Gastric Emptying of Three Different Size of Indigestible Radiopaque Markers in Healthy Subjects

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Abstract

The gastric emptying of indigestible solids is affected by the size, specific gravity, shape, consistency and the compressibility of the indigestible solids and depends largely on the composition of the meal. The threshold size is about 3.0mm in canine. But it is reported that the estimates made for dogs may not apply to humans. I evaluated whether the size of indigestible solids affects gastric emptying in healthy subjects with food which had the same specific gravity as the indigestible solids. We used three sets of 20 ring shaped radiopaque markers, which had the same specific gravity (1.2), shape, consistency, and compressibility, but different diameters (2.0 mm, 4.5 mm and 7.0 mm). After the subjects ingested the three sets of 20 markers with food, the number of markers evacuated from the stomach was counted every 15 min until all the markers were evacuated. The median numbers of discharged markers of 2.0 mm, 4.5 mm and 7.0 mm were 5 (0-5), 1 (0-3) and 3 (0-4) at 60 min, 15 (3-18), 10 (6-9) and 13 (11-16) at 120 min (median, 25th-75th percentile), respectively. There was no statistically significant difference between the numbers of the three types of discharged markers during observation. The lag time (the period from the time of ingestion of the markers to the time when the first marker left the stomach) of the 2.0 mm, 4.5 mm and 7.0 mm markers was 52.5 (45-105), 67.5 (60-105), and 52.5 (45-105) min, respectively, and there was no statistically significant difference. In conclusion, the radiopaque markers of different diameters (below 7.0 mm) left the stomach in the same pattern.

Key words: gastric emptying, human, radiopaque marker

Introduction

It has been reported that the gastric emptying of liquids, digestible solids, and indigestible solids do not take place at the same rate (Holt et al., 1982; Mojaverian et al., 1985). Studies on dogs have shown that the size and density of indigestible solids affect gastric emptying in the presence of food (Meyer et al., 1988), and that the threshold size was about 3.0 mm (Russell et al., 1985). Our study showed that ring shaped indigestible markers of 2.0 mm and 4.5 mm were evacuated in same manner but that there was a delay in the evacuation of 7.0 mm markers in canines. However, the estimates made for dogs may not apply to humans (Aoyagi et al.,...
In humans, the paper over 2.5 mm in diameter took longer to evaluate than the paper under 2.5 mm (Holt et al., 1982). Others reported that using polyethylene tubes of 2.0 mm diameter and different lengths (2.0 mm and 10.0 mm) does not affect gastric emptying (Smith et al., 1986) and the polyethylene tube of 2.0 mm diameter and 5.0 mm length emptied simultaneously during the emptying of digestible solids (Brogna et al., 1992). It has been reported that the density (Meyer et al., 1988), compressibility (Meyer et al., 1989), and the calories of a meal (Ewe et al., 1991; Mojaverian et al., 1985; Smith et al., 1986) has an effect on the gastric emptying of indigestible markers. But it has not been reported that different diameters of radiopaque markers made a difference in the gastric emptying rate in humans. The aim of this study was to investigate the effect of variation in indigestible marker diameters on the rate of gastric emptying in healthy subjects, by using three sizes of radiopaque markers of the same consistency.

**Materials and methods**

**Subjects**

We studied six healthy male volunteers with a median age of 24 years old (range 21–28 years old). No subject had a history of gastrointestinal disease and complaints. All subjects provided their informed consent to participate in the following protocol that had been approved beforehand by the ethical committee of Hiroshima University School of Medicine.

Three types of radiopaque markers were used: 1) a gelatin capsule of 20 SITZMARKS® (Konsyl Pharmaceuticals, INC. Texas, USA), which were ring shaped and whose diameter was 4.5 mm and thickness was 1.0 mm. 2) a gelatin capsule containing 20 markers, which were ring shaped and whose diameter was 2.0 mm and thickness was 1.0 mm (Kaigen Pharmaceuticals, JAPAN). 3) a gelatin capsule containing 20 markers, which were ring shaped and whose diameter was 7.0 mm and thickness was 1.0 mm (Kaigen Pharmaceuticals, JAPAN). Each type of marker was made of 33% of barium sulfate and 67% of polyvinyl chloride and had the same specific gravity, 1.2.

**Protocol**

After an overnight fast, the subjects simultaneously ingested three sets of radiopaque markers with 100 ml of water and ate a standard solid meal in a sitting position. The test meal consisted of rice, boiled salmon, egg, topping, and miso-soup (total 377 kcal, protein 21.2 g, glucose 42.4 g, fat 13.6 g). The specific gravity of the mixed foods was 1.2. Postprandial recordings were performed until all the markers had left the stomach. After ingestion of the markers, the number of markers emptied from the stomach was counted by fluoroscopy every 15 min.

