Ingestion of a large volume of water disturbs fructose absorption in young healthy women

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1. Introduction

High fructose corn syrup (HFCS) was developed industrially as an alternative to sucrose in the USA and came into wide usage during the period between 1970 and 1985. In Japan, the consumption of HFCS has been increasing since 1980, while that of sucrose has decreased. The most common use of HFCS is in soft drinks. Many studies have shown the relation between the intake of high-fructose-containing beverages and fructose malabsorption. High amounts of fructose often induce gastrointestinal symptoms, such as bloating, abdominal pain, and diarrhea. Unabsorbed fructose is transferred from the small intestine to the colon, and hydrogen is produced by colonic bacteria. Part of the hydrogen produced in the colon diffuses into the bloodstream and is excreted into the breath via the lung. Therefore, the quantification of hydrogen in the breath can be used to estimate incomplete fructose absorption. In a previous study, we showed that the intestinal transit time of fructose was approximately 60
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min. Accordingly, in the present study, we examined the effect of water intake at two different times (at 0.5 h or 1 h) after the ingestion of a fructose-containing beverage.

The highest consumers of fructose are adolescents and young adults in the USA, and this is probably also the case in Japan. Therefore, we enrolled young healthy Japanese women as subjects and examined the absorption of fructose-containing beverages by measuring the concentration of breath hydrogen (BH) after the intake of fructose-containing beverages.

2. Aim

The aim of our study is to elucidate the factors which are related to the absorption of fructose by measuring the concentration of BH in young healthy women.

3. Methods

(1) Subjects

Seventeen young healthy Japanese women with normal weight (BMI 18.5 ≤ BMI < 25) who did not release methane from the breath were enrolled as participants. Subjects were non-smokers, were not suffering from any apparent acute or chronic illness, and were not taking antibiotics during a month before the experiment. This study was approved by the Institutional Review Board of Sugiyama Jogakuen University School of Life Studies, and each subject gave written informed consent for study participation.

(2) Anthropometric and body composition measurement

Body weight and height were measured by standard methods. The waist circumference was assessed as the abdominal girth at the level of the umbilicus, and the hip was measured at the level of the greater trochanters. The waist-to-hip ratio (W/H) was calculated. Body composition including visceral fat area (VFA) was analyzed by an eight-polar bioelectrical impedance method, using InBody720 (Biospace, Tokyo, Japan).

(3) Fructose load test & experimental design

Each subject was studied on 4 occasions in a randomized crossover design. At each session, subjects ingested one of 4 beverages after a 12-h overnight fast. The beverages were prepared as follows: 10%F (Control): 25 g of fructose (Nisshin Seito, Tokyo, Japan) with 250 mL of water; 5%F: 25 g of fructose with 500 mL of water; 10%F + 0.5 hW: control beverage (0 h) and 250 mL of water at 0.5 h; 10%F + 1 hW: control beverage (0 h) and 250 mL of water at 1 h.

During the test, subjects avoided exercise, eating, and access to water. The experiments were performed at an interval of 1 week. Subjects avoided intake of alcohol, dairy products, and high-dietary fiber foods such as legumes, mushrooms, root vegetables, and seaweed for dinner on the day before the experiment, because these foods and liquids may affect BH excretion.

(4) Measurement of breath hydrogen concentration

Fructose malabsorption was measured by a breath hydrogen/methane analyzer (BGA-1000D, Laboratory for Breath Biochemistry Nourishment Metabolism, Nara, Japan). The terminal-expiratory gas was collected into the gas collection bag at the baseline (0 min), and every 15 min during a 180-min period. The gas samples were taken with subjects in the sitting position. Changes in BH were calculated as the difference from the baseline mean value (as 0 at 0 h) and shown as \( \Delta BH \). Incomplete fructose absorption was defined as a rise of \( \Delta BH \geq 20 \) ppm, which is highly specific for identifying carbohydrate malabsorption. Changes in the BH were quantified by calculating the incremental area under the curve ( \( \Delta AUC \) ), which was defined as the difference between the area under the curve from 0 min to 180 min and the area below the baseline (0 min).

