

Gastric Dysrhythmias and Nausea of Pregnancy

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Gastric dysrhythmias have been recorded from patients with a variety of nausea syndromes. The aim of this study was to measure gastric myoelectric activity in women with and without nausea during the first trimester of pregnancy. In 32 pregnant women gastric myoelectric activity was recorded for 30-45 min with cutaneous electrodes that yielded electrogastrograms (EGGs). Frequencies of the EGG waves were analyzed visually and by computer. Subjects rated their nausea at the time of EGG recording on a visual analog scale with 0 representing no nausea and 300 mm severe nausea. Gastric dysrhythmias were found in 26 pregnant subjects: Seventeen had tachygastrics (EGG frequencies of 4-9 cpm), five had 1- to 2-cpm EGG waves, and four had flat-line patterns. Mean nausea scores of the subjects with tachygastrics, 1- to 2-cpm, and flat-line patterns were 64.8 ± 13 , 93.4 ± 23 , and 77.2 ± 36 , respectively. Six pregnant subjects had normal 3-cpm EGG patterns, and their nausea scores averaged 2.8 ± 1.1 ($P < 0.05$ compared with nausea scores in subjects with tachygastrics, 1- to 2-cpm, and flat-line rhythms). Six subjects with gastric dysrhythmias during pregnancy were restudied after delivery; each of these subjects had normal 3-cpm EGG patterns and none had nausea. Thus, gastric dysrhythmias are objective pathophysiologic events associated with symptoms of nausea reported during the first trimester of pregnancy.

KEY WORDS: electrogastrography; pregnancy; vomiting; spectral analysis.

Nausea of pregnancy was described in antiquity (1). Today, the incidence of nausea during the first trimester of pregnancy varies from 50 to 80%, and surveys indicate that approximately 55% of pregnant women have daily episodes of vomiting (1-3). In hyperemesis gravidarum, the nausea and vomiting becomes severe, leading to hospitalization for weight loss and dehydration. Despite the frequency of nausea and the potential debilitation caused by

nausea of pregnancy, the pathophysiology of the syndrome is not understood.

Few studies of gastric motility have been performed early in human pregnancy because of radiation exposure or invasiveness of procedures. Although gastric emptying of liquids is delayed in the pregnant guinea pig (4), two studies of gastric liquid emptying performed in the third trimester of human pregnancy provided conflicting results (5, 6). Motor events of the stomach are controlled by myoelectrical activity called slow waves (also termed basic electrical rhythm, pacesetter potentials, or electrical control activity) (7). Slow waves propagate normally from proximal body to distal antrum at a frequency of 3 cycles per minute (cpm) (8). Disturbances in gastric slow-wave frequency, termed gastric dysrhythmias, are associated with a variety of syndromes in which nausea and vomiting are pre-

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dominant symptoms. These conditions include idiopathic nausea and vomiting (9–11), chronic dyspepsia (12), anorexia nervosa (13), diabetic gastroparesis (14), and motion sickness (15, 16).

We hypothesized that women with nausea of pregnancy may have altered gastric myoelectrical rhythms. Therefore, the aims of the present study were to use noninvasive electrogastrographic recording techniques to measure gastric myoelectrical activity in women in the first trimester of pregnancy and to correlate the intensity of their nausea at the time of the recording with their EGG rhythm.

MATERIALS AND METHODS

Subjects. EGGs and nausea scores were obtained from four groups of women: (1) pregnant subjects with nausea ($N = 26$), (2) pregnant women without nausea ($N = 6$), (3) postpartum subjects without nausea ($N = 6$), and (4) healthy, nonpregnant women ($N = 16$).

Thirty-two pregnant women who were undergoing routine prenatal care in the Obstetrics Clinic of the University Hospital volunteered for the study. The subjects reported nausea on at least one visit. None of the subjects had histories of gastrointestinal illness, and in the opinion of the attending obstetrician, each subject had typical nausea of pregnancy. Subjects with diabetes mellitus, hypertension, hydatidiform mole, hyperemesis gravidarum, or other major medical problems were excluded from the study. Each subject signed an informed consent approved by the Clinical Investigation Committee.

Average age of the 32 pregnant subjects was 27 years with a range of 19–35 years. Twelve women were primigravidas. The average duration of gestation at time of study was 10.9 weeks. Onset of nausea was noticed during the fifth week of pregnancy in most subjects. Seventy-six percent of the women had nausea on a daily basis; 33% percent vomited at least once a day. Only three women had nausea limited to the morning hours, ie, morning sickness; most of the women experienced nausea throughout the day.

