Gender-Related Differences in Gastric Emptying

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This study was undertaken to determine if men and women have similar rates of gastric emptying. Fifteen normal weight male subjects aged 20–53 yr (mean 30 yr) and 15 normal weight female subjects aged 20–45 yr (mean 32 yr) were studied. Each subject ingested an identical 300-g meal consisting of 150 g of beef stew and 150 g of orange juice. Technetium-99m- (^{99m}Tc) labeled liver pate was used as the radioactive marker for the solid phase; indium-111 DTPA ([^{111}In]DTPA) was the liquid marker. A scintillation camera and computer was used to measure the rate of emptying of the solid and liquid phases. Correction for radionuclide depth, decay, and crosstalk was performed. The half-emptying time for men was: solids 59.8 ± 3.7 min, liquids 30.3 ± 2.3 min, and for women was: solids 92.4 ± 7.5 min, liquids 53.8 ± 4.9 min. These differences were statistically significant (solids, $p = 0.00097$; liquids, $p = 0.00038$). We conclude that women empty both solids and liquids from their stomachs more slowly than men. Possible mechanisms for the difference in gastric emptying rates between men and women are discussed.

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Radionuclide gastric emptying studies have been widely used to measure gastric function in both research and clinical studies (*1–9*). The normal values for these studies are based on male controls or a mixed population, because it has been assumed men and women have identical rates of gastric emptying (*1–9*). In fact, in many studies the subjects' sex is not noted because it was considered irrelevant (*10,11*). In pregnant women, however, oral-to-cecal transit times are prolonged (*12*). A reduction in lower esophageal sphincter pressure and an increased prevalance of gastroesophageal reflux (*13–15*), and gallbladder stasis (*16,17*) have been reported to occur during pregnancy. Animal studies indicate that these effects may be due to smooth muscle relaxation caused by progesterone and estradiol (*13,15,18*).

We undertook a study of normal weight nonpregnant females to determine if nonpregnant women's stomachs empty both solids and liquids differently than men. We used a dual isotope radionuclide technique that corrects for radionuclide depth, decay, and crosstalk, which we used in previous studies of possible determinants of gastric emptying rates (*1–7,19,20*).

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MATERIALS AND METHODS

Subject Selection

Fifteen males and 15 females in good health, without history of gastrointestinal disease or symptoms, who were not on any medications (except two women who were on oral contraceptives), were used for the study population. All subjects in both groups were within normal weight categories for height.

Technique

Technetium-99m sulfur colloid- ([^{99m}Tc]SC) labeled liver pate was prepared by homogeneously mixing 5 mCi [^{99m}Tc] SC into 50 g of canned liver pate (*20*). This mixture was incubated for 10 min and then placed in a hot frying pan and stirred occasionally while frying for 10–15 min. The pate aggregates during frying into 2- to 5-mm particles. After frying, the pate is placed on an absorbent towel to remove any excess [^{99m}Tc]SC and grease. Each subject was fed a standard 300-g meal consisting of 150 g of beef stew and 150 g of orange juice. Six hundred microcuries of [^{99m}Tc]SC-labeled pate was mixed with the beef stew. Liquid emptying for each meal was also measured using 100 μCi of indium-111 DTPA ([^{111}In] DTPA), which was mixed into the orange juice. Meals were consumed in less than 5 min and imaging was begun immediately. Images were taken in the upright position at 15-min intervals using a large-field scintillation camera with a parallel-hole, medium-energy collimator. The subjects stood during imaging and sat between images. Anterior and posterior images were obtained over the 140-keV photopeak of ^{99m}Tc and over the 247-keV photopeak of ^{111}In using 20% energy windows. An external ^{99m}Tc point source was taped to the abdomen on the right costal margin to allow accurate horizontal and vertical repositioning for each set of anterior images. A posterior point source was similarly used for repositioning on the posterior images. Digital images were stored in a nuclear medicine computer system for data processing.

