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

Glutaric Aciduria Type 2 (GA2)

What is Glutaric Aciduria Type 2 (GA2)?

Multiple acyl-CoA dehydrogenation deficiency (MADD) ia disorder of fatty acid, amino acid and choline oxidation caused by defects in any one of two flavoproteins, electron transport flavoprotein (ETF) or ETF:ubiquinone oxidoreducatase (ETF- QO) which affect some 14 dehydrogenases.[1,2]

CLINICAL MANIFESTATIONS

Patients may present with cyclical vomiting, loss of appetite, progressive proximal muscle weakness particularly affecting neck, shoulder, hip and/or respiratory muscles but also chronic leg weakness and exercise intolerance with occasional rhabdomyolysis.[1] The clinical phenotype is heterogenous and has been classified into three groups: neonatal onset with congenital anomalies (type 1), neonatal onset without anomalies (type 2) and mild and/or later onset (type 3).[3]

The infant affected with this disorder presents with life-threatening illness in the first day of life presenting with tachypnea or dyspnea, profound metabolic acidosis and impressive hypoglycemia within a few hours of birth.[2] The later on-set of this disorder has presented with considerable variety. In adolescents and adults, muscular or cardiac symptoms or episodic vomiting are usually first features suggestive for MADD.[3]

PATHOPHYSIOLOGY

The metabolic defects result in impaired adenosine triphosphate (ATP) biosynthesis, excessive lipid accumulation in different organs and insufficient gluconeogenesis.3 The most characteristic pathological feature of MADD is increased intracellular neutral lipid storage, especially in skeletal muscle and liver which is observed as increased intracellular lipid droplets in both size and number.[4]

Inheritance: autosomal recessive[2, 3]

CONFIRMATORY TESTING

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

Overview of Disease Management

Therapeutic management mostly comprises a diet restricted in fat and protein and the avoidance of fasting.[1] Among the consequences of this disorder is a depletion of body stores of carnitine, thus, patients may benefit from carnitine supplementation.[2] Some forms of this disorder are responsive to riboflavin (100 to 300 mg/day)[2] and the clinical response to pharmacological doses of riboflavin is usually rapid and striking.[1] Initiation of management should be done in consultation with an attending physician/ metabolic specialist.

Prognosis

Early onset MADD is a disease with high mortality, the prognosis of late-onset MADD seems to be good; nevertheless, 5% of patient reported in literature had died mainly during metabolic decompensations and in some patients, death could not be prevented despite the known diagnosis of MADD.[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.

FATTY ACID OXIDATION DISORDERS

Glutaric Aciduria Type 2 (GA2)

WHAT TO DO

If unwell and cannot tolerate oral intake:

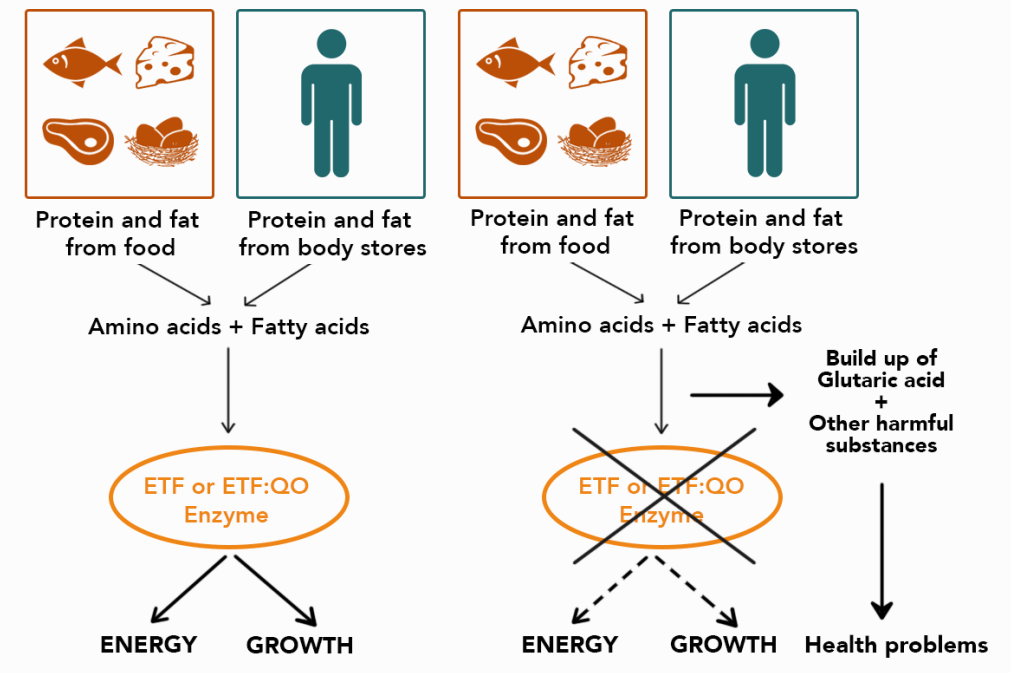
- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. May request for investigations (i.e. CBC, blood gas, kidney function etc.) as needed.
- May give fluid boluses if patient requires.
- Start D10% 0.3 NaCl at full maintenance. Assess patient clinically, 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:

- Insert oro- or nasogatric tube and start continuous feeding with oresol at maintenance rate
- Insert IV access. Monitor glucose levels. May request for investigations (i.e. CBC, blood gas, kidney func on 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 GA2 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] *Chapter 45. Mutiply acyl Coa dehydrogenase deficiency (MASS)/Glutaric aciduria type II/Ethylmalonic-adipic aciduria. Nyhan WL, Barshop BA and Ozand P. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 284-291*
[3] *Grunert S. Clinical and fenetical heterogeneity of late-onset multiple acyl-coenzyme A dehydrogenase deficiency. Orphanet J Rare Dis 2014;9(14):1-8.*
[4] *Liang WC and Nishino I. Riboflavin-responsive multiple acyl-CoA dehydrogenase deficiency: a frequent condition in the southern Chinese population. Neurol Clin Neurosci 2013;1:163-167.*