On the day of the study, 26 pregnant subjects had nausea during the recording of the EGG, and six pregnant subjects had little or no nausea. EGGs and gastrointestinal symptoms were also recorded after delivery in six of the these women who had experienced nausea during the first trimester of pregnancy.

In addition, 16 age-matched healthy women (average age 27 years, range 22–35 years) who were not pregnant underwent the same study protocol. These women had no histories of gastrointestinal illnesses or other medical problems.

Apparatus and Procedures. All subjects consumed a light breakfast of their choice 2 hr before the study in order not to disrupt their usual morning routine. During the EGG recording the patients were seated comfortably in a chair that reclined approximately 30 degrees.

Standard electrodes (Miniature Skin Electrodes, SensorMedics Corp., Anaheim, California) were positioned

on the abdomen to record the electrogastrogram. Three electrodes were positioned on the left upper quadrant and epigastric regions: the first electrode was positioned below the left rib margin in the midclavicular line, the third electrode was placed equidistant between the xiphoid process and the umbilicus, and the second electrode was positioned along a line between the first and third electrode. The fourth electrode served as a reference electrode and was positioned in the right upper quadrant along the line formed by the other three electrodes. The skin beneath the electrodes was abraded gently before attaching each electrode. The electrodes were connected to a rectilinear recorder (R611, SensorMedics) through nystagmus couplers (9859, SensorMedics). The low frequency cutoff was 0.016 Hz (time constant 10 sec), and the high frequency cutoff was 0.30 Hz. Sensitivities were adjusted as needed to obtain clear EGG signals. The EGG signal was recorded simultaneously on magnetic tape (Honeywell 101, Honeywell Instruments, Denver, Colorado) for computer analysis.

EGGs were recorded for 30–45 min. Subjects were asked to report any symptoms that occurred during the recording period, and symptoms were noted on the chart paper. At the end of the recording period, each subject indicated the overall intensity of their nausea during the session on a separate visual analog scale. The scale was a 300-mm line with 0 mm representing no nausea and 300 mm severe nausea, almost vomiting.

Visual and Computer Analysis of EGG Signals. The EGG signal with the least movement artifact was chosen for visual and computer analysis of the frequency of EGG waves. Three-cpm EGG waves (2.5–3.5 cpm) were considered normal; 4- to 9-cpm waves were considered tachygastrias; frequencies slower than 2.5 cpm were considered bradygastrias. The normal 3-cpm EGG waves were originally recorded by Alvarez (17), and many others since then have confirmed this normal 3-cpm frequency (9–13, 15, 16, 18, 19). Gastric slow waves and gastric dysrhythmias, such as tachygastrias and bradygastrias, may be recorded reliably from cutaneous electrodes or from mucosal and serosal electrodes (11, 18, 19). Computer analyses of approximately 30 min of EGG signals recorded from each patient were compared with visual interpretation of the EGG signal in order to confirm the predominant frequency peaks and to ascertain shifts in EGG frequency that may have eluded visual inspection. EGG data were rated without knowledge of nausea scores. Amplitude of EGG waves or spectral power were not quantified. Computer analysis of EGG records utilized analog to digital transformation, Fourier analysis, and running spectral analysis. Details of the method of computer analysis are presented in the Appendix.

Statistical Analysis. Nausea scores were ranked and submitted to ANOVA. The various subject groups were compared using Student-Neuman-Kuels for multiple pairwise comparisons. A P value of 0.05 or less was considered significant.

RESULTS

Nonpregnant Healthy Subjects. Fifteen of the 16 healthy women who were not pregnant had normal

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TABLE 1. EGG RHYTHMS AND NAUSEA SCORES IN PREGNANT WOMEN AND HEALTHY CONTROLS

