Abnormal gastric slow waves in patients with functional dyspepsia assessed by multichannel electrogastrography

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Lin, Xuemei, and Jiande Z. Chen. Abnormal gastric slow waves in patients with functional dyspepsia assessed by multichannel electrogastrography. Am J Physiol Gastrointest Liver Physiol 280: G1370–G1375, 2001.—The aim of this study was to utilize multichannel electrogastrography to investigate whether patients with functional dyspepsia had impaired propagation or coordination of gastric slow waves in the fasting state compared with healthy controls. The study was performed in 10 patients with functional dyspepsia and 11 healthy subjects. Gastric myoelectrical activity was measured by using surface electrogastrography with a specially designed four-channel device. The study was performed for 30 min or more in the fasting state. Special computer programs were developed for the computation of the propagation and coupling of the gastric slow wave. It was found that, compared with the healthy controls, the patients showed a significantly lower percentage of slow wave propagation (58.0 ± 8.9 vs. 89.9 ± 2.6%, P < 0.002) and a significantly lower percentage of slow wave coupling (46.9 ± 4.4 vs. 61.5 ± 6.9%, P < 0.04). In addition, the patients showed inconsistencies in the frequency and regularity of the gastric slow wave among the four-channel electrogastrograms (EGGs). It was concluded that patients with functional dyspepsia have impaired slow wave propagation and coupling. Multichannel EGG has more information than single-channel EGG for the detection of gastric myoelectrical abnormalities.

FUNCTIONAL DYSPEPSIA is a common but loosely defined clinical syndrome. It may be defined as episodic or persistent abdominal symptoms often related to feeding (3). These symptoms include vague epigastric or periumbilical discomfort, early satiety, postprandial fullness, bloating, regurgitation, nausea, and vomiting (32). On the basis of the combination of these symptoms, a number of investigators have attempted to subdivide functional dyspepsia into three categories: dysmotility-like, ulcer-like, and reflux-like dyspepsia (3). The pathophysiological mechanism of functional dyspepsia is unclear. Gastrointestinal motor disorders have been found in patients with functional dyspepsia, which presents as gastric hypomotility and uncoordinated antral duodenal contractions (4, 16, 21, 23, 34). Abnormal myoelectrical activities were seen in patients with chronic idiopathic nausea and vomiting (28). It has been implied that gastric motor disorders in these patients may be pathophysiologically attributed to gastric myoelectrical dysrhythmias (8, 13, 22, 26).

Gastric motility is regulated by gastric myoelectrical activity. The electrogastrogram (EGG) is an accurate noninvasive measurement of the gastric slow wave (8, 10, 18, 35). The frequency of gastric slow waves is measured in the EGG, whereas the contraction-related spike/second potentials are reflected in the EGG as an increase in amplitude (20, 35). Numerous studies have used this technique to detect gastric motility disorders (2, 8, 15, 17, 22, 24, 26, 27, 37–39, 41).

Previous studies have shown that abnormal gastric myoelectrical activities are associated with gastric motility disorders and gastrointestinal symptoms such as nausea and vomiting (1, 13, 19, 40), which are common in functional dyspepsia. Abnormal gastric myoelectrical activity has recently been reported in children with functional dyspepsia (14, 34) as well as in adult patients (13, 25). The study by Geldof et al. (25) reported no difference between the patients and healthy controls in the EGG parameters they analyzed. The quantitative assessment of the regularity of gastric slow waves was, however, not performed, and the postprandial state was studied after a relatively small test meal (275 kcal). Using single channel electrogastrography, we have recently reported that patients with functional dyspepsia had impaired gastric slow waves in the postprandial state but not in the fasting state (31).

Although there is an increasing interest in electrogastrography and an increased number of publications, the analysis of the EGG is based exclusively on spectral parameters derived from one single-channel EGG. In a recent study, we used a specially designed four-channel EGG device and found that the propagation of the gastric slow wave in normal controls could be identified from the multichannel EGGs (12). Inspired by this recent multichannel EGG study, we wondered whether the additional parameters (propagation and coupling of the gastric slow wave) obtained from the multichannel EGGs would provide more information on gastric myoelectrical abnormalities in patients with suspected motility disorders. The aim of this study was, there-
fore, to utilize the four-channel EGGs to investigate whether patients with functional dyspepsia had impaired propagation or coordination of gastric slow waves in the fasting state compared with healthy controls.

