Sorbitol malabsorption in normal volunteers and in patients with coeliac disease

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SUMMARY Sorbitol is a hexahydroxy alcohol used as a sugar substitute in many dietetic foods and as a drug vehicle. Previous studies have suggested that sorbitol ingestion may be an additional cause of non-specific gastrointestinal distress. We evaluated sorbitol malabsorption in 30 healthy volunteers, seven patients with untreated coeliac disease and nine patients with coeliac disease on a gluten free diet, using a four hour H₂ breath test. After ingestion of test solutions containing sorbitol 10 and 20 g and of four sweets (6.8 g sorbitol), 90%, 100%, and 62% of healthy volunteers, respectively had significantly raised H₂ excretion, indicating malabsorption of sorbitol. Of all healthy subjects tested, 45% after 10 g, 100% after 20 g, and 50% after four sweets complained of symptoms of carbohydrate intolerance during the eight hours after sorbitol. After a 5 g dose given at concentrations of 2%, 4%, 8%, 16%, malabsorption was shown in 10%, 12%, 22%, and 43% of the healthy volunteers. Symptoms of intolerance at 5 g were experienced only at concentrations of 8% and 16%. Unlike healthy volunteers and coeliac patients on a gluten free diet, 100% of untreated coeliacs malabsorbed a 2% solution of 5 g sorbitol. These results show that malabsorption and intolerance of sorbitol may result from ingestion of doses and/or concentrations usually found in many foods and drugs; they underline the need to consider this as a possible and hitherto underestimated cause of gastrointestinal symptoms.

Sorbitol, a hexahydroxy sugar alcohol occurring naturally in many fruits,^{1,3} is produced synthetically for commercial purposes by the catalytic reduction of glucose. Sorbitol is only partially absorbed,^{4,5} does not produce a rise in blood sugar when taken by mouth,⁶ and because of its sweetening power⁷ it is widely used as a sugar substitute in dietetic food and beverages and as a vehicle for suspending active drugs.

Recent studies, based on breath hydrogen (H₂) analysis, have shown that the majority of healthy adults malabsorb sorbitol⁸⁻¹⁰ and this is held to be the cause of functional bowel complaints after ingestion of sorbitol contained in sweets,¹¹ chewing-gum,^{12,13} dietetic food,¹⁴ and drugs.¹⁵

As sorbitol can be found in a number of commercial products at high concentration, we studied

the effect of varying amounts and concentrations of this substance on its malabsorption and intolerance in healthy volunteers and in patients with coeliac disease.

Methods

SUBJECTS

Thirty healthy volunteers, 15 women and 15 men, ranging in age from 22 to 61 years (mean 27±7), with no history of recent or recurrent gastrointestinal symptoms, recent antibiotic use, or diagnosis of gastrointestinal disease, took part in the study. Seven biopsy diagnosed untreated coeliac patients and nine coeliac patients on a gluten free diet were also studied. Informed consent was obtained from all the subjects taking part in the study.

TEST SOLUTIONS

All healthy volunteers were tested, on a single blinded basis, after an overnight fast, with two or

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more of the following solutions: 20 g in 250 ml water (8% solution; 447 mOsm/kg), 10 g in 250 ml water (4% solution; 224 mOsm/kg), and 5 g in 250 ml water (2% solution; 123 mOsm/kg). Five grams were also administered in 125, 62.5, and 31.2 ml water (4%, 8%, and 16% solution, respectively with corresponding osmolality of 221, 428, and 973 mOsm/kg). Eight healthy volunteers were also tested after having eaten two and four sweets each containing 1.7 g sorbitol. Untreated and treated coeliacs were tested with 5 g sorbitol in 250 ml water (2% solution). Serial testing was done at least two days apart. All subjects were known to be capable of producing H₂ after ingestion of 10 g lactulose.

All subjects were asked to report symptoms such as bloating, abdominal pain, and diarrhoea which may have occurred during the eight hour period after sorbitol ingestion. Subjects who had experienced at least one of these symptoms were defined as sorbitol intolerant.

BREATH H₂ TESTING

End expiratory breath samples were collected before and at 30 min intervals for four hours after ingestion of the test sugar solution. Samples were tested for H₂ concentration with a gas chromatograph (Microlyzer Model 12, Quintron, Milwaukee, WI, USA) and

Fig. 1 Maximum increase in breath hydrogen concentration over fasting baseline (Δ ppm) in healthy volunteers after the ingestion of 5, 10, and 20 g sorbitol in 250 ml water and two and four sweets containing 3.4 and 6.8 g sorbitol, respectively. Values above the dotted line indicate sorbitol malabsorption.