Pregnant women			Healthy controls		
Subject	EGG (cpm)	Nausea score	Subject	EGG (cpm)	Nausea score
Normal					
JG	3	6	SW	3	0
GB	3	6	MW	3	0
MW	3	3	EV	3	0
MP	3	0	KB	3	0
JE	3	2	LP	3	0
BZ	3	0	AD	3	0
Tachygastrica					
SP	7	131	LD	3	0
TE	5	134	JK	3	0
LR	5	47	LS	3	0
TW	4	37	JS	3	0
RM	7	25	TG	3	0
KH	8	179	LH	3	0
VP	5	90	JA	3	0
EM	4	82	KM	3	0
KL	6	116	BB	3	0
CG	5	90	NS	flat	0
JW	4	25			
BS	8	58			
WH	6	25			
ML	5	49			
SS	6	9			
CL	6	0			
Bradygastrica					
BD	1	34			
HM	2	44			
BS	1	110			
DC	1	142			
MR	1	137			
Flat line					
DR	flat	7			
CM	flat	78			
LF	flat	48			
SR	flat	176			

3-cpm EGG patterns (Table 1). Figure 1 shows the normal 3-cpm EGG signal and the corresponding spectral analysis with stable 3-cpm peaks in a nonpregnant subject. One healthy subject had a flat-line EGG pattern, which is shown in Figure 2. None of these nonpregnant subjects reported nausea or upper gastrointestinal symptoms at the time of the EGG recording.

Pregnant Subjects without Nausea. Six of the 32 pregnant subjects felt well and had little or no nausea at the time of the EGG study. Two of these subjects reported a nausea score of 6, two had scores of 2 and 3, and two reported no nausea. The mean nausea score was 2.8 ± 1.1 mm. The EGG pattern recorded from each of these women was the normal 3-cpm signal. Figure 3 shows the EGG tracing and spectral analysis from one of these pregnant subjects with a nausea score of 2. A clear

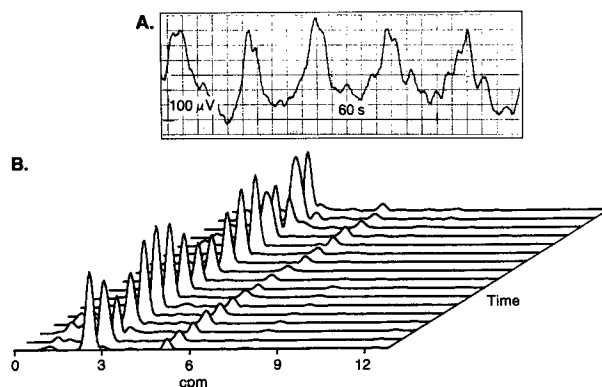


Fig 1. EGG tracing (A) and spectral analysis (B) from a recording from a healthy nonpregnant subject. The EGG tracing shows normal 3-cpm waves and the spectral analysis shows 3-cpm peaks. The peaks in the spectral analysis near 6 cpm are second harmonics of the first harmonic, which is 3 cpm, the normal EGG frequency. Harmonics are seen in the spectra as the periodic signal deviates from a sinusoidal wave. In this and the following figures, the minute and sensitivity standards are indicated on the EGG. The spectral analysis shows approximately 30 min of EGG data. Running spectral analyses are constructed by performing spectral analyses on successive segments of the digitized EGG signal, each of which is overlapped with preceding segments. Each line in the spectral analysis represents 5 min of EGG signal with a 75% overlap. Thus, each line represents 75 sec of new data added to the previous 225 sec of EGG data for a total of 5 min of EGG data per line.

3-cpm EGG signal is apparent; the spectral analysis also shows consistent peaks at 3 cpm and occasional peaks at 1 cpm.

Pregnant Subjects with Nausea. Twenty-six subjects reported nausea on the day of the study. Gastric dysrhythmias were present throughout the 30- to 40-min EGG recording period in 25 patients. One patient had an abrupt onset of nausea and gastric dysrhythmia and is described below.

Sixteen pregnant subjects had tachygastrics and reported nausea scores ranging from 9 to 179 during the EGG study period (Table 1). Figure 4 shows the

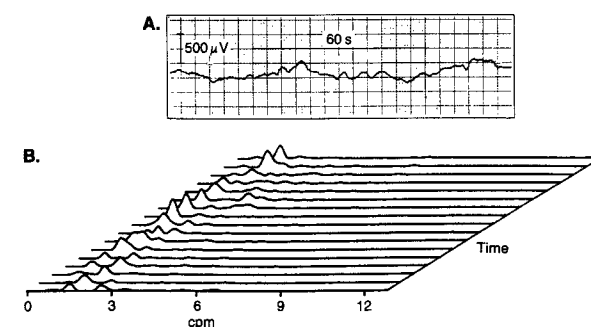


Fig 2. The EGG (A) from a healthy nonpregnant woman shows a flat-line pattern. The spectral analysis (B) shows regular 1-cpm peaks. This subject had no nausea.

