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-041/2022

FATTY ACID OXIDATION DISORDERS

Carnitine Palmitoyltransferase Type 1 (CPT1) Deficiency

What is Carnitine Palmitoyltransferase Type 1 (CPT1) Deficiency?

CPT1 is an ezyme of the outer mitochondrial membrane that converts long chain fatty acyl molecules to their corresponding acylcarnitines which are then transported across the inner mitochondrial membrane for ß-oxidation in the mitochondrial matrix. [1] CPT1 catalyzes the rate limiting step of long chain fatty acid import into the mitochondria and is the main regulatory enzyme of the system.[2]

CLINICAL MANIFESTATIONS

This disorder presents usually in infancy, often in the second six months, with acute hypoketotic hypoglycemia, metabolic acidosis with raised transaminases, hepatomegaly, hepatosteatosis and mild to moderate hyperammonemia during an episode of fasting brought in by an intercurrent, usually viral illness, or gastroenteritis.[1,3] Patients may present with a range of cardiac arrhythmias including sudden cardiac arrest and death may occur during an acute presentation but surviving infants may suffer with severe developmental delay and intellectual impairment as a result of cerebral bioenergetic failure.[1] Cardiac or skeletal muscle involvement is not common.[4]

PATHOPHYSIOLOGY

Three different isoforms exist including the liver, muscle and brain, with only the liver-type showing deficiency in humans.[3] Deficiency of CPT1 in the liver results in a failure of acylcarnitine formation and hence little or no entry of LCFA into mitochondria for oxidative metabolism.[1,3]

Inheritance: autosomal recessive[2]

CONFIRMATORY TESTING

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

Overview of Disease Management

The major element in management is the avoidance of fasting and in the presence of intercurrent infection or other cause of vomiting or anorexia in which the oral route is excluded, the provision of intravenous glucose is essential.[3] Reduction of intake of long chain fats appears prudent and medium chain triglycerides may be substituted.[1,3] Initiation of management should be done in consultation with an attending physician/ metabolic specialist.

Prognosis

Survival through infancy without symptoms has been reported and between episodes of metabolic decompensation individuals appear developmentally and cognitively normal unless there has been previous neurologic damage secondary to a metabolic decompensation.[4]

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-041/2022

FATTY ACID OXIDATION DISORDERS

Carnitine Palmitoyltransferase Type 1 (CPT1) Deficiency

WHAT TO DO

If unwell and cannot tolerate oral intake:

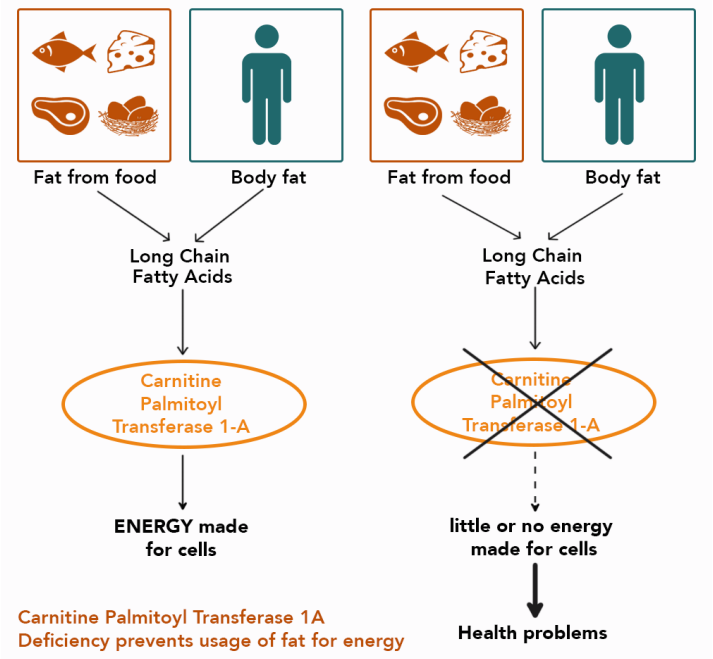
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. May request for investigations (i.e. CBC, CK, liver transaminases, blood gas, etc.) as needed.
- May give fluid boluses if patient requires.
- Start D10% 0.3NaCl at full maintenance. Assess patient clinically, if there is 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, CK, liver transaminases, blood gas, 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 CPT1 patient's breakdown of protein



[1] *Olpin SE. Pathophysiology of fatty acid oxidation disorders and resultant phenotypic variability. J Inherit Metab Dis 2013;36:645-658.*
[2] *Orgel A. Carnitine Palmitoyl transferase II: Enzyme Deficiency. hOp://www.userwebs.pomona.edu/~ejc14747/180/student%20presentations/Orgel%20carni ne%20paper.pdf Accessed 1 August 2014*
[3] *Chapter 39. Carnitine palmitoyl transferase I deficiency. Nyhan WL, Barshop BA and Ozand P. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 256-259.*
[4] *Bonnefont JP, Djouadi F, Prip-Buus C et al. Carnitine palmitoyltransferases 1 and 2: biochemical, molecular and medical aspects. Mol Asp Med 2004;25:495-520.*
[5] *Bilic E, Deliu M, Brinar V et al. Carni$ne palmitoyltransferase type 2 deficiency – case report and review of the literature. Nurol Croat 2013;62:57-62.*