FATTY ACID OXIDATION DISORDERS (FAOD)

FAOD includes:

- Medium chain acyl co-A dehydrogenase deficiency (MCADD)
- Very long chain acyl Co-A dehydrogenase deficiency (VLCAD)
- Long chain hydroxyacyl co-A dehydrogenase deficiency (LCHAD)
- Trifunctional protein deficiency (TFP)
- Carnitine Palmitoyl Transferase Deficiency Type 1 (CPT1)
- Carnitine Palmitoyl Transferase Deficiency Type 2 (CPT2)
- Carnitine Uptake Defect (CUD)
- Glutaric Aciduria Type 2 (GA2)

What are FAOD?

FAOD are a group of autosomal recessive disorders caused by the deficiency or absence of any of the enzymes needed for beta-oxidation. Children born with this condition appear normal at birth but untreated patients may present with low blood sugar which can lead to seizures, coma and death. One type of FAOD, VLCAD (or very long chain acyl-CoA dehydrogenase deficiency) may present with cardiomyopathy and increased creatine kinase (CK) levels.

Confirmatory Testing

Please refer to the table below:

FAOD	Confirmatory Testing
Medium chain acyl co-A dehydrogenase deficiency (MCADD)	Gene Testing and Plasma Acylcarnitine
Very long chain acyl Co-A dehydrogenase deficiency (VLCAD)	Gene Testing and Plasma Acylcarnitine
Long chain hydroxyacyl co-A dehydrogenase deficiency (LCHAD)	Gene Testing
Trifunctional protein deficiency (TFP)	Gene Testing
Carnitine Palmitoyl Transferase Deficiency Type 1 (CPT1)	Gene Testing
Carnitine Palmitoyl Transferase Deficiency Type 2 (CPT2)	Gene Testing and Plasma Acylcarnitine
Carnitine Uptake Defect (CUD)	Gene Testing and Plasma Acylcarnitine
Glutaric Aciduria Type 2 (GA2)	Gene Testing

Further confirmatory testing may be required after referral to a metabolic specialist.

FATTY ACID OXIDATION DISORDERS (FAOD)

Treatment of FAOD

Treatment is through the dietary restriction of fat. VLCAD patients are treated with a special milk formula containing medium chain triglycerides. Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent hypoglycemia.

WHAT TO DO

If unwell and cannot tolerate oral intake:

- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. For patients with VLCAD, collect samples for serum CK. May request for other investigations (i.e. CBC, Blood gas) as needed. May give fluid boluses if the patient requires it.
- Start D10% 0.3 NaCl at full maintenance. Assess the patient and clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
- Monitor input and output strictly (q6 hours). Check for the color of urine.

If unwell and can tolerate oral intake:

- Insert oro- or nasogastric tube and start continuous feeding with a high glucose formula
- Insert IV access. Monitor glucose levels. For patients with VLCAD, collect samples for serum CK. May request for other investigations (i.e. CBC, Blood gas) as needed. May give fluid boluses if the patient requires it.
- Start D10% 0.3 NaCl at 5-10 cc/hr.
- Monitor input and output strictly (q6 hours). Check for the color of urine.

**Patients with VLCAD may have rhabdomyolysis. Monitor CK levels and hydrate adequately. If CK levels continually rise, hemodialysis may be indicated.*
**Inform the metabolic doctor on call for further guidance regarding on-going management*
**If the patient is well, coordinate with a metabolic specialist regarding further management.*

NSRC-INT-037/2022

FATTY ACID OXIDATION DISORDERS

Medium Chain Acyl-CoA Dehydrogenase Deficiency

What is Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD)?

Medium chain acyl-CoA dehydrogenase (MCAD) deficiency is the most common defect of fatty acid oxidation.[1]

CLINICAL MANIFESTATIONS

MCAD deficiency has a very wide spectrum of clinical presentations ranging from benign hypoglycemia to coma and death.[2] Two presentations have been noted: (1) hypoketotic hypoglycemia or Reye syndrome which occurs within the first two years of life and (2) the chronic disruption of muscle function which include cardiomyopathy, weakness, hypotonia and arrhythmia.[2,3] In addition, MCAD deficiency has been shown to be associated with sudden infant death syndrome (SIDS).[4] A "metabolic stress" such as prolonged fasting often in connection with viral infections is usually required to precipitate disease manifestations but patients are completely asymptomatic between episodes.[2]

PATHOPHYSIOLOGY

MCAD catalyzes the initial step in the ß-oxidation of C12-C6 straight chain acyl-CoAs and MCAD deficiency results in a lack of production of energy from ß-oxidation of medium chain fatty acids and hepatic ketogenesis and gluconeogenesis.[4]

Inheritance: autosomal recessive[4]

CONFIRMATORY TESTING

Plasma acylcarnitine and gene testing. Further confirmatory testing may be required after referral to a metabolic specialist.