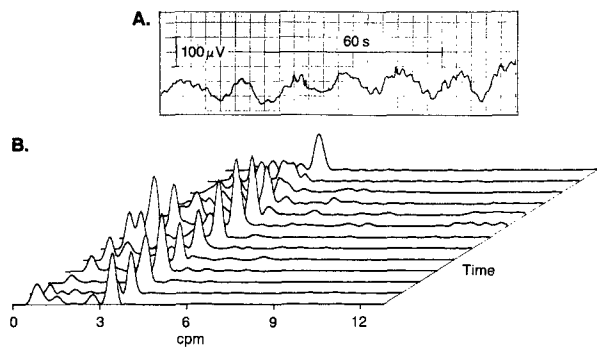


Fig 3. The EGG signal (A) shows clear 3-cpm waves and the spectral analysis (B) shows 3-cpm peaks recorded from a pregnant patient with virtually no nausea (score of 2, with zero indicating no nausea and 300 indicating severe nausea). Occasional 1-cpm peaks are present.

EGG and spectral analysis from a pregnant subject with nausea and 5- to 6-cpm tachygastrica. Respiratory rate is also shown and indicates the clear difference in respiratory and gastric frequencies. Little or no 3-cpm activity is seen in the spectral analysis computed from 30 min of EGG signal. This subject rated her nausea 90 during the study.

Figure 5 shows a 1- to 2-cpm EGG pattern in a pregnant subject with a nausea score of 34. The EGG tracing shows large, broad-based waves that last 30–60 sec. The spectral analysis also indicates the predominant peaks are in the low-frequency range of 1–2 cpm; there is little 3-cpm activity and little activity in the tachygastrica ranges. Nausea scores in the five subjects with 1- to 2-cpm EGG waves were 34, 44, 110, 137, and 142 (Table 1).

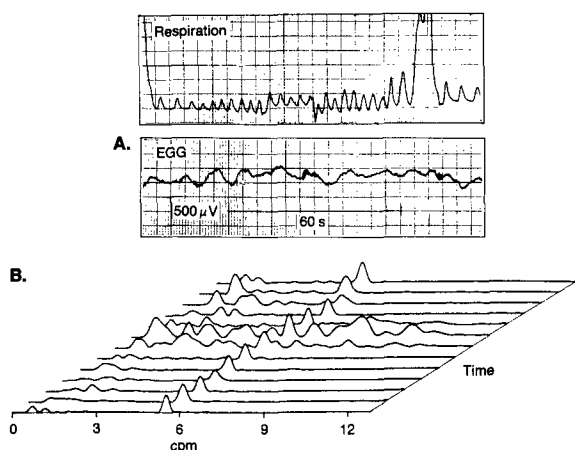


Fig 4. The EGG signal (A) shows a tachygastric pattern at approximately 5–6 cpm; the spectral analysis (B) also shows consistent peaks at 5 and 6 cpm as well as occasional low-frequency peaks. Note the absence of 3-cpm peaks. Nausea score reported by this subject was 90. Respiratory rhythm is also shown.

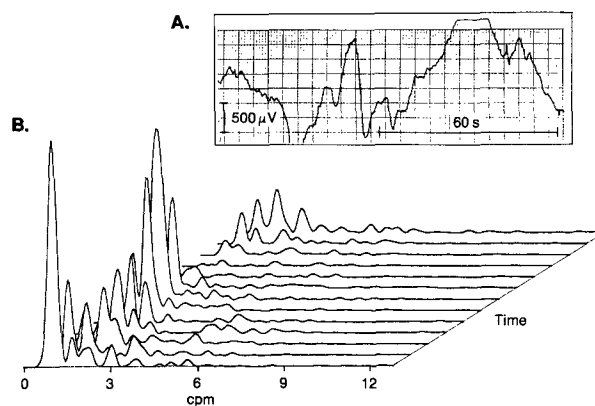


Fig 5. The EGG trace (A) shows large, broad-based waves that occupy 30–60 sec of time; the spectral analysis (B) also shows that 1- to 2-cpm peaks predominate. Note the absence of 3-cpm peaks in the spectral analysis. This subject rated her nausea 34.