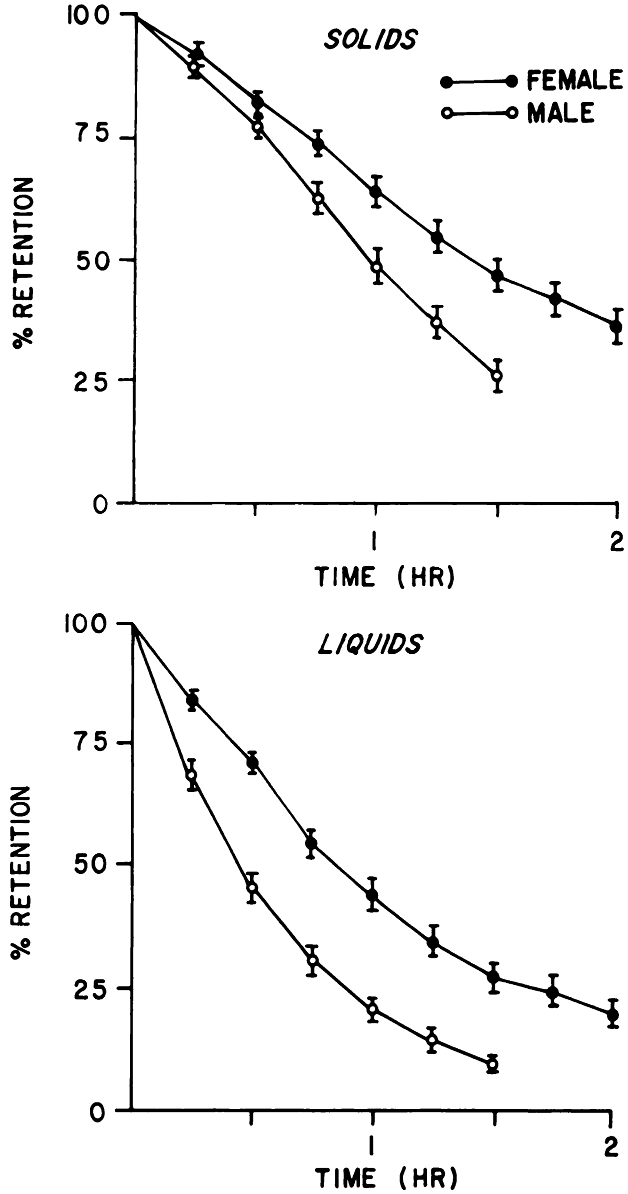

FIGURE 1
Solid and liquid gastric emptying curves for males and females. Bars indicate ± 1 s.e.m. Upper: Solid emptying for both males (0——0) and females (●——●) is linear. Emptying of solids is significantly slower for females than for males. Lower: Liquid emptying for both males and females is exponential. Emptying of liquids is significantly slower for females than for males.

The computer was used to generate a composite image of the anterior and the posterior images, respectively. A region of interest was manually defined to include the total stomach area on these images. Data were corrected for radionuclide interference and radioactive decay, and the geometric mean (GM) of the anterior and posterior counts was calculated. The GM was used to correct for attenuation of the radionuclides at depth within the body (*6,19,20*). The data were analyzed by the Biostatistics Department of our institution using the approximate degrees of freedom t-test.

RESULTS

The ages of the male population ranged from 21 to 53 yr, with a mean of 30 yr. Their height ranged from 66 to 74 in., with a mean of 69 in. Their weight ranged from 120 to 190 lb, with a mean of 168 lb. The solid half-emptying time was 59.8 ± 3.7 min (s.e.m.). The emptying curve was linear (Fig. 1). The liquid half-emptying time was 30.3 ± 2.3 min. The emptying curve was exponential.

The ages of the female population ranged from 23 to 44 yr, with a mean of 32 yr. Their height ranged from 60 to 68.5 in., with a mean of 65 in. Their weight ranged from 102 to 168 lb, with a mean of 130 lb. Two subjects were on oral contraceptives. The solid half-emptying time was 92.4 ± 7.5 min (s.e.m.). The emptying curve was approximately linear (Fig. 1). The liquid half-emptying time was 53.8 ± 4.9 min. The emptying curve was exponential (Fig. 1).

The differences between these two groups were statistically significant (solids, $p = 0.00097$; liquids, $p = 0.00038$). To be certain the two subjects on oral contraceptives did not skew the data, they were deleted from the female group and the statistical analysis was redone. The differences in gastric emptying rates between men and women remained statistically significant (solids, $p = 0.00689$; liquids, $p = 0.00095$).

