



Genetics Newborn Screening Program Health Professional Fact Sheet

FATTY ACID OXIDATION DISORDERS (FAOD) MEDIUM CHAIN ACYL-COA DEHYDROGENASE DEFICIENCY (MCADD)

Introduction

MCADD is an autosomal recessive disorder of fatty acid oxidation occurring in 1:10-15,000 live births. At conception, the sibs of an affected individual have a 25% risk of being affected, a 50% risk of being unaffected and carriers, and a 25% risk of being unaffected and not carriers. The risk could be 50% if one of the parents is also affected. Because asymptomatic parents and sibs may have MCAD deficiency, biochemical evaluation and/or DNA-based mutation analysis should be offered to both parents and all sibs.

MCADD results in an inability to break down medium chain fatty acids for ketone and ATP synthesis (**see figure**). MCAD is one of the enzymes involved in mitochondrial fatty acid β -oxidation, which fuels hepatic ketogenesis, a major source of energy once hepatic glycogen stores become depleted during prolonged fasting and periods of higher energy demands. The prognosis is good once the diagnosis is established and frequent feedings are instituted to avoid any prolonged period of fasting. It is hoped that pre-symptomatic identification and treatment of patients with MCADD will prevent any long-term problems.

Clinical Features

Affected individuals can be completely normal until prolonged fasting or infection leads to metabolic decompensation. This typically presents with hypoketotic hypoglycemia, seizures, vomiting, lethargy and coma. About 20% of infants with MCADD die during an acute episode when the diagnosis is not yet suspected. Survivors may suffer from neurological sequelae such as developmental delay, seizures, attention deficit hyperactive disorder or other behavioral abnormalities.

Diagnosis

Newborn screening—Tandem mass spectrometry identifies elevations in medium chain acylcarnitines, most notably octanoylcarnitine (C8-carnitine).

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

Clinical Diagnosis—Many children with MCADD are not diagnosed for weeks, months, or even years. The initial symptoms usually occur during infancy or early childhood, and often the first symptomatic episode occurs after a period of fasting. Symptoms may include extreme tiredness, skin clamminess, behavior changes, irritability, fever, diarrhea, and vomiting. The affected person may or may not have low blood sugar. If untreated, coma and even death could occur.

Situations that risk metabolic decompensation

Children with MCADD are often clinically asymptomatic. 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. Lethargy, vomiting, apneas or seizures are typical clinical features with or without hypoglycemia. Infants may be more subject to sudden death than older children.

Monitoring

Clinical observation is the most important tool for monitoring patients with MCADD. They should be observed for recurrent vomiting, refusal to eat, increased lethargy, apnea or seizures. In these situations, immediate evaluation in the emergency room is necessary. In situations of metabolic decompensation hypoglycemia can develop, but a normal blood glucose does not rule out metabolic instability and should never be a reason to delay therapy. It is also important for the primary care provider and the Metabolic Treatment Center to develop an on-going collaborative relationship in caring for these patients.

Treatment

- 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
- Restriction of dietary fat is controversial but it is reasonable during intercurrent infections; The Metabolic Treatment Center will set an patient's diet prescription that determines the optimum percentage of fat, carbohydrate, and protein.
- Carnitine supplements are provided in the case of a low blood carnitine level.
- Increased carbohydrate intake and cornstarch therapy is necessary during acute illness. The use of cornstarch therapy is an ongoing treatment and is even more necessary during acute illness
- 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 MCADD 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.
- All children with MCADD should have a yearly vaccine for influenza.
- There is no contraindication to any immunization because of MCADD.
- 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.

Surgical/surgical procedures

- Discuss any plans for surgical and dental procedures with the Metabolic Treatment Center
- Infants and children with MCADD can undergo necessary anesthetic/surgical procedures.
- Any surgical procedure constitutes a potentially catabolic situation.
- Any surgery should include hospitalization pre- and postoperatively.
- Preoperative fasting should be avoided with 10% dextrose being started preoperatively and continuing postoperatively until the child is eating and drinking well.
- 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.

Medium chain acyl-CoA Dehydrogenase Deficiency (MCADD)

