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Impaired Gastric Myoelectrical Activity in Patients with Chronic Renal Failure

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Dysmotility and delayed emptying of the stomach have been reported in patients with chronic renal failure (CRF). The aim of this study was to investigate whether gastric myoelectrical activity was impaired in patients with CRF using electrogastrography. The electrogastrogram (EGG) was recorded in 24 symptomatic patients with CRF (15 with diabetes) and 12 normal subjects. Two 30-min EGG recordings before and after a test meal were analyzed using spectral analysis methods. It was found that patients with CRF showed a significantly lower percentage of normal 2–4 cpm slow waves in both fasting and fed states in comparison with healthy controls (in fasting state: 88.9 ± 2.5% vs 67.4 ± 6.6%/63.2 ± 7.0%, $P < 0.01$; in fed state: 89.6 ± 1.8% vs 64.6 ± 6.2%/62.0 ± 8.3%, $P < 0.01$; controls vs diabetic patients/nondiabetic patients). Both patient groups showed a significantly higher prevalence of the abnormal EGG, which was defined as the percentage of 2–4 cpm slow waves lower than 70% (fasting state: 8% vs 60%/56%, $P < 0.01/0.05$; fed state: 0% vs 53%/56%, $P < 0.005/0.002$; controls vs diabetic patients/nondiabetic patients). No significant difference was observed in the regularity of the gastric slow waves between the two patient groups. The healthy controls showed a significant increase in the dominant power and frequency of the EGG after the test meal. However, this increase was absent in the two patient groups. It was concluded that patients with chronic renal failure have abnormal gastric myoelectrical activity, including impaired regularity of the gastric slow wave and a failed increase in the power of the EGG at 3 cpm. Electrogastrography is an attractive noninvasive method for the study of gastric motility in patients with severe chronic renal failure.

KEY WORDS: electrogastrography; motility; chronic renal failure; gastric emptying.

Chronic renal failure (CRF) is a chronic deterioration in renal function that leads to progressive destruction of the nephron mass. Gastrointestinal symptoms are common and are early manifestations of CRF. These symptoms include abdominal pain, nausea, vomiting, and early satiety (1). Impaired gastric motility has been reported in patients with CRF (2, 3). Gastric motility is regulated by gastric myoelectrical activity. Previous studies have shown that abnormal gastric myoelectrical activities are associated with gastric motility disorders and gastrointestinal symptoms, such as nausea and vomiting (4, 5), which are very common in CRF (6). Abnormal gastric myoelectrical activity was recently reported in children with CRF (7). However, it is unknown whether symptomatic adult patients with CRF have impaired gastric myoelectrical activity.

Gastric myoelectrical activity can be measured noninvasively using abdominal surface electrodes, a technique called electrogastrography (8). Previous studies have shown that the electrogastrogram (EGG) is an accurate measurement of the gastric slow wave (9–13). The frequency of gastric slow waves is measured

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in the EGG, whereas the contraction-related spike/second potentials are reflected in the EGG as an increase in amplitude (9, 14, 15). Numerous studies have shown the association of EGG abnormalities with gastric motility disorders and gastrointestinal symptoms (16–27).

The aim of this study was to investigate gastric myoelectrical activity in patients with CRF. It was hypothesized that: (1) gastric myoelectrical dysrhythmia might be found in patients with CRF using electrogastrography; and (2) patients with and without diabetes might show a difference in the EGG.

MATERIALS AND METHODS

Study Subjects

The study was performed on 12 asymptomatic normal subjects with no history of renal disease or gastrointestinal disease (7 men, 5 women, age 23–54 years, mean: 36 years) and 24 symptomatic patients with CRF who were diagnosed by clinical and laboratory measures (10 men, 14 women, age: 28–83 years, mean: 54 years). Fifteen of the patients had diabetes. All subjects were fasted for 6 hr or more prior to the study and had taken no medications with a known effect on gastrointestinal motility during the three days before the study. The study was approved by the Institutional Review Board at Integris Baptist Medical Center. Written consent was obtained from the subjects prior to the study.