Four subjects had flat-line gastric dysrhythmias even when higher sensitivity settings were used to record the EGG. As shown in Figure 6, the computer analysis of the flat-line EGG signals revealed a variety of low-power frequency peaks: 4- to 5-cpm, 1- to 2-cpm peaks, areas that had no frequency peaks, and intermittent 3-cpm peaks. Based on the actual EGG signal, however, such recordings were termed flat-line gastric dysrhythmias. Nausea scores reported by subjects with the flat-line pattern were 7, 78, 49, and 176 (Table 1).

One subject reported the sudden onset of nausea during the recording session. Figure 7 shows 10 min of continuous EGG signal that corresponds with this period of acute nausea and the spectral analysis of the entire 30-minute EGG recording. Before the onset of nausea, rhythmic EGG signals are seen. At the onset of nausea, the EGG signal disappears and respiratory rhythms appear in the recording. The EGG pattern during this period of nausea was

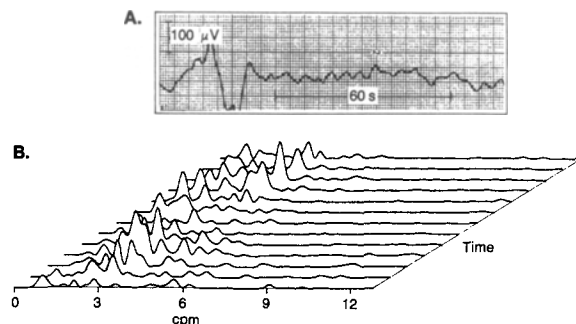


Fig 6. The EGG (A) shows a flat-line pattern despite increased sensitivity of the amplifier. The spectral analysis (B) shows a variety of peaks ranging from 1–2 cpm to 4 cpm, a pattern that is more variable than the flat-line pattern in Figure 2. This patient had a nausea score of 49.

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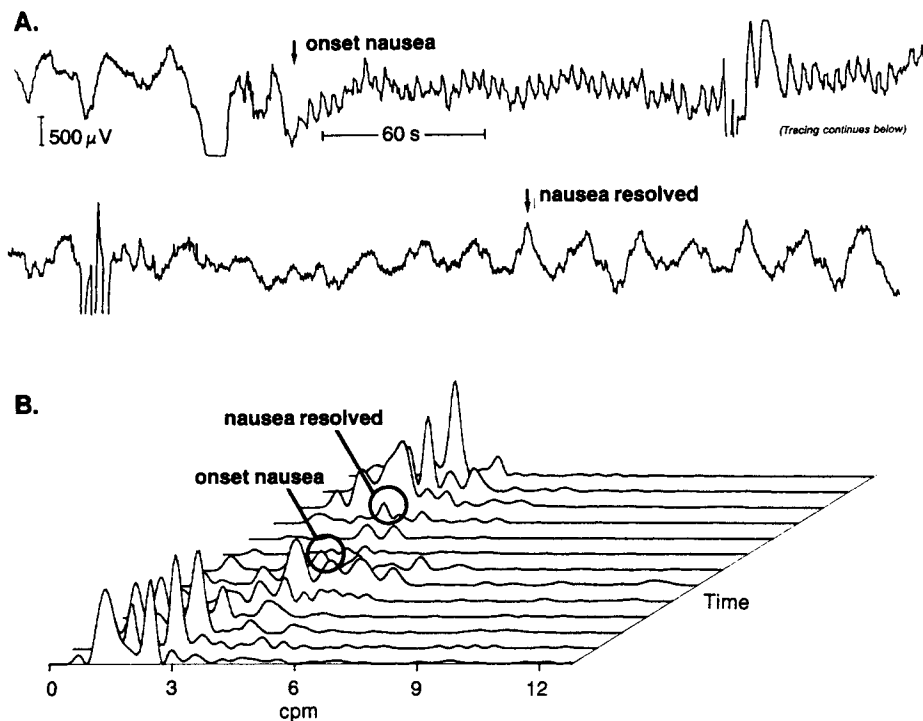


Fig 7. This continuous EGG tracing shows large-amplitude 3-cpm waves immediately before the onset of nausea and the appearance of a flat-line dysrhythmia during nausea (A). During the dysrhythmia period, respiratory activity at 16/min appears in the EGG tracing. Nausea resolved after the 3-cpm EGG pattern was reestablished. The computer analysis of the 30-min EGG recording (B) shows peaks near 3 cpm just before the onset of nausea and the flat-line dysrhythmia, which appears in the spectral analysis as the area of flat lines. The 3-cpm peaks reappear as the nausea resolves. The subject rated her intensity of nausea 176.

