CPT2: Carnitine Palmitoyltransferase 2 Deficiency

Carnitine palmitoyltransferase 2 deficiency, also known as CPT2 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 CPT2 deficiency, an enzyme that helps to prepare long-chain fatty acids for breakdown once they enter the mitochondria is not able to function properly. This prevents the body from creating needed energy during times of stress, illness, and fasting, which can lead to medical symptoms.

Genetics

People usually have two copies of the CPT2 gene, one inherited from each parent. CPT2 deficiency occurs when there are changes in both copies of the CPT2 gene (autosomal recessive inheritance). Someone who has a change in only one copy of the CPT2 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 CPT2 deficiency. Both males and females can have CPT2 deficiency.

Frequency

CPT2 deficiency is the most common FAOD, and usually presents in a mild form. Over 300 mild cases have been reported worldwide, and it is thought that CPT2 deficiency is under-recognized.

Signs and Symptoms

CPT2 deficiency can occur in both mild and severe forms. 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.

Patients with the severe form of CPT2 typically present as a baby. Signs and symptoms may include:

- Extreme tiredness (lethargy)
- Irritability
- Poor appetite
- A weakened heart muscle (cardiomyopathy)
- Abnormal heart rhythms (arrhythmias)
- Total failure of heart and lung function
- Low blood sugar with lack of ketones (hypoketotic hypoglycemia)
- Coma within days or weeks after birth (as a result of low blood sugar)

Patients with the mild form of CPT2 deficiency usually present in adolescence or early adulthood. Signs and symptoms may include:

- Brownish red urine indicating muscle breakdown (myoglobinuria)
- Muscle weakness or pain after exercise or other physical stress
- Muscle breakdown (rhabdomyolysis)
- High blood ammonia (hyperammonemia)

- Enlarged liver (hepatomegaly), especially when sick
- Enlarged, weakened heart (cardiomyopathy)
- Low blood sugar with lack of ketones (hypoketotic hypoglycemia)

Diagnosis

CPT2 deficiency can be diagnosed by:

- Clinical examination due to the signs and symptoms outlined above
- Measuring biochemical markers in the blood or urine (including acylcarnitine analysis and organic acid analysis)
- Measuring the amount of CPT2 activity in the blood or skin cells
- Performing a genetic test to look for changes in the CPT2 gene
- Prenatal testing of amniotic fluid or chorionic villi if there is a known family history of CPT2 deficiency

CPT2 deficiency can be identified by newborn screening; however, some mild cases may be missed during routine screening.

If there is a known family history of CPT2 deficiency, or if parents know they are known carriers, prenatal testing can be performed on amniotic fluid (the fluid surrounding a baby) or chorionic villi (a specific part of the placenta).

Treatment and Management

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

Treatment and management of CPT2 deficiency may include:

- Regular eating schedules to prevent of low blood sugar (hypoglycemia)
- Continuous feeding directly into the stomach in extreme cases
- Possible nutritional supplements like medium-chain triglycerides (e.g., MCT oil)
- Possible pharmacological treatment using triheptanoin (Dojolvi)

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:Carnitine palmitoyltransferase 2 deficiency - About the Disease

- The INFORM Network: CPT2 Deficiency | Fatty Acid Oxidation Disorders Diagnosis
- National Organization for Rare Disorders (NORD): Carnitine palmitoyltransferase 2 deficiency - NORD (National Organization for Rare Disorders)

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.