Determinants of liquid gastric emptying: comparisons between milk and isocalorically adjusted clear fluids

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Editor’s key points

- Milk has been considered equivalent to solid food in preoperative fasting guidelines because of its fat and protein content.
- The rates of gastric emptying were assessed ultrasonographically in healthy fasted volunteers who drank test beverages of varying composition.
- Gastric emptying of equal volumes of orange juice and non-human milk were similar if adjusted to the same caloric content.
- Gastric emptying of liquids depends primarily on caloric content rather than composition.

Background. Although current preoperative fasting guidelines apply restrictions to drinks containing milk because of delayed gastric emptying, the safe volume of milk that can be consumed up to 2 h before surgery on a theoretical basis has not yet been defined. We aimed to determine whether delayed gastric emptying depended mainly on the total amount of calories irrespective of compositional differences between milk and clear fluids.

Methods. We prepared five beverages with a uniform volume (500 ml) and step-wise increments in calories (0, 220, and 330 kcal), comprised mainly of non-human milk, pulpless orange juice, water, and gum syrup. The gastric emptying rate of each beverage was determined by ultrasound measurements of the gastric antral cross-sectional area after their ingestion by eight healthy fasting volunteers.

Results. The emptying rates of 500 ml of orange juice and 330 ml of non-human milk with 170 ml of water (both were 220 kcal) from the stomach were similar. Furthermore, 450 ml of orange juice with 50 ml of gum syrup and 500 ml of non-human milk (both were 330 kcal) left the stomach at similar rates. The 220 kcal beverages emptied faster than the 330 kcal beverages.

Conclusions. There were no significant differences in liquid gastric emptying after drinking equal volumes of either orange juice or milk as long as both had the same amount of calories. Liquid gastric emptying depends chiefly on the total caloric content.

Clinical trial registration. UMIN000012537.

Keywords: gastric emptying time; isocaloric fluids; preoperative fasting; ultrasonography

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The current ASA preoperative fasting guidelines recommended that patients fast from the intake of a light meal for 6 h or more before and clear fluids for 2 h or more before general anaesthesia.1 Avoiding the intake of non-human milk has also been recommended for 6 h before general anaesthesia because the gastric emptying time of non-human milk is considered to be similar to that of solid food. However, the gastric emptying rate of a mixture of 250 ml of tea with 50 ml of milk was recently shown to be the same as that of 300 ml of tea alone.2 Several studies previously reported that the gastric emptying rate of liquids may be mainly determined by the calories contained in liquids.3 – 5 Since 50 ml of milk has relatively few calories (~33 kcal), it may only slightly influence the gastric emptying rate. Thus, we hypothesized that the gastric emptying rate of a liquid is more strongly associated with its caloric content than with compositional differences between milk and clear fluids, and conducted the present study to examine this issue.

Methods

This study was registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (ref.: UMIN000012537). Ethical approval was received from the Hitachi, Ltd, Hitachi General Hospital Research Ethics Committee (approval number 2013-44). After obtaining written informed consent, eight healthy volunteers participated in this study. Subjects with medical conditions (such as diabetes mellitus, severe obesity, and gastric diseases) that might induce retention of stomach contents were excluded. According to guidelines for fasting before general anaesthesia, ingestion of solid food was stopped 6 h before, and of clear fluids 2 h before, the examination. Subjects ingested one of the five types of beverages containing different calories (0, about 220, and about 330 kcal) but a uniform volume (500 ml) over about 3 min. The order of beverage consumption was determined randomly according to a table of random...
numbers. In the first 60 min after beverage ingestion, the subject was kept in a sitting position at a 45° angle and underwent an ultrasound examination every 10 min. The subject was then free to move within the ward and was likewise examined every 30 min up to 120 min after beverage ingestion. An ultrasound assessment was performed in the right lateral position. The same subject had another beverage on a different day and underwent the same ultrasound examination. This pattern was repeated until all five types of beverages had been ingested with subsequent examinations.