Electrogastrogram

Surface electrogastrography was applied to record gastric myoelectrical activity. Before the placement of electrodes, the abdominal skin at the recording sites was cleaned with sandy skin-prep jelly (Omni Prep, Weaver & Co., Aurora, Colorado) to reduce impedance. The skin was rubbed until pinkish. The hair, if present, was shaved. Three silver–silver chloride ECG electrodes (Snap, Lombard, Illinois) were placed on the abdomen. One electrode (electrode 1) was placed at the midpoint between the xiphoid and the navel; one (electrode 2) was placed 5 cm to the left and 3 cm above this point; and a reference electrode (electrode 0) was placed in the lower quadrant close to the left costal margin. The bipolar EGG signal was derived from electrodes 1 and 2 and was amplified using a portable EGG recorder (Digitrapper EGG, Synectics Medical, Inc., Irving, Texas) with low and high cutoff frequencies of 1 and 18 cpm, respectively. Online digitization with a sampling frequency of 1 Hz was performed using an analog–digital converter installed on the recorder, and digitized samples were stored on the recorder.

Study Protocol

After a fast of 6 hr or more, the EGG recording was made in each subject for 30 min in the fasting state and 30 min after a standard test meal (two scrambled eggs and two pieces of toast plus 100 ml of water, 282 kcal, 32% protein, 46% carbohydrates, 22% fat). The symptoms scored included nausea, vomiting, abdominal pain, and early satiety, each graded from 0 to 3 (0, none; 1, mild; 2, moderate; 3, severe).

Data Analysis

At the end of the study, the EGG data stored on the recorder were downloaded to an IBM 486 personal computer. All data were subjected to computerized spectral analysis using programs previously developed in our laboratory (28). The following parameters were computed from the EGG using spectral analyses.

Percentage of Normal 2–4 cpm Slow Waves. The percentage of normal 2–4 cpm gastric slow waves, which reflects the regularity of gastric myoelectrical activity, was defined as the percent of time during which normal 2–4 cpm slow waves were present over the entire observation period. It was computed using the adaptive running spectral analysis method (29). Each EGG recording was divided into blocks of 1 min without overlapping. The power spectrum of each 1-min EGG was calculated and examined to see if the peak power was within the range of 2–4 cpm. The 1-min EGG was called normal if the dominant power was within the 2–4 cpm range. Otherwise, it was called dysrhythmia.

Percentage of Dysrhythmias. The percentage of gastric dysrhythmias was defined as the percent of time during which dysrhythmias were present over the entire observation period. It was computed using the same method as for the percentage of normal 2–4 cpm slow waves. If the peak power was outside the range of 2–4 cpm, it was called dysrhythmia. Gastric dysrhythmias included tachygastria, bradygastria, and arrhythmia. If the peak power was within the range of 0.5–2 cpm, the portion of the EGG was called bradygastria; if the peak power was within the range of 4–9 cpm, the portion of the data was called tachygastria. The 1-min EGG was defined as arrhythmia if its power spectrum showed no dominant peak in the range of 0.5–9 cpm.

EGG Dominant Frequency and Power. The frequency at which the overall power spectrum of an entire EGG recording had a peak power in the range of 0.5–9.0 cpm was defined as the EGG dominant frequency. The dominant frequency of the EGG has been shown to be equal to the frequency of the gastric slow wave measured from implanted serosal electrodes (13). It was computed using the smoothed power spectral analysis method (28). The smoothed power spectral analysis was used to produce the overall power spectrum of the EGG during each recording period, ie, the 30 minutes in the fasting state and the 30 min after the test meal.

The power at the dominant frequency in the power spectrum of the EGG was defined as the EGG dominant power. Previous studies (9, 11, 15) have shown that the relative change of the EGG dominant power reflects gastric contractility. Decibel (dB) units were used to represent the power of the EGG. Assuming a sinusoidal signal with an amplitude of A, power P in dB was expressed as $P(\mathrm{dB}) = 10 \times \log_{10}(A^2)$.

Change of EGG Dominant Power, δP. The change of EGG dominant power, δP, was defined as the difference between the EGG dominant powers after and before the test meal.

