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Gastric Emptying of a Carbohydrate-electrolyte Solution in Healthy Volunteers Depends on Osmotically Active Particles

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Abstract

Background: Preoperative ingestion of only clear fluids until 2 hours before induction of anesthesia is a common preoperative fasting regimen. Gastric emptying times, however, vary among clear fluids. We therefore investigated the gastric emptying of 2 clear glucose-electrolyte drinks.

Method: A 2-way crossover study was performed in 10 healthy volunteers. After fasting, the volunteers drank 500 mL of either OS-1®, an oral rehydration solution, or Pocari Sweat®, a popular sports drink, over 3 minutes in a standing position. Magnetic resonance imaging was performed before, immediately after, and 30 minutes after the drinking of each test fluid. The difference in gastric emptying between OS-1® and Pocari Sweat® was evaluated by comparing gastric fluid volume, flow rate, and residual ratio. We also compared the flow rates of sodium, potassium, carbohydrates, and osmotically active particles in the 2 test fluids.

Results: Gastric fluid volume 30 minutes after drinking was significantly smaller for OS-1® (76.0 ± 57.0 mL) than for Pocari Sweat® (158.1 ± 73.5 mL, p<0.01), although the volumes did not differ before or immediately after drinking. The flow rate was significantly faster for OS-1® (10.66 ± 3.34 mL) than for Pocari Sweat® (8.68 ± 3.02 mL/min, p<0.05), and the residual ratio was significantly smaller for OS-1® (21 ± 14% than for Pocari Sweat® (41 ± 19%, p<0.01). The flow rates of sodium, potassium, and glucose differed significantly between OS-1® and Pocari Sweat®, whereas the flow rate of osmotically active particles did not.

Conclusions: Gastric emptying is significantly faster for OS-1® than for Pocari Sweat®.
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Key words: gastric emptying, clear fluid, osmotically active particles

Introduction

Preoperative fasting is important in avoiding aspiration, a serious and even fatal complication during the induction of anesthesia. Strict preoperative fasting has been considered mandatory even if patients feel uncomfortable. Although preoperative fasting for 8 hours has been common practice in Japanese teaching hospitals[1], shorter fasting periods, 6 hours for meals and 2 hours for clear fluids, are used in the United States and Europe[2,3]. Evidence obtained in Japanese patients for the safety of these shorter fasting periods[4] led the Japanese Society of Anesthesiologists to adopt guidelines for preoperative fasting[5] comparable with European and American guidelines. Patients scheduled to undergo surgery are therefore allowed clear fluids until 2 hours before induction of anesthesia.

A clear fluid is defined as a nonparticulate fluid without fat, e.g., water, tea, or coffee with or without milk[2,3]. Many glucose-electrolyte solutions, regarded as clear fluids, are commercially available as sports drinks; these solutions have different caloric contents, osmolarity, and concentrations of ingredients. The gastric emptying rates of clear fluids have been found to differ[6–10], as have the gastric emptying rates and gastric residual volumes of glucose-electrolyte solutions. We therefore evaluated the gastric emptying rates of 2 clear carbohydrate-electrolyte solutions commonly available in Japan: OS-1®, which was developed for oral rehydration therapy; and Pocari Sweat®, a popular sports drink.

The mechanism responsible for the gastric emptying rate of clear fluids is poorly understood, although differences in gastric emptying rates have been observed[10–13]. Both OS-1® and Pocari Sweat® were both designed to be nearly isotonic but differ from each other in their caloric contents and concentrations of ingredients. We analyzed factors influencing their gastric emptying rates, focusing on the content and osmolarity of each fluid. Osmolarity is defined as the number of osmoles of solute per liter of solution. In this study, we used the term "osmotically active particles" for the solute, with an osmole being a unit of osmotic pressure equivalent to the amount of solute that dissociates in solution to form 1 mole (Avogadro's number) of particles (molecules and ions).

To determine gastric fluid volume (GFV), we used magnetic resonance imaging (MRI). Although scintigraphy is the gold standard for studying gastrointestinal functions, MRI has been shown to be a reliable means for measuring the gastric emptying of solid and fluid meals comparably with scintigraphy[14,15]. Furthermore, MRI is regarded as a noninvasive method that does not expose subjects to ionizing radiation[16].

In this 2-way cross-over study, we compared GFV and gastric emptying rate, measured with MRI, of OS-1® and Pocari Sweat® in 10 healthy volunteers. We also analyzed factors influencing gastric emptying rate, focusing on the content and osmolarity of each fluid.