considered a flat-line dysrhythmia. The 3-cpm EGG pattern was reestablished subsequently, and the subject reported the nausea resolved. Computer analysis shows peaks at or near 3 cpm in the early portions of the recording. However, the 3-cpm peaks abruptly disappear and flat lines are apparent during the period of nausea, which lasts approximately 4 min, the duration of the flat-line dysrhythmia as shown in the EGG signal. This subject rated the intensity of nausea 176 during this period. The spectral analysis also shows the return of 3-cpm peaks when the nausea resolved.

As shown in Figure 8, the six pregnant subjects who presented with normal 3-cpm signals had little or no nausea (2.8 ± 1.1), whereas those pregnant women presenting with gastric dysrhythmias had greater nausea scores: the four subjects with flat-line EGG patterns had an average nausea score of 77.2 ± 36 ; the five subjects with 1- to 2-cpm waves had an average nausea score of 93.4 ± 23 , and the 17 subjects with tachygastrias had an average nausea score of 64.8 ± 13 . One of the 17 subjects with tachygastria reported no nausea. Analyses of vari-

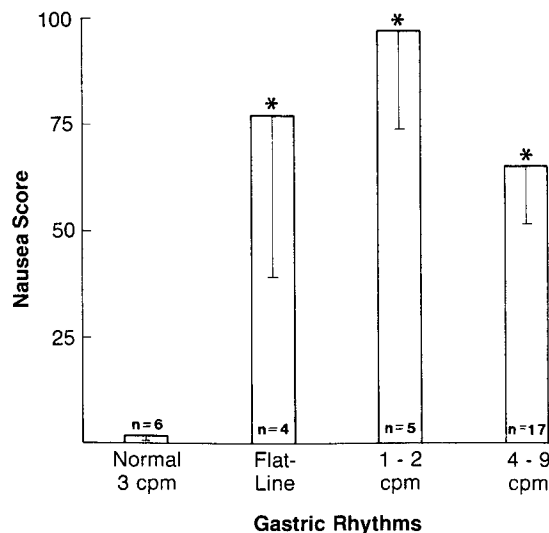


Fig 8. Nausea scores and gastric rhythms in pregnant women. Mean nausea scores were significantly greater ($P < 0.05$) in women with flat-line dysrhythmias, 1- to 2-cpm waves, and 4- to 9-cpm tachygastrias compared with pregnant women with normal 3-cpm EGG rhythms. Differences in nausea scores of subjects in the various gastric dysrhythmias were not significantly different.

