 to 9 cpm, bradygastria if in the range of 0.5 to 4 cpm, and arrhythmia if there was no dominant peak. If the percentage of tachygastria, bradygastria, or arrhythmia was more than 15%, it was defined as abnormal.

Postprandial-Preprandial Power Ratio

The relative change of EGG dominant power is defined as the power ratio before and after certain test meal. When dB units are used, the relative change of EGG dominant power is defined as the difference between dominant powers (in dB) before and after the test meal. Normally, the postprandial to fasting power ratio value is > 1. This may represent a true postprandial increase in the electrical activity of the stomach.[27]

Statistical Analysis

All data are presented as means ± standard error. Analysis of variance was used to identify any spatial difference among the 4-channel EGGs. Paired Student *t* test was applied to investigate differences in any of the EGG parameters between the patients and the controls and the differences before and after the test meal. A *P* value less than 0.05 was considered statistically significant.

RESULTS

The EGG tracings of the FD patients were grossly abnormal compared with the normal controls. The predominant rhythm in the normal controls was the regular slow wave with a frequency of about 3 cpm. The 4-channel recordings from the normal controls showed consistent amplitude and rhythmicity of the slow waves, whereas the recordings from the FD patients demonstrated a sharp contrast with irregular rhythms, diminished amplitude, and inconsistent spatial distributions (Fig. 1). Quantitative results are presented as follows:

Abnormal EGGs in FD Patients

The multichannel EGG was abnormal in 83.3% (60/72) of the patients, which included a decreased percentage (< 70%) of normal slow waves in 70.8% (51/72) of the patients, excessive tachygastria (> 15%) in 36.1% (26/72) of the patients, excessive bradygastria (> 15%) in 15.6% (10/64) of the patients, excessive arrhythmia (> 15%) in 62.5% (45/72) of the patients, and an abnormal response to the test meal (a postprandial decrease in dominant power) in 33.3% (24/72) of the patients.

Decreased Normal Slow Waves in FD Patients

Compared with the normal controls, the patients had a significant decrease in percentage of regular 2 to 4 cpm gastric slow waves in channels 1, 2, and 4 in the fasting state and in channel 3 in the fed state (Fig. 2). In the fasting state, the mean percentage of normal slow wave frequency in the patients among the 4 channels was 70.6% ± 2.2%, which was significantly lower than that in the controls (78.9% ± 3.0%, $P < 0.05$). In addition, there was a spatial difference in the percentage of normal slow waves in the FD patients in the fasting state (channel 4 of 71.1% ± 2.1% vs. channel 3 of 66.7% ± 2.1%, $P < 0.01$; Fig. 3). The most impaired region in the patients was from channel 3, approximately reflecting the distal antrum of the stomach.

