Improved Gastric Emptying Rate in Humans of a Unique Glucose Polymer with Gel-forming Properties

J. B. Leiper, K. Piehl Aulin & K. Söderlund
Dept. of Biomedical Sciences, Aberdeen University, Aberdeen, UK, and Dept. of Medical Science, University of Uppsala/LIVI, Falun, and Dept. of Physiology and Pharmacology, Karolinska Institute/Stockholm University College of Physical Education and Sports, Stockholm, Sweden


Background: The energy density of a nutrient drink is one of the main factors that affect the gastric emptying of the solution, while osmolality and viscosity are thought to have only a minimal influence.

Method: The rate of gastric emptying of two isoenergetic carbohydrate solutions with different osmolality and viscosity was determined using a double sampling gastric aspiration technique. Six healthy male subjects were studied on two occasions using approximately 550 ml of a solution containing 13.5% of carbohydrate either in the form of a mixture of monomeric glucose and short chain glucose oligomers (G-drink) or of long chain glucose polymers composed of 78% amylopectin and 22% amylose (C-drink).

Result: The half emptying time ($t_{1/2}$, median and range) for the viscous, markedly hypotonic (62 mosmol/kg) C-drink was faster (17.0 (6.2–31.4) min) than for the moderately hypertonic (336 mosmol/kg) G-drink (32.6 (25.2–40.7) min). The amount (median and range) of carbohydrate delivered to the small intestine was greater during the first 10 min after ingestion of C-drink (31.8 (15.8–55.9) g) than after ingestion of G-drink (14.3 (6.8–22.2) g). However, there was no difference in the blood glucose ($P = 0.73$) or serum insulin ($P = 0.38$) concentration at any time point after ingestion of the two test drinks.

Conclusion: The results of this study show that the carbohydrate present in C-drink, although it has the propensity to form a gel, empties from the stomach faster than that of an isoenergetic carbohydrate solution (G-drink) without potentiating increased circulating blood glucose or insulin levels.

Key words: Carbohydrates; energy density; gastric emptying; glucose; osmolality

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had a higher osmolality than that of C-drink. However, the effect of osmolality of carbohydrate solutions at the concentration used (13.5%) is not thought to markedly affect gastric emptying (11), and the high viscosity of C-drink would be expected to retard gastric emptying (14, 15).

The present investigation examined the rate of gastric emptying of isovolemic, isoenergetic solutions containing either Carbamyl or Glucidex as the sole carbohydrate.

Materials and Methods

A double sampling gastric aspiration technique was used to measure gastric emptying rate (16). Six healthy male subjects with no history of gastrointestinal or metabolic disease were enrolled for the study. Their physical characteristics were (median (range)); age, 23 years (20–27 years); height, 1.80 m (1.73–1.93 m) and body mass, 81 kg (64–83 kg). As a preliminary to the main trial, all potential subjects were initially screened to establish six individuals who could be successfully intubated with the oro-gastric tube. During these processes, the successful subjects underwent the major part of the protocol in order to establish the correct positioning of the tube in the stomach and to familiarize the subjects with the experimental procedures. Subjects gave their informed, written consent before participating in the study: the ethics committee of the Karolinska Institute, Sweden where the study was carried out approved the experimental protocol, which was in accordance with the Declaration of Helsinki.

The test carbohydrates used were Carbamyl PU 24-002 (Carbamyl AB, Kristianstad, Sweden), a potato based glucose polymer, with a mean molecular weight of between 500,000 and 700,000, consisting of 78% amylopectin and 22% amylose, and Glucidex IT 38 (Roquette Freres, Lille, France), a mixture of 15% dried glucose syrup, 13% disaccharides and 72% higher polysaccharides, with a mean molecular weight of 500, derived from maize starch. The two test solutions studied consisted of 75 g of carbohydrate in the form of either Carbamyl or Glucidex made up in 500 ml of tap water. This resulted in a similar total median (range) ingestion volume for the test drink; the Glucidex 62.0 (60–64) ml and the Carbamyl 62.0 (60–64) ml.

