Sorbitol Malabsorption and Nonspecific Abdominal Symptoms in Type II Diabetes

P. Vernia, C. Frandina, T. Bilotta, M.R. Ricciardi, G. Villotti, and F. Fallucca

Some data suggest that sorbitol intake may be responsible for diarrhea in diabetic patients. One hundred thirteen hydrogen breath tests were performed in type II diabetics (72) and normal controls (41) after oral loads of sorbitol ranging from 2.5 to 20 g in iso-osmolar solutions to assess the role of malabsorption of this compound in the genesis of abdominal symptoms. The prevalence of sorbitol malabsorption and abdominal symptoms, peak (Cmax H_2) and total (Ctot H_2) hydrogen production, and mouth to cecum transit time (MCTT) did not differ in type II diabetics and controls. Malabsorption was observed more frequently with the highest doses of sorbitol (10% of patients at a dose of 2.5 g and ~75% at 20 g). Symptoms, usually consisting of mild discomfort and abdominal distension, were observed only after sorbitol loads of 10 and 20 g in 27.2% of the diabetics and in 36.3% of the controls. Diarrhea was present in three subjects (two diabetics and one control) only at a dose of 20 g. These data indicate that it is highly unlikely for sorbitol to play a role in inducing diabetes diarrhea. A moderate (up to 10 g) sorbitol intake is not contraindicated in type II diabetics.

SORBITOL, a polyhydric alcohol present in a variety of fruits and plants, is synthesized for commercial use as a sweetener in drugs and foodstuff. Sorbitol is absorbed by the small intestine through a passive-diffusion mechanism, at a rate slower than that of other sugars. The malabsorbed sorbitol, which represents only a fraction of the ingested dose, is fermented by colonic bacterial flora through production of hydrogen and short-chain fatty acids, mostly acetic acid.[1]

In recent years, sorbitol intolerance has been reported in a large proportion of the normal adult population after an oral load as small as 10 g.[2-4] The clinical manifestations consist of nonspecific abdominal complaints (pain, distention, and bloating), but osmotic diarrhea has also been reported in both adults and children when ingesting high doses of sorbitol as water solutions or through sweets and beverages.[2,5] However, there are marked discrepancies in the literature concerning the prevalence of sorbitol malabsorption at a given dose and regarding the relationship between this finding and abdominal symptoms.[6,7]

Due to its sweetening power and being considered to reduce available calories, sorbitol is widely used as a sucrose substitute in foodstuff and beverages,[7] although only a minor caloric reduction may be expected from a compound with an energetic value of 2.8 kcal/g.[8] With respect to the general population, it can be stated that diabetic patients and obese subjects undergoing dietary restriction are more likely to ingest large amounts of sorbitol and are thus at a higher risk for sorbitol intolerance.

In a recent report, diabetics were shown to malabsorb 10 g sorbitol at the same percentage as normal controls.[9] However, since in sorbitol-using diabetics the prevalence of diarrhea was significantly higher than in nonusers, it was hypothesized that sorbitol could be involved in the genesis of diabetes diarrhea. Since the series of patients with sorbitol malabsorption was small, some patients were insulin-dependent and some were not, and the relationship between sorbitol intake and diarrhea was only indirectly inferred, this conclusion seems debatable.

The present investigation in a large series of diabetics was aimed at studying the prevalence of sorbitol malabsorption and evaluating the relationship between this finding and abdominal symptoms. Only non–insulin-dependent diabetics were included in the study both for ethical reasons, related to the prolonged fasting required by breath analysis, and to exclude the influence of neuropathy, the prevalence of which is far greater in type I than in type II diabetics. The study also aimed to identify the threshold dose above which sorbitol intake will probably result in symptoms, to provide dietary guidelines for sorbitol users.

SUBJECTS AND METHODS

The study was performed from 1990 through 1992 in 57 type II diabetic patients (29 men and 28 women, with a mean ± SD age of 57 ± 12 years) and in 35 healthy controls (21 men and 14 women aged 36 ± 14). Informed consent was obtained in all cases.