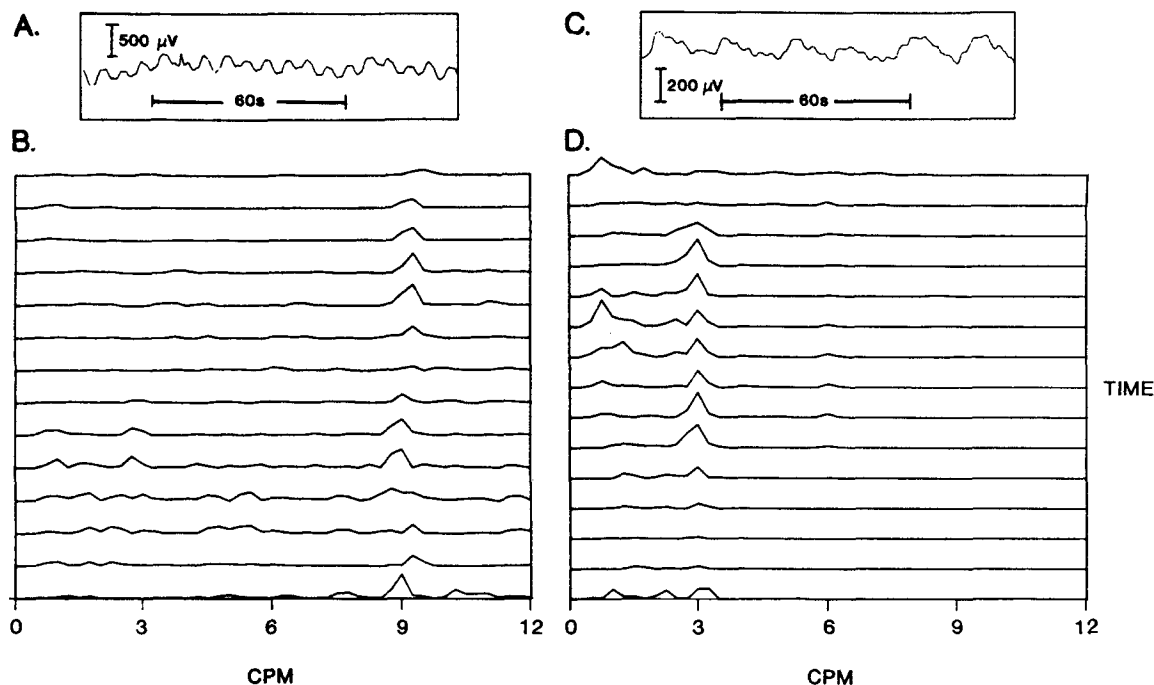


Fig 9. EGGs and spectral analysis from a patient during the first trimester of pregnancy and after delivery. The EGG (A) and spectral analysis (B) in the first trimester show a tachygastria (9 cpm) when the pregnant patient's nausea score was 137; in contrast, after delivery the EGG (C) and spectral analysis (D) show predominant 3-cpm waves and peaks, respectively, and the subject reported no nausea.

ance reveal significant differences in nausea scores among the groups ($P < 0.0014$). Mean nausea scores in the subjects with tachygastria, 1- to 2-cpm waves, and flat-line EGG pattern were significantly greater than nausea scores reported by the pregnant women who presented with 3-cpm patterns ($P < 0.05$). Intensity of nausea reported by subjects with the various gastric dysrhythmias did not differ significantly.

Postpartum Study of Subjects who had Nausea of Pregnancy. Six subjects with nausea, five with tachygastrics, and one with the 1- to 2-cpm wave pattern during the first trimester of pregnancy were restudied after delivery. None of these subjects reported nausea and a normal 3-cpm EGG pattern was recorded in each postpartum subject as shown in Figure 9, a recording from a subject who had had nausea and tachygastria during the first trimester of her pregnancy.

DISCUSSION

This study demonstrates for the first time that myoelectrical abnormalities of the stomach, ie, gastric dysrhythmias, are present in patients with nausea of pregnancy. In addition, the intensity of

nausea was significantly greater in the pregnant women with gastric dysrhythmias when compared with pregnant women who presented with normal 3-cpm EGG patterns. Finally, EGGs recorded from symptom-free, postpartum patients showed normal 3-cpm patterns, whereas they had had gastric dysrhythmias and nausea during early pregnancy. These findings indicate that gastric dysrhythmias are pathophysiologic events associated with first-trimester nausea.

Gastric dysrhythmias also have been recorded in patients with idiopathic nausea and vomiting, chronic dyspepsia, anorexia nervosa, and diabetic gastroparesis (9, 10, 12–15). Shifts from normal 3-cpm EGG rhythms to gastric dysrhythmias, evoked by glucagon infusions or by illusory self-motion, also correlate with reports of nausea (15–17). A sudden shift to a flat-line dysrhythmia (shown in Figure 7) in one of our pregnant subjects corresponded with her report of the sudden onset of nausea. Thus, the presence of gastric dysrhythmias and nausea symptoms in pregnant women is consistent with the previous studies cited above.

On the other hand, 3-cpm EGG waves reflect the normal gastric slow wave frequency (10–13, 15–19),

and the maintenance of 3-cpm activity is associated with normal sensations in the epigastrium. For example, healthy subjects who maintain normal 3-cpm EGG patterns during illusory self-motion do not report nausea or epigastric discomfort (15, 16). The establishment of 3-cpm activity (and decreased gastric dysrhythmias) correlated with improvement in symptoms such as nausea in diabetics with gastroparesis who were treated with domperidone (14). Similarly, the pregnant women who had nausea and gastric dysrhythmias during the first trimester were symptom-free and had established normal 3-cpm EGG rhythms in the postpartum period. Taken together, these findings support the concept that maintenance of normal 3-cpm EGG patterns is associated with well-being and lack of nausea, whereas the presence of gastric dysrhythmias is associated with symptoms of nausea. Treatment strategies designed to enhance 3-cpm EGG activity or to decrease gastric dysrhythmias may decrease nausea symptoms during first trimester pregnancy.

