Original Article

Fructose malabsorption in Thai adult

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Fructose malabsorption has not been well-defined in Thai populations but there has been increasing consumption of fructose-fortified drinks

Objectives: To assess the incidence of fructose malabsorption and intolerance in Thai normal subjects as well as the facilitating effect of glucose on fructose absorption.

Methods: Twenty-five gram of fructose was ingested by 77 subjects (37 men, 40 women; mean age 26 and 31 y, range 20-50 y and 21-50 y for men and women, respectively). Measurement of breath-H_2 levels after fructose ingestion in each subject up to 2 h was performed. Those who showed fructose malabsorption were later given 25 g of each glucose and fructose and second tests of breath-H_2 tests were done.

Results: Fructose malabsorption was found in eleven females with a significant rise in average breath-H_2 level at 30, 60, 90, and 120 min ($p < 0.001$), whereas none of the males had an abnormal breath-H_2 test. Only 1 of the 11 females with increased breath H_2 had gastrointestinal symptoms. In all the fructose malabsorbers, excess breath-H_2 reverted to normal when the fructose solution was mixed and administered with 25 g glucose ($p < 0.001$).

Conclusion: The incidence rate of fructose malabsorption was 11 of 77 subjects but these were female. One of the 11 had gastrointestinal symptoms. It was found that an equal amount of glucose would abolish fructose malabsorption.

Key Words: Breath-H_2 test, Fructose malabsorption, Fructose intolerance

Introduction

Fructose, one of the monosaccharides, is found either as free hexose in some fruits (pear, apple, grape),[1] honey, prepared foods and beverages, or as the by-product from enzymatic hydrolysis of disaccharide sucrose. It is absorbed across the enterocytes of the small intestine via glucose transporter 5 (GLUT5), a hexose membrane transporter, which is principally expressed on the brush border membrane of jejunal enterocytes. In contrast, other two monosaccharides, glucose and galactose, are transported by another carrier protein named sodium-dependent glucose cotransporter 1 (SGLT1). The gene encoding the GLUT5 protein, symbolized SLC2A5, is located on the short arm of human chromosome 1 (1p36.2).[2-4] The absorption rate of fructose is slower than that of glucose.

Breath-hydrogen analysis, a noninvasive test with high sensitivity and specificity,[5] has been used to determine the amount of hydrogen produced from fermentation of undigested carbohydrate that reached the large intestine by colonic bacteria. A positive result is demonstrated by a rise of breath hydrogen of $\geq$ 20 ppm after ingestion of carbohydrate.

Lactose intolerance has been considered a cause of abdominal discomfort especially in Asia, South America and Africa. Our previous study showed instances of lactose malabsorption and intolerance in Thai adults by the lactose hydrogen breath test and there was no difference in gender.[6] However, a problem of fructose intolerance is still undetermined whether it is clinically important despite the increasing consumption of high-fructose syrup-fortified foods as a sweetener substitution for sucrose. Gastrointestinal symptoms can be contributed to by fructose intolerance and disappear after restriction of fructose-containing foods.

Thus it was our aim in this study to find out the incidence of fructose malabsorption in Thai healthy adults and whether adding glucose to fructose solution can correct fructose malabsorption.

Subjects and methods

Subjects

The study was cross-sectional in design and conducted in the Division of Nutrition, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand between June 2001 and May 2002. All 79 recruited volunteers comprised 38 males (ages 20-50 y, mean 26 y) and 41 females (ages 21-50 y, mean 31 y). Inclusion criteria were as follows: 1) healthy physical condition, 2) non-smoker, 3) no history of current diarrhoea or constipation in the previous 2 wk, 4) not receiving antibiotics in the 2 wk prior to

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the study, 5) no consumption of slowly digested foods such as beans, bran, or high-fiber cereal on a day before the test. One male participant was excluded due to high baseline breath-H_2 concentration (>20 ppm). Another female subject was excluded because of incomplete conduct of the test. The conduct of this study was in accordance with Internationally agreed Ethical Codes for the conduct of Human Research. The subjects were informed about the purposes of the study and gave written informed consent.