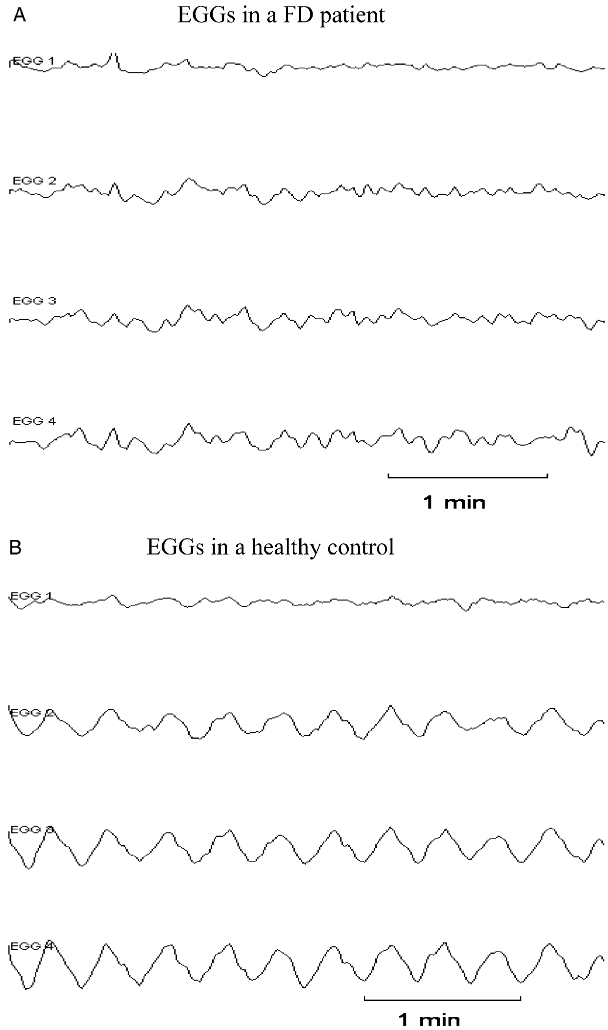

FIGURE 1. Typical 4-channel EGG tracings in a patient with FD fasting (A) and a healthy control (B).

Excessive Dysrhythmia in FD Patients

Arrhythmia (higher than 15%) was seen in 62.5% (45/72) of the patients, including 45.8% in the fasting state, 43.1% in the fed state, and 20.8% in both states. The mean percentage of arrhythmia in the fasting state in channels 1 to 4 were 17.4% ± 2.1%, 19.8% ± 2.6%, 20.7% ± 2.4%, and 16.8% ± 2.1%, respectively. All these values were significantly higher than those in the normal controls (channel 1 to 4: 7.6% ± 1.8%, 9.8% ± 1.9%, 10.5% ± 2.0%, and 9.5% ± 1.9%; channels 1 to 3, $P < 0.01$; channel 4, $P < 0.05$; Fig. 4). The highest percentage of arrhythmia was seen in channel 3 ($P < 0.01$, vs. channel 4). In the fed state, the mean percentages of arrhythmia for channels 1 to 4 were

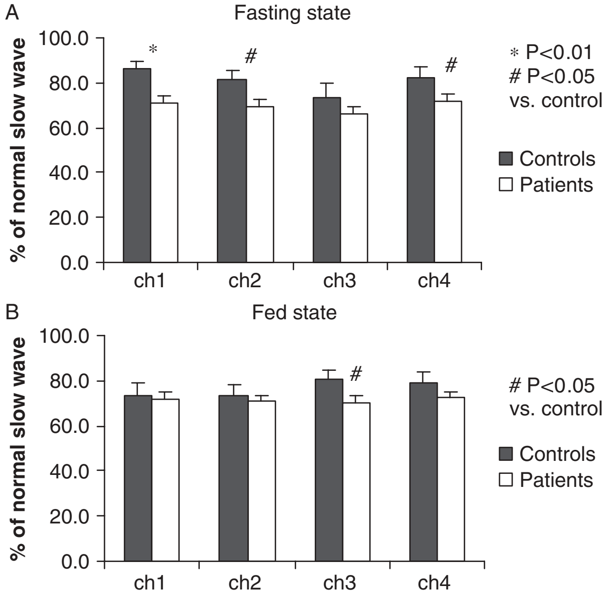

FIGURE 2. Percentage of normal slow waves in controls and patients with FD in the fasting (A) and fed (B) states.

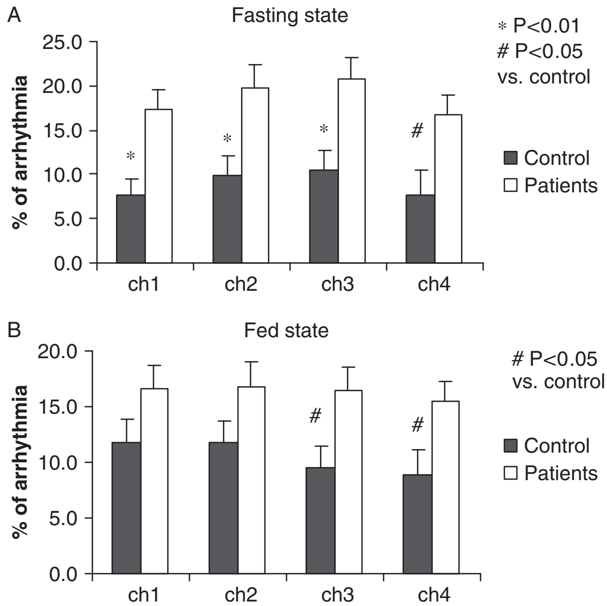

FIGURE 4. Percentage of arrhythmia in controls and patients with FD in the fasting (A) and fed (B) states.