Materials and Methods

The 10 subjects (5 men and 5 women) were healthy volunteers, aged 20 to 50 years, with a body weight ≥ 45 kg, a body-mass index of 18 to 30 kg/m², no gastrointestinal abnormalities, no history of abdominal surgery, and not taking any medications. Volunteers with contraindications to the use of MRI were excluded. Informed written consent was obtained from each volunteer before enrollment, and the study protocol was approved by the Ethics Committee of Nippon Medical School Hospital, Tokyo, Japan (approval #22-01-99), in January 2010 and was performed from October 2010 through August 2011 according to the principles of the Declaration of Helsinki of the World Medical Association (http://wma.net).

Protocol

This was a 2-way crossover study performed at an interval of at least 1 week. The test began at 3 or 4 p.m. Subjects were asked to start fasting at 9 or 10 a.m. but were allowed to drink clear fluids until 1 hour before the test. There were no dietary restrictions before fasting. Each subject drank 500

Table 1   main contents of OS-1® and Pocari Sweat®

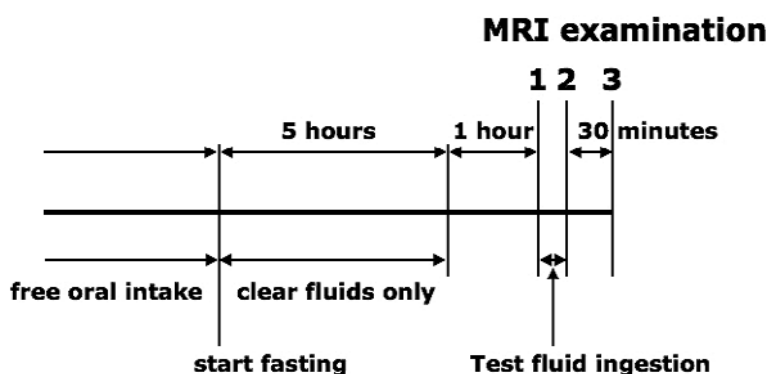|	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	Carbohydrate (g/L)	Osmolarity (mOsm/L)
OS-1®	50	20	50	25	270
Pocari Sweat®	21	5	17	62	340

PROTOCOL

Fig. 1   Time course of the experimental protocol. Subjects who started fasting at 9 a.m. ingested test fluids at 3 p.m. Subjects who started fasting at 10 a.m. ingested test fluids at 4 p.m.. 1: before test fluid ingestion, 2: immediately after test fluid ingestion, 3: 30 minutes after test fluid ingestion.

mL of OS-1® (Otsuka Pharmaceutical Factory Inc., Tokushima, Japan) or Pocari Sweat® (Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan) over 3 minutes while standing. The contents of OS-1® and Pocari Sweat® are shown in **Table 1**, and the protocol is shown in **Figure 1**.

Each subject underwent MRI 3 times during each test: before, immediately after, and 30 minutes after drinking the test fluids. The subjects lay on the scanner bed between the second and third MRI examinations.

Measurement of GFV

The GFV was measured with MRI on an Achieva 1.5-T scanning system (Royal Philips Electronics, Amsterdam, The Netherlands), with results assessed using the ViewForum R5.1 computing system (Royal Philips Electronics). The MRI protocol was gradient echo: balanced fast field echo; scan mode: 3 dimensions; echo time: 2.1 milliseconds; time to repetition: 4.2 milliseconds; slice thickness: 2 mm; number of slices: 70 to 100; fat suppression: spectral selection attenuated inversion recovery; number of

signal averages: 1, respiratory compensate: trigger; and coil: SENSE™ body coil.

The anatomical precision of the images constructed in the stomach was confirmed by an anesthesiologist and a radiological technologist, with each image obtained in the coronal, transverse, and sagittal planes. Following confirmation, the GFV was calculated automatically.

Evaluation of Gastric Emptying

Differences in gastric emptying between OS-1® and Pocari Sweat® were evaluated by comparing GFV throughout the protocol. We also calculated the flow rate, a marker of ease of elimination, and the residual ratio, a marker of the effect on change of GFV, using the following equations:

$$\text{flow rate} = (\text{volume}_s - \text{volume}_p)/\text{elimination time}$$
$$\text{residual ratio} = (\text{volume}_p/\text{volume}_s) \times 100$$

where volume_s (mL) indicates GFV immediately after ingestion; volume_p (mL) indicates GFV 30 minutes after ingestion; and elimination time (minutes) indicates the time between the beginnings of the second and third MRI examinations.

