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RAPID COMMUNICATION

Seventy-five gram glucose tolerance test to assess carbohydrate malabsorption and small bowel bacterial overgrowth

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Abstract

AIM: To investigate non-invasively the incidence of absorption of carbohydrates in diabetic patients during an oral glucose tolerance test (OGTT) and to determine whether malabsorption may be associated with insulin secretion and insulin resistance.

METHODS: A standard 75-g OGTT was performed in 82 diabetic patients. The patients received 75 g of anhydrous glucose in 225 mL of water after an overnight fasting and breath samples were collected at baseline and up to 120 min after ingestion. Breath hydrogen and methane concentrations were measured. Blood glucose and serum insulin concentrations were measured before ingestion and at 30, 60, 90, 120 min post-ingestion.

RESULTS: When carbohydrate malabsorption was defined as subjects with an increase of at least 10 ppm (parts per million) in hydrogen or methane excretion within a 2-h period, 28 (34%) had carbohydrate malabsorption. According to the result of increased breath test, 21 (75%) patients were classified as small bowel bacterial overgrowth and 7 (25%) as glucose malabsorption. Patients with carbohydrate malabsorption were older and had poor glycemic control as compared with those without carbohydrate malabsorption. The HOMA value, the sum of serum insulin during the test and the Δinsulin/Δglucose ratio were greater in patients with carbohydrate malabsorption.

CONCLUSION: Insulin resistance may be overestimated by using these markers if the patient has carbohydrate malabsorption, or that carbohydrate malabsorption may be present prior to the development of insulin resistance. Hence carbohydrate malabsorption should be taken into account for estimating insulin resistance and β-cell function.

Key words: 75-g OGTT; Carbohydrate malabsorption; Bacterial overgrowth; Breath test; Insulin resistance

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INTRODUCTION

The oral glucose tolerance test (OGTT) is a widely used procedure in the diagnoses of diabetes and intermediate stages of hyperglycemia. Plasma glucose and insulin responses during this test reflect the ability of pancreatic β-cells to secrete insulin and the sensitivity of tissues to insulin[1]. However, it was reported that 2%-20% of carbohydrates escape small intestinal absorption[2]. Based on this fact, digestion and absorption of carbohydrates may affect the results of OGTT. If the patient had carbohydrate malabsorption, plasma glucose and insulin responses during OGTT should be lower. Furthermore, an interesting observation was the outcome of OGTT yielding a remarkable intra-individual variability[3] and this was explained by the hypothesis that the velocity of the initial phase of glucose emptying from the stomach may depend on the grade of interdigestive antral motor activity at the time of glucose ingestion[4]. Although a many investigators have reported a close association between gastric emptying and insulin secretion, the prevalence of absorption of carbohydrates in diabetic patients has been unknown.

H_2 breath tests have been used to evaluate intestinal transit, bacterial overgrowth, and disaccharidase

deficiency[5-12]. Because bacteria represent the sole source of gut H_2 and CH_4, fasting breath H_2 and CH_4 gases have been used as markers of colonic fermentation[13,14]. As H_2 production increases when a small amount of carbohydrate is supplied to colonic bacteria, the measurement of breath H_2 concentration has been proposed as an indicator of carbohydrate malabsorption[6]. Similarly, breath CH_4 excretion, which reflects an indirect measurement of the metabolism of the anaerobic colonic flora, has been measured[15,16]. Methanogenic bacteria utilize H_2, carbon dioxide (CO_2), and then synthesize CH_4[17]. CH_4 absorbed from the colon reaches the lung and excretes into the breath[18].

The aim of the present study was to investigate non-invasively the incidence of malabsorption of carbohydrates in diabetic patients during OGTT and to determine whether malabsorption may be associated with insulin secretion and insulin resistance.

MATERIALS AND METHODS

Patients

A standard 75-g OGTT was performed in 82 diet-controlled diabetic patients (42 women and 40 men; age range 30-84 years, average 62 years) without abdominal symptoms. Patients treated with alpha-glucosidase inhibitors were excluded from this study. None of the patients had a history of use of PPI, H_2-receptor antagonist, antibiotics, steroids, or nonsteroidal anti-inflammatory drugs for a period of at least six month before the investigation. Patients who had a previous history of partial gastrectomy were also excluded from the study. The study was approved by our Local Ethical Committee.

