Effect of Meal Size and Test Duration on Gastric Emptying and Gastric Myoelectrical Activity as Determined with Simultaneous $^{[13]C}$Octanoate Breath Test and Electrogastrography in Normal Subjects Using a Muffin Meal

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Our purpose was to determine the effect of meal size on gastric emptying (GE) as measured by octanoate breath test (OBT), to determine the effect of the duration of breath collections on assessment of GE by OBT, and to determine the effect of meal size on gastric myoelectrical activity as measured by electrogastrography (EGG). Fourteen normal subjects underwent two modified $^{[13]C}$OBTs using muffin meals of 250 or 350 kcal mixed with 100 mg $^{[13]C}$sodium octanoate. $T_{1/2}$ for GE was determined for both the entire postprandial 6-hr breath collection and a truncated initial 4-hr data set. EGG was recorded for 30 min prior to the muffin meal and 4 hr postprandially. Using the 6-hr breath collection data, the $T_{1/2}$ was $177 \pm 7$ (mean $\pm$ SEM) for the 350-kcal meal compared to $153 \pm 7$ min ($P < 0.01$) for the 250-kcal meal. Using the 4-hr data, the $T_{1/2}$ for the 350-kcal meal was $244 \pm 32$ min compared to $165 \pm 12$ min ($P < 0.05$) for the 250-kcal meal. The ratio of postprandial to fasting EGG power of the dominant frequency for the 350-kcal meal ($1.9 \pm 0.4$) was higher than that for the 250-kcal meal ($1.3 \pm 0.6$). $T_{1/2}$ for the 350-kcal meal using 4- and 6-hr data was significantly correlated with the 4-hr power ratio ($r = 0.68$ and 0.67; $P < 0.05$, respectively), but poorly correlated for the 250-kcal meal. In conclusions, GE and EGG are affected by meal size. Using the muffin-based $^{[13]C}$OBT, $T_{1/2}$ for the 350-kcal meal was significantly longer than for a 250-kcal meal. Longer $T_{1/2}$ values were obtained with shorter breath sampling durations. The postprandial to fasting power ratio for the 350-kcal meal was greater than that for the 250-kcal meal.

KEY WORDS: octanoic acid; breath test; gastric emptying; electrogastrography.

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Assessment of gastric emptying (GE) can be helpful in the evaluation of patients with dyspeptic symptoms to determine if a gastric motor disorder is present (1, 2). Scintigraphy directly measures the amount of a radiolabeled meal that empties from the stomach (3). Breath tests employing stable non-radioactive isotopes offer an alternative to scintigraphy. With the [13C]octanoate breath test (OBT), a meal labeled with [13C]octanoate is consumed and breath samples are collected over several hours. Octanoic acid, a medium-chain fatty acid, is absorbed in the small intestine, transported to the liver bound to albumin, where it is oxidized to CO2, which is excreted by the lungs. GE is the rate limiting step for the excretion of octanoic acid. Thus, measurement of 13C in breath samples provides an indirect assessment of GE.

The [13C]OBT has been shown to be reproducible and to correlate with scintigraphy in measuring GE (4–8). Studies employing OBT, however, have used different meals and different durations of breath sampling (4, 5, 7). How these parameters affect GE as measured by OBT has not been carefully evaluated. Meal size and composition have previously been shown to affect gastric emptying by using scintigraphy and fluid collection techniques (9–12). Liquid meals empty more slowly with increasing concentrations of glucose (9, 10). These studies suggested an inhibitory feedback effect on gastric emptying by small intestinal contents (9, 10), with gastric emptying being regulated to allow a constant caloric delivery into the small intestine. A similar concept has been suggested for solid-phase gastric emptying using scintigraphy (11, 12). More recent studies show that although a larger meal prolongs the half emptying time, the rate on energy delivery from the stomach into the small intestine is still higher with larger meals (13).