The test solutions contained 20.0 ± 0.1 mg/l (mean ± s) phenol red as an essentially non-absorbed marker (17). The temperature of the solutions was essentially the same on both treatments and ranged from 19 to 21 °C. Solutions were injected into the stomach via the oro-gastric tube using two 60-ml catheter tip syringes (Beckton Dickinson Ltd, Cowley, UK). The syringes were used in order to ensure that the viscous C-drink would be rapidly transferred into the stomach; this procedure was completed within 60 sec for all test solutions. Although the test solutions were injected into the stomach, this will be referred to as ingestion.

Gastric emptying was measured using the method described by Beckers et al. (16). This technique is described here only briefly. A small sample of the test solution was collected before beginning the test. Immediately before the test solution was ingested, the residual content of the washed stomach was removed as completely as possible by aspiration. As soon as all the test solution had been ingested, the contents of the stomach were mixed using a 60-ml syringe to aspirate and immediately re-inject 20–30 ml at least 10 times; mixing took approximately 1 min. A sample (2.5 ml) of the gastric aspirate was then taken so that the volume of gastric residue before ingestion of the test solution could be calculated. Nine min after ingestion of the test drink, the gastric contents were mixed as before and a sample (2.5 ml) aspirated. Ten min after ingestion of the test drink, 5 ml of a 250 mg/l phenol red dye solution was added, and the contents mixed again before a second sample (2.5 ml) was aspirated at 11 min after ingestion. The volumes calculated from these two samples are referred to as those of the 10 min sample point. From the concentration of dye in the samples, the total volume in the stomach and the volume of test solution remaining at these times were calculated. The difference between the total gastric volume and the volume of test solution is the volume of gastric secretion and swallowed saliva. This procedure was repeated at 10-min intervals for a period of 60 min after ingestion of the test solution. The
concentration of phenol red in the 5-ml aliquot added at the 40 min and subsequent sampling points was increased from 250 to 500 mg/l to improve the sensitivity of the method (11). At the end of this period, 100 ml of distilled water was injected into the stomach, the contents mixed and removed by aspiration. The gastric volume at the end of the study was calculated from the concentration of dye in the aspirated wash solution: this procedure was used as a check of the final gastric volume as calculated by the method of Beckers et al. (16) and to check that the gastric tube was still correctly positioned. Phenol red was analysed spectrophotometrically after dilution (1:20) with NaOH–NaHCO₃ buffer (250: 500 mmol/l, pH 9.7), and osmolality was measured by freezing point depression (Roeblin model 13 Osmometer; Labex AB, Helsingborg, Sweden).

The quantity of energy delivered to the small intestine was calculated by multiplying the amount of carbohydrate (in grams) that was contained in the volume of test meal emptied from the stomach by the energy content of 1 g of carbohydrate (17.22 kJ).

Blood samples were obtained from an antecubital vein via an indwelling cannulae (Venflon 2 18G/32 mm; BOC Ohmeda AB, Helsingborg, Sweden): 5 min after insertion of the cannula a blood sample was collected (basal 1) and 5 min later a further blood sample was collected (basal 2). Additional blood samples were collected at 2, 5, 10, 15, 20, 30, 45 and 60 min after ingestion of the test drinks. Blood glucose concentration was measured on the whole blood immediately on collection using a dry chemistry technique (Accutrend alpha; Roche Diagnostics Scandinavia AB, Bromma, Sweden). Serum samples were collected by centrifugation from the clotted blood. Serum osmolality was measured on the day of collection (Roeblin model 13 Osmometer); aliquots of the serum were frozen at −20°C for later determination of insulin levels by radioimmunossay (RIA kit 52-1797-07; Pharmacia-Upjohn, Stockholm, Sweden) and albumin by a dry chemistry technique (Vitros 250; Johnson & Johnson, Stockholm, Sweden).

Statistical analysis

Initially the distribution of the data was examined using a normal probability plot and the derived correlation coefficient. All the gastric emptying, and blood glucose, serum insulin and serum albumin data were found not to be normally distributed, while serum osmolality data were essentially normally distributed. The data, which were not normally distributed, were analysed using the Friedman non-parametric two-way analysis of variance with factors for subjects, treatment and period in the model, or the Kruskal–Wallis non-parametric one-way analysis of variance with factors for subjects and treatment only when this was more appropriate. Where applicable, pairwise differences were assessed using Wilcoxon matched-pair signed ranks test. Where the assumption that the data were normally distributed was reasonably met, statistical analysis was carried out using a repeated measures analysis of variance (ANOVA) test with factors for subjects, treatments and period in the model, or with factors for subjects and treatment in the model where this was more appropriate. Where applicable, this was followed by application of the Tukey multiple range test to assess any differences between treatments. All tests were two-tailed and the conventional 5% level was used to determine statistical significance. Normally distributed data are reported as mean ± s, while non-parametric data are described as median with the range of minimum and maximum values.