Breath-hydrogen analysis

After 10-h overnight fasting, breath samples were taken at t = 0 (baseline) and 30, 60, 90, and 120 min following ingestion of 25 g fructose as a 10% (w/v) fructose solution. To assess the effect of equal amount of glucose to fructose on enhancement of fructose absorption, the subjects who were fructose malabsorbers re-collected their fasting breath samples after consuming 25 g fructose mixed with 25 g glucose as 20% (w/v) solution several weeks later. The subjects were not allowed to consume any food during the test and any symptoms of intolerance were noted such as flatulence, abdominal pain, passing of flatus, or loose stool.

End-expiratory alveolar air samples were collected by using an AlveoSampler (QT01091), a polyethylene bag assembled with a three-way stopcock that was fitted with a syringe for sample collection. Each 20 mL of breath sample was analyzed for H_2 level using chromatographic analytic method (QuinTron model 12i Microlyzer, QuinTron Instruments, Milwaukee, WI).[6] Fructose malabsorption was defined as an increase in breath-H_2 more than 20 ppm over the baseline level. Additionally, fructose intolerance was considered to be malabsorption plus the presence of one or more gastrointestinal symptoms.

Statistical analysis

Differences either between fructose absorber and malabsorber groups in females or between those for ingestion of fructose alone and a mixture of fructose with glucose were tested by using an unpaired *t*-test. Data were expressed as means $\pm$ SEMs and $p < 0.05$ was considered significant. Statistical analysis was performed with the use of SPSS software (version 11.5; SPSS Inc, Chicago, IL).

Results

There was no significant difference in mean ages of the female malabsorbers and the absorbers (30 $\pm$ 2.1 *vs*. 32 $\pm$1.6). In the male group, no significant change of average breath-H_2 level was observed during the study (Fig 1A). In contrast, 11 out of 40 (27.5%) female participants were fructose malabsorbers and their average breath-H_2 levels were significantly raised at 30, 60, 90, and 120 min of the test in the absence of difference in baseline values (Fig 1B). The incidence rate of fructose malabsorption was 0.14 (11 of 77) of the combined males and females.

Nine of the 11 female fructose malabsorbers were retested by ingesting a mixture of fructose and glucose solution and performing the breath-H_2 test several weeks later. There was no elevation of breath-H_2 level above 20 ppm during the second test (Fig 2). Moreover, the greatest

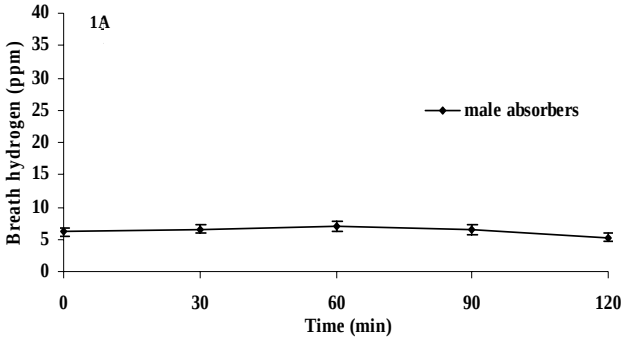

Fig 1A

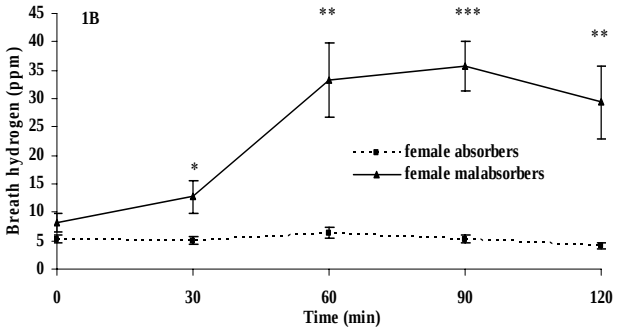

Fig 1B

Figure 1. Breath-H_2 analysis of fructose tolerance test. Of 20 ml alveolar air samples, hydrogen concentrations were assayed before and 30, 60, 90, and 120 min after ingestion of 25 g fructose as 10% (w/v) solution. In a 37 male group, no significant changes of breath hydrogen levels were found (Fig 1A). In contrast, 11 (27.5%) of 40 females, defined as fructose malabsorbers, showed positive breath-H_2 test presenting by a rise in breath-H_2 level more than 20 ppm over baseline while the remaining in the absence of change in H_2 level being fructose absorbers (Fig 1B). The results were means $\pm$ SEMs. *: $p < 0.05$, **: $p < 0.01$, ***: $p <$ 0.001 compared to fructose absorbers at the same time points.

decline occurred at the time point of 90 min.