The main objective of this study is to determine the effect of meal size on GE in normal subjects as determined by [13C]OBT. A secondary objective was to determine the effect of the duration of breath collections on GE determination by OBT. We also evaluated the effect of test meal size on gastric myoelectrical activity as measured simultaneously with electrogastrography (EGG) to determine if there is a correlation between EGG and GE parameters. In these studies, a muffin test meal was used in attempt to provide a convenient meal that could be easily standardized (14).

MATERIALS AND METHODS

Fourteen normal subjects [7 males and 7 females, ages of 19–46 years, body mass index = 25 ± 1.3 (mean ± SEM)] were enrolled in this study. The exclusion criteria were prior gastrointestinal surgery; the presence of gastroesophageal reflux disease, peptic ulcer disease, irritable bowel syndrome, or chronic gastrointestinal symptoms; pregnancy; disorders that interfere with the normal absorption of fats (such as chronic pancreatitis, colic spurs); and the use of medications known to affect gastrointestinal motility (such as catherics, antiarrhythmic, anticholinergic, and narcotic medications). Each subject underwent two simultaneous modified [13C]OBT and EGG recordings one week apart using muffin test meals of different sizes administered in random order. The subjects fasted overnight and abstained from caffeine, alcohol, and cigarettes for 12 hr prior to each study.

Test Procedures

[13C]Octanoate Breath Test (OBT). The muffin test meal was prepared on-site immediately before the study (14). The [13C]sodium octanoate (100 mg) was dissolved in water and mixed into either the 250-kcal (45 g CHO, 21 g fiber, 5.7 g protein, 5.4 g fat) or 350-kcal (63 g CHO, 3 g fiber, 8 g protein, 7.5 g fat) premeasured dry mix. After the [13C]sodium octanoate and water had been thoroughly mixed, the muffin meal was cooked using a microwave. Subjects were given 10 min to complete the meal with 150 cc water. Breath samples were obtained at 5 and 10 min before ingestion of the muffin meal and every 15 min for 6 hr thereafter using breath collection devices (Quintron, Milwaukee, Wisconsin, USA). Subjects were instructed to exhale normally into the mouthpiece of the collection device. Using this breath collection device, the end tidal volume of the breath sample fills the discard bag first, followed by the alveolar air, which enters the gas sample bag through a one-way septum valve. An evacuated 10 cc Extainer tube was inserted into the needle adapter to collect the breath sample from the filled gas sample bag, which was then reused for subsequent breath collections after emptying any residual air. The breath sample tubes were analyzed at Metabolic Solutions, Inc. (Nashua, New Hampshire, USA).

Electrogastrography (EGG) Recording. The Medtronic-Synectics EGG digitrapper (Minneapolis, Minnesota, USA) was used for EGG recording (2, 15). The abdominal skin was prepared for the cutaneous EGG electrodes. Abdominal hair, if present, was removed with a razor. The area was abraded with 4 x 4-in. gauze coated with skin preparation ointment (Omni prep) until the skin appeared slightly pinkish. Electrode cream (Signa Creme, Parker Laboratories, Orange, New Jersey, USA) was applied to each electrode placement site, allowed to soak in for 1 min and then removed with gauze. The EGG electrodes (Cleartrace electrodes; Medtronic Andover Medical, Inc., Haverhill, Minnesota, USA) were applied to the skin. One active electrode was placed on the midline halfway between the umbilicus and Xiphoid process. The other active electrode was placed on the left upper abdomen at a 30–45° angle 5 cm from the first midline active electrode. The reference electrode was placed on the subject's right side, 5 cm to the right of the midline electrode. EGG was recorded...
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for 30 min fasting and for 4 hr after the muffin meal using a sampling frequency of 4 Hz and movement average of 1. The symptom and meal buttons on the Medtronic-Synectics EGG digitrapper were used to record the breath sample collections and meal ingestion times, respectively.