The retention ratio in the stomach (the percent of the markers remaining in the stomach) was calculated on each roentgenograph. The lag time (the period from the time of ingestion of the markers to the time when the first marker left the stomach) and the half dose transit time (the time it took for 10 markers to be emptied from the stomach) were calculated.
Statistics

The results are expressed as median (25th–75th percentile). The statistical significance of
the differences between results was calculated by using Wilcoxon’s signed rank test and
Student’s paired t-test. A level of p < 0.05 was accepted as statistically significant.

Results

The representative data of the retention ratio in the stomach is shown in Fig. 1. The lag
time of the 2.0, 4.5, and 7.0 mm markers was the same, 105 min. The retention ratio in the
stomach at each time and the half dose transit time were also the same. There was no
statistically significant difference between the discharged numbers and the lag times of the
three types of markers at any time of observation. The emptying pattern of the three types
of markers showed a similar trend in other subjects.

The median numbers of discharged markers of the 2.0 mm, 4.5 mm and 7.0 mm were 5 (0–
5), 1 (0–3) and 3 (0–4) at 60 min, 15 (3–18), 10 (6–9) and 13 (11–16) at 120 min, (median, 25th–
75th%), respectively. The median rate of gastric emptying of the three types of markers was
meanly identical (Fig. 2). There was no statistically significant difference between the dischar
ded numbers of the three types of markers at any time of observation.

The lag time of the 2.0 mm, 4.5 mm and 7.0 mm markers was 52.5 (45–105), 67.5 (60–105), and
52.5 (45–105) min, respectively. There was no statistically significant difference between the
lag times of the three types of markers. The half dose transit time showed no significant
difference between the markers: 97.5 (81.7–117.3), 125.3 (92.5–157.5) and 100.0 (90.0–114.0) min in
2.0 mm, 4.5 mm and 7.0 mm, respectively (Fig. 3).

Fig. 1. Representative data of emptying time-courses. The emptying patterns of 2.0 mm (○),
4.5 mm (□) and 7.0 mm (△) radiopaque markers showed a similar trend.
Fig. 2. The median emptying time-courses from 6 subjects. They were given markers of 2.0 mm (○), 4.5 mm (□) and 7.0 mm (△) diameters. There were no statistically significant differences between the three types of markers at any time of observation.

Fig. 3. Individual lag time (A) and half dose transit time (B) of the markers of 2.0 mm, 4.5 mm and 7.0 mm diameters. There were no statistically significant differences between the lag times and the half dose transit times of the three types of markers.

Discussion

Several reports have shown that the gastric emptyings of liquids, digestible solids, and indigestible solids do not take place at the same rate (Holt et al., 1982; Mojaverian et al., 1985). Others reported that the maximum diameter necessary to make the indigestible solids empty together with digestible solids was a diameter of 2.0 mm (Meyer et al., 1988) and the polyethy-
Gastric emptying of radiopaque markers

It was also reported that the specific gravity, shape, consistency, compressibility (Meyer et al., 1989) and diameters (Meyer et al., 1988) of the indigestible solids and the calories of the food (Ewe et al., 1991; Mojaverian et al., 1985; Smith et al., 1986) may affect the gastric emptying. Studies on dogs have shown that size and density affect the gastric emptying in the presence of food (Meyer et al., 1985), and that the threshold size is about 3.0 mm (Russell et al., 1985). However, differences in the gastric emptying of indigestible tablets and granules between humans and animals have been reported, especially in large size dosage forms (Aoyagi et al., 1992). The present study was to clarify the affect of the diameters of indigestible solids in humans. It was reported in humans that in the fed state the pyloric sphincter is contracted and only small indigestible solids (less than 5.0 mm) are able to empty as “fortuitous emptying” with the meal, but large objects are not emptied in such a manner (Holt et al., 1982). It was also reported that the emptying of indigestible solids depends largely on the composition of the meal (Ewe et al., 1991). Not only the calories of the food but also differences in the specific gravity of the food and indigestible solids were probably one of the causes of the conflicting data and the different pattern of emptying. Thus, to clarify the affect of the diameters, we used food and indigestible solids of the same specific gravity, 1.2, and the subjects ingested the indigestible markers soon before eating food. Furthermore, to eliminate further causative factors on gastric emptying, we used markers of the same shape, specific gravity, consistency, and compressibility but different diameters. These markers, from 2.0 mm to 7.0 mm in diameter, were emptied from the stomach at the same rate in healthy subjects. The markers also had the same lag time and the same retention ratio in the stomach. Khosla et al. (1989) made a similar observation when studying radioisotope tablets.

In conclusion, this study clarified that different sizes of radiopaque markers between 2-7 mm in diameter show no difference in gastric emptying. We recommend the use of radiopaque markers for the diagnosis of the gastric emptying. To use the radiopaque markers clinically for the monitoring of gastric emptying, any diameter from 2-7 mm was suitable. If there were any problems, the smaller marker was less detectable than the larger one in specific gravity 1.2, and the larger one was less acceptable than the smaller one for ingestion. These problems will have to be settled before clinical use.

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