Results

The total volume of fluid in the stomach at any time includes not only the ingested test solution, but also any residual fluid, gastric secretions and swallowed saliva. Immediately after ingestion of the test solutions the total volume in the stomach (Table I) was similar on both trials. Over the 60-min period of measurement, the total volume remaining in the stomach was greater after ingestion of G-drink than after ingestion of C-drink ($P = 0.002$). Differences between the total stomach volumes on both trials were evident within 20 min of ingestion ($P = 0.046$) and these differences remained until the 50 min sampling point ($P = 0.031$). At the end of the period of measurement, although the volume remaining in the stomach appeared less on the C-drink trial than the G-drink trial, no difference could be detected ($P = 0.093$). The total gastric volume at the end of the study was essentially the same whether calculated from the concentration of dye in the aspirated wash solution or by the method of Beckers et al. (16) on both the C-drink trial (101 (8–230) and 94 (8–232) ml, respectively; $P = 0.87$) and G-drink trial (191 (157–281) and 197 (161–277) ml, respectively; $P = 0.52$).

The test drink volume remaining in the stomach is calculated separately to that of the total stomach volume and is shown in Fig. 1. While the test solution C-drink emptied from the stomach exponentially, G-drink followed a more linear pattern. The rate of gastric emptying of C-drink was faster than that for G-drink ($P = 0.001$). Differences between the two solutions were evident within 10 min of ingestion ($P = 0.045$) and these differences remained throughout the
rest of the measurement period. The time to empty half of the test solutions ($t_{1/2}$) from the stomach was calculated following logarithmic linearization of the data. The median (range) $t_{1/2}$ for C-drink was 17.0 (6.2–31.4) min which is substantially faster ($P = 0.013$) than that for G-drink (32.6 (25.2–40.7) min).

The median (range) rate of delivery of carbohydrate, and hence energy, to the small intestine was similar over each 10-min period following ingestion of G-drink, but not when C-drink ($P = 0.008$) was ingested (Fig. 2). Over the initial 10-min period after ingestion, the rate of carbohydrate delivery to the small intestine was faster from C-drink than from G-drink ($P = 0.031$), thereafter the rates were similar for the two solutions ($P = 0.24$). The cumulative delivery of carbohydrate to the small intestine was therefore greater ($P = 0.005$) from C-drink than from G-drink.

The disparity in the amount of carbohydrate delivered to the small intestine was not reflected by any difference in blood glucose or serum insulin or albumin levels between the trials (Table II). There were large inter-individual differences in the measured circulating levels of glucose, insulin and albumin on both trials that may have obscured any real differences in response to the two different drinks.

Serum osmolality remained essentially the same throughout both the C-drink and G-drink trials (Fig. 3), and there was no difference between trials. The osmolality of gastric aspirates following ingestion of the C-drink solution increased while those following ingestion of the G-drink solution decreased (Fig. 4).

Table II. Median (range) blood glucose, serum insulin and albumin levels measured on both trials

<table>
<thead>
<tr>
<th>Time</th>
<th>Basal 1</th>
<th>Basal 2</th>
<th>2 min</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>20 min</th>
<th>30 min</th>
<th>45 min</th>
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<tr>
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<td>C-drink</td>
<td>5.3</td>
<td>5.3</td>
<td>5.3</td>
<td>5.5</td>
<td>6.0</td>
<td>6.6</td>
<td>7.1</td>
<td>7.8</td>
<td>8.7</td>
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<td>(5.1–6.7)</td>
<td>(5.3–7.2)</td>
<td>(5.6–7.8)</td>
<td>(6.0–8.9)</td>
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<td>(5.4–13.1)</td>
<td>(4.3–13.0)</td>
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<tr>
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<td>5.4</td>
<td>5.2</td>
<td>5.4</td>
<td>5.9</td>
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<td>7.4</td>
<td>7.9</td>
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<td>(4.7–5.9)</td>
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<td>(5.6–8.0)</td>
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<td>6.8</td>
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<td>36.0</td>
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<td>7.0</td>
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<td>29.0</td>
<td>40.0</td>
<td>47.5</td>
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<td>Serum albumin (g/l)</td>
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<td>41</td>
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<tr>
<td>G-drink</td>
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Discussion