Data Analysis

[13C]Octanoate Breath Test. The breath samples were measured for 13CO2 at Metabolic Solutions, Inc. according to a previously described procedure (14). The amount of 13CO2 in the breath sample tubes was measured with a Europa Scientific 20/20 gas isotope ratio mass spectrometer using the Automated Breath 13C Analyzer option. The ratio of 12CO2 to 13CO2 (mass 45–44) was measured in the samples and compared to reference gases (5% CO2, 75% N2, 20% O2) calibrated with a standard of 13CO2. Data were expressed as the percent dose per hour and cumulative percent of dose over time. Curves fitted to the percent dose per hour and a cumulative percent of dose provided constants required to calculate the gastric parameters T1/2 and Tlag according the method of Ghoo et al (4). T1/2 was calculated from the cumulative percent dose curve as one half the maximum cumulative excretion of 13CO2 at infinite time.

EGG. The data stored in the EGG recorder were downloaded to an IBM compatible computer (NEC Powermate SX/251). The EGG recordings were analyzed using medtronic-synectics software program (ElectroGastroGram Version 6.40) with running spectral analysis and fast Fourier transformation as previously described (2, 15). The variables assessed were: (1) the dominant frequency of the EGG in the fasting and postprandial periods, (2) the power of the dominant frequency in the fasting and postprandial periods, (3) the ratio of postprandial to fasting power of the dominant frequency (P/F power ratio), and (4) percent time for the EGG frequency in the bradygastric (0.5–2.0), normal (2.0–4.0 cpm), tachygastria (4.0–9.0), and duodenal/respiratory (9.0–15.0) ranges for the fasting and postprandial periods. The P/F power ratio was determined for each hour postprandially as well as for the entire 4-hr postprandial period.

Statistical Analyses

Results are reported as either mean ± SD or mean ± SEM as noted. Student's paired t test was performed to determine significant differences. The coefficient of linear correlation (r) was performed to determine the relationship between two variables (16). P value < 0.05 was used as the criterion for statistical significance.

RESULTS

All 14 subjects completed two simultaneous modified [13C]OBT and EGG recording sessions without any adverse effects. All subjects finished ingesting the muffin meal within 10 min.

Gastric Emptying (GE) by Modified [13C]P-OBT. Gastric emptying values (Tlag and T1/2) were determined from the curves of the 13CO2 breath excretion over time according to the method of Ghoo et al (4). An example of 13CO2 breath curves using the two different muffin meals in the same subject is shown in Figure 1. The mean values for the Tlag and T1/2 of the 14 normal subjects are shown in Table 1. As seen in Figure 2, using the 6-hr breath collection data, the T1/2 was 177 ± 25 (mean ± SD) for the 350-kcal meal compared to 153 ± 27 min (P < 0.01) for the 250-kcal meal. Using only the initial 4-hr breath samples, the T1/2 for the 350-kcal meal was 244 ± 125 min compared to 165 ± 46 min (P < 0.05) for the 250-kcal meal. The T1/2 calculated from the truncated 4-hr data was longer than with the 6-hr data (P < 0.05) and showed more variability between subjects as in-

![Graph](image_url)

Table 1. Gastric Emptying Parameters (Tlag and T1/2) for Different Caloric Muffin Meals and Different Test Durations*

<table>
<thead>
<tr>
<th>Meal size (kcal)</th>
<th>Tlag gastric emptying (min)</th>
<th>T1/2 gastric emptying (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4 hr data</td>
<td>6 hr data</td>
</tr>
<tr>
<td>250</td>
<td>97.5 ± 6.1</td>
<td>99.2 ± 4.4</td>
</tr>
<tr>
<td>350</td>
<td>134.5 ± 13.5</td>
<td>113.7 ± 4.1b</td>
</tr>
</tbody>
</table>

*Results expressed as mean ± SEM; a, P < 0.05; b, P < 0.01 vs 250-kcal muffin meal.
There was a nonsignificant trend toward longer $T_{1/2}$ in females compared to males. For example, for the 250-kcal meal using the 6-hour data set, the $T_{1/2}$ for women was $163 \pm 22$ min (sd) compared to $143 \pm 29$ min for men ($P = 0.09$), and for the 350-kcal meal using the 6-hour data set, the $T_{1/2}$ for women was $183 \pm 27$ min compared to $172 \pm 24$ min for men ($P = 0.23$).