16.7% ± 2.0, 16.8 ± 2.2%, 16.4% ± 2.1% ($P < 0.05$, vs. controls), and 15.5% ± 1.7% ($P < 0.05$, vs. controls), respectively (Fig. 5).

For tachygastria, 26 of the 72 patients (36.1%) had a percentage of tachygastria higher than 15% (16 pts in the fasting state, 17 in the fed state and 8 in both states). In comparison with the controls, the percentages of tachygastria was significantly higher in channels 1 and 4 in the fasting state ($P < 0.01$), and in channel 3 in the fed state ($P < 0.05$). In addition, there was a spatial difference in the percentage of tachygastria in the FD patients in the fasting state (channel 2, 6.2% ± 0.9%; and channel 4, 5.8% ± 0.9%; vs. channel 3, 8.8% ± 0.8%; $P < 0.05$). The highest percentage of tachygastria was seen in channel 3, which was similar to incidence of arrhythmia.

Decreased Normal Slow Wave Coupling in Patients With FD

In the fasting state, there was no significant difference in slow wave coupling among the 4 channels between the FD patients and the normal controls (70.8% ± 2.1% vs. 75.1% ± 3.9%, $P > 0.05$). Postprandially, however, the percentage of slow wave coupling among the 4 channels in the FD patients was found to be significantly lower than the controls (70.8% ± 2.0% vs. 78.1% ± 3.0%, $P < 0.05$, Fig. 6).

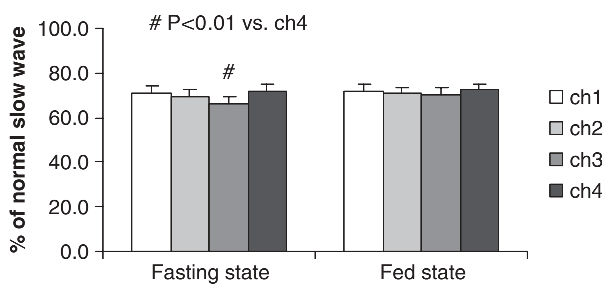

FIGURE 3. Spatial distribution of percentage of normal slow waves in the 4-channel EGG in the FD patients in the fasting and fed states.

Decreased Postprandial-Preprandial Power Ratio in FD Patients

The postprandial-preprandial power ratio in FD patients was found to be significantly smaller in channel 4 compared with the normal controls (0.83 vs. 2.00, $P < 0.05$). No significant difference was observed in other channels between the FD patients and the normal controls. The decreased power ratio was previously reported to be associated with a diminished gastric motor response to a test meal.[20,27] One third (33.3%) of the patients showed a decreased postprandial dominant power.

Gastrointestinal Symptoms in Patients With FD

The patients showed high symptom scores, particularly for nausea, upper abdominal pain, and bloating with an average symptom score of 2.5/4 for nausea, 2.3/4 for pain, and 2.1/4 for bloating, respectively. The other individual symptom score was 1.8 ± 0.04 for belch, 1.8 ± 0.05 for vomiting, 1.6 ± 0.06 for early satiety,

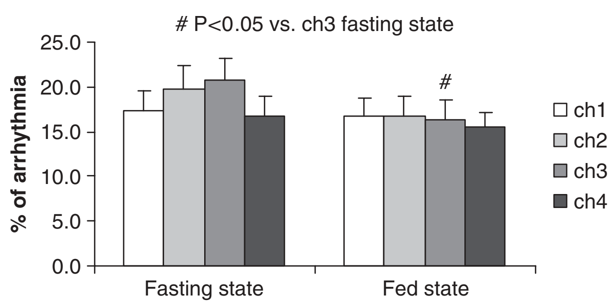

FIGURE 5. Spatial distribution of percentage of arrhythmia the 4-channel EGG in patients with FD in the fasting and fed states.