The present study has shown that a markedly hypotonic carbohydrate solution emptied faster from the stomach than an equal volume of an isoeenergetic carbohydrate solution with a higher osmolality. Although there were significant differences in the rate of emptying and hence the rate of carbohydrate delivery to the small intestine, there were no differences in the circulating levels of glucose, insulin or albumin between the two trials.

Water and dietary nutrients are absorbed primarily in the proximal region of the small intestine. The function of the stomach is to act mainly as a reservoir that allows a regulated amount of the ingestate to be delivered to the absorptive surface of the small intestine. Therefore, the rate of emptying of the gastric contents affects how quickly absorption occurs.

The energy density of the stomach contents is normally the main regulator of the emptying rate of similar volumes of nutrient solutions (5, 7–9, 11). The emptying rate of the 13.5% carbohydrate solution G-drink is of the order that would be expected for a relatively high energy solution (12), while that for the isoeenergetic C-drink was markedly faster. The effect of osmolality in the control of gastric emptying is usually marginal in carbohydrate solutions until the carbohydrate concentration is about 15% and the difference in osmolality of isoeenergetic solutions is in the order of 600–1000 mosmol/kg (11, 18–20). It is therefore surprising that C-drink, containing 13.5% carbohydrate as Carbamyl was emptied significantly faster from the stomach than the isoeenergetic G-drink when the average difference in osmolality between the solutions was only 275 mosmol/kg.

In addition, the greater viscosity of C-drink might have been expected to retard gastric emptying (14, 15). The incorporation of gel-forming carbohydrates such as pectin and guar gum to glucose solutions increases the viscosity of the fluids and normally slow the rate of gastric emptying (15, 21). This effect is generally thought to be due to a direct effect of greater force being required to evacuate a semi-solid gel from the stomach, and indirectly as the result of feedback inhibition caused by a slowing of intestinal absorption of glucose (15). However, others have demonstrated that the gastric emptying rates of semi-solid carbohydrate solutions are not all slowed in proportion to their viscosity, and that other related physical properties are more important (22, 23).

In one study, treatment of a starch paste with +amylase shortened the emptying time compared with an isoeenergetic glucose solution (23). This suggests that the rate at which carbohydrate polymers are hydrolyzed and absorbed in the intestine has a greater bearing on gastric emptying than the purely mechanical effect of viscosity.

Others have shown that the type of starch present in a carbohydrate meal can modulate gastric emptying (24) and hence affect the glycaemic response of carbohydrates. In the study of Mourot et al. (24), the rate of gastric emptying was fastest for potato, then bread, then rice, and slowest for spaghetti. These authors suggested that the differences in emptying rates were related to properties of the specific varieties of starch present in the carbohydrate meals rather than to variations in the energy density, meal volume or protein content of the ingested food. Interestingly, the carbohydrate present in C-drink was derived from potato starch while that present in G-drink was produced from maize starch.

At present it is not known how gastric emptying is regulated such that solutions of equal energy content empty at similar rates irrespective of whether the energy source is carbohydrate, protein or fat (2, 25). Although it is widely accepted that the receptors responding to energy density lie outside the stomach, it is not known whether they are positioned on the luminal or serosal side of the small intestine, or whether they respond to the same stimulus for each nutrient (25). While hyperglycaemia can slow gastric emptying and hypoglycaemia accelerate the emptying of
meals, the circulating levels of insulin, motilin, glucagon, gastrin, neuroepitope Y or somatostatin do not appear to have major effects on the regulation of gastric emptying (26). No other hormone or gastrointestinal peptide has as yet been identified as the equivocal regulator of gastric emptying of all energy sources. It is possible that the presence of nutrients at the brush border or in the portal blood is the main stimulus regulating gastric emptying of ingested food.