One hundred thirteen sorbitol tolerance tests were performed using the hydrogen breath test (72 tests in diabetics and 41 in controls). The following doses of sorbitol were tested: 2.5 g (group A, 10 diabetics and 10 controls); 5 g (group B, 29 diabetics and 11 controls); 10 g (group C, 22 diabetics and 10 controls); and 20 g (group D, 11 diabetics and 11 controls). Patients were randomly allocated to different doses of sorbitol and were then asked to undergo a further test at a lower dose in cases where the first test was positive and at a higher dose in those with negative results. After inclusion of at least 10 subjects in each study group, recruitment was discontinued.

After 24 hours of a low-fiber diet and 12-hour fasting, a hydrogen breath test was performed following an oral load of sorbitol administered in iso-osmolar water solutions. Osmolality was tested using a Fiske OSTm Osmometer (Fiske Associates, Needham Heights, MA). Alveolar air samples were collected into air-tight plastic syringes using a modified Haldane-Priestly tube,[10] before administration of sorbitol and every 30 minutes for 4 hours. Hydrogen concentration was measured in parts per million by means of a Quintron Model 12 Microlyzer gas chromatograph (Quintron Instrument, Milwaukee, WI). Excretion of hydrogen

From the Cattedra di Gastroenterologia 1 and Servizio Stati Disendocrini e Dismetabolici, II Clinica Medica, Universitá "La Sapienza," Roma, Italy.

Submitted May 31, 1994; accepted September 2, 1994.

Address reprint requests to P. Vernia, MD, Cattedra di Gastroenterologia 1, 2a Clinica Medica, Policlinico Umberto I, Viale del Policlinico, 00161 Roma, Italy.

0026-0495/95/4406-0019$03.00/0

was quantified as: (1) the peak hydrogen concentration (Cmax H_2); (2) the area under the curve of hydrogen concentration from 60 to 240 minutes, calculated with the triangular rule and expressed in arbitrary units of parts per million per hour (Ctot H_2); and (3) the time elapsed between administration of lactose and the first peak of an increased hydrogen excretion, representing the mouth to cecum transit time (MCTT).[11]

The test was defined as positive when the Cmax H_2 exceeded baseline values by 20 ppm in two or more samples. Tests that did not fulfill the above-mentioned criteria were defined as negative after testing for hydrogen production, following an oral load of 20 g lactulose. A single patient with a negative hydrogen breath test, who did not excrete increased amounts of hydrogen after lactulose was considered a hydrogen nonproducer and thus excluded from the present series. All symptoms occurring during the test and over the following 6 hours were recorded.

Data were analyzed using a χ^2 test, a t test for unpaired data, and the Wilcoxon signed-rank test.

RESULTS

When taking into account all data irrespective of the sorbitol dose, a minor degree of substrate malabsorption was found in 34 of 72 type II diabetics (47%) and in 20 of 42 controls (47%). Only one of the diabetics (10%) and one of the controls (10%) showed malabsorption at the dose of 2.5 g (group A); 11 diabetics (37%) and five controls (45%) tested positive at the dose of 5 g (group B); 15 diabetics (68%) and five controls (50%) tested positive at the dose of 10 g (group C); and seven diabetics (63%) and nine controls (81%) showed malabsorption at the dose of 20 g (group D) (Fig 1). In all the study groups, differences between diabetics and controls were not statistically significant.

In diabetics with a positive test, mean ± SD values for Cmax H_2 were 75.6 ± 57.3 ppm versus 57.0 ± 35.6 for controls. Due to the wide variation in values, this difference was not significant.

Ctot H_2 values at different doses of sorbitol were 77.3 ± 61.9 ppm/h (group B), 52 ± 38.8 (group C), and 99.1 ± 84.1 (group D) in diabetic patients with a positive test, and 57 ± 28.8 (group B), 40.4 ± 20.7 (group C), and 82 ± 47.6 (group D) in controls (mean ± SD). Data for all groups are graphically compared in Fig 2. Differences between diabetics and controls were not significant in all the study groups considered.

MCTT ranged from 60 to 240 minutes in diabetics, with a median value of 150 minutes, and from 60 to 240 minutes in controls, with a median value of 120 minutes (Fig 3). The difference calculated by the Wilcoxon signed-rank test was not significant.