There was a weak negative correlation between age and $T_{1/2}$ for the 350-kcal meal using 6-hour data ($r = -0.57; P = 0.03$).

**Gastric Myoelectrical Activity by EGG.** Figure 5 shows an example of an EGG tracing from a single patient representing two different meals administered on separate days. After meal ingestion, the EGG amplitude for the 350-kcal meal increased compared to fasting, whereas there was little change in the EGG amplitude for the 250-kcal meal. As seen in Table 2, the mean ratio of the postprandial to fasting power of the dominant frequency (P/F power ratio) for the entire 4-hour postprandial period from the 14 subjects for the 350-kcal meal was $1.9 \pm 0.4$, which tended to be higher, but not significantly, than for the 250-kcal meal ($1.3 \pm 0.6; P = 0.53$). When only the first 2-hour of the postprandial period were analyzed, the mean P/F power ratio for the 350-kcal meal was significantly higher than the 250-kcal meal ($2.4 \pm 0.6$ vs $1.5 \pm 0.5; P < 0.05$). The mean P/F power ratio for the 350-kcal meal for the entire 4-hour postprandial period and for the initial 2-hour postprandial period, but not for the 250-kcal meal, was significantly greater than 1 ($P < 0.05$), indicating an increase in EGG power after the test meal ingestion.

The mean ratios of the postprandial to fasting

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**Fig 2.** $T_{1/2}$ for gastric emptying results of a 250- and 350-kcal meal in normal subjects using 4-hr and 6-hr data for $[^13]$C-OBT gastric emptying analysis. Results expressed as mean ± SEM.

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**Fig 3.** Correlation between 4- and 6-hr breath collections for the OBT $T_{1/2}$ determinations. (A) Correlation between gastric emptying of 250-kcal meal in normal subjects using 4-hr and 6-hr data (same study day). (B) Correlation between gastric emptying of 350-kcal meal in normal subjects using 4-hr and 6-hr data (same study day).
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A. 4 hour test duration

B. 6 hour test duration

Fig 4. Correlation of $T_{1/2}$ for GE measured with the 250- and 350-kcal meals. There were moderate correlations between the $T_{1/2}$ values using the 250- and the 350-kcal meals performed on different days with either the 4-hr (A) or 6-hr data set (B).

The power of the dominant frequency (P/F power ratio) for each 1-hr postprandial measurement interval are shown in Figure 6. The mean P/F power ratios of both the 350- and 250-kcal meal were highest at the first hour postprandially, then gradually declined over time. The 350-kcal meal P/F power ratios for each 1-hr postprandial measurement interval tended to be greater than for the 250-kcal meal, being significant ($P < 0.05$) for the 1- to 2-hr period after meal ingestion. The mean P/F power ratios for the 350-kcal meal was greater than one for the first three 1-hr postprandial periods. For the 250-kcal meal, the mean P/F power ratio was greater, but not significantly, than one only for the first postprandial hour, then decreased to close to one for the remaining postprandial time periods.

Table 2 shows the EGG frequency ranges for the entire 4-hr postprandial period. The EGG dominant frequencies (DF) after the meal were not different over time between the 250- and 350-kcal meal. Most of the frequency ranges for both the 350- and 250-kcal meals were in the 2-4 cpm range. However, the 350-kcal meal had a slightly higher percentage of 2-4 cpm than the 250-kcal meal.

