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The modification of sucrose absorption by acarbose

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Summary

The effects of acarbose on the rate and time-course of sucrose absorption were determined in healthy children by means of the $^{13}$C-sucrose breath test and breath hydrogen assays. Each child was tested with and without prior acarbose administration (50 mg). According to the breath hydrogen assays, 25-90% of the sucrose was not absorbed after acarbose. The $^{13}$C breath test indicated delayed but complete absorption of the $^{13}$C. Thus, the sucrose unabsorbed after acarbose administration may be degraded by bacterial fermentation in the intestine, with absorption of the resulting organic acids.

Introduction

Slower absorption of carbohydrates from the gastro-intestinal tract may be of benefit in juvenile diabetics, when insulin secretion is deficient and cannot cope with the postprandial blood glucose increase. Therefore different groups of authors have been interested in the potential use of dietary fibres and enzyme inhibitors in the treatment of diabetes [1-4]. Acarbose, an $\alpha$-glucosidase inhibitor, is reported to prevent the breakdown of starch, disaccharides and sucrose by the corresponding enzymes [5, 6]. The aim of this study was to investigate the influence of acarbose on the rate and time course of sucrose absorption in healthy children by means of the $^{13}$C-sucrose breath test and breath hydrogen determination.

Methods

Orally administered $^{13}$C-sucrose, uniformly labelled (UL), will be converted
to $^{13}$C-UL-fructose at the site of the jejunal brush border. The $^{13}$C-mono-saccharides then absorbed will be metabolized afterwards to $^{13}$CO$_2$ and H$_2$O. The $^{13}$CO$_2$ exhilation is regarded as an index of sucrose absorption.

Breath hydrogen is produced in the human large intestine by bacterial fermentation from unabsorbed carbohydrates. Hydrogen diffuses into the blood stream and is eliminated via the lung. In breath hydrogen studies the amount of H$_2$ produced is considered to be a good index for comparing and calculating the loss of carbohydrates after loads with different sugars in the same individual [7]. To calculate sucrose malabsorption after acarbose an oral load with lactulose is recommended as a reference system, because lactulose is said not to be absorbed from the gut [7].

In 7 healthy children a $^{13}$C-enriched oral sucrose load (42.75 g sucrose per m$^2$ plus 2.85 mg/kg $^{13}$C-UL-sucrose) was performed. Each child was tested twice, with and without a previous administration of 50 mg of acarbose or a dummy tablet. Thus each child served as its own control. Expired breath samples were collected before the administration of the sucrose load and at intervals of 30-60 minutes up to 5-7 hours afterwards.

Breath samples were analysed for $^{13}$CO$_2$ by a mass spectrometer (Varian MAT 230), and for H$_2$ by gas chromatography (Varian M 3700; molecular sieve 50 Å, 36-60 mesh, argon). Details of methods are described elsewhere [8, 9].

To estimate sucrose malabsorption an oral load with lactulose was performed in some of the children.

Results

Following the ingestion of a $^{13}$C-enriched sucrose load $^{13}$C concentrations in breath rise and fall gradually, peaking at about 2.25 hours (range 2.2-5.5 hours). The intake of 50 mg of acarbose grossly altered the shape of the curve. It delayed, flattened and lowered the $^{13}$CO$_2$ peak (peaking time 2.75 hours, range 2.5-3.5 hours) and diminished the slope of the curve after peaking.

Figure 1 shows the $^{13}$C elimination in 1 child with and without administration of 50 mg of acarbose. The reproducibility of the method is shown by testing the same child twice.

The cumulative $^{13}$C elimination after acarbose decreased predominantly during the first 2-3 hours, when $^{13}$C elimination amounts to only 50% of the placebo values at 1 hour and to only 60% after 3 hours. However, after 5 hours the $^{13}$C elimination already reached 70% of the placebo values and in 1 child tested up to 7 hours no difference was found any longer (Fig. 2).

In healthy children an increase of breath hydrogen was never found after an oral sucrose load, indicating an almost complete absorption (Fig. 3). The
Fig. 1: The influence of 50 mg of acarbose (first test \(\cdot\rightarrow\cdot\), second test 6 months later \(\cdot\rightarrow\cdot\); placebo \(\cdot\rightarrow\cdot\)) on sucrose absorption, measured as cumulative \(\text{\textsuperscript{13}C}\) elimination, after an oral \(\text{\textsuperscript{13}C}\)-enriched sucrose load in a healthy boy.

Fig. 2: Cumulative \(\text{\textsuperscript{13}C}\) elimination in a diabetic child after an oral \(\text{\textsuperscript{13}C}\)-enriched sucrose load. Acarbose 50 mg \(\rightarrow\cdot\), placebo \(\cdot\rightarrow\cdot\).
Fig. 3: Breath hydrogen in a healthy boy following an oral sucrose load (with *—* and without ●—● concomitant administration of 50 mg of acarbose) and after an oral lactulose load ▲—▲.

Fig. 4: Influence of 50 mg of acarbose (white column; placebo hatched column) on breath hydrogen production (area under the curve) for 5 hours after an oral sucrose load. *: \( P < 0.005 \).
concomitant intake of 50 mg of acarbose increased the breath hydrogen elimination in children significantly (Figs 3 and 4).

Comparing the breath hydrogen production from the sucrose-acarbose load with that from a similar lactulose load, acarbose prevented sucrose absorption almost completely (i.e., about 75-90% of the sucrose administered in some of the children (Fig. 3). In others, only 25-50% of the sucrose intake seemed not to be absorbed from the small intestine.

Discussion

Using the $^{13}$C-sucrose and the $^{13}$C-glucose breath test it was shown in healthy children that an oral sucrose load is absorbed from the small intestine to the same extent and as quickly as glucose [8]. Furthermore, no increase in breath hydrogen was seen, indicating an almost complete absorption from the gut. From these 2 tests it appears that acarbose inhibits sucrose absorption. However, the difference in impairment of sucrose absorption calculated from both tests is quite large. Breath hydrogen levels after acarbose point to an extensive amount of sucrose not being absorbed from the small intestine (up to 90%); data from the $^{13}$C-sucrose breath test, on the other hand, show much less inhibition (about 50%) during the first 2 hours and a catch-up of ‘absorption’ thereafter.

For this apparent discrepancy 3 explanations may be offered:
1. lack of inhibition of acarbose on sucrose absorption in the lower small intestine,
2. a possible absorption of unchanged sucrose from the large intestine,
3. bacterial fermentation of saccharides and resorption of $^{13}$C-labelled cleavage products at the site of the large bowel.

These cleavage products of sucrose in the form of short-chain [10-14] organic acids will diffuse in the blood stream, will be metabolized and, entering the CO$_2$-HCO$_3^-$-pool, will be exhaled as $^{13}$CO$_2$.

The first rise in breath hydrogen appears about 90-120 minutes after the oral sucrose load, when unabsorbed saccharides reach the large intestine. Therefore, the increase of $^{13}$CO$_2$ during the first 2 hours reflects real sucrose absorption. However, afterwards the $^{13}$C elimination will enclose the uptake of $^{13}$C material in the form of either sucrose or cleavage products.

In conclusion, acarbose only delays but does not diminish the overall absorption, metabolism and elimination of $^{13}$C material after an oral $^{13}$C-enriched sucrose load. Acarbose 50 mg will inhibit sucrose absorption to about 50%. The unabsorbed rest is apparently not totally lost from the organism but can be salvaged for energy purposes because of bacterial fermentation to short-chain organic acids, which will diffuse into the blood stream.
References