With a sorbitol load of 2.5 and 5 g, no symptoms were experienced by any diabetic or control subjects during or after the test. In group C, only two diabetics (both with a positive test) and two controls (one with a positive and one with a negative test) experienced minor symptoms manifesting as abdominal tension (three cases) and slight abdominal pain (one case). The one control subject with a negative test complained of abdominal tension immediately after ingestion of the sorbitol solution, a fact that cast doubt as to the responsibility of sorbitol in inducing this symptom. In group D, seven patients (six with a positive and one with a negative test) experienced symptoms together with six controls, who all showed positive tests; however, the difference was not significant. More than one symptom was present in two diabetics and four controls. In five diabetics and four controls, symptoms consisted of gaseousness and abdominal tension, in one diabetic and four controls abdominal pain, and in two diabetics and one control one or two bowel movements with loose stools (mild diarrhea).

Symptoms occurred almost invariably within 30 minutes of the first Cmax H_2, with the exception of three diabetics and two control subjects in whom the delay was slightly longer, 60 minutes (in three cases) and 90 minutes (in one case). Although Cmax H_2 was higher in symptomatic versus nonsymptomatic malabsorbers in both the diabetes group (87.0 ± 58.2 ppm *v* 52.8 ± 37.5) and controls (75.8 ± 44.0 *v* 47.3 ± 21.0), the difference was not significant.

DISCUSSION

The prevalence of sorbitol malabsorption, the Cmax H_2, and the Ctot, as well as MCTT and the prevalence of symptoms, did not differ between type II diabetics and normal controls, indicating that in the two populations the response to sorbitol is identical.

The prevalence of sorbitol malabsorption appeared to increase with augmented loads of the substrate, ranging in both study groups from 10% at a dose of 2.5 g to approximately 75% at the highest tested dose (20 g). These results are in accordance with previous observations in healthy subjects[2-4] and diabetic patients.[9]

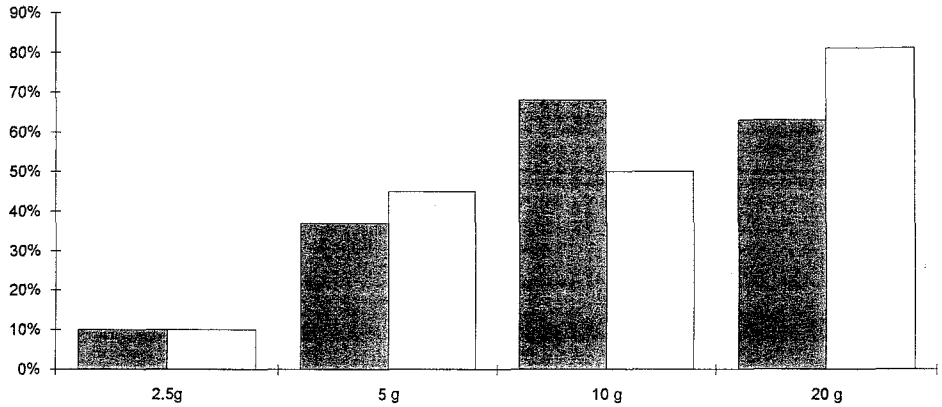

Fig 1. Prevalence of malabsorption after different oral loads of sorbitol in (■) diabetic patients and (□) normal controls.

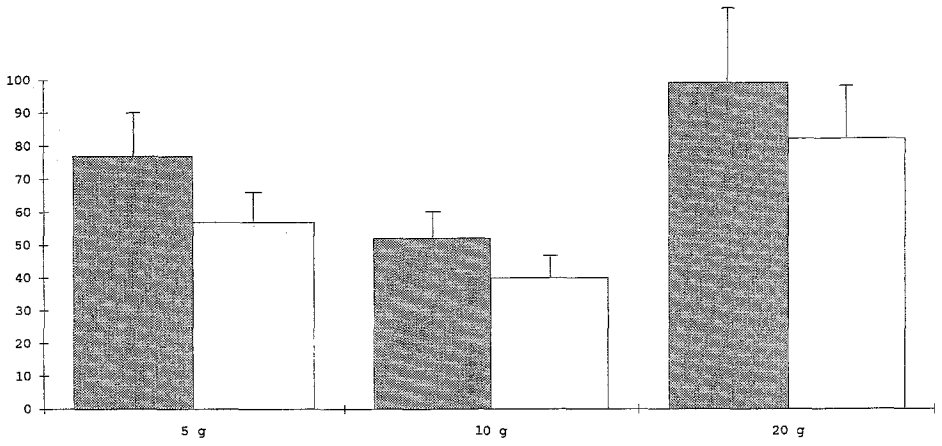

Fig 2. Mean ± SEM hydrogen production, expressed in arbitrary units (ppm/h), after different oral loads of sorbitol in (■) diabetic patients and (□) normal controls.