Definition of Abnormal EGG. We previously defined an

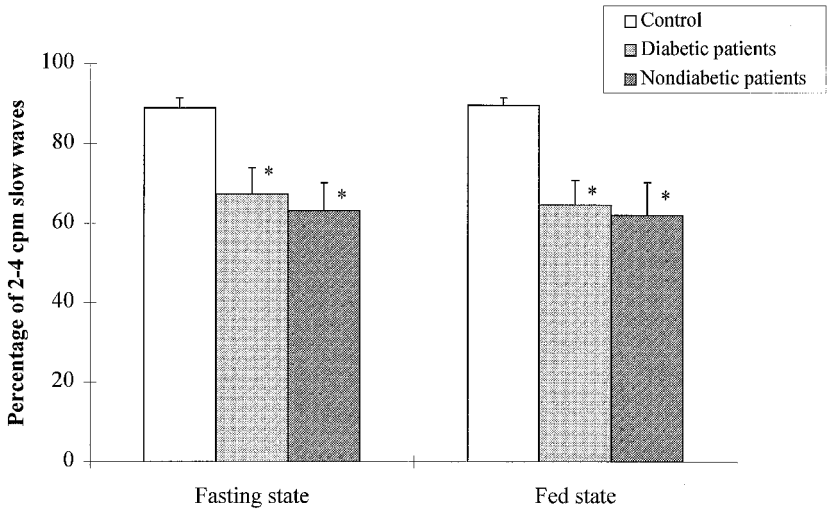

Fig 1. Percentage of 2–4 cpm slow waves in healthy subjects, nondiabetic patients, and diabetic patients. Both groups of patients showed a significantly lower percentage of 2–4 cpm slow waves in comparison with the healthy controls. There was, however, no significant difference between the two groups of patients. *$p<0.01$ in comparison with controls.

EGG recording with the percentage of normal slow waves below 70% in either the fasting or the fed state or a decrease in power at the dominant frequency after test meal as an abnormal EGG (30).

Statistical Analysis

All data are presented as mean ± SEM. Student's t test and chi-square test were used to investigate the difference of the EGG parameters between the patients and the controls and between the diabetic and nondiabetic patients. $P < 0.05$ was considered to be significant.

RESULTS

The patients with CRF showed a significantly lower percentage of normal 2–4 cpm waves in both fasting and fed states in comparison with the healthy controls (Figure 1). The healthy controls had a mean percentage of 2–4 cpm waves of 88.9 ± 2.5% in the fasting state and 89.6 ± 1.8% in the fed state. In contrast, the patients with diabetes had a mean percentage of 2–4 cpm waves of 67.4 ± 6.6% in the fasting state and 64.6 ± 6.2% in the fed state, and the nondiabetic patients had a mean percentage of 2–4 cpm waves of 63.2 ± 7.0% in the fasting state and 62.0 ± 8.3% in the fed state. There was, however, no difference between the two groups of patients. Figure 2 presents typical EGG recordings in the fasting state measured from a healthy subject and a patient, respectively. It can be seen that the EGG in the healthy subject had more regular 3 cpm slow waves than that in the patient. The running spectra of the EGG data presented in Figure 2 are shown in Figure 3. Regular 3 cpm slow waves were seen in the running power spectra of the EGG measured from the healthy subject, whereas the dominant 3 cpm slow waves were missing in the running power spectra of the EGG measured from the patient.

In our previous studies, an EGG was defined as abnormal if the percentage of 2–4 cpm slow waves was below 70%. Using this definition, we found that there was a significantly higher prevalence of the abnormal EGG in the patients with CRF than in healthy controls. In the fasting state, only 1 of the 12 healthy controls (8%) had an abnormal EGG (this particular subject had a percentage of 2–4 cpm slow waves of 69%, 1% below the defined normal level), whereas 9 of the 15 patients with diabetes (60%) had an abnormal EGG ($P < 0.01$ in comparison with the controls) and 5 of the 9 patients without diabetes (56%) had an abnormal EGG ($P < 0.05$ in comparison with the controls). In the fed state, all healthy subjects had a normal EGG, whereas 8 of the 15 patients with diabetes (53%) had an abnormal EGG ($P < 0.005$ in comparison with the controls), and 5 of the 9 patients without diabetes (56%) had an abnormal EGG ($P < 0.002$ in comparison with the controls). However, there was no significant difference in the prevalence of the abnormal EGG between the two patient groups in either fasting or fed state.

