
HMG-CoA Lyase Deficiency– Organic Acid Disorder

(Also known as 3-hydroxy-3-methylglutaric-CoA lyase deficiency)

What are organic acid disorders?

Organic acid disorders (also sometimes called organic acidemias) are a class of inherited metabolic disorders that occur when the body cannot break certain components of proteins (for example, branched-chain amino acids) and other substances. This leads to an accumulation of harmful substances in the blood and urine, which can cause serious health problems.

What is HMG Lyase Deficiency?

In the body, the breakdown of protein produces leucine and other amino acids. Leucine is further processed by an enzyme called 3-hydroxy-3-methylglutaryl-CoA lyase (HMG lyase). This enzyme is also important in producing ketone bodies, an important source of energy. HMG lyase deficiency occurs when this enzyme is not working well or is missing. This leads to the accumulation of harmful substances in the blood and a deficiency of ketone bodies.

What is its incidence?

HMG lyase deficiency is a rare disease. The incidence is unknown.

What causes the disease?

Mutations in the gene for HMG lyase results in enzyme that is not working well or is deficient.

What are the clinical features of the disease?

Although babies with HMG lyase deficiency are usually normal at birth, an episode of metabolic crisis leading to coma and death can be triggered by an illness or going without food for too long. The first episode usually occurs in infancy but can occur earlier or later in life. Increased amounts

of acidic substances may be found in the blood (acidemia) during a crisis. There may also be a lack of sugar and ketones (hypoglycemia and hypoketosis) in the blood. Other symptoms include lethargy, failure to thrive, vomiting, hypotonia, liver dysfunction and hyperammonemia (increased amounts of ammonia in the blood). They may also have hypotonia and seem irritable. In the long term, repeated episodes may cause brain damage and learning problems or mental retardation.

The presentation of HMG lyase deficiency is variable and there may be individuals with the disorder who are asymptomatic or do not develop symptoms until later in life.

How is the diagnosis confirmed?

The diagnosis of HMG lyase deficiency is confirmed by measuring urine organic acids to look for specific metabolites. Diagnostic testing is arranged by specialists at your local treatment centre.

What is the treatment of the disease?

The mainstay of treatment is to prevent fasting, especially when the child is ill. In an acute symptomatic episode, IV glucose and fluids are given. A low protein and/or low fat diet may be recommended in children with HMG lyase deficiency. Supplementation with carnitine may also be considered. Treatment can prevent metabolic crises and their sequelae. Treatment is coordinated by specialists at your local treatment centre.

What is the outcome of treatment?

If treatment is able to prevent episodes of metabolic crisis, children with HMG lyase deficiency have a good prognosis. However, response to treatment and therefore the outcome is variable.

Can a family have more than one child with HMG lyase deficiency?

HMG lyase deficiency is inherited as an autosomal recessive disorder. The parents of a child who has HMG lyase deficiency are assumed to be carriers for the disorder and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with the disorder. Prenatal testing for HMG lyase deficiency can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Unaffected siblings of a child with HMG lyase deficiency have a $2/3$ chance of being carriers. Carriers are healthy and do not have symptoms of HMG lyase deficiency.

Resources

<http://www.newbornscreening.info/Parents/organicaciddisorders/HMGCoA.html>

<http://www.oaanews.org/>

<http://www.geneclinics.org/>