Review

The clinical impact of carbohydrate malabsorption

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Abstract

Malabsorption of carbohydrates such as fructose, lactose or sorbitol can often be detected among patients suffering from so-called non specific abdominal complaints. Sometimes the differential diagnosis may be difficult. So far successful treatment consists of dietary interventions only. Nevertheless, many questions are remaining still unanswered.

Introduction

The high prevalence of carbohydrate malabsorption as well as the high rates of so called non-specific abdominal complaints cause serious problems. Worldwide up to 30% of the population is supposed to be affected by gastrointestinal complaints and although by far not all seek medical advice, yet this population constitute the majority of patients seen by gastroenterologists [1,2]. In each single case it may be necessary to evaluate the large variety of differential diagnoses. A particular challenging problem is the presence of carbohydrate malabsorption as it is often not easy to discriminate whether it is the cause of the complaints or just a mere coincidence.

Pathophysiology

Carbohydrates, a major source of calories are taken in different structures from mono-, di-, oligo- onto polysaccharides. On the passage to the small intestine they are degraded enzymatically until finally the brush-border enzymes hydrolyse these into monosaccharides to be further absorbed via different carrier systems [3]. Malabsorption may be caused by two different mechanisms. With an underlying intestinal disease, for example coeliac disease or infections, the absorption of all sugars is restricted, while in the case of a single transport defect there is only an incomplete absorption of carbohydrates that are absorbed through this particular pathway.

Lactose, fructose and sorbitol are the most important sugars involved in eliciting gastrointestinal symptoms in case of incomplete absorption. Lactose containing products such as milk belong to the most important nutrients of mankind. Fruits and vegetables with large contents of fructose and sorbitol are of growing importance in our diet and have many favourable nutrimental aspects. Moreover, fructose and specially sorbitol are increasingly applied as sweetener by food manufacturers or in so-called sugar-free sweets.

The rare primary lactose malabsorption affecting newborns is an autosomal – recessive disorder that causes serious problems in the nourishment of infants and is treated by strict dietary avoidance of lactose-containing food and beverages [4]. Different mutations affect the structure and hence the activity of the enzyme [5].

In contrast to this rare disorder lactose malabsorption of adults is the most frequent malabsorption throughout the whole world. Usually at the age of 5–7 years the production of lactase in the intestinal brush border decreases and malabsorption occurs as a physiological consequence, however, often without clinical symptoms even in spite of ongoing intake of lactose [6–8]. In some parts of the world (especially among Caucasians in the northern part of Europe) genetically caused lactase persistence is dominating with enabling the permanent intake of lactose. Maybe even this capacity is the cornerstone of Milchwirtschaft. Nucleotide polymorphism explaining persistent lactase activity was found to be prevalent in northern Europeans, however, not in other ethnic groups with persistent lactase activity, thus leaving many open questions [9–12].

Fructose is considered to pass the brush-border by GLUT 5 a member of the glucose transporter family. But meanwhile a significant effect of GLUT 2 as complementary factor has been shown [13,14]. A deficiency – congenital as well as acquired – causes malabsorption. For therapeutical purpose it is important to know, that
the presence of glucose stimulates the absorption of fructose, while sorbitol does worsen it [15]. Sorbitol is absorbed only in very small amount in most humans. Absorption is assumed to take place by diffusion [16,17].

**Symptoms**

Most patients with symptomatic carbohydrate malabsorption complain of flatulence, distension, diffuse abdominal pain with colics, sometimes with concomitant diarrhoea. Headache after the intake of the sugar which is malabsorbed may even occur. It could be demonstrated, that successful dietary restrictions not only stop gastrointestinal complaints, but also may improve the mood; the effect on plasma tryptophan levels has been suggested as a possible pathway [18,19]. However, symptoms are generally non-specific and there is no leading symptom for a single sugar [2].

The abdominal symptoms are considered to be caused by an increased osmotic load of the malabsorbed sugar remaining in the small intestine with increased intraluminal water and consecutive accelerated transit. The production of gas is associated with the action of bacteria in the colon and diarrhoea occurs if the increased amount of intraluminal water cannot be reabsorbed in the colon.

However, these usual explanations bear some limitations. First, about half of all malabsorbers are free of complaints, even if they ingest the incompletely absorbed sugar. Moreover, from the above quoted studies of lactose malabsorption we know that the condition starts within the first decade of life but symptoms occur - if ever- often much later. Similar data are available about children with fructose malabsorption showing malabsorption rates nearly identical to those of adults [20,21] indicating that the underlying disturbance is present already early in childhood, however, often without concomitant symptoms.