There was a slight difference in the percentage of tachygastria between the patients with diabetes and those without diabetes (Figure 4). In the fasting state, the percentage of tachygastria was 10.59 ± 4.35% in

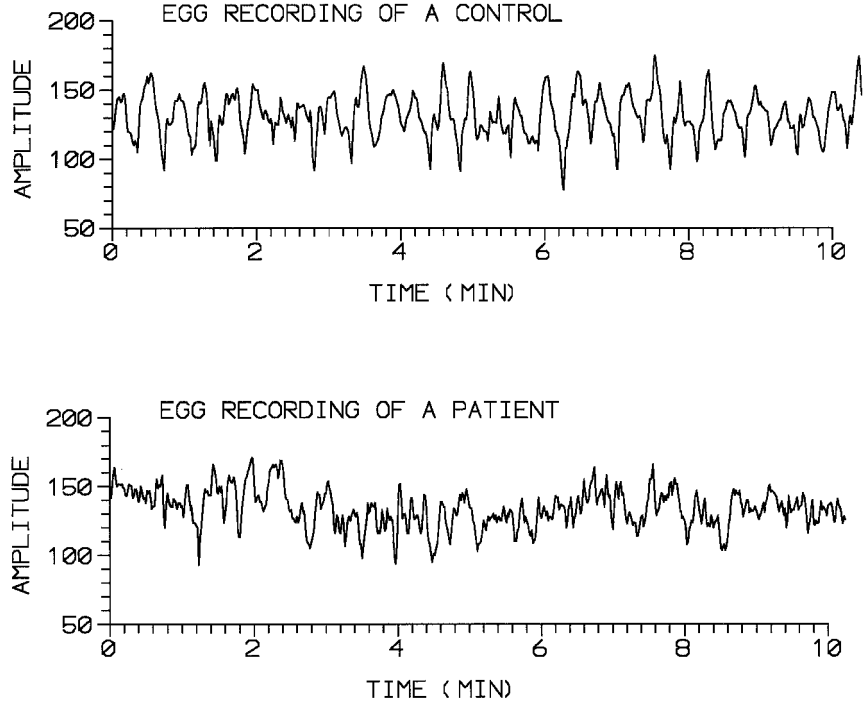

Fig 2. Typical EGG recordings from a healthy control and a patient with chronic renal failure. Regular 3 cpm slow waves were seen in the normal subject but not in the patient.

the nondiabetic patients and 4.26 ± 1.38% in the diabetic patients ($P = 0.09$). In the fed state, the percentage of tachygastria was 10.13 ± 3.52% in the nondiabetic patients and 7.75 ± 1.64% in the diabetic patients ($P > 0.05$).

Different responses in the power of the EGG at the dominant frequency (or dominant power) were observed among the three subject groups. As shown in Figure 5, the healthy controls had an average increase of 2.53 ± 1.18 dB in the dominant power of the EGG (a 3-dB increase in power is equivalent to a 50% increase in the amplitude of the EGG), whereas the patients with diabetes had an average increase of 1.25 ± 1.20 dB, and the patients without diabetes had an average increase of −1.39 ± 1.57 dB ($P < 0.05$ in comparison with the controls). In our previous studies, the response of the EGG to a test meal was defined as abnormal if there was no increase in the dominant power of the EGG. Using this definition, it was found that 3 of the 12 controls (25%) had an abnormal response to the test meal, whereas 7 of the 15 patients with diabetes (47%) had an abnormal response to the test meal, and 7 of the 9 patients without diabetes (78%) had an abnormal response to the test meal ($P < 0.01$ in comparison with the controls). The prevalence of an abnormal response of the EGG to the test meal was significantly higher in the patients without diabetes than those with diabetes ($P < 0.05$).