Most of the subjects who had positive breath-H_2 test had no gastrointestinal symptom; only one fructose malabsorber developed abdominal discomfort. None of the fructose absorbers had abdominal symptoms during the test; meanwhile, 1 of 11 (9%) fructose malabsorbers appeared fructose-intolerant.

Discussion

Fructose malabsorption in healthy adults was found at the incidence of 11/77 and one of these (9%) was classified as fructose intolerance due to presenting with abdominal discomfort. Gotze et al.[5] reported that 36% (108/293) of German populations with gastrointestinal symptoms showed fructose malabsorption and 79 of these 108 (73%) had clinical symptom following their fructose breath test. Their higher incidence of fructose malabsorption and intolerance may be due to different status of the target subjects. In this study, all of subjects found to be fructose malabsorbers were female, whereas none of the males had abnormal breath-H_2 test or any symptoms. GLUT5, which is responsible for fructose transporter across brush border of enterocytes, is regulated by the gene named SLC2A5; solute carrier family 2 (facilitated glucose/fructose transporter) member 5. Although the gene SLC2A5 is located on chromosome 1, it is unclear why only female subjects

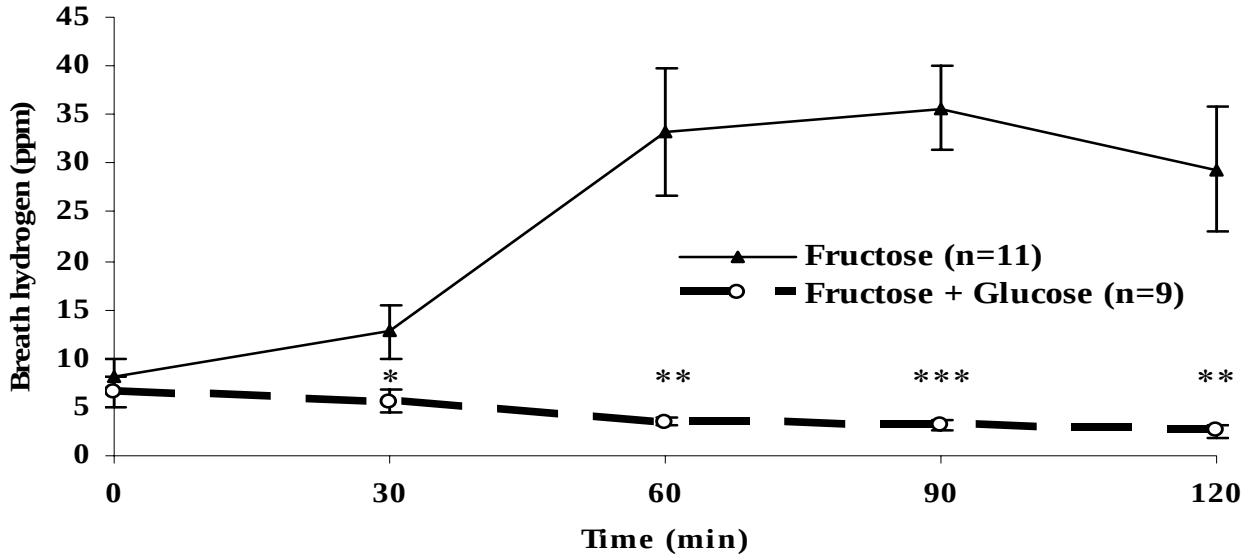

Figure 2. Reversed fructose malabsorption by 25 g glucose. To assess facilitating effect of glucose on fructose absorption, breath-H_2 test was undergone in 9 of 11 female fructose malabsorbers after consumption of a 250-mL mixture of 25 g glucose with 25 g fructose. Consequently, marked decrease in H_2 concentration was observed. Data were presented as means $\pm$ SEMs. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$ compared to only 25-g fructose consumption.

here presented as fructose malabsorbers. In contrast to lactose,[7] data of fructose malabsorption and intolerance related to ethnicity, age, and sex are not clearly available.