On the other hand, with respect to the prevalence of symptoms, our findings markedly differ from those reported by some investigators.[5,12] Both in the diabetes group and in the control group, most malabsorbers did not complain of abdominal symptoms. Only when the load of sorbitol was greater than 20 g did the majority of malabsorbers experience some abdominal discomfort, and some of them also experienced abdominal pain and/or diarrhea. An even lower prevalence of symptoms than that in the present series was reported by Beaugerie et al,[1,7] according to whom no subjects experienced marked gastrointestinal symptoms at a dose of 20 g sorbitol; 43 and 57 g sorbitol, respectively, were needed to induce abdominal pain and diarrhea in 50% of subjects, respectively. A similar discrepancy with other series may have several explanations. First, with respect to the osmolality of solutions, this factor was not maintained at a constant level by some investigators, although hyperosmotic fluids may accelerate intestinal transit time and enhance the probability of malabsorption and fermentation of substrate. Results similar to those reported in the present series were found by Jain et al,[3] who used isoosmolar solutions. Second, intestinal transit time could influence the prevalence of symptoms. However, notwithstanding the fact that MCTT was not reported by all investigators, this factor is unlikely to be responsible for the differing results, since the timing of increased excretion of hydrogen was found to be identical in asymptomatic and symptomatic malabsorbers.[9] In addition, in our series MCTT was identical in both diabetics and controls. Third, some genetically controlled factors could have influenced the prevalence of symptoms. A higher probability of gastrointestinal complaints was reported in non-whites (55%) versus whites (43%) after a load of 10 g sorbitol.[12] In a subsequent study by the same investigators, clinically severe sorbitol intolerance was more frequent in non-whites.[3] All subjects in our series were whites. Fourth, the ability to ferment substrate to hydrogen may vary among individuals. Due to a higher production of gaseous fermentation products, those with higher fermentation rates are more likely to experience a greater amount of symptoms.[12] However, since in our series Ctot H_2 and Cmax H_2 were not significantly different in symptomatic versus asymptomatic sorbitol malabsorbers, this does not seem to occur. Moreover, in this study diarrhea was associated with hydrogen excretion rates lower than those of most subjects with abdominal pain, suggesting that a reduced rather than an increased ability to ferment substrate is present in this condition, which is probably due to decreased colonic transit time. The fermentation rate is thus unlikely to be responsible for the varying prevalence of symptomatic patients in different series. The variable response of the bowel to gaseous distention could to some extent explain the differing results of the different series, unless patients with irritable bowel syndrome, an extremely frequent condition in Western countries, were included in some series. If such is the case, the high

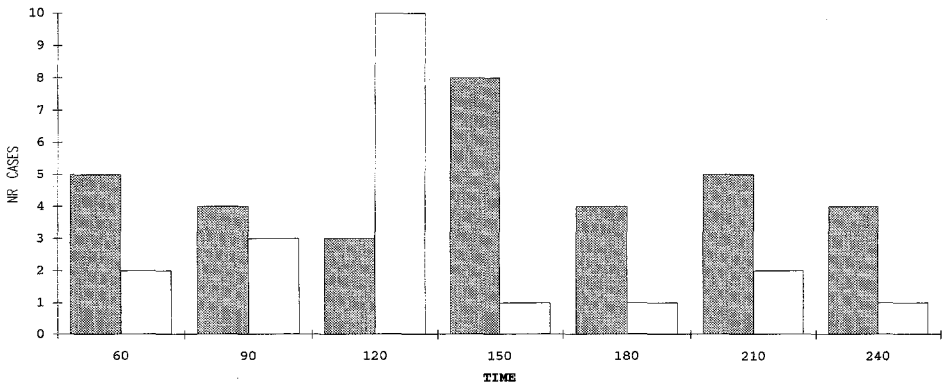

Fig 3. MCTT in (■) diabetics (median, 120 minutes) and (□) normal controls (median, 150 minutes). Number of cases on x axis.

sensitivity of these subjects to intestinal distention[13] may have affected the results.