While all three subject groups showed normal dominant frequencies within 2–4 cpm in both fasting and fed states, there was a difference in the change of the dominant frequency after the test meal between the controls and the patients. As shown in Figure 6, the healthy controls showed a significant increase in the dominant power of the EGG after the test meal (2.84 ± 0.08 cpm vs 3.09 ± 0.07 cpm, $P < 0.005$), whereas neither the patients with diabetes (2.92 ± 0.11 cpm vs 2.80 ± 0.14 cpm, $P > 0.05$) nor the patients without diabetes (3.25 ± 0.18 cpm vs 3.08 ± 0.19 cpm, $P > 0.05$) showed such an increase. The mean value of the dominant frequency in both patient groups actually decreased after the test meal.

Four symptoms were scored, including nausea, vomiting, abdominal pain, and early satiety, each graded from 0 to 3 with 0 meaning no symptoms and 3 the most severe. A total symptom score was calculated for each patient, and then an average total symptom score for each group of subjects was computed. The average total symptom score was 0 for the healthy controls, 6.06 ± 0.58 for the patients with diabetes, and 6.44 ± 1.26 for the patients without diabetes. There was a significant difference in the symptom score between the controls and patients, but

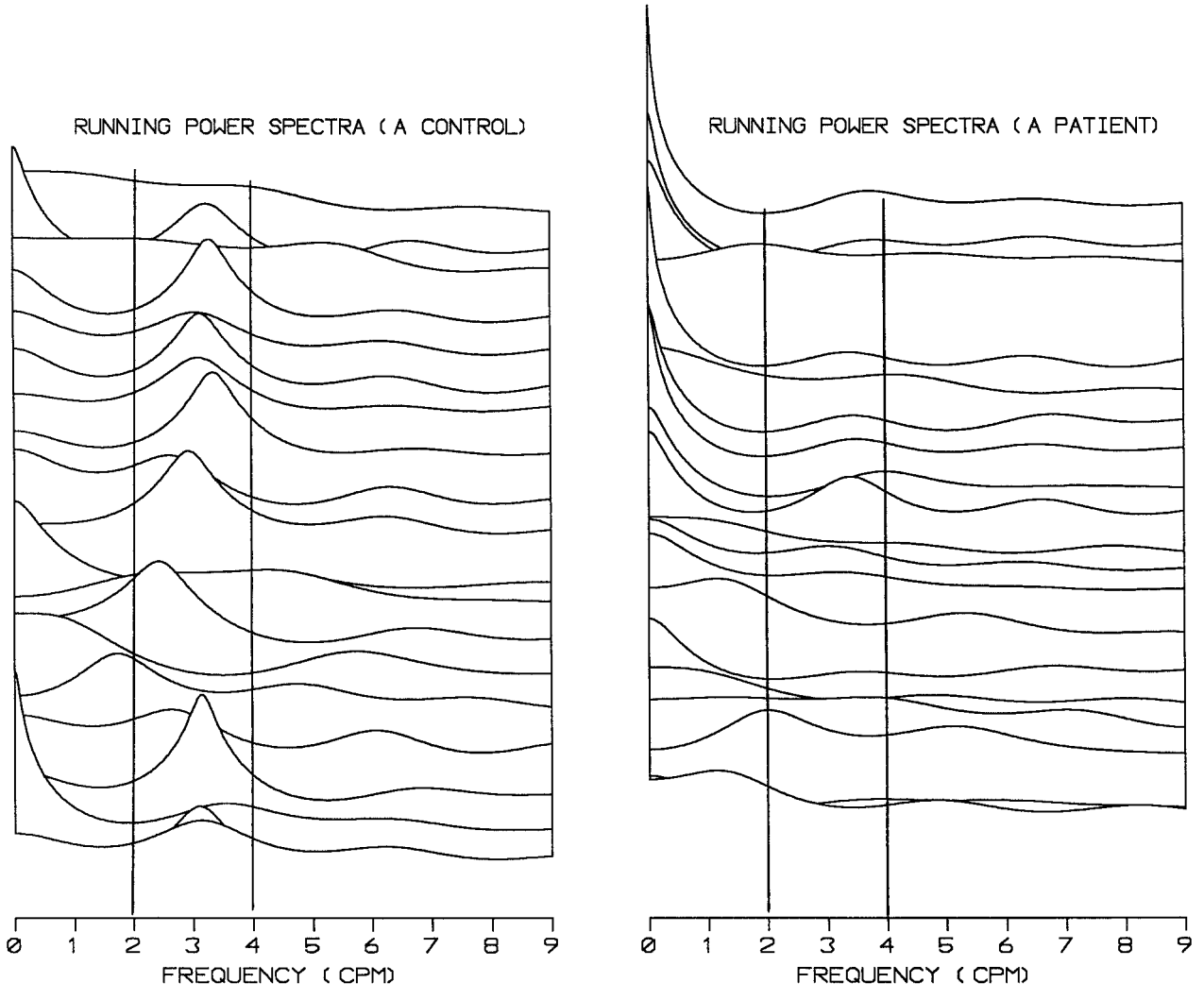

Fig 3. Running power spectra of the EGG analyzed by the adaptive spectral analysis method. Each curve in the figure starting from the bottom to the top represents the power spectrum of 1-min nonoverlapping EGG data. Spectral peaks were seen in the 2–4 cpm frequency range in a majority of the power spectra in the healthy subject (left panel). The running power spectra of the EGG obtained from the patient (right panel) showed an absence of spectral peaks in the 2–4 cpm frequency range.