Fig. 2 Percentage of intolerant subjects after ingestion of 5, 10, and 20 g sorbitol in 250 ml water and two and four sweets containing 3.4 and 6.8 g sorbitol, respectively. Black bars: subjects with bloating, cramps and diarrhoea; shadowed bars: subjects with bloating and cramps; white bars: subjects with only bloating.

results were expressed in parts per million (ppm). A rise of at least 20 ppm over fasting baseline was considered evidence of sorbitol malabsorption. The cumulative H₂ excretion, over the four hour test, was estimated by calculating the area under the curve of H₂ concentration against time with the equation for the sum of the areas of consecutive trapezoids as proposed by Kotler *et al.*¹⁶

STATISTICAL ANALYSIS

The results were statistically analysed by the Student's *t* test and the linear correlation test.

Results

The rise in breath H₂ concentration over baseline (Δ ppm) after the ingestion of 5, 10, and 20 g sorbitol in 250 ml water and two sweets containing 3.4 g sorbitol and four sweets containing 6.8 g sorbitol is shown in Figure 1. After ingestion of both 10 g and 20 g the mean Δ ppm was significantly higher than after ingestion of 5 g. Although the mean rise in breath H₂ concentration was higher after 20 g than after 10 g, no significant difference was found between these two groups. The ingestion of four sweets (6.8 g) caused an increase in breath H₂ excretion significantly higher than after two sweets (3.4 g).

Sorbitol malabsorption was found in one of 10 healthy volunteers (10%) after 5 g solution, 18 of 20 (90%) after 10 g solution, six of 6 (100%) after 20 g solution, one of 8 (12%) after two sweets, and five of 8 (62%) after four sweets. A rise $\geq$ 20 ppm in breath H₂ excretion was observed as early as 30 min and as late as 110 min after sorbitol ingestion.

The proportion of intolerant subjects rose with increases of sorbitol doses and concentrations (Fig. 2). All but one of the intolerant subjects were malabsorbers but the malabsorbers were not all intolerant.

Figure 3 shows that there was no significant difference in mean Δ ppm values after administration of 5 g solution of sorbitol at different concentrations. While only one subject of 10 (10%) was shown to malabsorb a 2% solution, however, one of eight (12%), two of nine (22%), and three of seven (43%) were shown to malabsorb 5 g of sorbitol in 4%, 8%, and 16% solution, respectively. Only one subject after 8% solution and two subjects after 16% solution experienced symptoms of intolerance.

Five grams in a 2% solution were also given to seven untreated coeliacs and nine coeliacs on a gluten free diet. As shown in Figure 4, excretion of H_2 was significantly higher in untreated coeliacs than in both healthy volunteers and treated coeliacs. No significant difference was found between healthy volunteers and coeliac patients on a gluten free diet. It was not possible to evaluate intolerance in the untreated coeliacs as most of them already suffered from the symptoms that we attribute to carbohydrate malabsorption.

A significant correlation between Δ ppm values and cumulative H_2 excretion ($r=0.85$, $p<0.001$) was found in all tests carried out and Figure 5 shows Δ ppm values and total H_2 excretion in the group of subjects, divided into tolerant and intolerant, to whom 10 g of sorbitol in 250 ml water were administered. No significant difference was found between

Fig. 3 Maximum increase in breath hydrogen concentration over fasting baseline (Δ ppm) in healthy volunteers after the ingestion of 5 g sorbitol test solutions at different concentrations (2%, 4%, 8%, and 16%). Values above the dotted line indicate sorbitol malabsorption.

Fig. 4 Maximum increase in breath hydrogen concentration over fasting baseline (Δ ppm) in 10 healthy subjects, seven untreated coeliac patients and nine coeliac patients on a gluten free diet after the ingestion of 5 g sorbitol in 250 ml water (2% solution). Values above the dotted line indicate sorbitol malabsorption.

tolerant and intolerant subjects either in Δ ppm values or total H_2 excretion.

Discussion

Sorbitol absorption is incomplete⁴ and it is well known that ingestion of 20–30 g can produce osmotic diarrhoea in most subjects.¹⁷ According to the recent literature the frequency of malabsorbers, after ingestion of 10 g sorbitol, ranges from 70%–80%, if a rise of 20 ppm is taken as an index of malabsorption.^{8–10} At this dose, even though there was marked inter-subject variability in H_2 production, we found an even higher frequency of malabsorption (90%). It was also found that 10% of subjects malabsorbed 5 g and 100% 20 g of sorbitol.

Our results, in agreement with those of other studies,^{8–10} seem to confirm that sorbitol malabsorption is dose related. By increasing the dose from 5 to

Fig. 5 Breath H₂ production evaluated in both mean Δ ppm and total H₂ excretion in 11 tolerant and nine intolerant healthy subjects after ingestion of 10 g sorbitol in 250 ml water (4% solution).

