Fructose Intolerance

Fructose intolerance is an error in fructose metabolism caused by deficiency of the enzyme aldolase B. After ingestion, fructose is degraded to fructose-1-phosphate in the liver by fructokinase. Then, fructose-1-phosphate is degraded by aldolase B into dihydroxyacetone-phosphate (DHAP) and glyceraldehyde. A deficiency of aldolase B results in the accumulation of fructose-1-phosphate in cells and phosphate trapping. This accumulation has downstream effects on gluconeogenesis and glycogenolysis and the regeneration of ATP. Symptoms include hypoglycemia, vomiting, jaundice, cirrhosis and potentially kidney failure. This disease is inherited in an autosomal recessive fashion. Diagnosis is aided by dietary history, especially in infants who become symptomatic after breast feeding is supplemented by fructose containing foods. Treatment is based around strict avoidance of fructose in the diet. It is important to distinguish this disease from essential fructosuria, which causes a clinically benign elevation of fructose in the blood and urine.

PLAY PICMONIC

Pathophysiology

Deficiency of Aldolase B

Down-arrow Aldo-lace (B) Bee

Fructose-1-phosphate is degraded by aldolase B into dihydroxyacetone-phosphate (DHAP) and glyceraldehyde (GA). A deficiency of aldolase B results in the accumulation of fructose-1-phosphate in cells and phosphate trapping.

Fructose 1-P To DHAP And GA

Fruit-toast (1) Wand-Fonz-fairy to Dhapper Dog-hat or Glitter-pie

Fructose-1-phosphate is degraded by aldolase B into dihydroxyacetone-phosphate (DHAP) and glyceraldehyde (GA).

Accumulation Of Fructose-1-Phosphate

Fruit-toast (1) Wand-Fonz-fairy

A deficiency of aldolase B results in the accumulation of fructose-1-phosphate in cells. This traps phosphate in an unusable form that does not return to the general phosphate pool, resulting in depletion of phosphate and ATP stores. This has downstream effects on gluconeogenesis and glycogenolysis and the regeneration of ATP.

Inhibition Of Glycogenolysis

Inhibiting-chains with Glider-lights

Glycogenolysis is the breakdown of glycogen to glucose-1-phosphate and glucose. In hereditary fructose intolerance, the accumulation of fructose-1-phosphate in cells leads to trapping of phosphate which decreases the amount of ATP available to cells. Decreased ATP leads to inhibition of glycogenolysis and gluconeogenesis.

Inhibition Of Gluconeogenesis

Inhibiting-chains with Glue-genie

Gluconeogenesis is a metabolic pathway that results in the generation of glucose from substrates such as lactate, glycerol, and glucogenic amino acids. In hereditary fructose intolerance, the accumulation of fructose-1-phosphate in cells leads to the trapping of phosphate which decreases the amount of ATP available to cells. Decreased ATP leads to inhibition of glycogenolysis and gluconeogensis.

Clinical Features

Hypoglycemia

Hippo-glue-bottle

Due to inhibition of glycogenolysis and gluconeogenesis, individuals with hereditary fructose intolerance suffer from hypoglycemia.

Vomiting

Vomit

Vomiting is a common nonspecific symptom in hereditary fructose intolerance. Vomiting can also be seen secondary to hypoglycemia in this disorder.

Jaundice

Jaundice-janitor

Jaundice is yellowing of the skin and conjunctival membranes caused by hyperbilirubinemia, and it is often caused by liver disease. Aldolase B is preferentially expressed in the liver and deficiency can cause liver damage with presentation of jaundice.

Cirrhosis

C-roses-on-liver

Cirrhosis is characterized by fibrosis and scarring of the liver, leading to loss of function. Because aldolase B is expressed in the liver, deficiency can cause liver damage and cirrhosis.

Autosomal Recessive

Recessive-chocolate

This disease is inherited in an autosomal-recessive fashion.