

Prevalence of Gastric Myoelectrical Abnormalities in Patients with Nonulcer Dyspepsia and *H. pylori* Infection

Resolution After *H. pylori* Eradication

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The aims of this study were to investigate the effects of *H. pylori* eradication on gastric myoelectrical activity and dyspeptic symptoms. Sixty-two subjects with *H. pylori* infection and no active peptic ulcer participated in this study, which involved three sessions. Anti-*H. pylori* therapy consisting of clarithromycin and omeprazole was given for two weeks. Gastric myoelectrical activity was measured using surface electrogastronomy and dyspeptic symptoms were scored at each session. A [¹⁴C] urea breath test was performed at baseline and one month after treatment. In comparison with baseline, the percentage of normal slow waves was significantly increased and the mean total symptom score was significantly reduced one and three months after therapy ($P < 0.05$). Approximately 40% of patients with nonulcer dyspepsia symptoms and *H. pylori* infection have abnormal gastric myoelectrical activity, which may be normalized following the eradication of *H. pylori* infection. The normalization of gastric myoelectrical activity may be one explanation for the significant symptom improvement in this subset of the dyspepsia population after *H. pylori* eradication.

KEY WORDS: myoelectrical activity; electrogastronomy; *H. pylori* eradication; nonulcer dyspepsia; stomach.

H. pylori is a spiral bacterium that infects the lining of the stomach and predisposes the patient to gastritis and ulcer. Studies have shown that patients with *H. pylori* infection and nonulcer dyspepsia have a mildly

increased rate of solid phase gastric emptying (1). In some studies, eradication of *H. pylori* infection has relieved the clinical symptoms of nonulcer dyspepsia (2), while in others there has been no significant difference noted (3). However, very few studies have assessed the effect of *H. pylori* infection on gastric myoelectrical activity (4).

Two types of myoelectrical activities have been observed in the human stomach: slow waves (or electrical control activity, basic electrical rhythm) and spike potentials (or electrical response activity) (5). Slow waves are present all the time and originate near the junction of the proximal one third and distal two thirds of the gastric corpus. They are characterized by regular recurring changes in potentials, propagating circumferentially and distally towards the pylorus

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with increasing velocity and amplitude. The frequency of the normal slow wave is about 3 cycles/minute (cpm) or 0.05 Hz in humans (5, 6). Spike potentials are directly associated with antral contractions. The antral muscles contract when slow waves are superimposed with spike potentials. The frequency and propagation of the antral contractions are determined by the gastric slow wave.

Gastric myoelectrical activity can be measured by placing electrodes on the abdominal surface. The cutaneous recording of gastric myoelectrical activity is termed the electrogastrogram (EGG) (7). Previous studies (8, 9) have shown that the frequency of the gastric slow wave can be detected on the EGG, whereas spikes are reflected on the EGG as an increase in amplitude. When correctly recorded and analyzed, the noninvasive EGG provides information on the frequency and relative amplitude of antral slow waves (9). Electrogastrography has been successfully applied to investigate gastric myoelectrical activity in both normal subjects and patients with gastroparesis and nonulcer dyspepsia (10–22).

The aims of this study were to investigate the patterns of gastric myoelectrical activity in subjects with *H. pylori* infection and to determine the effect of *H. pylori* eradication on gastric myoelectrical activity and the status of dyspeptic symptoms using the noninvasive electrogastrographic technique.

MATERIALS AND METHODS

Subjects

Sixty-two subjects (35 men, 27 women, age 27–77 years) with *H. pylori* infection confirmed by the [¹⁴C] urea breath test (UBT) and no active peptic ulcer, as excluded by upper gastrointestinal endoscopy, participated in this study. Patients were excluded if they had any chronic or acute disease or conditions that might influence the outcome of this study, including taking an investigational drug during the preceding month or previous gastric resection. The research protocol was approved by the Human Investigation Committee at the University of Virginia Health Science Center, and a written consent form was signed by all subjects before the study. The *H. pylori* status in each subject was determined by using the UBT (previously described), which has a sensitivity and specificity of over 90% (23).

