Rapid Communication

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

Yoshihisa Urita, Susumu Ishihara, Tatsuo Akimoto, Hiroto Kato, Noriko Hara, Yoshiko Honda, Yoko Nagai, Kazushige Nakanishi, Nagato Shimada, Motonobu Sugimoto, Kazumasa Miki

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.

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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 in diabetic patients has been unknown.

H2 breath tests have been used to evaluate intestinal transit, bacterial overgrowth, and disaccharidase

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deficiency\cite{5-12}. Because bacteria represent the sole source of gut H\textsubscript{2} and CH\textsubscript{4}, fasting breath H\textsubscript{2} and CH\textsubscript{4} gases have been used as markers of colonic fermentation\cite{13,14}. As H\textsubscript{2} production increases when a small amount of carbohydrate is supplied to colonic bacteria, the measurement of breath H\textsubscript{2} concentration has been proposed as an indicator of carbohydrate malabsorption\cite{5}. Similarly, breath CH\textsubscript{4} excretion, which reflects an indirect measurement of the metabolism of the anaerobic colonic flora, has been measured\cite{15,16}. Methanogenic bacteria utilize H\textsubscript{2}, carbon dioxide (CO\textsubscript{2}), and then synthesize CH\textsubscript{4}\cite{17}. CH\textsubscript{4} absorbed from the colon reaches the lung and excretes into the breath\cite{18).

The aim of the present study was to investigate noninvasively 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\textsubscript{2}-receptor antagonist, antibiotics, steroids, or nonsteroidal anti-inflammatory drugs for a period of at least six months 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\textsubscript{2} and CH\textsubscript{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 above the baseline before the first 40 min, whereas patients had carbohydrate malabsorption without small bowel bacterial overgrowth.

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\textsubscript{2} and/or CH\textsubscript{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\textsubscript{2} and/or CH\textsubscript{4} greater than 10 ppm above the baseline at 70 min and later. Of 28 patients with an increase of H\textsubscript{2} and/or CH\textsubscript{4} 21 (75%) patients were classified as small bowel bacterial overgrowth and 7 (25%) as carbohydrate malabsorption (Figure 3). All comparisons of groups were made using the Mann-Whitney U test. A P value less than 0.05 was considered statistically significant.

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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.
There is increasing evidence that postprandial hyperglycemia has a major role in the pathogenesis of diabetic macrovascular complications. It is widely recognized that postprandial glycaemia 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. 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. 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. Some previous studies also described approximately 35% of the variance in initial postprandial blood glucose concentrations after a 75-g oral glucose load. 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.

In the present study, 34% (28/82) patients without abdominal symptoms, including diarrhea, had carbohydrate malabsorption, including 7 patients classified as small bowel 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.

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

DISCUSSION

Impaired intestinal and gastric motility are frequent findings in diabetic patients. 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. 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. 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 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.

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