3-hydroxy-3-methylglutaryl-CoA Lyase Deficiency

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3-hydroxy-3-methylglutaryl-CoA lyase deficiency (also known as HMG-CoA lyase deficiency) is an uncommon inherited disorder in which the body cannot process a particular protein building block (amino acid) called leucine. Additionally, the disorder prevents the body from making ketones, which are compounds that are used for energy during periods without food (fasting).

Keywords: genetic conditions

1. Introduction

The signs and symptoms of HMG-CoA lyase deficiency usually appear within the first year of life. The condition causes episodes of vomiting, diarrhea, dehydration, extreme tiredness (lethargy), and weak muscle tone (hypotonia). During an episode, blood sugar levels can become dangerously low (hypoglycemia), and a buildup of harmful compounds can cause the blood to become too acidic (metabolic acidosis). If untreated, the disorder can lead to breathing problems, convulsions, coma, and death. Episodes are often triggered by an infection, fasting, strenuous exercise, or other types of stress.

HMG-CoA lyase deficiency is sometimes mistaken for Reye syndrome, a severe disorder that develops in children while they appear to be recovering from viral infections such as chicken pox or flu. Most cases of Reye syndrome are associated with the use of aspirin during these viral infections.

2. Frequency

HMG-CoA lyase deficiency is a rare condition; it has been reported in fewer than 100 individuals worldwide. Most people diagnosed with this disorder have been from Saudi Arabia, Portugal, or Spain.

3. Causes

Mutations in the *HMGCL* gene cause HMG-CoA lyase deficiency. The *HMGCL* gene provides instructions for making an enzyme known as 3-hydroxymethyl-3-methylglutaryl-coenzyme A lyase (HMG-CoA lyase). This enzyme plays a critical role in breaking down dietary proteins and fats for energy. Specifically, it is responsible for processing leucine, an amino acid that is part of many proteins. HMG-CoA lyase also produces ketones during the breakdown of fats. Ketones are compounds that certain organs and tissues, particularly the brain, use for energy when the simple sugar glucose is not available. For example, ketones are important sources of energy during periods of fasting.

If a mutation in the *HMGCL* gene reduces or eliminates the activity of HMG-CoA lyase, the body is unable to process leucine or make ketones properly. When leucine is not processed normally, a buildup of chemical byproducts called organic acids can result in metabolic acidosis. A shortage of ketones often leads to hypoglycemia. Metabolic acidosis and hypoglycemia can damage cells, particularly in the brain, resulting in serious illness in children with HMG-CoA lyase deficiency.

3.1. The gene associated with 3-hydroxy-3-methylglutaryl-CoA lyase deficiency

- HMGCL

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- 3-hydroxy-3-methylglutaryl-coenzyme A lyase deficiency
- 3-OH 3-CH3 glutaric aciduria
- 3-OH 3-methyl glutaric aciduria
- 3HMG
- Deficiency of hydroxymethylglutaryl-CoA lyase
- HMG
- HMG-CoA lyase deficiency
- Hydroxymethylglutaric aciduria

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