Electrogastrogram (EGG)

Gastric myoelectrical activity in each subject was measured using surface electrogastrography. Prior to the placement of electrodes, the abdominal surface where electrodes were to be positioned was shaved, if necessary, and cleaned with sandy skin-prep paste (Omni Prep, Weaver & Co., Aurora, Colorado, USA) to reduce the impedance. Three silver–silver chloride ECG electrodes (NDM, Dayton,

Ohio, USA) were placed on the abdominal skin surface over the stomach. Two active electrodes were connected to yield a bipolar EGG signal: one was placed at the midpoint between the xiphoid and the navel; the other was placed 5 cm to the left and 3 cm above this point. One reference electrode was placed in the lower quadrant near the left costal margin. The EGG signal was recorded by a portable EGG recorder (Synectics, Irving, Texas) with low and high cutoff frequencies of 1 and 18 cpm, respectively, and simultaneously digitized and stored on the recorder. The analog-to-digital converter was 8-bit and the sampling frequency was 1 Hz. All recordings were made in a quiet room with subjects in a supine position. They were asked not to talk and to remain as still as possible during the recording to avoid motion artifacts.

Study Protocol

A baseline and two follow-up studies were performed on all subjects. The baseline study included a UBT in the fasting state for confirmation of *H. pylori* status, followed by an EGG test. The recording of the EGG lasted for 30 min in the fasting state and 60 min after a solid test meal of a 500-kcal turkey sandwich consumed within 15 min. Then each subject was treated with clarithromycin (500 mg twice daily) and omeprazole (40 mg every day or 20 mg twice daily) for two weeks. The two follow-up studies were performed at one month and three months after the treatment, respectively. The first follow-up study included a UBT to test *H. pylori* status and an EGG test as described above, whereas the second follow-up study included only an EGG test. Symptoms of heartburn, fullness, nausea, and abdominal pain experienced during the previous week were each graded as 0 to 3 (0 = none, 1 = mild, 2 = moderate, 3 = severe) during patient interviews at baseline and one and three months after treatment.

Data Analysis

The EGG data stored on the EGG recorder were downloaded to an IBM 486 personal computer using the software Multigram (Synectics Medical, Inc., Irving, Texas, USA). All data were subjected to computerized spectral analyses using computer programs developed by authors (24). Before computer analysis, all recordings were visually inspected for identifying motion artifacts; the time periods containing these motion artifacts were deleted. The following parameters were computed from the EGGs using spectral analysis methods.

EGG Dominant Frequency and 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 of the EGG was defined as the EGG dominant power. The smoothed power spectral analysis method (25) was used to calculate the EGG dominant frequency and power during each recording period, including a 30-min baseline and a 60-min postprandial. Decibel (dB) units were used to express the power of the EGG.

Change of EGG Dominant Power. The change of EGG dominant power (δp) was defined as the difference between the EGG dominant powers after and before the test meal. This was equivalent to the power ratio in linear scale (26).

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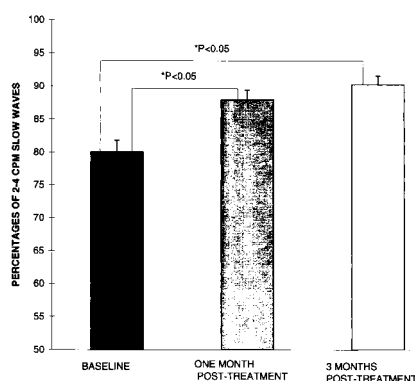


Fig 1. The mean percentages of 2- to 4-cpm slow waves observed in the EGG at baseline and one and three months after treatment. The mean percentage of the 2- to 4-cpm slow waves in the 62 subjects was significantly increased during the course of treatment ($P < 0.05$).

Percentage of Normal Slow Waves (or Dysrhythmias).

The percentage of normal gastric slow waves (or dysrhythmias) was defined as the percent of time during which normal 2- to 4-cpm slow waves were present (or absent) over the entire observation period. It was computed using the adaptive spectral analysis method (27). Each EGG recording was divided into nonoverlapping 2-min blocks. The power spectrum of each 2-min block was computed and examined to determine if the dominant peak power was within the range of 2–4 cpm. The 2-min EGG was categorized normal if the dominant power was within 2–4 cpm. Otherwise, it was categorized as dysrhythmia including bradygastria (0.5–2.0 cpm) and tachygastria (4.0–9.0 cpm).