**METHODS**

**Subjects**

The study was performed in 10 patients with functional dyspepsia (8 females, 2 males, mean age 40.2 yr) and 11 healthy subjects (5 females, 6 males, mean age 37.3 yr). All patients were clinically confirmed, with a negative endoscopy within 3 mo before the study, to be without any mechanical obstructions or organic diseases. None of the patients had been diagnosed for gastroesophageal reflux, chronic intestinal pseudoobstruction, irritable bowel syndrome, 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 concomitant medication limited to prokinetic agents, anticholinergic agents, or calcium channel blockers were excluded from the study. The selection of these patients was based on the Rome II criteria and a symptom score with a history of the symptoms of ≥6 mo duration (continuous or intermittent). The following symptoms were evaluated as mild, moderate, or severe and were respectively scored from 1 to 3: nausea, vomiting, anorexia, early satiety, postprandial bloating or distension, upper abdominal discomfort or pain, and belching. An aggregate score of ≥6 was required for enrollment in the study. The healthy subjects had no history of gastrointestinal diseases and were free of gastrointestinal symptoms. Body mass index ranged from 17 to 32 kg/m² (24.6 ± 1.6) in the patients and 18 to 26 kg/m² (22.4 ± 2.9) in the controls. None of the subjects took medications the week before or during the study. The research protocol was approved by the institutional review board at the Integris Baptist Medical Center of Oklahoma, and written consent forms were signed by all subjects before the study.

**Multichannel Electrogastrography**

Gastric myoelectrical activity in each subject was measured using surface electrogastrography with a specially designed multichannel device (Medtronic-Synectics, Shoreview, MN). The device consisted of four identical amplifiers with cutoff frequencies of 1.8 and 16.0 cpm. A 12-bit analog-to-digital converter was installed in the recording device for online digitization of the EGG. The sampling frequency was 4 Hz. The device was tested before the study with a multichannel signal generator, and it was confirmed that the amplifiers did not generate any phase shifts among different channels when an identical sinusoid of 3 cpm was sent to the input of each channel. Before the attachment of electrodes, the abdominal surface where electrodes were to be positioned was shaved, if hairy, and cleaned with sandy skin prep paste (Omni Prep, Weaver and Aurora, CO) to reduce impedance. Six silver/silver chloride electrocardiogram electrodes (3M Red Dot, St. Paul, MN) were placed on the abdominal skin as shown in Fig. 1, including four active electrodes (electrodes 1–4), one reference electrode (electrode 0), and a ground electrode. Electrode 3 was placed 2 cm above the middle point between the xiphoid process and the umbilicus; electrode 4 was 4 cm on the right horizontal to electrode 3, and electrodes 2 and 1 were placed 45° upper left of electrode 3 with an interval of 4–6 cm depending on the size of the subject. The common reference electrode (electrode 0) was placed at the cross-point of two lines, one horizontal-connecting electrode 1 and one vertical-connecting electrode 3. The ground electrode was placed on the left coastal margin horizontal to electrode 3. Connection of each of the four active electrodes to the common reference electrode derived four-channel EGG signals. The study was performed for ≥30 min in the supine position after a fast ≥6 h. The subjects were allowed to watch regular TV and were asked to stay awake, not to talk, and to remain as still as possible during the whole recording period to avoid motion artifacts.

**Data Analysis**

**Percentage of slow wave propagation.** Cross-covariance analysis was performed to compute the propagation of the gastric slow wave from the EGG. The calculation was performed on a minute-by-minute basis. In this method, the first sum of the multiplication of the corresponding samples in two EGG signals was calculated. The second sum was computed by shifting the second EGG signal one sample forward or backward, and the nth sum was obtained by shifting the second EGG signal by nth samples forward or backward. The time lag between the two time series was determined by the number of samples shifted backward or forward, which resulted in the maximum sum. The time lag between the most proximal and most distal channels was calculated every 1 min using this method. The average value for the whole recording period was obtained from these values of the time lag. A minute was defined as propagated if the time lag was >3 s. The percentage of propagation was defined as the percentage of time during which the time lag was >3 s between the most proximal and most distal channels.

**Percentage of slow wave coupling.** Cross-spectral analysis was developed to compute the percentage of slow wave coupling. The percentage of slow wave coupling was defined as the percentage 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 EGG recording was divided into blocks of 1 min without overlapping. The power spectrum of each 1-min EGG was calculated, and the
controls (P, lower than that shown (89.9 \pm 58.0\%).

