BC Newborn Screening Program Information Sheet

Guanidinoacetate Methyltransferase Deficiency (GAMT) Cerebral Creatine Deficiency

What is GAMT Deficiency?

GAMT is an enzyme required for the synthesis of creatine. Creatine is particularly important in the brain where it provides a short-term energy pool. Deficiency of the GAMT enzyme leads to inadequate levels of creatine in the brain and the toxic buildup of a compound called guanidinoacetate. This combination leads to dysfunction in brain cells.

What is its incidence?

GAMT deficiency is a rare disease that affects less than 1 in every 300,000 babies born in BC.

What causes the disease?

Mutations in the gene for GAMT result in impairment or complete deficiency of the enzyme.

What are the clinical features of the disease?

Babies with GAMT deficiency are indistinguishable from healthy babies for the first few weeks of life. Without treatment however, low creatine and high guanidinoacetate levels can cause severe and irreversible damage to the brain. Guanidinoacetate levels rise within 24 hours of birth and newborns with elevated levels and genetic changes in the GAMT gene are investigated further.

How is the diagnosis confirmed?

The diagnosis of GAMT deficiency is confirmed by testing guanidinoacetate in urine and blood along other possible genetic tests. Diagnostic testing is arranged by specialists at BC Children's Hospital.

What is the treatment of the disease?

The mainstay of treatment is to provide supplementation of creatine along with dietary changes to limit the production of guanidinoacetate. This may involve restricted intake of some natural protein and supplementation with special medical formula.Treatment is coordinated by specialists at BC Children's Hospital.

What is the outcome of treatment?

If treatment is started early, children with GAMT deficiency have a good prognosis. However, this is a very rare disorder and only a small number of children have been treated from birth worldwide.

Can a family have more than one child with GAMT?

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

Resources

https://rarediseases.info.nih.gov/diseases/2578/guanidinoacetate-methyltransferase-deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=3