Based on several previous reports of EGG parameters in both normal subjects and patients (11, 13, 14, 18), an EGG recording was defined as abnormal if the percentage of normal 2- to 4-cpm slow waves was lower than 70% in either fasting or fed state and/or if there was an absence of a normal increase in the postprandial EGG dominant power ($\delta p < 0$).

Statistical Analysis

The EGG parameters and symptom scores, defined above, at baseline and one and three months after the treatment were compared with ANOVA, Student's *t* test and χ^2 analysis (28). Statistical significance was assigned for $p < 0.05$. All data were presented in mean \pm SEM.

RESULTS

Using the definition of abnormality of the EGG described in the previous section, we found that 39% of the patients with *H. pylori* infection had an abnormal EGG at baseline (15 patients had lower than 70% of the 2- to 4-cpm slow waves in either fasting or fed state and 9 patients had a decrease of EGG power after the test meal). Gastric myoelectrical activity in

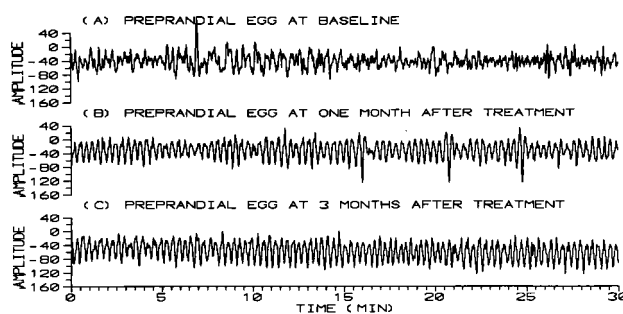


Fig 2. Examples of 30-min EGG recordings from one subject at baseline and one and three months after treatment. The rhythmicity of the EGG was significantly improved following the course of treatment.

patients with *H. pylori* infection was significantly improved following the course of therapy aimed at eradication of *H. pylori*, with 16% patients remaining abnormal one month after treatment ($P < 0.004$, χ^2 analysis) and 11% three months after treatment ($P < 0.0004$, χ^2 analysis). Gastric dysrhythmias recorded in this study included bradygastria and tachygastria. No difference was found in the frequency of occurrence of these two types of dysrhythmias.

A significant increase in the percentage of 2- to 4-cpm slow waves was found during the course of the study. The mean percentage of the 2- to 4-cpm slow waves in the 62 subjects was $80.0 \pm 1.8\%$ at baseline, $87.9 \pm 1.4\%$ one month after anti *H. pylori* therapy ($P < 0.05$, in comparison with baseline), and $90.2 \pm 1.3\%$ three months after treatment ($P < 0.05$, in comparison with baseline, see Figure 1.) An example of EGG recordings and their running power spectra are presented in Figure 2 and 3.

The postprandial change in EGG dominant power was not affected by treatment. The mean value of the postprandial increase of EGG dominant power was 4.70 ± 0.72 dB at baseline, 4.86 ± 0.61 dB one month after treatment, and 4.52 ± 0.62 dB three months after treatment.

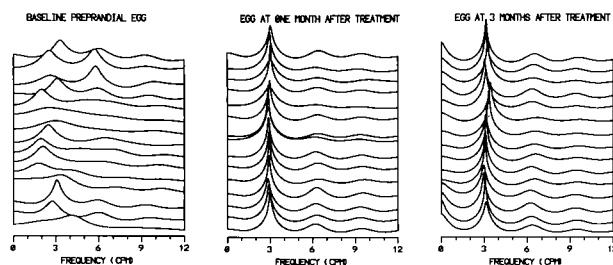


Fig 3. Running power spectra of the EGGs in Figure 2 at baseline and one and three months after treatment. The percentage of 2- to 4-cpm slow waves was significantly increased after the treatment in comparison with the baseline.

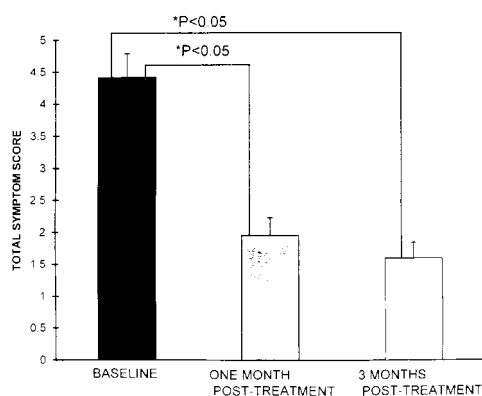


Fig 4. Mean total symptom scores in the 62 subjects at baseline and one and three months after treatment. The mean total symptom score was significantly reduced following the course of therapy aimed at eradication of *H. pylori* ($P < 0.05$).

