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My46 Trait Profile

HMG CoA lyase deficiency

Other Names: 3-hydroxy-3-methylglutaryl-CoA lyase deficiency, Hydroxymethylglutaric aciduria

HMG CoA lyase deficiency is a rare genetic condition characterized by the body's inability to break down a certain amino acid called leucine or make ketones. It is caused by mutations in the HMGCL gene that makes an enzyme called hydroxymethylglutaryl-CoA lyase.

Characteristics of HMG CoA lyase deficiency

HMG CoA lyase deficiency is a rare inherited metabolic disorder in which the body is unable to metabolize (i.e., break down and use) certain proteins and fats properly because it is not producing enough of an enzyme called hydroxymethylglutaryl-CoA lyase (also known as HMG CoA lyase). As a result, other compounds can build up in blood, urine, and tissues. Too much of these compounds can be harmful to the body and cause health problems.

People with HMG CoA lyase deficiency have difficulty breaking down the amino acid leucine and with producing ketones. Ketones are important compounds that can be used for energy by certain organs in the body. Because individuals with HMG CoA lyase deficiency cannot produce ketones, they are at risk for developing low blood sugar (hypoglycemia) and other problems if they do not eat for a length of time. Signs and symptoms of HMG CoA lyase deficiency usually appear in the first year of life, and can range from mild to life-threatening. Certain activities can trigger episodes of health problems called metabolic crises. These include fasting (not eating for a long time), infections or stress. During an episode, individuals with HMG CoA lyase deficiency may have vomiting, weak muscle tone (hypotonia), excessive tiredness (lethargy), and rapid breathing (tachypnea). Seizures or coma may also occur.

Diagnosis/Testing

Most individuals with HMG CoA lyase deficiency have changes or mutations in the HMGCL gene. This gene makes the enzyme hydroxymethylglutaryl-CoA lyase that is responsible for both breaking down the amino acid called leucine, and for producing ketones. Mutations in the HMGCL gene that cause this enzyme to not be made or to not be made properly result in many of the health problems seen in individuals with HMG CoA lyase deficiency.

Many babies with HMG CoA lyase deficiency are diagnosed early in life through newborn screening (NBS). NBS tests a spot of blood from the baby's heel, and looks to see if the 3-hydroxymethyl-3-methylglutaryl-coenzyme A lyase is working properly. NBS test results are confirmed with additional blood and urine chemical tests, and possibly genetic testing of the HMGCL gene.

Management/Surveillance

Individuals with HMG CoA lyase deficiency are typically managed by a team of specialty providers that can include: geneticists, genetic counselors, primary care doctors, nutritionists, and social workers. The amino acid leucine is found in many of the foods we eat, usually in what we would call "protein-rich foods." This also includes breast milk and infant formulas. This means it is very important for individuals with HMG to follow a customized low-protein diet. This diet usually includes a medical formula specially made to provide all amino acids except for isoleucine to ensure good nutrition. Specific medications and vitamin supplements (i.e. L-carnitine) are also often prescribed.

It is recommended that an emergency treatment plan, often documented by an "Emergency Letter" is made to ensure

that during times of illness or other metabolic stress, a child with HMG CoA lyase deficiency will be assessed for signs and symptoms of a metabolic crisis (e.g., poor feeding, vomiting, lethargy, excessive sleepiness, irritability) and given appropriate medical attention. Failure to do receive appropriate treatement can lead to coma and sometimes, death. It is of upmost importance that individuals with HMG adhere to their specific diet and treatment plans to avoid metabolic stress and/or crisis. In general, the earlier the individual is diagnosed and treated, the better the outcome.

Mode of inheritance

HMG CoA lyase deficiency is inherited in an autosomal recessive pattern. This means that an individual has to inherit two HMGCL mutations (i.e., one from each parent) to be affected with HMG. If both parents are carriers of an HMGCL mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with HMG CoA lyase deficiency. Babies born in the United States are screened for HMG CoA lyase deficiency by newborn screening.

Risk to family members

Parents of a child with HMG CoA lyase deficiency are carriers of HMG CoA lyase deficiency. If a sibling of a child with HMG CoA lyase deficiency is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of HMG.

Special considerations

None

Resources

Baby's First Test: 3-Hydroxy-3-methylglutaric aciduria
http://www.babysfirsttest.org/newborn-screening/conditions/3-hydroxy-3-methylglutaric-aciduria
Genetics Home Reference: HMG CoA Lyase Deficiency
http://ghr.nlm.nih.gov/condition/3-hydroxy-3-methylglutaryl-coa-lyase-deficiency
Medical Home Portal: HMG CoA Lyase Deficiency
http://www.medicalhomeportal.org/newborn/hmg-coa-lyase-deficiency
Organic Acidemia Association
http://www.oaanews.org
STAR-G Newborn Screening
http://www.newbornscreening.info/Parents/organicaciddisorders/HMGCoA.html

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