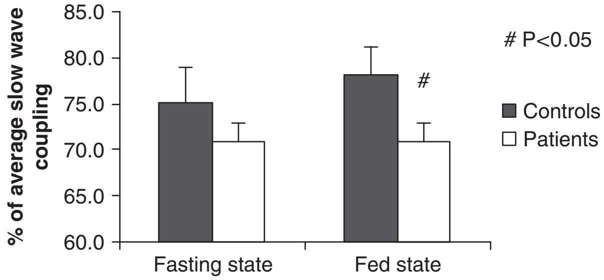

FIGURE 6. Percentage of average slow wave coupling in FD patients and normal controls.

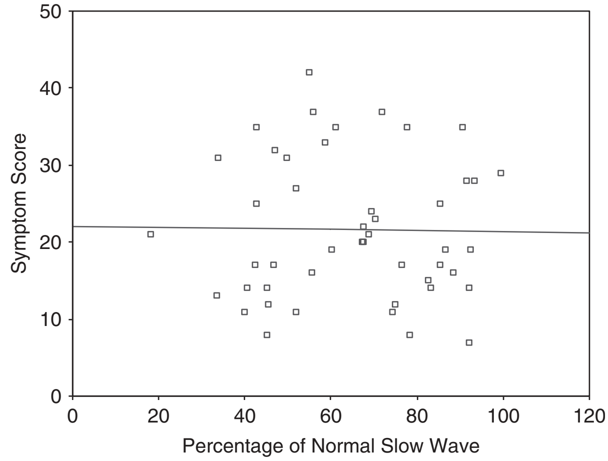

FIGURE 8. Correlation between the percentage of normal slow waves and symptom scores in FD patients with EGG assessment.

1.4 ± 0.03 for diarrhea, 1.3 ± 0.07 for regurgitation, 1.3 ± 0.04 for acid regurgitation, 1.2 ± 0.02 for anorexia, 1.1 ± 0.03 for heartburn, and 0.6 ± 0.04 for chest pain (Fig. 7). The mean total score was 19/48 for all 12 epigastric symptoms. No correlation was noted between the symptom score and % of normal slow waves ($R = 0.05$, $P = 0.83$; Fig. 8), % of bradygastria ($R = 0.04$, $P = 0.85$), % of tachygastria ($R = 0.03$, $P = 0.92$), or % of arrhythmia ($R = 0.07$, $P = 0.76$).

DISCUSSION

In this study, multichannel electrogastrography was performed in a large number (72) of patients with FD. Abnormalities were observed in the rhythmicity and spatial distribution of the gastric slow waves. These include (1) a decreased percentage of normal gastric slow waves in both fasting and fed states, attributed to an increased percentage of tachygastria and arrhythmia; (2) a reduced percentage of slow wave coupling among the 4 channels; and (3) a decreased postprandial-preprandial power ratio.

The conventional single-channel EGG reveals information on the rhythmicity or regularity of gastric slow waves and the response of the slow wave to the test meal. In a previous study using conventional single-channel EGG in FD patients, we found that the regularity of gastric slow waves was relatively lower in the patients only in the fed state.[28] This was in agreement with another study using multichannel EGG but in relatively small sample sizes.[25] But conflicting results have been reported in the literature regarding slow wave abnormalities in the fasting state.[29] In the current study, we found that the percentage of normal gastric slow waves was decreased not only in the fasting state, but also in the fed states. Our findings are similar to those in previous studies reported by Lin et al.[30] In addition, we noted that the percentage of normal slow waves was lowest in channel 3 and the highest percentage of arrhythmia or tachygastria was also in channel 3. This suggests that in FD patients, the stomach is not homogeneous electrophysiologically and that there exists local abnormalities in the rhythmicity of the slow wave. Channel 3 is roughly above the distal antrum, and it is known that the ectopic pacemaker is usually located in the distal antrum. This was supported by the results in our previous study. Qian et al[31] used internal serosal electrodes and recorded gastric slow waves in dogs under various interventions that induced dysrhythmic and reported that the lowest percentage of normal slow waves was in the distal antrum. Thus the multichannel EGG, as used in this study, improved the detection of abnormal gastric myoelectrical activity in FD patients, provided additional information in the spatial distribution of the EGG parameters, including spatial distribution of the frequency, amplitude, and percentage of the normal waves, and coupling of the gastric slow waves.