Procedures

The patients received 75 g of anhydrous glucose in 225 mL of water in the sitting position after an overnight fasting. Breath samples were collected at baseline and at 5, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, and 120 min after ingestion. Breath H_2 and CH_4 concentrations were measured with breath analyzer TGA-2000 (TERAMECS, Kyoto) and expressed in parts per million (ppm). Linear accuracy response range was 2 to 150 ppm. An increase of at least 10 ppm within a 2-h period is indicative of bacterial overgrowth or glucose malabsorption[19]. Venous blood samples were obtained before ingestion and at 30, 60, 90, and 120 min after ingestion and blood glucose and serum insulin concentrations were measured.

Calculations

The homeostasis model assessment (HOMA), fasting serum insulin, the sum of serum insulin during the test, and the Δinsulin/Δglucose ratio were used as indexes of insulin resistance. The HOMA value was calculated as follows: HOMA = fasting plasma glucose (mg/dL) × fasting insulin (pmol/L)/405. The Δinsulin/Δglucose ratio was calculated as follows: (insulin at 30 min - insulin at baseline)/(glucose at 30 min - glucose at baseline).

Statistical analysis

All values were expressed as means ± SD. Comparisons of groups were made using the Mann-Whitney *U* test. A *P* value less than 0.05 was considered statistically significant.

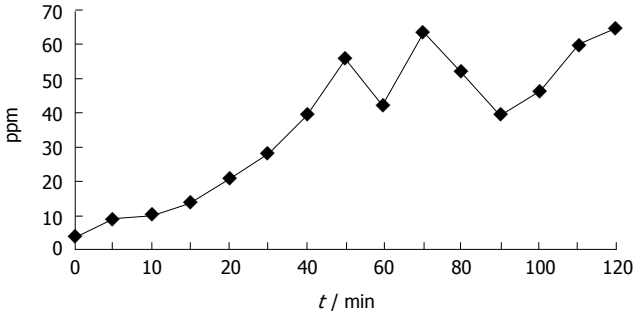

Figure 1 Changes in breath hydrogen concentration during OGTT in the patient with suspicious of small bowel bacterial overgrowth. An increase of H_2 greater than 10 ppm above the baseline was found at 15 min.

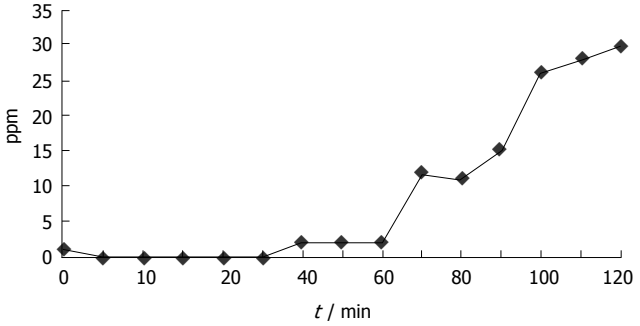

Figure 2 Changes in breath hydrogen concentration during OGTT in the patient with suspicious of carbohydrate malabsorption. Breath H_2 concentration increased gradually from the beginning and reached 10 ppm over the baseline at 70 min and later.

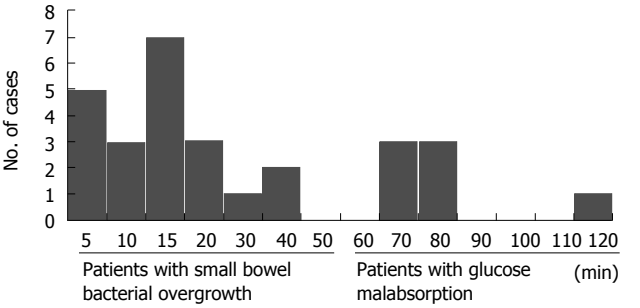

Figure 3 Distribution of time when breath hydrogen and/or methane levels increased more than 10 ppm over baseline.

RESULTS

Incidence of carbohydrate malabsorption

When carbohydrate malabsorption was defined as subjects with an increase of at least 10 ppm within a 2-h period, 34% (28/82) patients had carbohydrate malabsorption. As shown in Figures 1 and 2, small bowel bacterial overgrowth was defined as an increase of H_2 and/or CH_4 greater than 10 ppm above the baseline before the first 40 min, whereas carbohydrate malabsorption without small bowel bacterial overgrowth was defined as an increase of H_2 and/or CH_4 greater than 10 ppm above the baseline at 70 min and later. Of 28 patients with an increase of H_2 and/or CH_4, 21 (75%) patients were classified as small bowel bacterial overgrowth and 7 (25%) as carbohydrate malabsorption (Figure 3). All

Table 1 Characteristics of 82 patients with diabetes mellitus classified according to carbohydrate malabsorption status

	Carbohydrate malabsorption (+)	Carbohydrate malabsorption (-)	*P* value
n	28	54	
Age	63.3 ± 10.3	59.2 ± 9.7	0.34
HbA1c	7.1 ± 1.7	6.4 ± 1.5	0.17
HOMA	2.0 ± 2.1	1.9 ± 1.9	0.22
ΣIR	107.0 ± 95.3	117.0 ± 76.2	0.08
ΔIR/ΔBG	0.18 ± 0.27	0.14 ± 0.21	0.06

28 patients had no abdominal symptom during OGTT.