The percentage of slow wave propagation was less obvious in the patients than in the controls (see the gastric slow wave in the four-channel EGGs was

RESULTS

A

B

1 min

200 \mu V

slow waves in two 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 four channels was computed, and the values were then averaged.

Spectral Analysis

Spectral analysis of the EGG was performed to derive the following EGG parameters in each channel.

EGG dominant frequency/power. The frequency at which the EGG power spectrum had a peak power in the range of 0.5–9.0 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 two parameters were calculated by using the smooth-power spectral analysis method (5).

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 (30). In this method, each EGG recording was divided into blocks of 1 minute without overlapping. The power spectrum of each 1-min EGG was calculated and examined to see whether the peak power was within the range of 2–4 cpm. The 1-min EGG was called normal if the peak power was within the 2–4 cpm range; otherwise, it was defined as dysrhythmia.

Statistical Analysis

All data are presented as means \(\pm\) SE. Analysis of variance (ANOVA) and paired student’s t-tests were applied to investigate the difference observed in the time lag, percentage of propagation, and percentage of coupling. A P value of \(<0.05\) was considered significant.

RESULTS

Both visually and quantitatively, the propagation of the gastric slow wave in the four-channel EGGs was less obvious in the patients than in the controls (see Fig. 2). The percentage of slow wave propagation was 58.0 \(\pm\) 8.9\% in the patients, which was significantly lower than that shown (89.9 \(\pm\) 2.6\%) in the healthy controls (P \(< 0.002\)). Similarly, the averaged time lag between the most proximal channel and the most distal channel was significantly smaller in the patients than in the healthy controls (4.52 \(\pm\) 1.02 vs. 9.58 \(\pm\) 0.31, P \(< 0.001\)).

In addition to the impairment in propagation, the patients also showed abnormality in slow wave coupling. The percentage of slow wave coupling was significantly lower in the patients than in the controls (46.9 \(\pm\) 4.4 vs. 61.5 \(\pm\) 6.9\%, P \(< 0.04\)).

Although the average percentage of the normal slow waves was lower in the patients than in the controls, the difference was not statistically significant. In the healthy controls, there was no difference in the percentage of normal slow waves among the four channels (channels 1–4: 95.9 \(\pm\) 1.6, 95.7 \(\pm\) 2.0, 94.5 \(\pm\) 1.9, and 94.7 \(\pm\) 1.6\%, respectively; P \(=\) 0.9, ANOVA). In the patients, however, the percentage of normal slow waves was \(~10\%) lower in channel 3 than in the rest of the channels, although the difference was not statistically significant (channels 1–4: 76.7 \(\pm\) 4.3, 77.8 \(\pm\) 4.2, 69.8 \(\pm\) 6.5, and 78.3 \(\pm\) 5.9\%, respectively; P \(=\) 0.7, ANOVA). The difference was significant, however, between channels 3 and 4 (P \(< 0.02\)).

Similar disagreement among the four channels in the dominant frequency of the EGG, which was not seen in the controls, was noted in the patients. The dominant EGG frequency was found to be lower in channel 2 than in the other channels (channels 1–4: 3.05 \(\pm\) 0.05, 2.76 \(\pm\) 0.12, 2.91 \(\pm\) 0.1, and 2.93 \(\pm\) 0.1 cpm, respectively; P \(=\) 0.3, ANOVA), and the difference between channels 1 and 2 was statistically significant (P \(< 0.03\)). On the other hand, in the controls, no difference was noted in the dominant frequency among the four channels (channels 1–4: 3.09 \(\pm\) 0.06, 3.11 \(\pm\) 0.09, 2.97 \(\pm\) 0.07, and 3.03 \(\pm\) 0.07 cpm, respectively; P \(=\) 0.6, ANOVA; Fig. 3).

With regard to the dominant power of the EGG, the results were in converse; there was a difference among the four channels in the controls but not in the patients. As shown in Fig. 4, there was no difference in

Fig. 2. Original recording from a healthy subject (left) and a patient (right).

Fig. 3. Dominant frequency in both patients and healthy controls among the four channels.
the dominant power among the four channels in the patients. In the controls, however, the dominant power in channel 3 was higher than that in channel 1 (P < 0.01) and the dominant power in channel 4 was higher than that in channels 1 and 2 (P < 0.02).

