VLCAD: Very Long-Chain Acyl-CoA Dehydrogenase Deficiency

Very long-chain acyl-CoA dehydrogenase deficiency, also known as VLCAD deficiency, is a type of genetic condition categorized as a fatty acid oxidation disorder (also known as a FAOD). The body usually gets its energy by breaking down, or burning, fats and sugars. People with FAODs cannot properly break down certain types of fats. For those with VLCAD deficiency, the enzyme that is needed to break down very long-chain fats is unable to function properly. This prevents the body from creating needed energy during times of stress, illness, fasting, and exercise, which can lead to medical symptoms.

Alternative Names

- VLCAD

Cause and Genetics

People usually have two copies of the ACADVL gene, one inherited from each parent. VLCAD deficiency occurs when there are changes in both copies of the ACADVL gene (autosomal recessive inheritance). Someone who has a change in only one copy of the ACADVL gene is called a carrier, and they usually do not have any medical symptoms. If both parents are carriers, there is a 1 in 4 chance with each pregnancy that their child will have VLCAD deficiency. Both males and females can have VLCAD deficiency.

Frequency

The exact frequency of VLCAD deficiency is unknown. Some studies estimate that as many as 1 in 30,000 people have VLCAD deficiency. Routine newborn screening has found that VLCAD deficiency is more common than previously thought, but many of these babies did not show symptoms in early life.

Signs and Symptoms

The signs and symptoms of VLCAD deficiency vary from mild to severe and can happen at any age. Whether your child was diagnosed via newborn screening may also affect when, if, and how these symptoms present. Always check with your doctor if your child is doing something out of "their" normal, as every child may present with symptoms a little differently. People with VLCAD deficiency may experience different symptoms as they age.

Signs and symptoms of VLCAD deficiency in babies may include:

- Low blood sugar that can be life-threatening (hypoglycemia)
- A specific type of low blood sugar only seen in FAODs (hypoketotic hypoglycemia)
- Coma within days or weeks after birth (as a result of low blood sugar)
- High levels of ammonia in the blood (hyperammonemia)
- Abnormal heart rhythm (arrhythmia)

As babies grow from about ages two months to two years they may experience other symptoms including:

- Extreme tiredness (lethargy)

- Muscle weakness
- Irritability
- Enlarged liver when sick (hepatomegaly)
- Enlarged weakened heart muscle (cardiomyopathy)
- Abnormal heart rhythm (arrhythmia)
- Muscle pain and dark urine (myoglobinuria) caused by muscle breakdown (rhabdomyolysis)
- Total lung and heart function failure

During childhood and early adulthood episodes of low blood sugar associated with life-threatening comas usually become less common but patients may still experience:

- Periodic muscle pain caused by skeletal muscle breakdown (rhabdomyolysis)
- Dark-brown urine (a sign of myoglobinuria/rhabdomyolysis)
- Poor muscle tone (hypotonia)
- Heart problems (cardiomyopathy)
- Abnormal heart rhythm (arrhythmia)

The potential for muscle breakdown (rhabdomyolysis), is increased by illness, stress, cold/heat and exercise, and should be treated promptly. Some people with a milder form of VLCAD deficiency may only have episodes of muscle pain after severe illness or heavy exercise. Some people with VLCAD deficiency do not have signs or symptoms between episodes. Others may continue to have poor muscle tone (hypotonia) or chronic heart problems/failure.

Diagnosis

Most cases of VLCAD deficiency are identified by routine newborn screening. If newborn screening is suggestive of VLCAD deficiency, additional tests may be performed including:

- Measuring biochemical markers in the blood or urine
- Measuring VLCAD protein activity from blood or skin cell samples (cultured fibroblasts)
- Performing a genetic test to look for changes in the ACADVL gene or a group of genes that can cause FAODs

In some cases, a diagnosis of VLCAD deficiency can be made before birth. If there is a family history, prenatal testing can be performed on amniotic fluid (the fluid surrounding a baby) or chorionic villi (a specific part of the placenta).

Some pregnant mothers will experience a life threatening condition called HELLP syndrome during pregnancy. This may include high blood pressure, abnormal liver functions, and decreased blood clotting.

Some individuals with VLCAD deficiency may not be diagnosed until later in life if their newborn screening wasn't completed properly or if they were not screened at all. Others may also have a milder form of VLCAD deficiency that did not cause signs or symptoms in early life.

Treatment and Management

Before beginning any treatment or therapy, consult with your physician.

Management and treatment of VLCAD deficiency may include:

- Specialized medical formulas
- Regular eating schedules to prevent low blood sugar (hypoglycemia)
- Continuous feeding directly into the stomach in severe cases, especially at night
- Low-fat, high-carbohydrate diet
- Medicine called triheptanoin (Dojolvi)
- MCT oil supplementation
- Possible supplements including carnitine (Carnitor) and riboflavin (Vitamin B2)
- Intravenous (IV) sugar-containing fluids called D10 to treat metabolic crisis

In some mild cases monitoring exercise, avoiding cold/heat exposure, and not fasting may be enough to control and manage symptoms.

Parents should call their health care provider immediately if babies show symptoms like excessive sleepiness, vomiting, diarrhea, a fever, poor appetite, or an infection. Medical treatment should be sought immediately if there is loss of consciousness or severe confusion (decompensation), as these are signs of dangerously low blood sugar.

Patients should discuss the appropriate preparation for anesthesia with their metabolic team.

All patients should have an emergency protocol letter, written and signed by their doctor, that details their prescribed treatment during crisis and in emergency room settings, to manage severe episodes.

Clinical Trials

For specific details on other clinical trials, visit the MitoAction Clinical Trials page or www.clinicaltrials.gov.

Resources

- The National Institutes of Health: VLCAD deficiency - About the Disease
- The INFORM Network: VLCAD Deficiency | Fatty Acid Oxidation Disorders Diagnosis
- Baby's First Test: Newborn screening information for very-long-chain acyl-CoA dehydrogenase deficiency
- Nutrition management guidelines: Nutrition management guideline for very-long chain acyl-CoA dehydrogenase deficiency (VLCAD): An evidence- and consensus-based approach

Connecting with others who are impacted by a rare disease allows for important information to be shared about day-to day life, prevents isolation, and gives hope. Please contact MitoAction for peer support opportunities at 888-MITO-411 or email mito411@mitoaction.org. Other resources we recommend are:

- New Patient Kit for FAODs
- Planning and Preparation
- Monthly Expert Series
- Energy in Action Podcast

MitoAction does not provide medical advice, diagnosis, treatment, or legal advice. It is essential that all those living with or caring for someone with a Mitochondrial or FAOD disease have an emergency protocol letter. These letters, which are written and signed by a doctor, share details about prescribed treatment during crises and in emergency room settings. Always check with your doctor if you or your child has concerns as everyone may present with symptoms differently. Before beginning any treatment or therapy, please consult with your physician.