no significant difference between the two groups of patients.

DISCUSSION

In this study, we have found that: (1) Patients with CRF showed a significantly lower percentage of normal 2–4 cpm waves in both fasting and fed states. There was a significantly higher prevalence of the abnormal EGG (the percentage of normal 2–4 cpm slow waves below 70%) in the patients with CRF in both fasting and fed states. (2) In comparison with healthy controls, patients with CRF showed less increase in the amplitude of the EGG after the test meal. The prevalence of an abnormal response of the EGG to the test meal (no increase or a decrease in EGG dominant power after the test meal) was significantly higher in patients with CRF. (3) There was a significant increase in the dominant frequency in the controls after the solid test meal; this increase, however, was not observed in patients with CRF. (4) There was no significant difference in the regularity of the gastric slow wave between the patients with diabetes and those without diabetes, although the nondiabetic patients had a slightly higher percentage of tachygastria in the fasting state. The prevalence of an abnormal response to the test meal in EGG dominant power was significantly higher in nondiabetic patients than in diabetic patients. No significant difference was

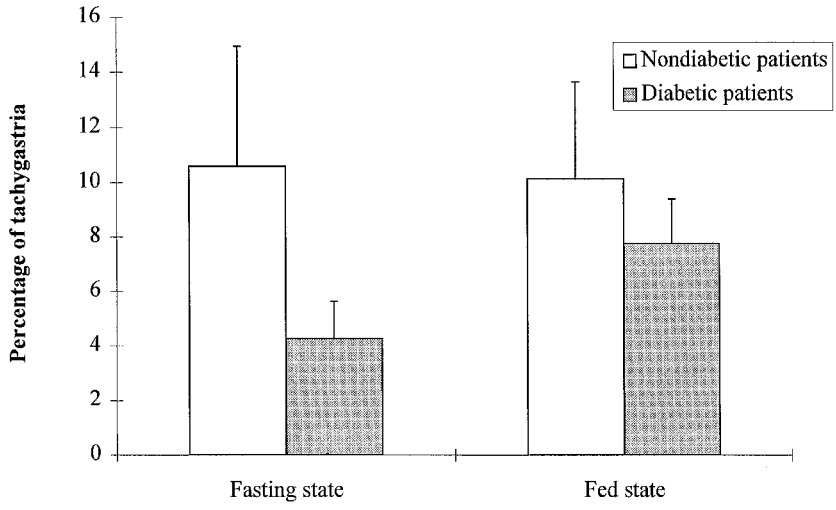

Fig 4. The percentage of tachygastria observed in the fasting and fed EGG in patients with and without diabetes. The nondiabetic patients showed a higher percentage of tachygastria than the diabetic patients. The difference was, however, not statistically significant.

found in the symptom scores between the two groups of patients, although the nondiabetic patients had a slightly higher score.