Table 2　Demographic data of subject

Age (years)	Height (cm)	Body Weight (kg)	Body-mass index (kg/m²)
32.1 ± 5.1	165.1 ± 9.2	60.6 ± 12.6	22.1 ± 3.1

mean ± sd

To explore factors affecting the elimination of clear fluids, the flow rates of sodium, potassium, carbohydrates in calorie, and osmotically active particles were calculated, using the following equation:

flow rate = concentration of a solute × (volume$_s$ − volume$_p$)/elimination time

Statistical Analysis

Two-way analysis of variance for repeated measurements was used to compare GFV following the ingestion of OS-1® and Pocari Sweat® throughout the protocol. Post-hoc analysis was performed with the Bonferroni test. Wilcoxon signed rank tests were used to estimate flow rates, residual ratios, and factors affecting them following the ingestion of OS-1® and Pocari Sweat®. All results are presented as mean ± SD. A *P*-value less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed using GraphPad Prism version 5.0b for Macintosh (GraphPad Software Inc., San Diego, CA, USA).

Results

Ten subjects were enrolled in this study; their demographic characteristics are shown in **Table 2**. The mean times between the completion of drinking and the start of MRI examination were similar between OS-1® (5.9 ± 1.7 minutes) and Pocari Sweat® (5.3 ± 1.1 min, P>0.05), as were the durations of MRI examinations (5.5 ± 3.6 minutes for OS-1® and 5.6 ± 2.6 minutes for Pocari Sweat®, P>0.05). The 3-directional MRI images showing gastric fluid were well constructed **(Fig. 2)**, and the GFV was calculated on the basis of these images. Immediately after the drinking of 500 mL of OS-1® and Pocari Sweat®, the residual volumes decreased by 120 to 150 mL.

We observed a significant difference in GFV 30 minutes after ingestion, whereas the GFVs before and immediately after ingestion did not differ significantly **(Table 3)**. The time course of change in GFV significantly differed between OS-1® and Pocari Sweat® (p<0.05, F(2, 36)= 3.51). The gastric emptying flow rate was significantly faster for OS-1® (10.66 ± 3.34 mL/min) than for Pocari Sweat® (8.68 ± 3.02 mL/min, P<0.05; **Fig. 3**), and the residual ratio was significantly smaller for OS-1® (21 ± 14%) than for Pocari Sweat® (41 ± 19%, P<0.01; **Fig. 4**). The residual ratio was smaller for OS-1® than for Pocari Sweat® in each subject **(Fig. 5)**. The flow rates of sodium, potassium, and glucose differed significantly for OS-1® and Pocari Sweat®, whereas the flow rates of osmotically active particles did not **(Table 4)**.

Discussion

We found that the gastric emptying flow rate was significantly faster for OS-1® than for Pocari Sweat®. Analysis of the flow rate of each ingredient showed that gastric emptying was adjusted to keep the flow rate of osmotically active particles constant. Sodium, potassium, and glucose were not independent controllers of gastric emptying. Rather, our findings suggest that each ingredient is integrated as osmotically active particles to adjust the gastric emptying of clear fluids. The flow rate of osmotically active particles is likely maintained at approximately 3.0 mOsm/min.

One study has found that the relative percent change in GFV of clear water decreases monotonically for 60 minutes[17]. In that study, GFV was measured with MRI every 10 minutes for 1 hour after ingestion of clear water, and the 50% and 75% reduction times of GFV were 18 ± 9 minutes and 24 ± 3 minutes (mean ± SD), respectively. We evaluated changes in GFV by measuring this variable immediately after ingestion and approximately 30 minutes after ingestion. In
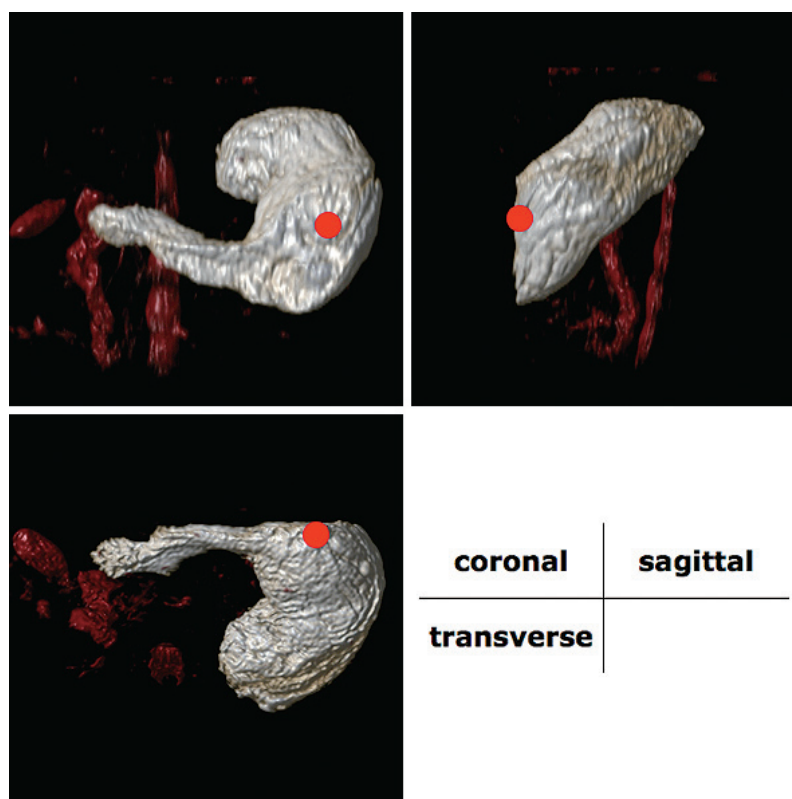
Fig. 2 MRI determination of the GFV. Patients were examined in the supine position, with fluid detected in the 3-directional images. The surface level of fluid is indicated by a red circle in each image.