The five beverages studied are shown in Table 1. Each equi-volumetric beverage (500 ml) contained one of the three main ingredients, including water, pulpless orange juice, or non-human milk. Gum syrup was used to adjust total calories in the O+S group. The composition profiles of pulpless orange juice and non-human milk such as total calories and content of each of the three major nutrients were based on nutrition facts provided as merchandize information. The osmolality and viscosity of each beverage were measured three times, and the average value of three measurements was calculated. Osmolality was determined using a freezing point depression osmometer (3D3; Advanced Instruments Inc., Norwood, MA, USA). Viscosity was measured using a B-type rotational viscometer (RB-80L; Toki Sangyo Co., Tokyo, Japan) under the conditions of 60 rpm and 25 (0.3°) C.

Previous studies have shown that 250–300 ml of water leaves the stomach in < 30–60 min, and liquid gastric emptying is exponential; therefore, we expected 500 ml of water to leave the stomach within the observational period of 120 min. Three different caloric contents were examined in the present study because the Enhanced Recovery After Surgery (ERAS) group has recommended that it is safe and feasible to ingest 400 ml of 12.6% glucose solution (about 200 kcal in 400 ml) up to 2 h before surgery. Lower and upper values of calorie intake were established based on this level, that is, 0 and 330 kcal, which was equivalent to 1.5 times this standard. Water or gum syrup was added where appropriate to achieve the pre-set caloric content.

The volume of stomach contents was determined from the cross-sectional area (CSA) of the gastric antrum measured by ultrasonography (Hi Vision AVIUS, Hitachi Aloka Medical, Ltd, Tokyo, Japan). The gastric antrum was imaged in a sagittal to right parasagittal plane using the left lobe of the liver, the pancreas, the abdominal aorta, or the inferior vena cava as anatomical landmarks, as described. The CSA of the gastric antrum was calculated according to the following formula using the anteroposterior (AP) and cranio-caudal (CC) diameters, as described.

\[
\text{Antral CSA} = \pi \times \text{AP} \times \text{CC}/4
\]

Gastric volume was calculated from the antral CSA, as described.

\[
\text{volume} = -372.54 + 282.49 \times \log(\text{CSA}) - 1.68 \times \text{weight}
\]

When calculated volume was <0 ml, it was considered to be 0 ml. Measurements were performed at baseline, every 10 min for 60 min, and then at 30 min intervals for 120 min after beverages were ingested. To ensure technical uniformity, all measurements were performed by one evaluator (T.O.).

### Statistics

Repeated-measures analysis of variance and the Student–Newman–Keuls (SNK) tests were performed to determine differences in CSA and gastric volume of all measurements up to 120 min. \(P<0.05\) was considered statistically significant. Measured values were expressed as mean [standard deviation (SD)]. Statistical analyses were carried out using Excel Statistical Program File Ystat 2013 (developed by S. Yamazaki, Igakutosyo Syuppan Co., Ltd, Tokyo, Japan).

### Results

Eight healthy male participants completed this study with the following physical characteristics [medians (inter-quartile range)]: age 27 (24–27) yr; height 171 (165–177) cm; weight 65 (59–67) kg; and BMI 22 (21–23) kg m\(^{-2}\). Figures 1 and 2 show typical ultrasound images generated during the study. In the case of the M and M+W groups, hyperechoic particles were occasionally observed suspended in a hypoechoic fluid (Fig. 2), which is consistent with coagulation of milk induced by stomach acids. All of these disappeared gradually during the observational period of 120 min, and were not responsible for delayed gastric emptying.

