Propionic Acidemia (PROP), Methylmalonic Acidemia (MUT), and Cobalamin Defects (Cbl A,B) - Organic Acid Disorders

What are organic acid disorders?

Organic acid disorders (also called organic acidemias) are a class of inherited metabolic disorders that occur when the body cannot breakdown 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 are PROP, MMA and CblA,B? What causes these diseases?

People with propionic academia (PROP) and methylmalonic acidemia (MUT) cannot properly process two substances (propionyl-CoA and methylmalonyl-CoA) that are produced in sequential steps during the breakdown of some amino acids. This leads to elevated levels of propionic and methylmalonic acids in their blood.

Propionic acidemia is caused by a defect in the enzyme propionyl-CoA carboxylase. Methylmalonic acidemia can be due to a defect in an enzyme methylmalonyl-CoA mutase (MUT) or if there is a deficiency or a problem with processing vitamin B12 (the cobalamin defects, Cbl A,B), which is a cofactor of this enzyme.

What is the incidence?

Propionic academia, methylmalonic academia and cobalamin defects are estimated to affect about 1 in every 20,000 to 40,000 babies born in BC.

What are the clinical features of these diseases?

Although babies with propionic academia, methylmalonic academia, or cobalamin defects are normal at birth, without treatment they may have an episode of metabolic acidosis with encephalopathy, which can progress to coma and death. Other symptoms include lethargy, failure to thrive, vomiting, hypotonia, and seizures. Increased amounts of ammonia and acidic substances may be found in the blood (hyperammonemia and acidemia). The presentation of methylmalonic academia and cobalamin defects are variable and there may be individuals with these disorders who are mildly affected or are asymptomatic, but may still be at risk for an acute metabolic crisis.

How is the diagnosis confirmed?

The diagnosis of PROP, MUT, or CblA,B is confirmed by looking for certain substances in the blood and urine.

Specific urine organic acid profiles, and specific acylcarnitine and amino acid profiles in the blood are helpful in confirming the diagnosis and differentiating these disorders. Enzyme studies and mutation analysis of the genes involved in the metabolism of propionyl and methylmalonyl CoA may also assist in confirming the diagnosis. Diagnostic testing is arranged by specialists at BC Children's Hospital.

The BC Newborn Screening Program is a collaboration of BC Women's Hospital & Health Centre, BC Children's Hospital and the BC Perinatal Health Program, all part of the Provincial Health Services Authority.

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What is the treatment of the disease?

A low protein diet is often recommended in children with PROP and MUT. Vitamin B12 injections may also be suggested if a problem with vitamin B12 metabolism (CblA,B) is identified. Affected children should also avoid going long periods without food. Supplementation with carnitine and antibiotics may also be considered. Treatment can prevent metabolic crises and their sequelae. 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 and to decrease the level of acid in the blood.

Treatment is coordinated by specialists at BC Children's Hospital.

What is the outcome of treatment?

If treatment is able to prevent episodes of metabolic crisis, children with propionic and methylmalonic academia can have a good prognosis. However, response to treatment and therefore the outcome is variable. Even with treatment, some children may still have developmental delays.

Can a family have more than one child with PROP, MUT or CblA,B?

PROP, MUT, and CblA,B are inherited as autosomal recessive disorders.

The parents of a child who has PROP, MUT, or CblA,B 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 PROP, MUT, or CblA,B 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 PROP, MUT, or CblA,B have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of PROP, MUT, or CblA,B.

Resources

http://www.newbornscreening.info/Parents/organicaciddisorders/MMA.html
http://www.newbornscreening.info/Parents/organicaciddisorders/PA.html
http://www.oaanews.org/
http://www.geneclinics.org/

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