State of CT
Genetics Newborn Screening Program
Health Care Provider Fact Sheet

CARNITINE PALMITOYLTRANSFERASE DEFICIENCY II (CPT II)

Introduction

Deficiency of CPT II activity is the most common inherited disorder of lipid metabolism affecting skeletal muscle. CPT II activity is located on the inner mitochondrial membrane. The CPTase enzyme system, in conjunction with acyl-CoA synthetase and carnitine/acylcarnitine translocase, provides the mechanism whereby long-chain fatty acids are transferred from the cytosolic compartment to the mitochondrial matrix to undergo beta-oxidation.

There are three distinct clinical forms of CPT II deficiency: the common adult myopathic form, the lethal neonatal form affecting many body systems, and the severe infantile form which has liver, heart and skeletal muscle involvement. The most common is the "classical" muscular form of CPT II deficiency. Patients with this defect generally present in adulthood with muscle pain and stiffness and, in severe cases, myoglobinuria (the presence of dark-colored urine caused by the release of myoglobin from damaged muscle tissue) due to prolonged exercise, fasting, mild infections, emotional stress, sleep deprivation, extremes in temperature, or general anesthesia during surgery. Most patients present with their first episode between 15 and 30 years of age, but it has been reported in all ages including young children. Most affected patients are males, although the disorder is inherited in an autosomal recessive manner. Between episodes, serum CPK levels are usually normal. Fasting ketogenesis is decreased in some patients, although they rarely show the acute decompensation common in other defects of ß-oxidation. Carnitine levels are usually normal in plasma and in tissues. Cardiac dysfunction is rarely seen. Renal failure, as a result of episodes of myoglobinuria, is found in 25 percent of patients. Permanent muscle weakness is rare. Lipid storage in muscle is found in 20 percent of patients; hepatic lipid storage is rare. Death may occur from renal failure or from respiratory insufficiency if the respiratory muscles are involved in an acute attack.

The infantile form, hepatocardiomuscular type, is very rare, with only a few cases reported. Symptoms include fasting hypoketotic hypoglycemia, elevated liver transaminases and carnitine deficiency hepatomegaly, coma, seizures, cardiomegaly, arrhythmia, skeletal muscle involvement and marked lipid accumulation in muscle. Patients may survive if recognized and treated aggressively. These infants usually have dysmorphic features including cystic renal dysplasia, cataracts and neuronal migration defects, specifically brain dysplasia and/or intracerebral calcifications. Another rare disorder linked to CPT II deficiency is manifest in infancy as hypoketotic hypoglycemia, hepatomegaly and hepatic failure, cardiomegaly and arrhythmias, lethargy, seizure, and coma.

Diagnosis

Newborn screening—Tandem mass spectrometry: C0- free carnitine, C16 palmitoyl carnitine, C16, C18:1, and C16/C2 or C18/C2.

Confirmation—a second sample may be requested or follow up testing will be done at the Metabolic Treatment Center at Yale or UCONN Genetics.

Situations that risk metabolic decompensation

Metabolic decompensation can be triggered by the catabolic processes that occur in the course of an infection, after an immunization or with a prolonged period of fasting.

Monitoring

Clinical observation is the most important tool for monitoring patients with CPT II. It is important for the primary care provider and the Metabolic Treatment Center to develop an on-going collaborative relationship in caring for these patients.

Treatment

The treatment of CPT II deficiency is variable and often patient-specific considering the wide variation in symptoms and lifestyles. There are certain things affected individuals can do to prevent symptoms. Most try to avoid the triggers such as prolonged vigorous exercise, fasting, and extremes in temperature. Individuals with CPT II deficiency try to keep their water intake high, especially if they are athletes. However, there are specific treatment regimens for CPT II-deficient patients, including the administration of MCT Oil (medium-chain triglycerides) or carnitine that should be established on a case by case basis under the supervision of Metabolic Treatment Center at Yale or UCONN Genetics.

- Avoid fasting.
- Feed at regular intervals during the day and limit overnight fasting
- Should not go without food intake longer than 4 hours for the first 4 months of life; 6 hours for ages 4-8 months; and no longer than 8 hours thereafter
- High carbohydrate, low fat diet. MCT oil supplement to supply the medium chains for beta-oxidation.
- Supplementation with L-carnitine restores plasma carnitine levels to nearly normal.
- If the child is vomiting or refuses to eat, (s)he needs to be taken to an emergency room for IV administration of 10% dextrose.
- The parents usually have an emergency protocol with them. This protocol, provided by the Metabolic Treatment Center, contains basic information about the disorder, necessary diagnostic investigations and guidelines for treatment.
- Infants and children with CPT II should have regularly scheduled visits at the Metabolic Treatment Center.

Illness

- Any illness can potentially lead to metabolic decompensation
- Prevention and/or early intervention is of particular importance
- Provide high-carbohydrate feedings including cornstarch
- Avoid dehydration
- Closely monitor blood glucose and intake; even if blood glucose is normal, metabolic decompensation can occur.
- Consult with the Metabolic Treatment Center within 24 hours of the onset of the illness

Immunization

- Immunizations must be kept current.
- There is no contraindication to any immunization because of CPT II.
- Parents and physicians should be alerted to the need for immediate evaluation if high fever, lethargy or vomiting occurs in the first 24 hours.
- After an immunization without any other clinical symptoms, administration of acetaminophen or ibuprofen is warranted.
- Influenza or influenza-like illnesses may cause major muscle breakdown so an annual influenza vaccination is recommended.

Surgical/surgical procedures

- Discuss any plans for surgical and dental procedures with the Metabolic Treatment Center
- Patients who need to have surgery with general anesthesia, should alert their physician to the need for alternative anesthetics that do not trigger symptoms. Several cases resembling malignant hyperthermia have been reported in patients with CPT deficiency. In one, kidney shut down was caused by accumulation of myoglobin after muscle destruction. More recently, a malignant hyperthermia event in childhood was associated with a mutation in the CPT II gene . Although this patient had decreased CPT II enzyme activity, there were no symptoms in the absence of anesthesia. Preoperative fasting should be avoided with 10% dextrose being started preoperatively and continuing postoperatively. Any surgery should include hospitalization pre- and postoperatively.
- If complicated surgery, or a postoperative period, as an inpatient is required, the procedure should be done at a hospital with a metabolic service.

Growth and development

- It is crucial to closely monitor all growth parameters on a regular basis.
- In cases with neurological deficits, the child should be referred to an early intervention program and developmental progress closely monitored by both the metabolic team and the primary care provider.

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