
3-Methylcrotonyl-CoA Carboxylase (3MCC) Deficiency – Organic Acid Disorder

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 3MCC Deficiency?

In the body, the breakdown of protein produces leucine and other amino acids. An enzyme called 3-Methylcrotonyl-CoA Carboxylase further processes leucine. 3MCC deficiency occurs when this enzyme is not working well or is missing. This leads to the accumulation of harmful substances in the blood.

What is its incidence?

3MCC deficiency is a rare disease that affects about 1 in every 50,000 babies born in Ontario.

What causes the disease?

Mutations in the gene for 3-methylcrotonyl-CoA carboxylase results in enzyme that is not working well or is deficient.

What are the clinical features of the disease?

Although babies with 3MCC 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 at a few months of age. Increased amounts of ammonia and acidic substances may be found in the blood (hyperammonemia and acidemia) during a crisis. Other symptoms include lethargy,

failure to thrive, vomiting, hypotonia, seizures, breathing problems, and liver problems. They may also have hypotonia and seem jittery and irritable. In the long term, repeated episodes may cause brain damage and learning problems or mental retardation.

The presentation of 3MCC deficiency is variable and there may be individuals with the disorder who are asymptomatic or do not develop symptoms until later in life. Occasionally, asymptomatic women who have 3MCC deficiency will have infants who appear to have 3MCC deficiency on the newborn screen but are found later not to be affected. This finding is a transient state in the newborn as it is a reflection of the mother's metabolic status.

How is the diagnosis confirmed?

The diagnosis of 3MCC deficiency is confirmed by measuring urine organic acids. Diagnostic testing is arranged by specialists at your regional treatment centre.

What is the treatment of the disease?

The mainstay of treatment is to prevent fasting, especially when a child is ill. In an acute symptomatic episode, IV glucose and fluids can be given, along with other medications that can help the body to get rid of harmful substances. In the long term, a low protein diet may be recommended. Supplementation with carnitine may also be considered. This can prevent metabolic crises and their sequelae. Treatment is coordinated by specialists at your regional treatment centre.

What is the outcome of treatment?

If treatment is able to prevent episodes of metabolic crisis, children with 3MCC deficiency have a good prognosis. However, response to treatment and therefore the outcome is variable.

Can a family have more than one child with 3MCC Deficiency?

3MCC deficiency is inherited as an autosomal recessive disorder. The parents of a child who has 3MCC 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 3MCC 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 3MCC deficiency have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of 3MCC deficiency.

Resources

<http://www.newbornscreening.info/Parents/organicaciddisorders/3MCC.html>

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

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