A number of studies have previously investigated gastric motility in patients with CRF. Some investigators failed to demonstrate delayed gastric emptying using the scintigraphic technique (31–35). Two most recent studies, however, have shown gastric dysmotility and delayed gastric emptying in symptomatic patients with CRF using applied potential tomography and real-time ultrasonography, respectively (2, 3). Our data support these two previous studies. The lower percentage of normal 2–4 cpm slow waves and a smaller increase or a decrease in the dominant power of the EGG after the test meal in patients with CRF observed in this study are indicative of gastroparesis according to one of our previous studies (36). In that previous study, simultaneous recordings of gastric emptying and electrogastrography were made in 97 patients with symptoms suggestive of gastroparesis (36). The same definition of the abnormal EGG was used, and the results showed that an abnormal postprandial EGG predicted delayed gastric emptying with an accuracy of 78%, and the abnormal re-

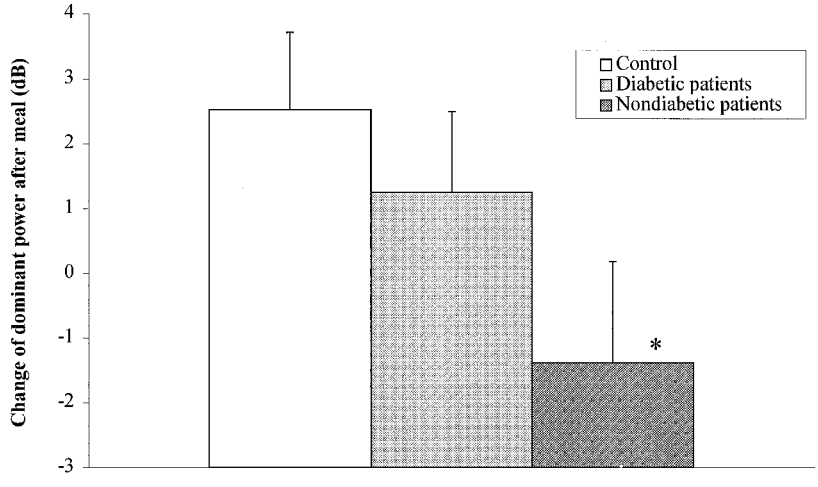

Fig 5. Changes of the dominant power of the EGG after the test meal in three groups of subjects. The healthy controls showed the highest increase in the dominant power of the EGG, whereas the nondiabetic patients showed an average decrease in the dominant power of the EGG after the test meal. *$p<0.05$ on comparison with controls.

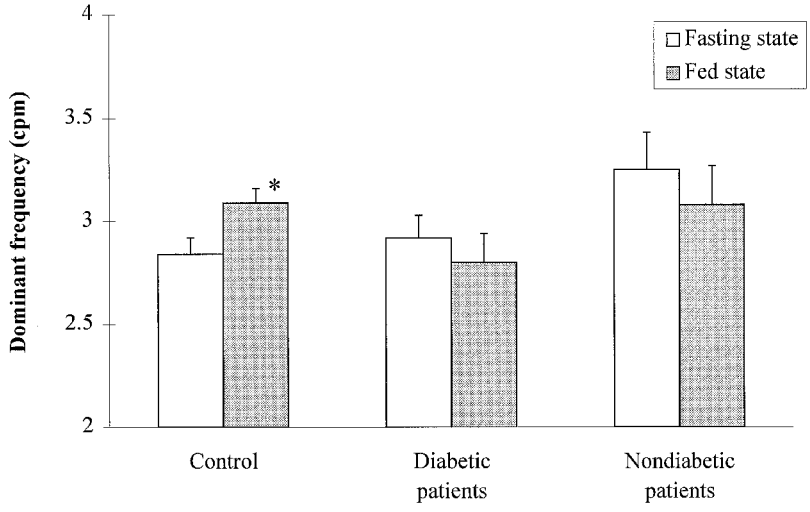

Fig 6. Changes of the dominant frequency of the EGG after the test meal in the three subject groups. The controls showed a normal increase in the dominant frequency of the EGG after the test meal. Both patient groups, however, showed no significant changes in the dominant frequency of the EGG. There was actually an averaged decrease in both groups of patient. $*p<0.05$ on comparison with fasting state.