The rate at which nutrients are digested and transported across the intestinal mucosa may play an important role in regulating gastric emptying. The rapid rate of gastric emptying of C-drink could be related to the glucose polymer composition present having a faster rate of intestinal absorption, and hence more rapid removal of the nutrient from the luminal surface, compared to that of the carbohydrate present in G-drink. However, the gel-like properties of Carbamyl would tend to decrease the velocity at which this polymer would reach the hydrolytic enzymes bound to the intestinal villi (27) and would therefore tend to delay digestion and absorption. Another possibility is that it is a viscosity-related slowing of the rate of diffusion that delays the interaction between the carbohydrate emptied from the stomach and the brush border binding sites of the hydrolyzing enzymes or glucose transporters (28). Such an effect might mask the nutrient content of an ingested solution and allow an initial rapid rate of gastric emptying: as emptying continued the carbohydrate content in the duodenum would rise, eventually leading to an increase in the concentration gradient that could overcome the inhibitory effect on diffusion and trigger the feedback inhibitor loop to the stomach that would cause the emptying rate to slow. However, as liquids empty from the stomach faster than solids (3), gastric emptying rate is not always proportional to the viscosity of the stomach contents (22, 23) and increasing viscosity usually slows gastric emptying (14, 15). It is unlikely that the latter postulated mechanism is an important regulator of normal gastric emptying.

The other perplexing finding in the present study was that no difference could be shown in circulating levels of either glucose or insulin between the two trials. Within 10 min of ingestion approximately 50% of the total carbohydrate content of C-drink was emptied into the duodenum while less than 20% had been delivered by G-drink. As the subsequent rates of carbohydrate delivery every 10 min were similar from both solutions, although the volume of C-drink in the stomach was significantly less than that of G-drink, it is unlikely that there was a substantial amount of Carbamyl remaining unabsorbed in the small intestine. The similarity in circulating albumin concentrations between the two trials would suggest that there was no difference in the blood volume that could mask an increase in total content of circulating glucose or insulin levels. In addition, the rate of restoration of muscle glycogen levels was faster when this same Carbamyl solution was ingested following heavy glycogen-depleting exercise than when a similar amount of Glucidex was consumed (13). This suggests that a greater amount of carbohydrate was absorbed and transported to the muscles on the Carbamyl trial compared with the Glucidex trial. Therefore, it must be assumed that the lack of a difference in circulating glucose levels between the two trials in the present study is not due to a slower rate of intestinal absorption of Carbamyl. Bornet et al. (22) suggested that the glycaemic index of carbohydrate solutions was determined more by the rate of hydrolysis of the carbohydrates than by the gastric emptying rate or viscosity of these solutions. They found small, but significant, differences in the gastric emptying rate of their isoenergetic starch solutions, but no difference could be detected in the glycaemic and insulinaemic responses between the starch solutions, although these responses were lower than that produced by an isoenergetic glucose monomer solution. In the present study, while a slower rate of hydrolysis of the carbohydrate present in C-drink than in G-drink could promote a faster rate of gastric emptying of C-drink it cannot explain the faster rate of glycogen re-synthesis that occurs with C-drink.

If some of the Carbamyl solidified within the stomach and became effectively insoluble soon after ingestion, this would have given the appearance of a rapid exit of the solution equivalent to the volume of beverage, and hence amount of phenol red, that had solidified. This is thought unlikely, although the C-drink required greater effort to mix and aspirate compared with the G-drink no blockages were ever encountered. In addition, during the washout procedure at the end of each study, some of the solidified material is likely to have dissolved in the distilled water wash, resulting in an apparent increase in the measured total volume in the stomach compared to that calculated by the method of Beckers et al. (16): no such differences were seen between these two methods of estimating the final volumes. The fact that C-drink enhances post-exercise glycogen re-synthesis, suggesting a rapid rate of absorption of the carbohydrate present in this drink also argues against the result of the present study being an artefact.

The present study suggests that Carbamyl is a unique carbohydrate polymer that empties from the stomach at a rate that is faster than would be expected from its energy density without potentiating a greater increase in circulating levels of glucose or insulin compared with that elicited by an isoenergetic carbohydrate that is emptied more slowly. While the hypotonicity of the Carbamyl containing drink may have contributed to its rapid emptying rate it is unlikely to be the main factor.

Acknowledgements

We would like to thank Professor R. J. Maughan for suggesting this study, and Carbamyl AB, Kristianstad, Sweden, and Roquette Freres, Lille, France, for kindly donating the carbohydrates used in this study.
References