(5) Estimation of abdominal symptoms

Abdominal symptoms (abdominal pain, bloating, flatulence, and borborygmus) were recorded by the visual analog scales (VAS, 0 to 10 cm) at the baseline (0 min) and every 15 min after the intake of test beverages during a 180-min test period. The results were expressed as the sum of the individual scores of abdominal symptoms.

(6) Statistics

All data are expressed as means ± SEM. Statistical analyses were performed using StatView ver. 5.0 (SAS Institute, NC, USA). Differences in the time-course changes from the baseline values were analyzed using repeated measure one-way ANOVA, followed by the post-hoc test of Fisher’s PLSD. The measured value differences at each time point in the 10%F vs. 5%F trials and the 10%F + 0.5 hW vs. 10%F + 1 hW trials were assessed by an unpaired t-test. \( p < 0.05 \) was considered to be significant in all analyses.

4. Results

The physical characteristics of subjects are shown in Table 1. There were no significant differences in any of the physical characteristics in the 4 trials.

Changes in BH in the 4 trials are shown in Fig. 1. BH in the 10%F, 10%F + 0.5 hW, and 10%F + 1 hW trials were significantly increased at 45 or 60 min (\( p < 0.05 \) each), and...
peaked at 75 or 90 min, and returned to the baseline level at 120 or 135 min. BH in the 5% F trial was significantly increased at 45 min (p<0.05) and peaked at 75 min, but did not return to the baseline level at 180 min.

△BH in the 4 trials are shown in Fig. 2. △BH in the 5% F trial was significantly higher than that in the 10% F trial at 150 and 165 min (p<0.05 each). △BH in the 10% F + 0.5 hW vs. 10% F + 1 hW trials was not significantly different at any time point. The numbers of subjects with △BH ≥20 ppm were as follows: 10 in the 5% F trial, 8 in the 10% F + 1 hW trial, 5 in the 10% F trial, and 3 in the 10% F + 0.5 hW trial.

The △AUC-BH is presented in Fig. 3. The △AUC-BH in the 5% F trial was significantly larger than that in the 10% F trial (p<0.05). The △AUC-BH in the 10% F + 0.5 hW vs. 10% F + 1 hW trials were not significantly different.

The sum of the individual abdominal symptoms score is presented in Fig. 4. Asymptomatic subjects were as follows: 5 in the 10% F and 10% F + 0.5 hW trials, and 4 in the 5% F and 10% F + 1 hW trials. However, there were no significant differences in the strength of each symptom and the number in the 4 trials. The number of cases of acute diarrhea was as follows: 2 in the 10% F + 0.5 hW trial and 1 in each of the other trials, and the symptoms occurred at 45-105 min after fructose ingestion.

5. Discussion

The frequency of fructose malabsorption increases with higher amounts and concentrations of fructose intake. Changes in BH after the ingestion of 10% fructose beverage containing 25 g of fructose in 10 healthy adult subjects showed 5 subjects with fructose malabsorption, i.e., 50%. In the present study, the △AUC-BH in the 5% F trial was significantly larger than that in the 10% F trial, suggesting that a large volume of water suppressed fructose absorption even at the lower concentration. Our current hypothesis on fructose malabsorption in the 5% F trial is presented in Fig. 5. The △AUC-BH in the 5% F trial is suggested to have been increased by the effect of the increased generation of gas in the colon. There was no significant difference in the 10% F + 0.5 hW vs. the 10% F + 1 hW trials, suggesting that fructose absorption was not affected by the water taken after the ingestion of fructose-containing beverage, and ingested fructose rapidly moved into the colon within 0.5 h.

Fructose is transported into the enterocytes through a specific fructose transporter, GLUT5, located at the intestinal membrane. Absorption of fructose by facilitated diffusion, which does not need adenosine 5-triphosphate, differs from that of glucose. The contact of fructose with the intestinal brush-border membrane may also have been decreased by a large amount of water, and the transfer of fructose into the enterocytes by facilitated diffusion may have become slower. It is likely that unabsorbed fructose, together with a large amount of water, rapidly shifted into the colon from the small intestine and increased the production of hydrogen, methane, and fatty acids by bacterial anaerobic fermentation.

