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-042/2022

FATTY ACID OXIDATION DISORDERS

Carnitine Palmitoyltransferase Type 2 (CPT2) Deficiency

What is Carnitine Palmitoyltransferase Type 2 (CPT2) Deficiency?

Carnitine Palmitoyltransferase Type II (CPT2) is responsible for the last step of the carnitine dependent transport system.[1] In these disorders, long-chain acylcarnitines are translocated across the inner mitochondrial membrane but are not effciently converted to acyl-CoAs.[2]

CLINICAL MANIFESTATIONS

CPT2 has three phenotypes: (1) a fatal neonatal-onset form with non-ketotic hypoglycemia, liver disease, hypotonia, cardiomyopathy and congenital abnormalities; (2) infantile form with or without cardiac disease presents with liver and skeletal muscle involvement with episodes of decompensation and; (3) adult form presenting with muscle pain, stiffness and myoglobinuria.[1, 3] The episodes are triggered by exertional exercise, cold, fever, infection or prolonged fasting.[3,4] CPT2 presents frequently in adults with rhabdomyolysis and myoglobinuria triggered most often by prolonged exercise.[4]

PATHOPHYSIOLOGY

In the adult form of CPT2 deficiency, the triggering circumstances of myolysis attacks are consistent with the fact that long chain fatty acids are the main energy source for skeletal muscle during fasting or prolonged exercise.[1,3,4] It has been speculated that increased concentration of long-chain acylcarnitines in patient with the severe form of CPT2 deficiency may promote cardiac arrhythmia.[2] Why the two clinical presentations of CPT2 deficiency differ both in age of onset and tissue expression pattern remains unresolved.[2,3]

Inheritance: autosomal recessive[1]

CONFIRMATORY TESTING

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

Overview of Disease Management

Similar to all fatty acid oxidation defects, long term dietary therapy is aimed at preventing any period of fasting; restriction of long chain fat intake along with medium chain triglyceride supplementation is recommended and in the muscular form, preventive rhabdomyolysis attacks is based on frequent meals with carbohydrate extra-intake before and during prolonged exercise.[2] Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Prognosis

The clinical condition of patients is normal between recurrent attacks and the frequency of attacks are variable ranging from asymptomatic to lethal but in all cases the symptomatology is restricted to the skeletal muscles without liver or heart involvement.[2]

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.

FATTY ACID OXIDATION DISORDERS

Carnitine Palmitoyltransferase Type 2 (CPT2) Deficiency

WHAT TO DO

If unwell and cannot tolerate oral intake:

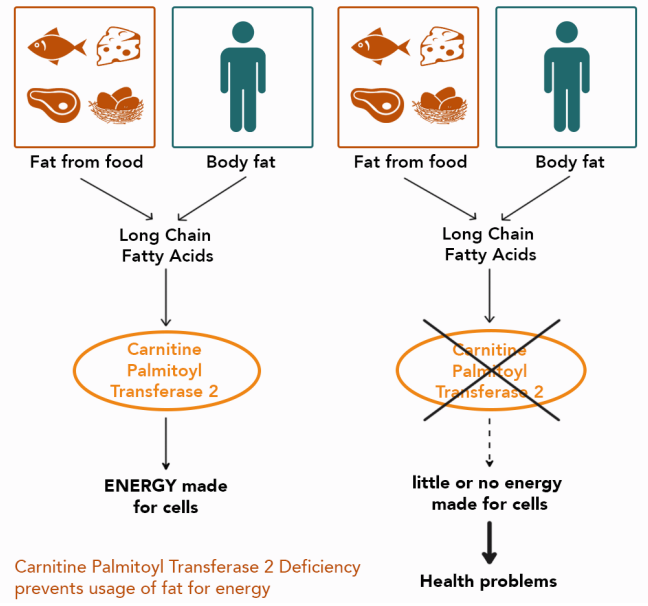
- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. Collect samples for urine ketones and serum creatine kinase (CK). May request for investigations (i.e. CBC, liver transaminases, blood gas, etc.) as needed.
- May give fluid boluses if pa ent requires.
- 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). Check color of urine and may request for urinalysis to check for urine myoglobin.

If unwell and can tolerate oral intake:

- Encourage regular feeding
- Insert IV access. Monitor glucose levels. Collect samples for urine ketones and serum creatine kinase (CK). May request for investigations (i.e. CBC, liver transaminases, blood gas, etc.) as needed.
- Start D10% 0.3NaCl at 5-10 cc/hr
- Monitor input and output strictly (q6 hours). Check color of urine and may request for urinalysis to check for urine myoglobin.

**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 CPT2 patient's breakdown of protein



Carnitine Palmitoyl Transferase 2 Deficiency prevents usage of fat for energy

[1] *Orgel A. Carnitine Palmitoyltransferase II: Enzyme Deficiency. http://www.userwebs.pomona.edu/~ejc14747/180/student%20presentations/Orgel%20carni ne%20paper.pdf Accessed 1 August 2014*
[2] *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.*
[3] *Olpin SE. Pathophysiology of fatty acid oxidation disorders and resultant phenotypic variability. J Inherit Metab Dis 2013;36:645-658.*
[4] *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.*