The present data indicate that the sorbitol dose required to induce gastrointestinal symptoms is greater than that reported by some investigators. The modalities of sorbitol ingestion are also of prime importance, since complex foodstuff slows gastric emptying and thereby increases the tolerated dose.[14-15] The concurrent presence of fructose, which competes with sorbitol absorptive mechanisms, increases the probability of malabsorption[5,16] and pertinent symptoms, whereas the presence of glucose enhances absorption of sorbitol.[14] In our series, a single 10-g dose of sorbitol and, probably, also a far greater total daily load were well tolerated by the vast majority of normal controls and type II diabetics.

Our data do not support the view that sorbitol may play a relevant role in inducing diarrhea in type II diabetes.[17] Given that dietary sorbitol does not contribute to intracellular concentrations of this compound and thus does not play a role in the genesis of diabetes complications, the intake of reasonable amounts of sorbitol is not contraindicated in type II diabetic patients.

ACKNOWLEDGMENT

We wish to thank Alexandra Gaumert, MA, for translating the manuscript to English.

REFERENCES

1. Beaugerie L: Digestion des glucides et troubles fonctionnels intestinaux. Gastroenterol Hepatol 26:67-70, 1990

2. Hyams J: Sorbitol intolerance: An unappreciated cause of functional gastrointestinal complaints. Gastroenterology 84:30-33, 1983

3. Jain N, Patel V, Pitchumoni C: Sorbitol intolerance in adults. Prevalence and pathogenesis on two continents. J Clin Gastroenterol 9:317-319, 1987

4. Corazza G, Strocchi A, Rossi R, et al: Sorbitol malabsorption in normal volunteers and in patients with coeliac disease. Gut 29:44-48, 1988

5. Hyams J, Etienne N, Leichtner A, et al: Carbohydrate malabsorption following fruit juice ingestion in young children. Pediatrics 82:64-68, 1988

6. Beaugerie L, Flourie' B, Marteau P, et al: Digestion and absorption in the human intestine of three sugar alcohols. Gastroenterology 99:717-723, 1990

7. Beaugerie L, Flourie' B, Pellier P, et al: Tolerance clinique, absorption intestinale et valeur energetique de quatre polyols pris a' jeun. Gastroenterol Clin Biol 15:929-932, 1991

8. Wang YM, Van Eys J: Nutritional significance of fructose and sugar alcohols. Annu Rev Nutr 1:473-475, 1981

9. Badiga M, Jain N, Casanova C, et al: Diarrhea in diabetics: The role of sorbitol. J Am Coll Nutr 6:578-582, 1990

10. Metz G, Gassull A, Leed AR, et al: A simple method for measuring hydrogen in carbohydrate malabsorption by end-expiratory sampling. Clin Sci Mol Med 30:237-240, 1976

11. Bond J, Levitt M: Investigation of small bowel transit in man utilizing pulmonary hydrogen (H_2) measurements. J Lab Clin Med 85:546-555, 1975

12. Jain NK, Rosenberg DB, Ulahannan MJ, et al: Sorbitol intolerance in adults. Am J Gastroenterol 9:678-681, 1985

13. Ritchie J: Pain from distention of the pelvic colon by inflating a balloon in the irritable bowel syndrome. Gut 14:125-132, 1973

14. Beaugerie L, Nath SK, Desjeux JF: Le mucose stimule l'absorption du sorbitol a travers la muqueuse jejunale humaine. Gastroenterol Clin Biol 13:379-382, 1989

15. Zumbe' A, Brinkworth RA: Comparative studies of gastrointestinal tolerance and acceptability of milk chocolate containing either sucrose isomalt or sorbitol in healthy consumers and type 2 diabetics. Z Ernahrungswiss 31:40-48, 1992

16. Rumessen JJ, Gudmand-Hoyer E: Malabsorption of fructose-sorbitol mixtures. Interactions causing abdominal distress. Scand J Gastroenterol 22:431-436, 1987

17. Wegener M, Borsch G, Schaffstein J, et al: Gastrointestinal transit disorders in patients with insulin-treated diabetes mellitus. Dig Dis 8:23-26, 1990