DISCUSSION

Radionuclide gastric emptying studies are used extensively for both research and clinical studies of gastric function (*1–9*). The normal values for these studies are based on all male or mixed populations, because it has been assumed that men and women have identical rates of gastric emptying (*1–9*). In fact, in many studies, the sex of the subjects is not noted because it was not considered relevant (*10,11*). Indeed, studies comparing gastric emptying in elderly men and women have found no significant difference (*22*).

We have previously looked at a number of possible determinants of the rate of gastric emptying including meal size, meal composition, subject age and weight, and the measurement technique (*1–7,18,20*). Like other investigators, our previous studies have used male subjects. We undertook this study to determine if gender affects gastric emptying.

In our study, we found the rates of gastric emptying of both solids and liquids to be slower in women. The mechanism for these differences is not known. The most likely explanation appears to be the effects of female sex hormones, primarily progesterone and estradiol, on the gastrointestinal tract. A reduction in lower esophageal sphincter (LES) pressure and an increased prevalence of gastroesophageal reflux occur during pregnancy, a time when these hormones are significantly elevated (*13–15*). In animals, progesterone is associated with a decrease in LES pressures and a decrease in the length-tension response of esophageal smooth muscle to pentagastrin, acetylcholine, norepinephrine, and bethanechol (*13–15,23*). Gallbladder stasis also has been described in pregnancy (*16,17*). Studies on isolated gallbladder smooth muscle indicate that progesterone inhibits its contractility (*23*).

Using breath hydrogen concentration after lactulose ingestion to measure gastrointestinal transit, Wald found the mouth-to-cecum transit time prolonged in pregnancy (*12*). This was most marked during the third trimester (when progesterone and estradiol are at their highest levels). Wald also found a minimal prolongation of the mouth-to-cecum gastrointestinal transit rate during the luteal phase of the menstrual cycle when the progesterone levels are peaked (*13*). However, both the above studies observed total gastrointestinal transit time, not gastric emptying, per se.

In the nonpregnant woman, it does not appear that the rate of gastric emptying is affected by the menstrual cycle. Using a dual isotope radionuclide technique, Horowitz et al. found no difference in gastric emptying rate during the follicular phase compared with the luteal phase of the menstrual cycle (*24*). These authors suggested that the gastrointestinal transit slowing found by Wald et al. was due to a preferential effect of progesterone on the intestinal smooth muscle, rather than gastric smooth muscle. This lack of change in gastric emptying with the menstrual cycle was also confirmed in animal studies. In rats, no change in gastrointestinal transit was found in cycling, compared with pregnant animals (*18*). However, castrated female animals had a significantly faster transit time. These investigators felt this data indicated that sex hormones are responsible for slowing gastrointestinal transit in these animals, but that the absolute levels of the hormones (i.e., cycling versus pregnant rats) was not important.

The mechanism by which sex hormones may cause a decrease in motility is not known. Estradiol receptors have been identified in gastrointestinal tissues (*13*). Progesterone receptors have been identified in other progesterone-responsive tissues and may be present in the gastrointestinal tract, as well (*13*). Finally, motilin, a gastrointestinal hormone with smooth muscle stimulating effect whose target organs are the LES, stomach, small and large intestine, and gallbladder, is diminished in pregnancy (*25*). Perhaps progesterone acts indirectly by decreasing the plasma level of this peptide, thereby, slowing gastric emptying.

To our knowledge no previous studies have used dual isotope radionuclide techniques to directly address the question of slower gastric emptying in non-pregnant women versus men. However, in a study to establish normal values with a dual isotope gastric emptying technique, Notivol et al. also noted a significant difference in gastric emptying in control males and females (*26*), although their study differed from ours in several ways. In that study, imaging was delayed until 15 min after meal ingestion. Subsequent imaging was performed at 30-min intervals. Their lack of finding of exponential emptying of liquids, as had been described by most other groups, raises questions about their technique (*1–7,9–11,26*).

In our study we used a dual isotope technique, which we have used in a number of previous studies (*1–7,19*). We have shown that the label, ^{99m}Tc liver pate, demonstrates equal performance to intracellularly labeled chicken liver (*21*). To correct for depth, we used GM correction. This technique reduces the error in gastric emptying studies by 10%–56% (*6,19,21*). In addition, we corrected for decay and crosstalk (*19*).

We conclude that gastric emptying of solids and liquids is slower in women than in men. The most likely explanation is an effect of sex hormones, especially progesterone and estradiol, on gastrointestinal motility.

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