

CASE REPORT

Adult hereditary fructose intolerance

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Abstract

Hereditary fructose intolerance (HFI) is an under-recognized, preventable life-threatening condition. It is an autosomal recessive disorder with subnormal activity of aldolase B in the liver, kidney and small bowel. Symptoms are present only after the ingestion of fructose, which leads to brisk hypoglycemia, and an individual with continued ingestion will exhibit vomiting, abdominal pain, failure to thrive, and renal and liver failure. A diagnosis of HFI was made in a 50-year-old woman on the basis of medical history, response to IV fructose intolerance test, demonstration of aldolase B activity reduction in duodenal biopsy, and molecular analysis of leukocyte DNA by PCR showed homozygosity for two doses of mutant gene. HFI may remain undiagnosed until adult life and may lead to disastrous complications following inadvertent fructose or sorbitol infusion. Several lethal episodes of HFI following sorbitol and fructose infusion have been reported. The diagnosis can only be suspected by taking a careful dietary history, and this can present serious complications.

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Key words: Adults; Fructose intolerance; Diet; Fructose; Sorbitol

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INTRODUCTION

Hereditary fructose intolerance (HFI) is an autosomal recessive inborn error of metabolism that results from a deficiency of fructose 1-phosphate aldolase in the liver, intestine and kidney.

The estimated incidence is 1 in 20 000 live births^[1] and the carrier frequency is 1 in 70, but the prevalence of HFI in adults is unknown. The clinical symptoms were first described by Chambers and Pratt in 1956^[2].

Affected individuals fail to metabolize fructose completely in the liver, intestine and kidneys because of deficiency of fructose 1-phosphate aldolase and ingestion of fructose, sorbitol or sucrose causes abdominal pain, vomiting and symptomatic hypoglycemia. The syndrome typically appears in the newborn at the time of weaning from the breast when food containing sucrose or fructose is given. Continued ingestion results in poor feeding, growth retardation, gradual liver and kidney failure acidosis, and eventually death^[3]. Affected children soon develop an aversion to all foods and protect themselves by self-imposed fructose and sucrose restriction.

The strict dietary exclusion leads to normal growth and longevity. Nevertheless, complete elimination of this sugar from the diet is difficult to achieve, especially for undiagnosed adults, without professional advice. These people may suffer symptoms throughout life and represent a diagnostic challenge for attending physicians. Furthermore, potentially lethal complications may result from inadvertent infusion of fructose- or sorbitol-containing solutions in a hospital setting^[4,5].

CASE REPORT

A 50-year-old German woman presented with a long life history of aversion to sugary foods. She reported being breast fed until the age of 2 years, and her mother said that she refused the usual sucrose-containing formulas. She described nausea, vomiting, diffuse abdominal pain and hypoglycemic symptoms even after the smallest amount of sugar or fruit. Her 2-year-old brother died after receiving an intravenous infusion in hospital, while her parents and three siblings are asymptomatic. She takes no regular medications. On examination, she

Table 1 FTT using 250 mg/kg body weight showing glucose, phosphate, uric acid and magnesium levels in the blood following injection of fructose

Time (min)	Glucose (mg/dL)	Phosphate (mmol/L)	Uric acid (mg/dL)	Magnesium (mmol/L)
0	87	1.000	5.1	0.72
15	67	0.77	6.74	0.84
30	61	0.64	7.74	0.8
45	60	0.80	7.58	0.88
60	68	0.83	7.58	0.91

had mild thoracic scoliosis with no neurological defect. Otherwise, physical examination was unremarkable.

Results of laboratory investigations including full blood count, urea, creatinine, electrolytes, full biochemical profile, amylase lipase and lipid studies, liver function tests and insulin level were within normal ranges. A fructose tolerance test (FTT) using 250 mg fructose per kilogram body weight was performed. At 0, 15, 30, 45 and 60 min after fructose injection, blood samples were taken for analysis of glucose, phosphate, uric acid and magnesium. A typical abnormal FTT was observed after the infusion, i.e. a drop in serum glucose and serum phosphate and rise in serum uric acid and magnesium concentration occurred (Table 1).

Thirty minutes after fructose injection, she developed significant dizziness, sweating, tremor and abdominal pain that were closely observed, and by 60 min her symptoms improved. The diagnosis was further confirmed by histochemical analysis of an endoscopic biopsy specimen from the small intestine, which showed 70% reduction in aldolase B activity in the mucosa, and molecular analysis of leukocyte DNA extracted from a blood sample using PCR amplification revealed that she had inherited two doses of the mutant gene, one from each parent, as the cause of the disease.

DISCUSSION

Fructose is a natural component of many plants and is distributed widely among most fruits and vegetables. Fructose is metabolized primarily in the liver and to some extent in the kidney, small intestine and adipose tissue^[6]. Deficiency in aldolase B in the liver, kidney and small intestine causes fructose intolerance^[7]. After ingestion, fructose rapidly enters the hepatocytes where fructokinase phosphorylates it to fructose 1-phosphate. Fructose 1-phosphate accumulates in HFI because of deficiency of the enzyme fructose 1-phosphate aldolase, which splits fructose 1-phosphate into glyceraldehydes and dihydroxyacetone phosphate.

The accumulation of fructose 1-phosphate results in inhibition of other enzymes, namely phosphorylase, liver fructose 1-6 bisphosphate aldolase and fructokinase. This results in impaired glycogenolysis and glyconeogenesis, and may induce hypoglycemia^[8]. Early exclusion of fructose and sucrose from the diet is accompanied by dramatic improvement; otherwise, growth is retarded and

progressive liver and renal disease are likely, and may lead to death^[9-11]. Diagnosis can be achieved by FTT and tissue diagnosis by direct assay of aldolase B activity in the liver, intestine or renal tissue. Recently, the use of PCR-based procedures has made the diagnosis simpler^[12,13].

The infusion of fructose- or sorbitol-containing solutions in patients with unsuspected disease leads to potentially fatal hepatorenal failure. More than 20 cases have been reported in Germany where the use of fructose or sorbitol solutions is long established^[14,15]. Our patient is alive at the age of 50 years with previously undiagnosed HFI, and did not have complications of the disease. This patient illustrates the importance of a careful dietary history and awareness of disease symptoms. In contrast, incorrect diagnosis and unawareness of possible pediatric problems in adult life may lead to catastrophic complications, while early recognition leads to effective management.

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