Table 3 Gastric Fluid Volume

	before drinking	immediately after drinking	30 min after drinking[a]
OS-1®	24.0 ± 15.7	348.0 ± 80.0	76.0 ± 57.0
Pocari Sweat®	25.8 ± 14.5	388.6 ± 44.7	158.1 ± 73.5

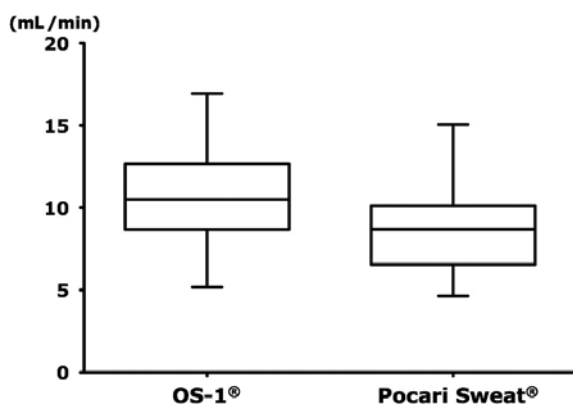[a]: $p < 0.01$ (OS-1® vs Pocari Sweat®), mean ± sd (mL)

Fig. 3 Flow rates of gastric emptying of clear fluid, as determined with MRI. The rate was significantly faster for OS-1® (10.66 ± 3.34 mL/min) than for Pocari Sweat® (8.68 ± 3.02 mL/min, $p < 0.05$).
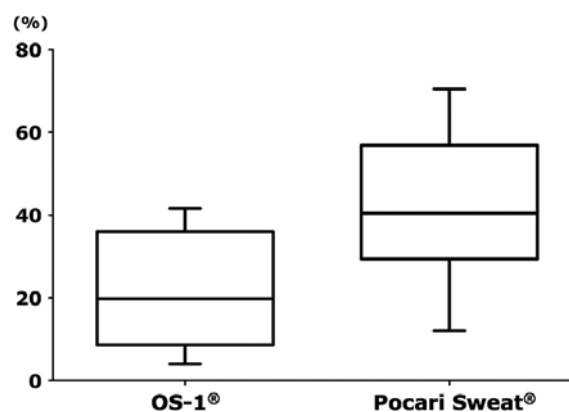

Fig. 4 Residual ratios of GFV for OS-1® and Pocari Sweat®. The ratio was significantly smaller for OS-1® (21 ± 14%) than for Pocari Sweat® (41 ± 19%, $p < 0.01$).

comparison, the mean time for 50% gastric emptying of a 10% dextrose solution was approximately 25 minutes and showed a monoexponential time course[18]. These findings suggest that the residual ratios at 30 minutes of clear water and of 10% dextrose solution were 5% to 10%[17] and approximately 50%[18], respectively. We found that the residual ratios at 30 minutes were 21 ± 14% for OS-1[®] and 41 ± 19% for Pocari Sweat[®]. Thus, our 2 sampling points for GFV, separated by 30 minutes, could be considered to be included in the monoexponential and linear phases of gastric emptying.

The interval between the completion of the drinking of the test fluids and the start of MRI examination and the duration of each MRI examination were each 5 to 6 minutes. If these time periods are considered, the residual volume immediately after the drinking of the test fluids was consistent with previous findings showing that following the ingestion of 750 mL of 120 mM NaCl, 200 to 500 mL was eliminated from the stomach

Fig. 5 Residual ratios of individual volunteers. Squares represent OS-1[®], and triangles represent Pocari Sweat[®]. The data for each individual are connected with a line.

within 5 minutes[19].