The improvement of gastric myoelectrical activity was found to be associated with eradication of *H. pylori* infection. One month after treatment, 46 of the 62 subjects (74%) were cured of *H. pylori* infection, and 40 of these 46 subjects (87%) had normal EGGs. Eighteen of 24 subjects (74%) with abnormal EGGs at the baseline were cured of *H. pylori* infection at one month follow-up, and 15 of these 18 cured subjects (83%) showed a normalization of the EGG.

A significant improvement on the symptoms was observed during the follow-up interviews. As shown in Figure 4, the mean total symptom score was 4.41 ± 0.37 at baseline, 1.95 ± 0.28 one month after treatment ($P < 0.05$, in comparison with the baseline), and 1.59 ± 0.25 after three months ($P < 0.05$, in comparison with the baseline). The symptom score for abdominal pain was found to be associated with the status of the EGG. At the baseline, the symptom score for abdominal pain was significantly higher in the patients with abnormal EGGs than in patients with normal EGGs (1.69 ± 0.35 vs 0.83 ± 0.20 , $P < 0.05$). The normalization of the EGG was associated with a significant decrease in the symptom score of abdominal pain. Specifically, 18 of the 24 subjects with abnormal EGGs at baseline were cured of *H. pylori* infection one month after therapy, and the mean symptom score of abdominal pain in these 18 subjects was significantly reduced one month after therapy in comparison with these patients at the baseline (1.44 ± 0.27 vs 0.56 ± 0.25 , $P < 0.05$, see Figure 5.) This reduction in abdominal pain was also present at three months with a mean pain score of 0.28 ± 0.18 ($P < 0.05$, compared to the baseline) in the 16 patients whose EGG remained normal. Two of six patients with abnormal EGGs at baseline whose

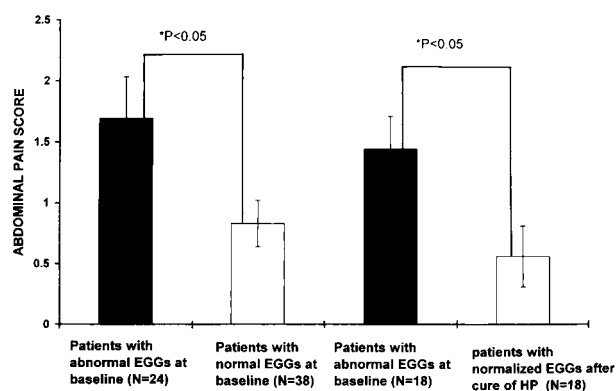


Fig 5. Mean abdominal pain score in patients with abnormal and normal EGGs at baseline and in patients with abnormal EGGs at baseline that normalized after one month of treatment. At baseline, the abdominal pain score was significantly higher in patients with abnormal EGGs than in patients with normal EGGs. The normalization of the EGG after one month of treatment was associated with a significant reduction in the abdominal pain score.

H. pylori was not eradicated one month after therapy had persistently abnormal EGGs. The mean abdominal pain score in these six patients was not significantly reduced one month after therapy (1.5 ± 0.6 vs 0.8 ± 0.5 , $P = 0.2$).

DISCUSSION

We have found in this investigation that 39% of nonulcer patients with *H. pylori* infection had abnormal EGGs. The treatment of *H. pylori* infection with clarithromycin and omeprazole significantly reduced the prevalence of EGG abnormalities in these patients. Specifically, the treatment significantly increased the percentage of normal 2- to 4-cpm gastric slow waves. There was no significant improvement in the postprandial change of EGG dominant power, which was normal before the treatment course. A majority (74%) of the patients were cured of *H. pylori* infection, and the overall score for dyspepsia symptoms was significantly reduced one month after treatment. The improvement of gastric myoelectrical activity seemed to be associated with the eradication of *H. pylori* infection. In particular, the severity of abdominal pain and its subsequent improvement after *H. pylori* eradication paralleled the status of the EGG.