**Fig. 4. Dominant power in both patients and healthy controls among the four channels.**

DISCUSSION

In this study, we present a novel method, multichannel electrogastrography, for the study of gastric myoelectrical abnormalities in patients with functional dyspepsia. It was found that, compared with the healthy controls, the patients with functional dyspepsia had impaired gastric slow wave propagation and coordination. This was reflected in the decreased percentages of slow wave propagation and coupling and in the inconsistencies in the percentage of the normal slow wave and its dominant frequency measured from different channels.

With few exceptions (7, 12), single-channel electrogastrography has been used exclusively for the measurement of gastric myoelectrical activity. Although some investigators had recorded multichannel EGGs previously, the results were reported on the basis of an analysis of a single selected channel. With the methodology of multichannel electrogastrography, information on the propagation and coordination of the gastric slow wave can also be provided.

The feasibility of the detection of gastric slow wave propagation was first reported about 10 years ago (7). With the aid of either ultrasound or X-ray for the localization of the stomach, forward propagation was observed in the majority of the subjects and the total phase shift among the four channels was comparable to that reported in this study (7). In another study (6), retrograde propagation of tachygastria slow waves was observed in a few patients with gastroparesis. The methodology applied in the current study was first described in a recent study (12). In this current method, localization of the stomach was not performed. This makes it more practical and feasible in both clinical and research settings. Computer simulations performed by Kothapalli (29) using a three-dimensional model as well as those performed in our laboratory (30) also predicted that propagation of the gastric slow wave may be detected from the phase shift between different positional EGG channels. In this study, we have shown that patients with functional dyspepsia have impaired slow wave propagation.

In addition to the detection of slow wave propagation, we have defined a new parameter, the percentage of slow wave coupling. Although the former reflects the propagation of slow waves, i.e., whether the slow wave propagates distally, orally, or simultaneously, the latter represents the coupling or consistency of the slow wave frequency along the gastric axis. A zero percentage of coupling indicates that the slow wave has different frequencies in the four channels. That is, if the slow waves at different locations have different frequencies, they are by no means coupled. The definition given in this study was determined experimentally. We have found that the specific definition given in this study maximizes the difference between controls and patients. Our data suggest that this parameter is useful for the identification of slow wave uncoupling in patients with functional dyspepsia. It is believed that it can also be used to identify slow wave uncoupling in other categories of patients with suspected motility disorders.

Although the regularity of gastric slow waves was relatively lower in the patients, its absolute value in a majority of the patients was in the normal range in the fasting state. This was in agreement with our previous study (31), in which we used conventional single-channel electrogastrography and found that gastric myoelectrical activity was impaired only in the fed state. Conflicting results have been reported in the literature regarding slow wave abnormalities in the fasting state (19, 25). In the current study, we noted that the percentage of normal slow waves was lowest in channel 3. This suggests that the stomach was not homogeneous electrophysiologically and that there existed local abnormalities in the rhythmicity of the slow wave. Channel 3 is above the distal antrum, and it is known that the ectopic pacemaker is usually located in the distal antrum. In a recent study, Qian and Chen (33) used internal serosal electrodes and recorded gastric slow waves in dogs under various interventions that induced dysrhythmia. It was found that the lowest percentage of normal slow waves was in the distal antrum, supporting the results in the current study. Similarly, inconsistency in the dominant frequency of the slow wave among the four channels was noted. This also suggests disordination of the gastric slow wave.

It is well known that, under normal conditions, the slow wave has a higher amplitude in the distal antrum than in the body. The results that we obtained in the normal controls were in agreement with this, i.e., higher EGG dominant power in the distal channel than...
in the proximal channel. This was not noted in the patients, however, suggesting that the antrum might be impaired with regard to the strength of the gastric slow wave.

Numerous previous studies with single-channel electrogastrography have shown that most abnormalities in gastric myoelectrical activity can be detected only in the fed state. Using multichannel electrogastrography, however, we are now able to identify abnormalities in slow wave propagation and coupling in the fasting state. On the other hand, it should be pointed out that, on the basis of previous experiments and computer simulations (9, 12), we found that the method of multichannel electrogastrography presented in this study is less capable of detecting slow wave propagation in the fed state (9, 12). Accordingly, the current study was not extended to include the fed state.

In conclusion, the propagation of the gastric slow wave is detectable from the multichannel EGG recordings by use of an appropriate recording device and appropriate arrangement of the electrodes. The quantitative analysis of the multichannel EGGs provides useful information on the coupling or uncoupling of the gastric slow wave. Patients with functional dyspepsia have impaired propagation and coordination of the gastric slow wave.

REFERENCES