Correlation of OBT with EGG. The correlation between the 4-hr EGG P/F power ratio and the $T_{1/2}$ for GE using the 6-hr breath collection data for both 250- and 350-kcal meal are shown in Figure 7. There was a moderate correlation between $T_{1/2}$ using the 6-hr breath collection data and the 4-hr EGG postprandial/fasting power ratio for the 350-kcal meal ($r = 0.67; P < 0.01$). In contrast, there was a poor correlation between the 4-hr EGG P/F power ratio and $T_{1/2}$ for GE with the 250-kcal meal ($r = 0.18, P = 0.53$). We also analyzed the correlation between the 4-hr EGG P/F power ratio and the $T_{1/2}$ using the 4-hr breath collection data from both the 250- and 350-kcal meal. The 4-hr P/F power ratio was moderately correlated with $T_{1/2}$ from 4-hr data for the 350-kcal meal ($r = 0.68, P < 0.01$). There was a poor correlation between the 4-hr P/F power ratio with $T_{1/2}$ using the 4-hr breath collection for the 250-kcal meal ($r = 0.074; P = 0.801$).

We further investigated the relationship between the EGG power ratio and $T_{1/2}$ for GE by correlating the EGG power ratio calculated with different durations of the postprandial period with the $T_{1/2}$ value by OBT. Interestingly, we found that the longer postprandial recording period yielded stronger correlations between P/F power ratio and $T_{1/2}$ for the 350-kcal meal. The $r$ value for the correlations between

![Fig 5. EGG tracings from the same patient with the two different meals on separate days. This condensed EGG tracing illustrates the effects of the meal size on the change in EGG amplitude. After meal ingestion, the EGG amplitude for the 350-kcal meal increased compared to fasting, whereas there was no apparent change for the 250-kcal meal.](image-url)
\( T_{1/2} \) for the 350-kcal meal using 6-hr breath collection data and P/F power ratios using 1-, 2-, 3-, and 4-hr EGG data were 0.57 \((P < 0.05)\), 0.63 \((P < 0.05)\), 0.69 \((P < 0.01)\), and 0.67 \((P < 0.01)\), respectively.

**DISCUSSION**

The octanoate breath test (OBT) is used in Europe and in the United States, primarily for pharmaceutical clinical research studies of new prokinetic agents. Efforts have been made to refine the OBT beyond a research tool to a practical, standardized diagnostic test for the clinical evaluation of patients with symptoms suggestive of gastroparesis. This study uses an easy-to-prepare muffin meal along with a practical breath collection system to conveniently and reliably measure solid-phase gastric emptying (GE). Previous studies with a muffin meal have successfully demonstrated the ability of this modified OBT to measure GE in healthy volunteers as compared to scintigraphy (14). This modified muffin-based OBT also detected an increase in gastric emptying by the promotility agent, erythromycin (14). In the current study, the modified muffin-based OBT was further evaluated by investigating the effect of meal size and test duration on the \( T_{1/2} \) for gastric emptying as determined by the OBT.

Our results indicate that gastric emptying is affected by test meal size. Using the muffin based \([^{13}C]\)OBT, \( T_{1/2} \) for the larger 350-kcal meal was significantly longer than for a 250-kcal meal. Whether this is due to the higher caloric content, fat content, or volume of the 350-kcal muffin meal is not known. Previous studies have demonstrated that increasing the caloric content of the meal of fixed composition delayed the half emptying time of gastric emptying using scintigraphy (11, 17). Similar to our study, a progressive delay in the \( T_{1/2} \) for GE using scintigraphy was seen with increasing both the meal energy content and volume despite constant meal composition (17). A 300-kcal egg meal for gastric emptying provided less intersubject variability and minimal intra-subject variability than smaller (150 kcal) or larger meals (600 kcal) in normal subjects (17). Gastric emptying is regulated by inhibitory neural feedback from the small intestine in response to nutrients; larger caloric meals have stronger inhibitory effects on gastric emptying (11, 18, 19). Gastric emptying has been suggested to be regulated to allow a constant caloric delivery into the small intestine (11, 12). More recent studies suggest that although a larger meal prolongs the half emptying time, when expressed as the amount of food entering the small intestine, the rate of energy delivery from the stomach into the small intestine is still higher with a larger meal (13).