The mechanism of the gastric emptying of fluids is strikingly different from that of solids. The antrum determines the rate of the gastric emptying of solids by its grinding and trituration of large solids into smaller particles. The pylorus prevents solid particles from entering the duodenum until they have been triturated into particles 2 to 3 mm in size. The process is regulated by the stomach and duodenum. The vagal and enteric nerves[20], and hormones such as cholecystokinin and secretin[12,21], stimulate the duodenum to provide feedback to the stomach to increase pyloric pressure and to decrease antral contractility[20,22].

In contrast, ingested fluids are rapidly distributed throughout the entire stomach, rather than staying in the fundus. The emptying of fluids begins immediately, either monoexponentially[13,18,19] or linearly[9,14,17], in response to the fundal pressure gradient. The duodenum continues to provide feedback to the stomach when fluids are ingested. Carbohydrates[7,9,23] and triglycerides[24,25] in the duodenum inhibit gastric emptying. Duodenal glucose infusion inhibits gastric emptying as a function of the log of the number of calories[9]. Gastric emptying of glucose solutions is regulated by a negative-feedback or a closed-loop system involving the stomach and duodenum[23]. When solutions of 3 different glucose concentrations (0.05, 0.125, and 0.25 g/mL) were introduced through the gastric tube by gravity, the gastric emptying rates, expressed as the rate of glucose in calories, were similar, with a mean overall rate of 2.13 ± 0.08 kcal/min[23]. The same study evaluated the effect of direct glucose infusion into the duodenum on gastric emptying of physiological saline. Regardless of the volume or concentration of glucose, the gastric emptying of physiological saline was maintained at 0.46 ± 0.04 minute per intraduodenal glucose calorie[23]. These findings

Table 4   The flow rate of each content of OS-1[®] and Pocari Sweat[®]

	Na (mEq/min)[a]	K (mEq/min)[a]	Carbohydrate calories (kcal/min)[a]	Osmotically active particles (mOsm/min)
OS-1[®]	0.53 ± 0.17	0.21 ± 0.07	1.07 ± 0.33	2.88 ± 0.90
Pocari Sweat[®]	0.18 ± 0.06	0.04 ± 0.02	2.15 ± 0.75	2.95 ± 1.03

[a]: p<0.01 (OS vs PS), mean ± sd

suggest that there is a steady state of the balanced outcome of 2 reciprocally interdependent functions, gastric delivery and its postpyloric inhibition, and that a closed-loop system regulates the flow of glucose in calories[23].

We calculated the flow rate of gastric elimination of each ingredient of OS-1® and Pocari Sweat® to determine factors regulating gastric emptying. There were significant differences in the flow rates of sodium, potassium, and calorie of carbohydrate between OS-1® and Pocari Sweat®, whereas the flow rates of osmotically active particles were similar, 2.88 ± 0.90 mOsm/min and 2.95 ± 1.03 mOsm/min, respectively. These findings suggest that the gastric emptying of clear fluids is regulated to maintain the flow of osmotically active particles constant, at approximately 3 mOsm/min.

Although glucose has been found to regulate the gastric emptying of liquids[7,23,26] via a closed-loop system[23], the regulated flow of glucose in calories was not observed in the present study. Other factors have been proposed, including triglycerides[24,25] and osmolality[7,27], and our results suggest that osmotically active particles are another possible regulatory factor. The discrepancies may be due to differences in tested solutions. The test solutions in previous studies were made of anhydrous (or monomeric) glucose and distilled water only[7,23]. One study, which used solutions containing electrolytes, suggests that glucose regulates gastric emptying and that osmolality has a limited effect[26]. Although they differed from our present findings, previous findings suggest the involvement of osmolality in the gastric emptying of liquids containing electrolytes[26]. Electrolytes, such as sodium and potassium, do not appear to be factors in the regulation of gastric emptying[28], whereas osmolality may affect gastric emptying in the presence of electrolytes. Further studies are required to determine the mechanism underlying gastric emptying of clear fluids, such as glucose-electrolyte solutions.

In conclusion, gastric emptying is significantly faster for OS-1® than for Pocari Sweat®, with the rate regulated to keep the flow of osmotically active particles constant, at approximately 3.0 mOsm/min. The mechanisms by which clear fluids are sensed in the stomach and duodenum remain unknown. Further investigations are required to determine the mechanism of the gastric emptying of clear fluids.

Conflict of Interest: The authors have no conflict of interest to declare.

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