The mean CSA and mean gastric volume were significantly higher 40 min after ingestion and thereafter in the O+S group than in the O group (\(P<0.01\); SNK test; \(n=8\); Figs 3 and 4). The mean CSA and mean gastric volume were significantly higher 40 min after ingestion and thereafter in the M group than in the M+W group (\(P<0.01\); SNK test; \(n=8\); Figs 3 and 4). No significant difference was noted in the mean CSA or mean

<table>
<thead>
<tr>
<th>Component</th>
<th>W group</th>
<th>O group</th>
<th>O+S group</th>
<th>M group</th>
<th>M+W group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water (ml)</td>
<td>500</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>170</td>
</tr>
<tr>
<td>Pulpless orange juice (ml)</td>
<td>0</td>
<td>500</td>
<td>450</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Non-human milk (ml)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>500</td>
<td>330</td>
</tr>
<tr>
<td>Gum syrup (ml)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>500</td>
<td>330</td>
</tr>
<tr>
<td>Total volume (ml)</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>Total calories (kcal)</td>
<td>0</td>
<td>220</td>
<td>329</td>
<td>332</td>
<td>219</td>
</tr>
<tr>
<td>Protein (g dl(^{-1}))</td>
<td>0</td>
<td>0.70</td>
<td>0.63</td>
<td>3.25</td>
<td>2.15</td>
</tr>
<tr>
<td>Carbohydrate (g dl(^{-1}))</td>
<td>0</td>
<td>10.3</td>
<td>15.82</td>
<td>4.80</td>
<td>3.17</td>
</tr>
<tr>
<td>Lipid (g dl(^{-1}))</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.80</td>
<td>2.51</td>
</tr>
<tr>
<td>Osmolality (mOsm litre(^{-1}))</td>
<td>2</td>
<td>547</td>
<td>867</td>
<td>249</td>
<td>166</td>
</tr>
<tr>
<td>Viscosity (mPa s)</td>
<td>0.973</td>
<td>2.790</td>
<td>1.920</td>
<td>1.857</td>
<td>1.487</td>
</tr>
</tbody>
</table>
gastric volume at any time point between the O and M+W groups or between the M and O+S groups (Figs 3 and 4). The mean CSA was significantly lower in the W group than in the other groups at 10–60 min ($P < 0.01$; SNK test; $n = 8$; Figs 3 and 4). The mean gastric volume was significantly lower in the W group than in the other groups at 10–60 min ($P < 0.01$; SNK test; $n = 8$; Figs 3 and 4). No significant difference was noted in the mean CSA between the W, O, and M+W groups at 120 min (Figs 3 and 4), or the mean gastric volume between the W, O, and M+W groups at 90 and 120 min (Figs 3 and 4). The mean CSA in the W group returned to the value measured at baseline 40 min after ingestion, and did not significantly change to the end of the observation period.

**Discussion**

The current ASA preoperative fasting guidelines recommend fasting from the intake of a light meal for 6 h or more before and clear fluids for 2 h or more before general anaesthesia.\(^1\) The gastric emptying time of milk is considered to be similar to that of solid food; avoiding its ingestion 6 h before general anaesthesia has been recommended because the fat and protein contained in milk are considered to delay gastric emptying. Therefore, milk has been regarded as an exception. However, a recent study demonstrated that the gastric emptying rate of a mixture of 250 ml of tea with 50 ml of milk was similar to that of 300 ml of tea alone,\(^2\) which indicated that addition of a small to moderate volume of full fat milk to tea/coffee did not significantly delay gastric emptying.

An important issue to be considered is why a small to moderate volume of milk is feasible. In other words, the critical determinant of gastric emptying, such as fat content, total calories, or both, has yet to be identified. The caloric content of 50 ml of milk is $\sim 33$ kcal, which has a negligible influence on liquid gastric emptying. Because of its high fat content, milk is higher in calories than other beverages with the same volume. This might explain why milk has been distinguished from other beverages such as clear fluids. Therefore, the

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**Fig 1** (A) Sagittal sonogram of the gastric antrum after ingestion of 500 ml of orange juice. The antrum can be found between the left lobe of the liver and the pancreas, at the level of the aorta or inferior vena cava. The antrum appeared distended with a hypoechoic fluid content. (a) Sagittal sonogram of the empty gastric antrum. Arrow, antrum; L, liver; P, pancreas; Ao, aorta.