The frequency of fructose malabsorption depends on carbohydrate dose ingested. Compared to this study carried out with 25 g fructose, several reports showed higher frequency of fructose malabsorption in keeping with ingestion of more fructose (37.5-50 g).[8-9] It is more physiological to intake 25 g of fructose because our previous study showed fructose content of commercial fruit juices in a range of 4.25 to 15.5 mg/250 mL.[1] Moreover, from food label of nutrition facts, we find that one serving size (250 mL) of beverage sweetened with high-fructose syrup or crystalline fructose available in Thailand contains as much as 22.5 g fructose. It is of note that consumption of pure high fructose-fortified beverages may lead to clinical symptoms.

Fructose malabsorption was abolished after addition of glucose to fructose solution. Fujisawa et al. demonstrated such glucose-facilitating effect on absorptive capacity of fructose in the rat model.[10] They showed that dose-dependent enhancing effect of glucose correlated to hydrogen excretion and the maximum effect occurred when administration of equal amounts of fructose and glucose. In our data, the study was carried out under the condition of a mixture of similar quantity of glucose and fructose.

As previously described,[1] even though some fruit juices contain similar fructose concentration, they had a different glucose content resulting in a varied ratio of fructose to glucose: 2:1, 1.7:1, 1.28:1 for apple juice, pear juice and grape juice, respectively. In addition, there is sorbitol in pear juice. The clinical study by Hyams et al. showed that excess breath-H_2 excretion was found in all subjects, 50% and 25% of the participants after ingestion of pear juice (containing 2% sorbitol), apple juice (0.5% sorbitol) and grape juice (no sorbitol), respectively.[11] Both factors including a higher ratio of fructose to glucose than 1:1 and the presence of sorbitol clearly have an influence on incomplete absorption of the carbohydrates. The improvement in gastrointestinal symptoms and self-rated health of dietary fructose intolerance occurred if fructose is eliminated from the diet.[12] On the other hand, it may be that such effects of fruits and/or fruit juices containing more fructose than glucose may have a role in the management of constipation.

This study presents the relatively low incidences of fructose malabsorption and intolerance in Thai adults compared to Europeans. All fructose malabsorbers were females, in whom a positive breath-H_2 test can be reversed by the fructose absorption-enhancing effect of glucose. Further research is needed to evaluate whether fructose malabsorption related to gender has a genetic basis and to assess fructose malabsorption at different ages and with regard to ethnicity.

Acknowledgements

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泰國成年人之果糖吸收不良

在泰國，添加果糖的飲料消耗量日漸增加，而果糖吸收不良在泰國族群尚未被完整定義。

目的：評估果糖吸收不良及耐受不良在泰國正常人的盛行率及葡萄糖對果糖吸收的影響。

方法：77 名研究對象(37 名男性，40 名女性；男女平均年齡分別為 26 歲及 31 歲，範圍在 20-50 歲及 21-50 歲)食用 25 公克的果糖。每名研究對象在食用果糖兩個小時後測量呼出氫氣的含量。有果糖吸收不良的人，之後再給予葡萄糖及果糖各 25 公克，並測量第二次呼氣中氫氣的含量。

結果：11 名女性有果糖吸收不良現象，她們在 30、60、90 及 120 分鐘，呼氣中氫氣含量顯著上升(p<0.001)，反之沒有任何一名男性其呼氣氫氣測量不正常。在 11 名呼氣中氫氣含量上升的女性中只有 1 名有腸胃道症狀。在所有果糖吸收不良者，當攝取果糖溶液混合 25 公克的葡萄糖後，會使呼氣中過多的氫氣恢復正常(p<0.001)。

結論：果糖吸收不良的發生率在 77 名研究對象中有 11 名，且均為女性。11 名研究對象中有一名有腸胃道症狀。此研究結果發現等量的葡萄糖可以消除果糖吸收不良。

關鍵字：呼吸氫氣測試、果糖吸收不良、果糖不耐症。