As shown in Table 1, the values of HbA1c were 7.11% ± 1.70% and 6.43% ± 1.46% in patients with and without carbohydrate malabsorption (including small bowel bacterial overgrowth), respectively. Patients with carbohydrate malabsorption were older and had poor glycemic control when compared with those without carbohydrate malabsorption.

Carbohydrate malabsorption and insulin resistance

The HOMA values in the patients with carbohydrate malabsorption (2.0 ± 2.1) were greater than those without carbohydrate malabsorption (1.94 ± 1.86), but did not reach statistical significance ($P = 0.22$). Similarly, the sum of serum insulin during the test and the Δinsulin/Δglucose ratio were also greater in patients with carbohydrate malabsorption than those without carbohydrate malabsorption (Table 1), but the difference was not significant.

DISCUSSION

Impaired intestinal and gastric motility are frequent findings in diabetic patients[19,20]. However, there is a wide range of symptoms in gastrointestinal motility disorders, and the degree of motility disorders correlate poorly with severity of symptoms. Intestinal peristalsis as well as gastric acid secretion are the most important factors protecting against the small bowel bacterial overgrowth[21]. Although delayed gastrointestinal transit potentially causes bacterial overgrowth, in contrast, a rapid transit may also cause diarrhea due to an increase in intraluminal contents that reach the cecum. It is, therefore, possible that both rapid and delayed gastrointestinal transit cause diarrhea because of bacterial overgrowth or carbohydrate malabsorption. However, patients with bacterial overgrowth may also be asymptomatic[22]. Although gastrointestinal symptoms are present in 50%-70% of diabetic patients, the association between symptoms and bacterial overgrowth in diabetic patients has been unknown.

In the present study, 34% (28/82) patients without abdominal symptoms, including diarrhea, had carbohydrate malabsorption, including 7 patients classified as small bowel bacterial overgrowth. It has been unclear how much of small bowel bacterial overgrowth is opposed to carbohydrate malabsorption. The results of the present study suggest that carbohydrate malabsorption occurs more often in diabetic patients than small bowel bacterial overgrowth.

There is increasing evidence that postprandial hyperglycemia has a major role in the pathogenesis of diabetic macrovascular complications[23,24]. It is widely recognized that postprandial glycemia is potentially dependent on a number of factors, including the rate of carbohydrate entry into the small intestine, small intestinal digestion and absorption, insulin secretion, peripheral insulin sensitivity, and hepatic and muscle glucose metabolism[25]. In addition, postprandial secretion of insulin is prompted as much by the incretin hormones as by entry of glucose into the blood, and the release of incretins is dependent on rates of nutrient entry into the small intestine[26,27]. Our observations confirmed that one third of patients with diet-controlled type 2 diabetes and without abdominal symptoms had carbohydrates malabsorption, which might contribute to postprandial hyperglycemia[25]. Some previous studies also described approximately 35% of the variance in initial postprandial blood glucose concentrations after a 75-g oral glucose load[28,29]. Since patients with carbohydrate malabsorption tended to be older and to have poor glycemic control as compared with those without carbohydrate malabsorption, it is possible that patients with long-standing or poor-controlled diabetes may more often have carbohydrate malabsorption. Conversely, the result and its interpretation of 75-g OGTT might be influenced by carbohydrate malabsorption.

A standard 75-g OGTT has also been used to assess insulin resistance and insulin release. For example, fasting plasma insulin concentrations have been used as an index of insulin resistance, and the 30-min ratio of changes in plasma insulin and glucose has been used as an index of β-cell function[30,31]. Insulin resistance, evaluated by the HOMA value, the sum of serum insulin during the test, and the Δinsulin/Δglucose ratio were greater in patients with carbohydrate malabsorption than those without carbohydrate malabsorption. However, these differences were not significant. This suggests that insulin resistance might be overestimated by using these markers if the patient has carbohydrate malabsorption, or that carbohydrate malabsorption might be present prior to the development of insulin resistance. In conclusion, it is more desirable that carbohydrate malabsorption should be taken into account for estimating insulin resistance and β-cell function.

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