And most important in more than 50% of all affected patients history reveals that symptoms began after gastrointestinal infection and/or an antibiotic therapy.

These observations were our basis for two small investigations that showed that the degradation of the malabsorbed sugar in anaerobic stool cultures correlates with the occurrence of symptoms in affected patients. Moreover, this augmented degradation of sugar interpreted as increased colonic bacterial activity was accompanied by a change of pattern of the short chain free fatty acids in favour of butyrate [22,23].

Although data on colonic fermentation and its role in the pathogenesis of these non-specific abdominal complaints are increasing the mechanism is still by far not completely understood, thus, selective therapeutic interventions being not available at the moment [24,25].

**Prevalence**

Taken together the deficiency of lactase is the most common enzymatic defect in the world. However, there are significant regional differences in its prevalence. The overwhelming majority in Asia and Africa as well as the indigenous people in America and Australia are affected while in Europe there is a significant decline from south to north. Malabsorption rates between 70% and 100% in Italy and Turkey are in contrast to rates below 10% in Scandinavia [26]. Furthermore, it is of great interest that there are isolated populations like some tribes, for example, in Africa with low rates of lactase deficiency and a lifestyle (migratory cattlemen) distinct from that of their environment [27].

Malabsorption rates for fructose and sorbitol are very similar in all studies throughout the world. They vary according to the dosage and the concentration of the tested sugar. After the intake of 50 g fructose in 250 ml water (20% solution) 60–70% of patients as well as control subjects show malabsorption, while the rate is at about 40% when 25 g (10% solution) is used [2]. As for sorbitol the test dosages are less standardized, but even after the intake of only 10 g malabsorption rates close to 100% are reported [2]. It is not only the similar rates in patients and healthy controls that is remarkable, but also the fact that about 50% of all malabsorbers are non-symptomatizing. In lactose malabsorbers the occurrence of concomitant symptoms is more heterogeneous [2].

**Diagnosis**

Although there are direct methods to detect carbohydrate malabsorption that are available, yet only indirect methods are used in clinical routine practice. The application of a tube in the coecum to collect and measure a malabsorbed sugar is inappropriate for routine purposes. Even the determination of the enzymatic activity of disaccharidases in small intestinal biopsies is rarely used. In the past glucose measurement in blood was used to evaluate lactose malabsorption. However, the implementation of H2-tests mainly by Levitt and Donaldson [28] made the diagnosis much easier. Although meanwhile C13 exhalation tests are also available yet the H2-exhalation test has become the method of choice for the investigation of carbohydrate malabsorption.

After the intake of a sugar in case of incomplete intestinal absorption the sugar passes to the colon and is degraded there by local bacterial flora into hydrogen, methane, carbon dioxide and short chain free fatty acids. A small amount of hydrogen is absorbed into the blood and is exhaled during the first passage through the lungs. A rise in hydrogen in the exhaled gas (over 20 ppm) indicates carbohydrate malabsorption [29]; apart from intestinal bacterial overgrowth there is no other pathway for production of this gas. The increase in hydrogen to over 20 ppm as indicator of malabsorption is broadly accepted, however, not repeatedly evaluated. Further parameters such as at least a doubling of the initial hydrogen value are arbitrary to avoid false positive results. The extent of the increase of hydrogen has been reported to correlate with symptoms in some studies [30] an observation we could not confirm in many series. The concomitant measurement of methane in addition to hydrogen is possible, but not widely spread. So far, it is not really clarified whether it improves the accuracy of the test so far. However, there are interesting observations of symptoms in methane producers [31].

In practice after an overnight fast the patient has to drink a solution of a special amount of the investigated sugar (mostly 50 g lactose, 25 g fructose while for sorbitol various quantities are used) usually dissolved in 250 ml of water. Before the ingestion and then every 10 (with lactulose) or 30 min after hydrogen production is measured using ion-sensitive electrodes. During the fructose test it is also strongly recommended to measure the blood sugar to be able to discriminate the more dangerous fructose intolerance, an aldolase deficiency of the liver. In those patients, who may have very similar symptoms as patients with the simple malabsorption, severe hypoglycaemia may occur and even lethal complications are possible. Therefore, in this context it is to point out that the term fructose intolerance should be strictly applied for these patients with the severe liver enzyme deficiency.