The greatest number of subjects with △BH ≥20 ppm, which is defined as incomplete fructose absorption, was found in the 5% F trial. Nevertheless, there was no significant difference in the VAS of abdominal symptoms among the 4 trials, and there was no correlation between the △AUC-BH and each gastrointestinal symptom. These symptoms are attributed to intestinal and/or colonic distention due to the osmotic effect of incompletely absorbed fructose.

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<th>Table 1 Anthropometric characteristics</th>
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Values are presented as the means ± SEM.
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Fig. 1 Changes of BH concentration in the 4 trials.

Values are presented as the means ± SEM. *p<0.05 compared with the baseline (0 min).

Fig. 2 ΔBH in the 4 trials.

* p<0.05 compared with the 10% F trial.

Fig. 3 ΔAUC-BH in the 4 trials.

Values are presented as means ± SEM. *p<0.05 compared with the 10% F trial.
fructose, rather than the effect of gases produced by colonic bacterial fermentation\(^7\). It is difficult to quantify fructose malabsorption by the breath test only. In this study, although BH and abdominal symptoms had great differences among individuals, the breath test provided a valuable non-invasive diagnostic strategy.

In the present study, only fructose was ingested, but fructose is usually contained with glucose in soft drinks or foods, and fructose absorption is promoted by glucose\(^5\). Sucrose is composed of fructose and glucose, and it is normally completely absorbed\(^8\). When the amount of fructose is greater than that of glucose, fructose malabsorption could be induced\(^5\). The abnormality of BH was less in the HFCS-55 (55% fructose and 45% glucose) ingestion compared with the ingestion of fructose only, and symptoms such as abdominal pain, bloating, and flatulence were not observed after the HFCS-55 ingestion\(^2\).

HFCS is classified into 3 different types by the Japan Agricultural Standard\(^2\), as follows: high-fructose liquid sugar (fructose ≥90%), fructose-glucose liquid sugar (fructose 50% - <90%), and glucose-fructose liquid sugar (fructose <50%). The products that contain HFCS include soft drinks, which account for ca. 50% of the total, followed by milk beverages, seasoning, bread, and cold desserts\(^7\). Fructose malabsorption is likely to develop in infants, and the majority of infants experience fructose malabsorption after 0.5 g/kg of fructose ingestion\(^6\). HFCS is often added to fruit-flavored juice or sports drinks\(^7\). Even 100% apple or pear juice contains more fructose than glucose\(^6\). Thus, the attention to the use of these beverages is necessary because of the low amounts of fructose that can be tolerated by babies and infants compared to adults.
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Also, patients with irritable bowel syndrome were reported to be sensitive to fructose and HFCS ingestion\(^1\). Ingestion of HFCS in healthy subjects did not cause the abdominal symptoms, but the patients with irritable bowel syndrome were more likely to develop abdominal symptoms\(^2\).

There are many reports that fructose may have adverse effects on human health. Our previous study demonstrated that the ingestion of fructose with fat exacerbates postprandial lipidemia in young healthy women\(^{30}\). In the USA, many studies have shown the relation between the intake of sugar-sweetened beverages and weight gain\(^{20}\). Overconsumption of fructose- or HFCS-containing beverages may enhance the risk of metabolic syndrome, which is becoming a serious problem not only in the USA but also in Japan. The World Health Organization proposed that added sugars should provide no more than 10% of dietary energy\(^{21}\). However, the influence of intake of fructose and HFCS on health remains to be clarified, and very little data about the effects on the Japanese people are available. For the present, there is no evidence-based data on the upper limit of the intake of fructose and HFCS for maintaining health in the dietary intake reference for Japanese\(^{26}\). Elucidation of the influence of fructose and HFCS ingestion is mandatory to protect the health of the Japanese population, and a strategy of dietary education for children and adolescents about this issue must be formulated as soon as possible in Japan.

6. Conclusion

The present study demonstrated that fructose-containing beverages are liable to cause gastrointestinal symptoms, and fructose absorption, even at a low concentration, may be disturbed by the intake of a large volume of water.

Acknowledgements

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