**Fig 2** Sagittal sonogram of the gastric antrum after ingestion of 500 ml of milk. (a) The antrum appeared distended with a hyperechoic content, suggesting curdled milk. (a) With time, the hyperechoic content changed into hyperechoic particles suspended in a hypoechoic fluid, suggesting curdled milk. Arrow, antrum; L, liver; P, pancreas; Ao, aorta.
slower gastric emptying of milk compared with clear fluids of the same volume could be due to the higher caloric content due to its high fat content. Several studies previously indicated that the most significant factor determining gastric emptying of fluids is the calories contained in the fluids.\textsuperscript{3–5} Maerz and colleagues\textsuperscript{12} reported that the gastric emptying rates of sugar, protein, and fat components with the equivalent calories were the same in rats. Maughan and colleagues\textsuperscript{3} investigated the time course of changes in stomach contents after the ingestion of a glucose solution and soybean protein in healthy volunteers, and reported that gastric emptying time was the same when calories were equal. Calbet and Holst\textsuperscript{13} demonstrated that gastric emptying was equivalent among milk protein solutions with the same energy content, independent of the protein fractions, even in the case of a total casein protein solution, which had a lipid content that was seven-fold higher than that of the other protein solutions. Based on this background, we hypothesized that gastric emptying rate of a liquid is associated more strongly with its caloric content than with compositional differences, that is, between milk and clear fluids.

The present results provide important insights for preoperative fasting guidelines. Although orange juice contains less protein than milk and no fat, no significant difference was observed in liquid gastric emptying after drinking either pulpless orange juice or milk as long as both had equivalent caloric content. These results indicate that liquid gastric emptying chiefly depends on total amount of calories (energy density) rather than compositional differences such as fat content, osmolality, or viscosity. A reason why differences in fat content exert a considerable impact on liquid gastric emptying can be explained in terms of its high energy density per gram. This result is supported by findings of previous studies performed under experimental and clinical settings. Neither a drink with milk added nor a drink consisting almost exclusively of milk should be routinely restricted for the simple reason that they contain milk. Hence, beverages available before surgery should be defined from the perspective of both caloric content and volume. As described above, 250–300 ml of water should leave the stomach in <30–60 min,\textsuperscript{6} which suggests that 600 ml of water should leave the

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3}
\caption{Changes in the antral CSA over time after ingesting one of the five different beverages. *$P<0.01$ significant difference between the M group and M+W group by the SNK multiple comparisons test; \#$P<0.01$ significant difference between the O+S group and O group by the SNK multiple comparisons test; \#*$P<0.01$ significant difference between the W group and the other groups by the SNK multiple comparisons test. Values are expressed as mean (SD) ($n=8$ in each group). W group: 500 ml of water (0 kcal), O group: 500 ml of 100% orange juice (220 kcal), O+S group: 450 ml of 100% orange juice +50 ml of gum syrup (total: 330 kcal in 500 ml), M group: 500 ml of non-human milk (330 kcal), M+W group: 330 ml of non-human milk +170 ml of water (total: 220 kcal in 500 ml).}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure4}
\caption{Changes in calculated gastric volume based on the measured antral CSA over time after ingesting one of the five different beverages. *$P<0.01$ significant difference between the M group and M+W group by the SNK multiple comparisons test; \#$P<0.01$ significant difference between the O+S group and O group by the SNK multiple comparisons test; \#*$P<0.01$ significant difference between the W group and the other groups by the SNK multiple comparisons test. Values are expressed as mean (SD) ($n=8$ in each group).}
\end{figure}
stomach within 120 min of ingestion. The ERAS group has encouraged preoperative carbohydrate loading with 400 ml of a 12.6% glucose solution, which is equivalent to about 200 kcal. We find that the average stomach volume after ingestion of 500 ml of fluid containing a caloric content equivalent to 220 kcal (the O and M+W groups) returned to baseline and was not significantly different from 500 ml of water at 120 min. In contrast, when ingesting 500 ml of fluid equivalent to 330 kcal (the O+S and M groups), the average stomach volume at 120 min was about 100 ml. Based on these results, ingestion of beverages meeting the following requirements up to 2 h before elective surgery appears to be acceptable: not exceeding 220 kcal in calories and 500 ml in volume. Under these conditions, patients can have a choice of milk tea, coffee with milk, and also cafe au lait, and beverages consisting almost exclusively of milk.

