Galactosemia

What is Galactosemia?

Galactosemia is a rare genetic metabolic disorder that is inherited in an autosomal recessive manner. It is an inborn error of carbohydrate metabolism characterized by elevated levels of galactose and its metabolites due to enzyme deficiencies involved in its metabolism. Galactose is the sugar found mainly in milk and dairy products. It is also produced by the body. Milk contains a sugar called lactose, and during digestion, lactose is broken down into the sugars glucose and galactose. Glucose can immediately be used as a source of energy by the body, but galactose needs to be further broken down before it can be utilized. The birth incidence of classic galactosemia is about 1 per 47,000 in the Caucasian population. The Philippine NBS data as of December 2018 gives a prevalence of 1 : 134,439.

PATHOPHYSIOLOGY

The galactose metabolic pathway with multiple enzymatic steps is shown. The enzymes allow the subsequent conversion of galactose to galactose-1-phosphate by GALK (1); galactose-1-phosphate and uridine diphosphate glucose (UDP glucose) to glucose-1-phosphate and UDP-galactose by GALT (2) and the interconversion of UDP-glucose and UDP-galactose by GALE (3). Children with galactosemia have very little or entirely lack an enzyme that helps the body break down galactose. There are three different enzyme problems that can lead to galactosemia. In the first type or classic galactosemia, the enzyme that is reduced or missing is called galactose-1-phosphate uridyl transferase (GALT). The GALT enzyme enables the body to break down galactose into glucose. The second type of galactosemia is due to a deficiency in uridine diphosphate galactose 4-epimerase (GALE). Its severe type clinically resembles classic galactosemia. The third type, is due to a deficiency in galactokinase (GALK), and presents primarily as cataracts in untreated patients.

Clinical Features

Patients can present with feeding problems, failure to thrive, hepatocellular damage, bleeding, and sepsis in untreated infants. In approximately 10% of individuals, cataracts are present. Failure to thrive is the most common initial clinical symptom of classic galactosemia. Vomiting or diarrhea usually begins within a few days of milk ingestion. Jaundice of intrinsic liver disease may be accentuated by the severe hemolysis occurring in some patients. Cataracts have been observed within a few days of birth. There appears to be a high frequency of neonatal death due to E. coli sepsis in patients with classic galactosemia.

The association of jaundice and hemorrhagic diathesis in the first 2 weeks of life is a clinical presenta on in which galactosemia must be considered. Coagulopathy may also be present in galactosemia with little evidence of liver disease. Galactosemia also causes learning and language problems in children, bone mineral density problems and ovarian failure in girls.

Treatment and Monitoring

Dietary elimination of milk and milk products containing lactose is the treatment for all types of galactosemia. There is no chemical or drug substitute for the missing enzyme at this me. An infant diagnosed with galactosemia will have to be on a soy-based formula. Dietary management under the close supervision of a metabolic dietician and a metabolic doctor is a must. Regular monitoring of blood galactose levels and regular evaluation by the genetic metabolic team is important for optimal treatment.

Prognosis

Despite an early galactose-free diet, long-term complications have been noted in older children and adults with classic galactosemia because of endogenous galactose production. These include speech problems, poor intellectual function, neurologic deficits (predominantly extrapyramidal findings with ataxia), and ovarian failure in females. Thus, the need for regular monitoring and evaluation is important.