HMG-CoA Lyase Deficiency

What is HMG-CoA Lyase Deficiency?

It is an organic acid disorder due to a deficiency in one of the enzymes involved in catabolism of leucine. This enzyme is called 3-hydroxy-3-methylglutaryl-CoA lyase (HMG-CoA lyase), this enzyme is also important in producing ketone bodies, an important source of energy. This leads to the accumulation of harmful substances in the blood and a deficiency in ketone bodies.

What causes the disease?

Mutations in the HMGCL gene are a potential cause of the HMG-CoA lyas enzyme deficiency.

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 eventually death can be triggered by an illness or going without food for too long. The first episode usually occurs at 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, learning problems, or mental retardation. The presentation of HMG lyase deficiency is variable and there may be individuals with the disorder who are asymptomatic (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. DNA molecular testing of the HMGCL gene may help also in confirming the diagnosis

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 D10% and fluids are given. A low protein and/or low fat diet may be recommended to children with HMG lyase deficiency. Supplementation with carnitine may also be considered. Treatment can prevent metabolic crises and their sequelae. A Biochemical genetics specialist and a Metabolic Genetics dietitian should coordinate the treatment.