There are several limitations of this study. First, we evaluated stomach contents after ingestion of beverages using only one modality, ultrasonography. Ultrasonography was previously shown to be as good as scintigraphy, which is considered the gold standard for testing emptying of stomach contents. Furthermore, Bouvet and colleagues reported that ultrasonography was useful for evaluating stomach contents before emergency surgery. Simple, non-invasive ultrasonography has been attracting attention as a method that can be used to evaluate stomach contents and is considered to provide accurate data. Secondly, the subjects were both physically and mentally healthy. None had a complication that could influence gastric emptying or the presumed anxiety that accompanies the wait for surgery. In actual clinical settings, the majority of patients undergoing surgery are more likely to be elderly and have comorbidities. Considering these conditions, the results of the present study should not be applied to the general population undergoing anaesthesia and surgery. In addition, although the number of subjects (n=8) was small, the variability of the data was also small, which resulted in significant differences. Thirdly, gastric emptying rate of fluids is known to be regulated by several factors other than caloric content, for example, osmolality and viscosity; that have to be considered. Maughan and colleagues reported that while osmotic pressure affected gastric emptying rate, its influence was smaller than that of calories. Moreover, Murray and colleagues demonstrated that osmotic pressure did not strongly influence gastric emptying. Juvonen and colleagues showed that oat bran-enriched beverages with a lower viscosity were discharged from the stomach faster than those with higher viscosity. Although the difference in viscosity was very large (250 mPa s compared with >3000 mPa s), the difference in gastric emptying rate (measured by the blood level of acetaminophen) was only 1.1-fold greater. These studies indicate that osmolality and viscosity affect gastric emptying rate of fluids; however, these factors only have a small impact. In the present study, no significant difference was observed in liquid gastric emptying between the isocaloric groups regardless of an osmotic difference of over three-fold. Likewise, liquid gastric emptying in the O group and M+W group, whose energy contents were isocalorically adjusted, was not significantly different in spite of a difference in viscosity of over two-fold. Thus, it is reasonable to conclude that differences in osmolality and viscosity of orange juice and non-human milk had no practical impact on liquid gastric emptying. However, the results of the present study cannot be applied to other beverages with very high osmolality, viscosity, or both. Finally, we need to address the issue of changes from a liquid to a solid form depending on the type of beverage. Milk can coagulate in the acid environment in the stomach, which might delay gastric emptying. We did not observe a delay in gastric emptying in any case in the M and M+W groups, even when image patterns suggesting curdled milk. Although the amount of milk used in the present study (up to 500 ml) exerted little or no influence on gastric emptying rate, this issue remains unsolved when more milk is ingested.

In conclusion, the results of our study indicate that liquid gastric emptying chiefly depends on total amount of calories rather than compositional differences, while differences in fat content exert a considerable impact on the total amount of calories. Ingestion of beverages meeting the following requirements up to 2 h before elective surgery appears to be acceptable: not exceeding 220 kcal in calories and 500 ml in volume (except for beverages with very high osmolality, viscosity, or both). Further investigations should lead to simplification of preoperative fasting guidelines to permit more types of beverages before elective surgery, thereby allowing patients to have more choices according to dietary preferences.

Authors’ contributions
T.O. contributed to the study design, conduct of the study, data collection, data analysis, and manuscript preparation. H.T. contributed to the study design, data analysis, and helped with manuscript preparation. A.S. gave advice on drafting the manuscript.

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Declaration of interest
None declared.

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