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.*

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FATTY ACID OXIDATION DISORDERS

Trifunctional protein (TFP) Deficiency

What is Trifunctional Protein (TFP) Deficiency?

The mitochondrial trifunctional protein (TFP) is a multienzyme complex of the ß-oxidation cycle composed of four ß- subunits harbouring long-chain enoyl-CoA hydratase and long chain L-3-hydroxyacyl-CoA dehydrogenase and four ß- subunits encoding long chain 3-ketoacyl-CoA thoilase.1 General or complete TFP deficiency is defined and occurs when markedly decreased activity of all three enzymatic components, LCHAD, long chain 2,3 enoyl CoA drasate and LKAT exist.[2]

CLINICAL MANIFESTATIONS

General TFP deficiency has three phenotypes: the lethal phenotype presenting with lethal cardiac failure or sudden death due to arrhythmias, the hepatic phenotype and the neuromyopathic phenotype that has later-onset, episodic, recurrent skeletal myopathy with muscular pain and weakness often induced by exercise or exposure to cold and peripheral neuropathy.[2, 3]

It is important to note that fetuses with complete TFP deficiency can cause maternal liver diseases of pregnancy.[2]

PATHOPHYSIOLOGY

Mitochondrial fatty acid ß-oxidation is a major energy-producing pathway.[4] Any defect in any enzyme may cause the characteristic signs and symptoms which include hypoketotic hypoglycemia.[2]

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

Treatment includes avoidance of fasting, reduced long-chain fat intake, supplementation with medium chain triglycerides, supplementation with fat-soluble vitamins, and avoidance of other potential stressors such as prolonged exercise.[2] Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Prognosis

Patients with metabolic crises do well unless the hypoglycemia and seizures are prolonged and cause developmental delay, older onset patients with rhabdomyolysis can reduce episodes significantly with dietary management and do well.[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

Trifunctional protein (TFP) Deficiency

WHAT TO DO

If unwell and cannot tolerate oral intake:

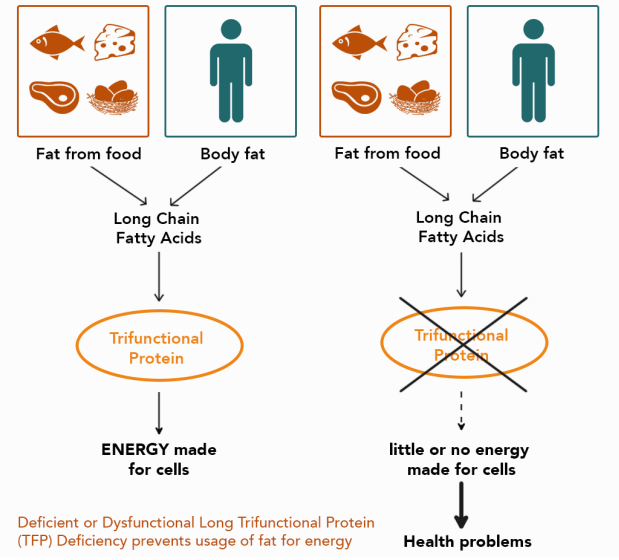
- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. Collect samples for urine ketones and serum creatine kinase (CK). May request for investigations (i.e. CBC, liver transaminases, blood gas, etc.) as needed.
- May give fluid boluses if the patient requires 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). 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 TFP patient's breakdown of protein



[1] *Speikerkoetter U, Khuchua Z, Yue Z et al. General Mitochondrial Trifunctional Protein (TFP) Deficiency as a results of either a or ß-subunit mutations exhibits imilar phenotypes because mutation in either subunit alter TFP complex expression and subunit turnover. Ped Res 2003l55(2):1-7.*
[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] *Kamijo T, Wanders RJA, Saudubray JM et al. Mitochondrial Trifunctional Protein Deficiency. J Clin Invest 1994;93:1740-1747.*
[4] *Nyhan WL, Barshop BA and Ozand P. Chapter 37: Carnitine transporter deficiency. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 246-250.*
[5] *http://ghr.nlm.nih.gov/condi on/mitonchondrial-functional-protein-deficiency Accessed 30 April 2012*