The majority of gastric dysrhythmias recorded during the first trimester of pregnancy were 4- to 9-cpm tachygastrias. The tachygastrias were stable, rapid undulations in the EGG signal (Figures 4 and 9A). In contrast, tachygastrias evoked in healthy subjects during vection-induced motion sickness are abrupt in onset, transient, and chaotic dysrhythmias, which often vary from 4 to 9 cpm in a single subject (15, 16). Furthermore, the mean nausea score of the 17 pregnant women with stable tachygastrias was 64, whereas the mean nausea score of 21 healthy subjects with vection-induced acute tachyarrhythmias was >180, as recorded on the same visual analog scale (unpublished observations). These findings suggest that certain characteristics of gastric dysrhythmias, such as frequency (bradygastric vs tachygastric), duration (acute vs chronic), and amplitude (low vs high), may be relevant to the intensity of nausea perceived by an individual.

The frequency of the gastric dysrhythmias did not appear crucial in subjects with nausea of pregnancy, however, because no significant differences in nausea scores were found in subjects with tachygastrias, 1- to 2-cpm waves or flat-line pattern. The duration of gastric dysrhythmias may be important, however, since acute shifts in gastric rhythm appear to be very nauseogenic, as shown in vection-induced motion sickness (15, 16) and in the pregnant subject who shifted abruptly from a 3-cpm rhythm to a flat-line pattern. Intermittent gastric dysrhythmias lasting 2–4.9 min were recorded in

patients with anorexia nervosa (13), but the presence of nausea was not reported. Gastric dysrhythmias lasting 1–10 min were recorded after glucagon infusions in healthy subjects who experienced nausea (18); however, the duration and intensity of nausea were not quantitated. Our studies in motion sickness suggest that acute shifts from normal 3-cpm gastric rhythms to gastric dysrhythmias of short duration (4–15 min) are associated with more intense nausea than the continuous, long-duration (30–40 min) gastric dysrhythmias found in nausea of pregnancy.

The low-frequency EGG signals recorded from the pregnant women with nausea formed two distinct patterns: 1- to 2-cpm waves and flat-line dysrhythmias. The 1- to 2-cpm waves and flat-line pattern also have been recorded in diabetics with nausea, vomiting, and gastroparesis (14). You et al recorded low-frequency dysrhythmias termed bradygastrics in patients with idiopathic nausea and vomiting (10). The 1- to 2-cpm EGG signals correlate with strong antral contractions in the dog (20), but the canine fundus also produces 1 per minute contractions (21). Bradygastrics are induced by intraarterial infusion of epinephrine in dogs (22, 23) and increasing doses of catecholamines are associated with retching (22). The origins and underlying mechanisms of the 1- to 2-cpm waves and the flat-line dysrhythmias in man are unknown.

EGG methods may be used safely to record gastric myoelectrical activity during pregnancy in order to study the natural history of gastric myoelectrical disturbances and nausea symptoms. By correlating the different gastric myoelectrical patterns with selected neuroendocrine measures, ie, catecholamines, progesterone, human chorionic gonadotrophin, or gut hormones (whose release is altered during pregnancy) (24), the mechanism(s) of nausea of pregnancy and the associated gastric dysrhythmias may be further elucidated.

APPENDIX

The EGG signal, stored previously on magnetic tape, was channeled to the A/D conversion board in the laboratory computer (Sperry IT, UNISYS, New York) where it was digitized at 4 Hz. The digitized signal was zero-centered and filtered to remove high frequency (>18 cpm) and very low frequency (<1 cpm) components, which may alter the frequencies of interest (1–15 cpm) in the digitized EGG signal. The filters used were fourth-order elliptical filters

with a 200 milli-dB passband ripple. The low-pass filter had a high-frequency band edge at 0.5 Hz with an attenuation of -90 dB in the stopband. The high-pass filter had a high-frequency band edge at 0.015 Hz with required attenuation of -90 dB in the stopband.

After the digital filtering described above, the time series was Fourier transformed and the spectral density estimates were calculated. The spectral analysis provided information concerning the frequencies contained in the signal. The spectral analysis used in these studies utilized a Hanning window and yielded spectra with frequency bin widths of 0.002084 Hz. The EGG spectra calculated from a discrete time period, ie, the Fourier transformation, were graphed in a pseudo three-dimensional plot called a running spectral analysis or spectral analysis in this text.

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