sponse of the EGG predicted delayed gastric emptying with an accuracy of 75%. That is, a majority of patients with an abnormal postprandial EGG or an abnormal response to the test meal have delayed gastric emptying. Based on the conclusion of that previous study, the data of this current study would suggest that most of the patients with CRF had delayed gastric emptying of the solid meal.

Little is known about gastric myoelectrical activity in patients with CRF. The studies by Ravelli et al (2, 7) were the only experiments investigating gastric myoelectrical activity in CRF. Their studies were performed in pediatric patients with CRF, and gastric myoelectrical activity was also recorded using electrogastrography. They studied 17 children with severe CRF and symptoms of anorexia and vomiting. A majority of patients were found to have gastric dysrhythmias, including bradyarrhythmia, tachyarrhythmia, and arrhythmia. However, no quantatative figures such as the percentage of 2–4 cpm slow waves or exact definition of gastric dysrhythmias was given. In this paper, gastric myoelectrical activity in adult patients with CRF was recorded and analyzed using a more quantatative method. The consistency between this current study and the previous studies by Ravelli et al suggests that noninvasive electrogastrography is a reliable technique for the measurement of gastric myoelectrical activity, as demonstrated in a number of previous studies (9–13). In patients with severe renal failure, electrogastrography may be a good noninvasive alternative to gastric manometry for the study of gastric motility.

The EGG in healthy subjects usually has unique responses to a test meal (24, 37–40). These include a substantial increase in the amplitude or dominant power of the EGG and a slight (5% to 10%) but significant increase in the dominant frequency of the EGG after a solid test meal. The dominant frequency of the EGG may show a decrease or nonsignificant increase if the test meal is composed of liquid or liquid–solid (39). These phenomena were also observed in the normal subjects in this study. However, the increase in the dominant power of the EGG observed in this study was not as substantial as reported in the literature. A one- to twofold increase in amplitude a 6- to 10-dB increase in dominant power is usually observed in the healthy subject after a solid test meal of 500 kcal or higher (40). In this study, however, only a less than 3-dB increase in the dominant power of the EGG was observed in the normal subjects. Moreover, about 25% of the healthy subjects showed a decrease in EGG dominant power after the meal, which has rarely been reported in previous studies. This abnormal response to the test meal in the healthy subjects is believed to be caused by the lower-calorie test meal (282 kcal) used in this study. This implies that a relatively high-calorie test meal is needed to produce a normal response of the EGG for a normal subject. The reason for the selection of the 280-calorie test meal in this study was that patients

with severe gastrointestinal symptoms were not able to finish a whole test meal high in calories. One other factor that would result in an abnormal response of the EGG to the test meal is the fat content. A few studies have previously showed that a higher percentage of fat in the test meal may decrease gastric myoelectrical activity (41). However, the percentage of fat in the test meal used in this study was relatively low and should not impair gastric myoelectrical activity.

No significant difference was found in EGG parameters between the patients with diabetes and those without diabetes except that nondiabetic patients showed more abnormal responses to the test meal. While 47% of the patients with diabetes had an abnormal response to the test meal, 78% of the patients without diabetes had an abnormal response to the test meal. No data were available to explain this difference. Although the patients with diabetes had a lower symptom score than the patients without diabetes, the difference was marginal and not significant. No significant correlation between the symptom score and the EGG parameters was found in this study.

In conclusion, patients with chronic renal failure have abnormal gastric myoelectrical activity, including impaired regularity of the gastric slow wave and a failed increase in the amplitude of the EGG. Electrogastrography is an attractive noninvasive method for the study of gastric motility in patients with severe chronic renal failure.

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