In practice it is also important to perform a lactulose breath test. Lactulose cannot be split in the human small intestine and, therefore, causes an increase in hydrogen production. As a considerable number of patients have no hydrogen producing bacteria false negative results cannot be excluded without a lactulose test done. Moreover, this test (sometimes in combination with the glucose test) can give some hints to the intestinal transit time and the occurrence of intestinal bacterial overgrowth that may otherwise cause false positive results [2].
A further advantage of breath tests is that many other sugars can be tested at different dosages and concentrations, as well as combinations of sugars or even complete meals.

Finally, all investigated patients should be asked about complaints during and the day after the test for a better correlation and evaluation of the clinical importance of the result.

Newer developments in diagnostic methods in suspected cases of lactose malabsorption using genetic testing have to be further evaluated in clinical practice [32], but there are some doubts whether they can substitute tolerance tests. Nevertheless, they may be helpful in special situations [33].

**Treatment**

After establishing the diagnosis a strict dietary regimen is recommended for a limited period of time (about 14 days). The intake of the incompletely absorbed sugar should be avoided as much as possible. If the patient remains free of symptoms, this is considered a confirmation of the diagnosis - especially if symptoms reappear after dietary non-compliance.

If the diagnosis seems adequately confirmed, a modification of the diet is possible. Generally, for all sugars there is the option of allowing a controlled intake of small amounts of the sugar concerned that can be tolerated. An even better way for tolerating the sugar is by mere dilution that is if this sugar is added to a meal or the intake follows a meal. Adaptation of the small intestine, that means better tolerance due to continuous ingesting of increasing amounts, however, seems not possible [30].

Moreover, there are also more specific dietary options. In case of lactose-malabsorption dairy products free of lactose as well as products such as yoghurt or kefir which contain organisms able to provide some lactase activity can be used [34]. Finally, especially for lactose containing liquids there is the possibility of adding lactase [35].

Fructose malabsorbers do not need a complete abstinence of fructose containing products. Based on the fact that all can tolerate saccharose, a disaccharide consisting of fructose and glucose different malabsorption studies have been performed by our group as well as others in which we added glucose and other carbohydrates to fructose in fructose malabsorbers. In the presence of equimolar amounts of glucose, fructose is tolerated and no malabsorption is detectable in breath tests. Sugars activating the glucose carrier system have the same effect while others such as, for example, sorbitol even augment the incomplete absorption and may deteriorate clinical symptoms [36–39].

Concerning sorbitol malabsorption avoidance of the sugar is the only option. The intake of small quantities of sorbitol containing food may be attempted, preferably following meals to increase dilution.

These treatment options have been investigated in several studies. All of them have methodological problems (documentation of adherence, description of the dietary regimen, assessment of improvement as well as others) but show similar results.

In a study by our group [40] with a prospective and a retrospective part to evaluate a possible placebo effect we observed a significant improvement in 60–100% of patients according to the degree of compliance. However, 30–50% also reported improvement in spite of only poor to moderate compliance. This may be a hint that in some cases symptoms may disappear again after some time or probably and even more important that the initial diagnosis was not the cause of the symptoms as malabsorption persisted.

Another long-term investigation [41] showed clinical improvement in 81% after 1 month persisting in 67% of cases over 1 year.

The fact that many patients with non-specific complaints feel better for some weeks after colonoscopy (cleansing of colon being suggested as a reason) led to attempts to influence the bacterial flora of the colon. However, the reported effect of malabsorption on the butyrate production [23] and possible detrimental effects [42] on colonic diseases (including carcinogenesis) lead to reluctance against approaches with antibiotics and all attempts to modify the bacterial composition of the colon [43,44].

In conclusion, carbohydrate malabsorption is an important differential diagnosis in patients with non-specific abdominal complaints. Whereas malabsorption of lactose is well accepted in the community for long, malabsorption of fructose and sorbitol has meanwhile gained broader attention. Although diagnosis is simple, yet the clinical importance of the diagnosis of malabsorption in the single patient is sometimes difficult to estimate. At present dietary modification is the cornerstone of treatment. Still open questions remain not only in the diagnosis but more important in the pathogenesis of symptoms and the possible influence of degradation products on more serious diseases such as colonic neoplasms deserve further investigation.

**Conflicts of interest**

The authors declared that there was no conflict of interest.

**References**