Our study also demonstrated that the \( T_{1/2} \) values for gastric emptying obtained with \([^{13}C]\)OBT are affected by the duration of breath sampling. A shorter duration of breath collection yielded longer values for \( T_{1/2} \) with more variability. The longer duration of breath sampling appears to give a more precise value for gastric emptying. Using a 220-kcal egg meal, Camicari and coworkers have suggested that \([^{13}C]\) breath tests with intermittent breath collections can give
gastroduodenal emptying results that are comparable with scintigraphy (8, 20). Preliminary studies have suggested that this shortened approach can be performed with the simplified muffin meal in studies that simultaneously measure gastric emptying with OBT and scintigraphy (14).

In this study, we simultaneously measured EGG activity with the OBT. EGG is a noninvasive method for studying gastric myoelectrical activity (3). Normal EGG responses to solid meals include an increase in the dominant frequency, power of the dominant frequency, and the percentage of the dominant frequency in the normal 2–4 cpm range (21–23). However, there is no standard meal for the EGG study (21, 23). Our study demonstrates that EGG parameters, primarily the EGG postprandial/fasting power ratio, are also affected by test meal size. Using a muffin test meal, the postprandial/fasting power ratio for the larger 350-kcal meal was greater than that for the 250-kcal meal. We found that only the larger 350-kcal muffin meal induces normal EGG responses, as indicated by an increase in power of the dominant frequency and higher percentage of the time that the dominant frequency is in 2–4 cpm range. The smaller 250-kcal muffin meal had little effect on the EGG power ratio. These results suggest that 350-kcal muffin test meal appears to be a better “gastric stimulating” meal than a 250-kcal meal and might be a better meal to be used as a standard meal for subjects undergoing EGG or gastric emptying by the 

\[^{13}\text{C}\text{OBT}\]. Other studies have also suggested that reduced caloric meals fail to generate the expected postprandial EGG changes and may not be appropriate for use as test meals (23). In other tests of gastric motor function, such as antroduodenal manometry, often a larger (300–400 kcal) meal is used to ensure transformation from the fasting to fed-type gastric motility pattern (3).

Many studies have reported an increase in the EGG power of the dominant frequency after meal ingestion (22, 24, 25). This increase has been suggested to be either from an increased amplitude or strength of antral contractions (26) or gastric distension from the test meal (27). We found a moderate positive correlation between the \(T_{1/2}\) for gastric emptying and postprandial/fasting power ratio of the dominant frequency for the 350-kcal meal. If the increase in power was related to the strength of antral contractions and to gastric emptying, one might expect a negative correlation; for example, an increased EGG power ratio related to a shorter \(T_{1/2}\). Thus, our observations support the role of gastric distension in the increase in EGG power of the dominant frequency after meal ingestion.

The EGG postprandial/fasting power ratio correlated significantly with \(T_{1/2}\) for the 350-kcal meal, whereas there was poor correlation for the 250-kcal meal. For the 350-kcal meal, using the initial postprandial hour, this correlation between the EGG postprandial/fasting power ratio of the dominant fre-
quency and the $T_{1/2}$ for gastric emptying was moderate ($r = 0.57$). However, longer postprandial periods (e.g., 2, 3, or 4 hr after the meal) produced stronger correlations between postprandial/fasting power ratio of the dominant frequency and $T_{1/2}$ (e.g., $r = 0.63$, 0.69, and 0.67, respectively). This observation indirectly supports the rationale of using a postprandial EGG recording period of longer than 1 hr. Other studies have suggested increasing the postprandial EGG recording period to 2 hr to detect gastric myoelectric abnormalities in symptomatic patients (28, 29).

In conclusion, our results indicate that gastric emptying as measured by $^{13}$CO$_2$Obt and EGG are both affected by the test meal size. The test duration also affects gastric emptying values derived using the ObT. Our results also suggest that the larger 250-kcal muffin test meal appears to be a better gastric stimulating meal than a 250-kcal meal for subjects undergoing EGG or gastric emptying by the $^{13}$CO$_2$Obt method. It is possible that the test meal size may also affect the sensitivity of EGG and GE studies in detecting patients with gastric motor disorders.

REFERENCES