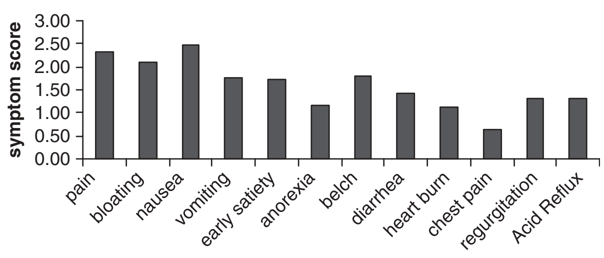

FIGURE 7. Symptom distribution in FD patients.

The spectral analysis of the multichannel EGGs provides relevant information regarding the coupling or uncoupling of the gastric slow wave. It is well known that smooth muscles in different regions of the stomach generate slow waves with different frequencies when measured from muscle strips. The smooth muscles in the proximal part of the stomach produce slow waves with higher frequencies, and those in the distal portion of the stomach produce slow waves with lower frequencies. When the smooth muscles are coupled in the whole stomach, the proximal part of the stomach that fires at the highest frequency drives the other parts of the stomach to the same high frequency (usually about 3 cpm). That is, when the gastric slow wave is coupled, it propagates distally. When gastric slow waves at different locations are uncoupled, however, they may have different frequencies and the multichannel EGG recordings may reveal different dominant frequencies at different locations or channels. In this study, we found that the percentage of slow wave coupling was significantly lower in FD patients compared with the controls. This implies that the gastric slow waves in the stomach were not consistent or appropriately coordinated in patients with FD. Similar findings were reported in patients with systemic sclerosis.[32] It is believed that the multichannel EGG may become a useful tool to study the uncoupling of the gastric slow wave in other categories of patients with suspected gastric motility disorders.

The origin of postprandial symptoms in FD is unclear. Although a number of physiologic abnormalities have been well demonstrated in this situation, their relationship to symptoms has not been definitely established.[33] Various mechanisms may explain why symptoms after a meal may arise independent of either the appearance of gastric dysrhythmias or their potential consequences, such as antral hypomotility and delayed gastric emptying. Koch et al[34] reported that the establishment of normal 3-cpm gastric myoelectrical activity and resolution of dysrhythmias, not normalization of emptying rates, was associated with improvement in upper gastrointestinal symptoms in patients with diabetic gastroparesis. Hu et al[35] found that electrical acustimulation reduced the severity of symptoms of motion sickness and concurrently decreased gastric tachyarrhythmia. Upper abdominal discomfort, bloating, and nausea may be caused by impaired fundal relaxation leading to increased intragastric pressure and antral overdistention produced by displacement of food from the proximal to the distal stomach.[36–39] Furthermore, increased sensitivity to gastric distention due to visceral hyperalgesia may also be involved in symptom production.[40] The elucidation of the roles of each of these physiologic abnormalities in the pathogenesis of FD demands further studies, which will probably require multiple and sophisticated methods to approach several mechanisms. A recent study suggested that disturbances of gastric myoelectrical activity are unlikely to play a role in the origin of postprandial upper abdominal discomfort and bloating in dysmotilitylike FD.[41] Similar to these previous studies, the observation made in the present study did not support any one-to-one correlations between the EGG and the symptoms. However, general associations between abnormal EGGs and gastric symptoms have been consistently reported: Friesen et al[42] found that an abnormal EGG was associated with a higher mean postprandial pain severity in FD children; Parkman et al[43] found that FD patients with both delayed gastric emptying and abnormal EGG had more severe symptoms.

In conclusion, gastric myoelectrical activity is impaired in most patients with FD. The impairment is reflected as a decreased percentage of regular 2 to 4 cpm slow waves and an excessive amount of arrhythmia as well as an abnormal spatial distribution of EGG parameters among the 4 channels, suggesting an impaired coordination of gastric slow waves. Thus multichannel EGG can provide more information in the detection of abnormal gastric myoelectrical activity and in the spatial distribution of the EGG parameters in FD patients.

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