Noninvasive electrogastrography was applied in this study to record gastric myoelectrical activity in patients with *H. pylori* infection. Alternative methods to measure gastric myoelectrical activity include the use of serosal electrodes (8, 29, 30) or intraluminal electrodes (31). The practical application of the serosal electrodes is very limited due to its invasive nature.

While it is feasible, the intraluminal technique may not provide a reliable measurement of gastric myoelectrical activity due to the fact that the contact between the electrodes and the gastric mucosa is not always guaranteed during recording. Electrogastrography is the most commonly used method for the study of gastric myoelectrical activity. It is attractive not only because it is noninvasive but also because it does not disturb the ongoing physiological process of the stomach. Previous studies have shown that the dominant frequency of the EGG accurately reflects the frequency of the gastric slow wave (8, 29, 30). The relative change of EGG power at the dominant frequency reflects the contractility of the stomach (8, 32–35). The percentage of 2- to 4-cpm slow waves observed in the EGG represents the regularity of the gastric slow wave.

This study showed that approximately 40% of symptomatic patients with *H. pylori* infection had abnormal EGGs. Numerous previous studies have shown that a vast majority of normal subjects have a normal EGG, i.e., the percentage of 2- to 4-cpm slow waves is higher than 70% in both fasting and fed states, and there is a postprandial increase in EGG dominant power (13, 26). The data analysis method used in these previous studies was the same as in the current study. Abnormal EGGs have been reported in subjects with motion sickness (10), pregnant women with nausea and vomiting (15, 36), and in several clinical settings, such as patients with gastroparesis (13, 37, 38), and functional dyspepsia or unexplained nausea and vomiting (12, 14, 18, 39). The prevalence of the abnormal EGG in symptomatic patients with *H. pylori* infection reported here is much higher than that in healthy subjects but lower than in patients with gastroparesis. More than 75% of patients with gastroparesis have been reported to have abnormal EGGs (13, 37, 38).

The postprandial increase of EGG power at the dominant frequency is a typical observation of the EGG after the test meal in normal subjects (11, 13, 14, 19, 31, 34, 35). The increase is dependent upon the content of the test meal. After a regular test meal of 500 kcal, the postprandial EGG usually shows a one- to twofold increase in amplitude or a 6- to 12-dB increase in the dominant power (22). The patients with *H. pylori* infection in this study showed an increase of 4.7 dB at the baseline. This value was slightly lower compared to healthy subjects and suggests that a minority of the patients might have delayed gastric emptying (17). Our data indicated that the eradication of *H. pylori* infection was not associ-

ated with the postprandial increase of EGG power. This is in agreement with the previous findings that showed eradication of *H. pylori* infection did not affect gastric emptying (1).

Our data suggest that the attempted eradication of *H. pylori* infection using clarithromycin and omeprazole seemed to normalize gastric myoelectrical activity. This improvement was due to the normalization of the rhythmicity of the gastric slow wave since the postprandial power change was initially normal and did not change. Some recent preliminary studies (40, 41) reported a similar improvement in the rhythmicity of the gastric slow wave by treatment with omeprazole in patients with peptic ulcer disease. The status of *H. pylori* infection was, however, not reported in these studies. Gastrointestinal symptoms such as those listed in this study are common in patients with *H. pylori* infection. The eradication of *H. pylori* infection has been reported to relieve symptoms (2), and gastric emptying of a solid meal is believed to be slightly faster in *H. pylori*-infected individuals. However, a change in gastric emptying after *H. pylori* eradication could not explain the symptom reduction we observed. The concurrent improvement in clinical symptoms and the rhythmicity of the gastric slow wave noted in this study suggests an association of gastric dysrhythmias and the clinical symptoms. The improvement of gastric myoelectrical activity may be one explanation for symptom improvement, particularly abdominal pain. Our data indicated that the subset of patients with an abnormal EGG has a significantly higher score of abdominal pain and that the normalization of the EGG led to a significant reduction in their symptom score of abdominal pain.

In summary, about 40% of patients with *H. pylori* infection have abnormal gastric myoelectrical activity. A combination treatment of clarithromycin and omeprazole cures *H. pylori* infection in a majority of patients, significantly improves the clinical symptoms, and results in an improvement in gastric myoelectrical activity. The improvement in gastric myoelectrical activity may be one explanation for symptom improvement, particularly abdominal pain, and has important implications in planning and interpreting future nonulcer dyspepsia research.

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