Overview of Disease Management

Treatment consists of avoidance of prolonged fasting by instituting frequent feedings with a carbohydrate rich diet and provision of supplementary nocturnal uncooked cornstarch.[2] Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Prognosis

Most authors report a mortality rate of 20-25% during the initial decompensation. Although the majority of children survive their initial episode, a significant amount of children who survived and perhaps children who have experienced clinically unrecognized episodes, suffer from long term sequelae and about 40% are judged to have developmental delay.[2] Long term outcome remains dependent on constant monitoring for early signs of illness and rapid medical intervention to prevent complications.[3]

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state, correct the acidosis and prevent essential amino acid deficiency.

NSRC-INT-037/2022

FATTY ACID OXIDATION DISORDERS

Medium Chain Acyl-CoA Dehydrogenase Deficiency

WHAT TO DO

If unwell and cannot tolerate oral intake:

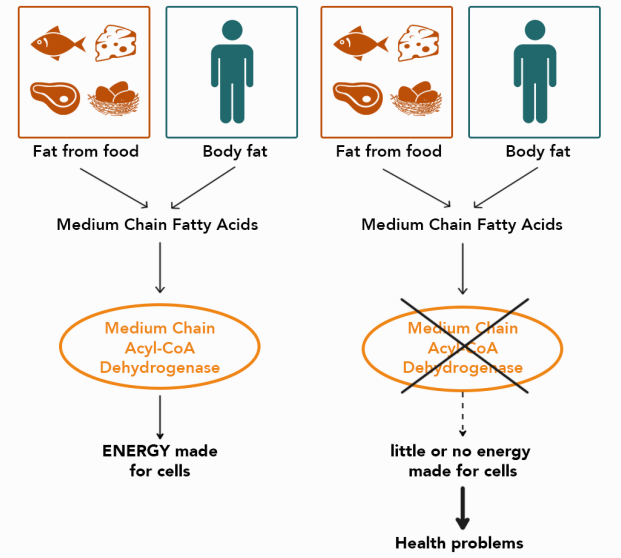
- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. May request for investigations (i.e. CBC, etc.) as needed.
- May give fluid boluses if the patient requires it.
- Start D10% 0.3NaCl at full maintenance. Assess the patient and clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5x the maintenance.
- Monitor input and output strictly (q6 hours).

If unwell and can tolerate oral intake:

- Encourage regular feeding
- Insert IV access. Monitor glucose levels. May request for investigations (i.e. CBC, etc.) as needed.
- Start D10% 0.3NaCl at 5-10 cc/hr
- Monitor input and output strictly (q6 hours).

*Inform the metabolic doctor on call for further guidance regarding on-going management
*If the patient is well, coordinate with a metabolic specialist regarding further management.

Normal breakdown of protein vs MCADD patient's breakdown of protein



[1]Strauss AW, Andersen BS and Bennett MJ. Chapter 5: Mitochondrial Fatty Acid Oxidation Defects in Sarafoglou K, Hoffman GF and Roth KS (eds). Pediatric Endocrinology and Inborn Errors of Metabolism. New York:McGraw Hill, 2009 pp 60-62.
[2] Hsu HW, Zytkovicz TH, Comeau AM et al. Spectrum of Medium chain acyl-coA dehydrogenase deficiency detected by newborn screening. Pediatrics 2008;121:e1108-e1114.
[3] Nyhan WL, Barshop BA and Ozand P. Chapter 40: Medium chain acyl-CoA dehydrogenase deficiency. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 260-265.
[4] Wilson CJ, Champion MP, Collins JE et al. Outcome of medium chain acyl-CoA dehydrogenase deficiency after diagnosis. Arch Dis Child 1999;80:459-462.
[5] Liebig M, Schymik I, Mueller M et al. Neonatal screening for very long chain acyl-CoA dehydrogenase deficiency: enzymatic and molecular evalua$on of neonates with elevated C14:1-carnitine levels. Pediatrics 2006;118(3):1064-1069.