20 g in the same volume of water, however, the concentration of the solution also increases, and we decided to ascertain the effects of different concentrations on malabsorption by administering 5 g sorbitol at four different concentrations. Our results confirm that on 5 g sorbitol, by doubling the concentration of the solution from 2% to 4% to 8% to 16%, the frequency of sorbitol malabsorption increases from 10% to 12% to 22% to 43% respectively, even if this is not accompanied by a proportional increase in H₂ excretion. The frequency of malabsorption after ingestion of 6.8 g sorbitol in the form of four sweets is equal to 62%. The higher frequency of sorbitol malabsorbers on increasing the concentration of the 5 g solution can be explained by the fact that a hyperosmotic solution speeds intestinal transit and therefore worsens malabsorption.¹⁸ As our results show that the frequency of malabsorption after a solution of 10 g sorbitol in 250 mg (224 mOsm/kg) is greater than after a solution of 5 g in 31.2 ml (973 mOsm/kg), it seems that sorbitol malabsorption depends more on the dose than the osmolality.

In patients with malabsorption as a result of untreated coeliac disease the ingestion of the smallest and least concentrated dose used, 5 g in a 2% solution, provoked a highly significant increase in H₂ excretion as compared with healthy subjects. All the untreated coeliac patients resulted as sorbitol malabsorbers and this, to a certain extent, was predictable as in villous atrophy there is a reduced absorption of hydrophilic solutes of low molecular weight such as mannitol, another polyhydric alcohol with the same molecular weight as sorbitol (182.17).¹⁹ Even though we were unable to evaluate sorbitol intolerance in our coeliac patients, it is possible to speculate that ingestion of even small quantities of sorbitol may worsen symptoms such as bloating, abdominal pain, and diarrhoea.

Of our healthy volunteers, 45% after ingestion of

10 g and 100% after 20 g were sorbitol intolerant. No subject showed symptoms of intolerance after ingestion of a 2% solution of 5 g, however, two of seven (28%) did after 5 g in 16% solution. Also the severity of intolerance proved to be dose and concentration dependent as the majority of subjects tested suffered from diarrhoea only after 20 g. It must not be forgotten, however, that in the cases of sorbitol intolerance reported in literature, the daily intake of sorbitol varied by only a few grams¹³ to 170 g.¹²

As expected, not all the malabsorbers showed signs of sorbitol intolerance and, in agreement with other studies,^{8,9} we found no significant correlation between the presence of symptoms and the amount of breath H₂ production evaluated either in Δ ppm or total H₂ excretion over four hours after ingestion of 10 g. This can be explained on the basis of inter-individual differences in pain response to gut distension²⁰ or in efficiency of 'colonic salvage' of malabsorbed carbohydrates.²¹

In conclusion, our results confirm that nearly all healthy volunteers malabsorb sorbitol at a 10 g dose and that the percentage of malabsorbers at 5 g is concentration related.

The increasing use of sorbitol as an artificial sweetener may be clinically relevant¹¹⁻¹⁵ and recently the need to look closely at sorbitol malabsorption as an important cause of gastrointestinal distress of unknown origin has been emphasised.²² At present, there are a large number of dietetic foods and drugs on the market which contain sorbitol in doses and/or concentrations that, according to our study, could cause malabsorption and intolerance (Table). We suggest that habitual consumers of dietetic foods,

Table Sorbitol content of natural and dietetic foods and drugs

Natural foods	
Pears	up to 4.6 g/100 g dry weight ¹
Peaches	up to 1.0 g/100 g dry weight ¹
Prunes, dried	up to 2.4 g/100 g dry weight ¹
Plums	up to 15.8 g/100 g dry weight ²
Sweet cherries	up to 12.6 g/100 g dry weight ²
Apple juice (conc)	up to 5.4 g/100 g fresh weight ³
Pear juice (conc)	up to 12.0 g/100 g fresh weight ³
Dietetic foods*	
Sugar free gum	up to 2.5 g/piece
Sugar free mints	up to 2.0 g/piece
Diabetic jams	up to 57.0 g/100 g
Diabetic chocolate	up to 40.0 g/100 g
Drugs (syrops)†	
Multivitamins	up to 8.0 g/dose (53% solutions)
Bronchodilators	up to 5.0 g/dose (50% solutions)
Expectorants	up to 5.7 g/dose (57% solutions)

*Products commercially available in Italy; †Contents declared by the Italian pharmaceutical companies (Repertorio Farmaceutico Italiano, 1986).

diabetics and weight watchers, or users of drugs which contain sorbitol should be better informed, by the producers, about the possible onset of functional bowel complaints. The consumption of sorbitol through non-essential foods, such as chewing-gum and sweets, should be discouraged.

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