NURSING GUIDELINES FOR THE MANAGEMENT OF CHILDREN WITH FATTY ACID OXIDATION DEFECT

Revision 1

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1.0 STATEMENT:

The objective in preparation of Nursing Guidelines for Management of Inherited Metabolic Disorders (IMD) is to increase the knowledge base of nursing staff involved in the delivery of care to patients with an IMD, provide a resource material for reference and ultimately ensure the consistent delivery of high quality care to patients attending the National Centre for Metabolic Disorders (NCIMD).

Readers of this document are reminded that prescription of dietary regimes and all medications (including insulin, minerals, vitamins and trace elements) is the responsibility of the Metabolic Consultant. These guidelines may only be used under the supervision and guidance of a Metabolic Consultant.

The document authors wish to thank the various Doctors, Nurses, parents and patients who have worked in and attended the National Centre throughout the years, contributing greatly in the process to our knowledge and experience of Inherited Metabolic Disorders.

2.0 SCOPE:

These guidelines are a point of reference for all nursing and medical staff in relation to the care of a child with a Fatty Acid Oxidation Defect or suspected of having a Fatty Acid Oxidation Defect.

3.0 DEFINITIONS:

Mitochondrial Fatty Acid Oxidation Defects (FAODs) are genetic metabolic deficiencies in which the body is unable to oxidise (breakdown) fatty acids to create energy. There are three main components to fatty acid oxidation: 1. carnitine cycle, 2. ß-oxidation cycle, 3. Electron transfer (Morris & Spiekerkoetter, 2012). Individual defects are identified under each component of the mitochondrial fatty acid oxidation pathway (Morris & Spiekerkoetter, 2012). Treatment and outcomes depend on the different disorders of fatty acid oxidation and also on the severity of the enzyme defect present (Spiekerkoetter et al, 2009). This guideline refers to the more common of the ß-oxidation defects.

Fatty acids present in muscle and other tissues, are long term energy sources and are utilised during periods of fasting or illness when glucose stores are depleted. Fatty acids are the preferred fuel for the heart, and also serve as an essential source of energy for skeletal muscle during sustained exercise. The use of fatty acids by the liver provides energy for gluconeogenesis. The liver also uses fatty acids to synthesise ketones, which serve as a fat derived fuel for the brain.

Oxidation takes place in the mitochondria with specific enzymes mediating the process. In long chain FAODs, the enzyme deficiency prevents the breakdown of fatty acids from long chain fats, which under normal circumstances would be utilised for energy. Nonetheless, medium chain fats can be broken down and utilised for this purpose. Therefore, in conditions such as Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency, Mitochondrial Trifunctional Protein (MTP) deficiency and Long-chain Hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, medium-chain triglycerides (MCT) are substituted in these long chain FAODs. Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCADD) deficiency is the most common among this group (Zschocke & Hoffmann, 2011). The difference between medium and long chain defects is that there is no fat restriction in MCADD (note: MCT is contraindicated for patients with MCADD) and its mainstay of treatment is to avoid fasting, however, milder forms of VLCAD deficiency are treated in the same manner as MCADD (Zschocke & Hoffmann, 2011).

4.0 PRESENTATION:

There is wide variation in presentation of FAODs, even within the same family. Clinical features are thought to occur due to the inability to oxidise fatty acids and the accumulation of toxic metabolites.

4.1 Clinical presentation may include:

- Hypoglycaemia after fasting.
- Fasting can precipitate severe encephalopathy (Wajner and Amaral, 2016).
- Lethargy / chronic tiredness.
- Persistent vomiting, especially during an intercurrent illness.

- Acute and chronic liver disease +/- jaundice.
- Cardiomyopathy and peripheral myopathy.
- Exercise / illness induced rhabdomyolysis (Morris & Spiekerkoetter, 2012)

As these defects are inherited in an autosomal recessive manner (Morris & Spiekerkoetter, 2012), there may be a positive family history of unexplained illness and sudden infant death. HELLP Syndrome (haemolysis, elevated liver enzymes and low platelets) is associated with heterozygous mothers for LCHAD or MTP deficiency (Morris & Spiekerkoetter, 2012).

Recognition of the fatty acid oxidation disorders is often difficult, because patients can appear well until exposed to prolonged fasting.

4.2 New born Screening

Given their frequency, due to the improved clinical outcome achieved by pre-symptomatic initiation of treatment, MCADD deficiency was included in the national new born blood spot screening programme in Ireland in December 2018.

5.0 DIAGNOSIS:

5.1. Diagnosis is *suspected* in patients with the above history and the following:

- Acylcarnitine profile – elevated disease specific acylcarnitines. However, can be normal in patients with milder enzyme deficiencies.
- Urine for organic acids – elevated medium chain (and sometimes long chain) dicarboxylic acids during fasting or illness.
- Total and Free Carnitine (serum) – Free carnitine is often low because of acylcarnitine accumulation.
- Elevated Creatinine Kinase (CK).

5.2. Diagnosis is *confirmed by:*

- Enzyme Assay - Skin biopsy.
- Mutation Analysis.

5.3. Trivial illness can result in metabolic decompensation leading to:

- Abnormal liver function
- Hypoketotic Hypoglycaemia (often a late sign).
- Hepatomegaly.
- Raised Liver Transaminases (AST and ALT).
- Elevated ammonia.

- **Intermittent Rhabdomyolysis**

- Elevated Creatinine Kinase (CK)
- Myoglobinuria. Myoglobin is a reddish pigment in muscle similar to haemoglobin in blood. It stores oxygen until needed by the mitochondria (the organelles in which ATP generation occurs).
- Muscle weakness causing pain and tenderness.
- Elevated Lactate
- Metabolic acidosis on venous/capillary blood gas

More severe illness presents with a further exacerbation of the aforementioned symptoms and

- **Cardiomyopathy**

5.4. Usual reasons for admission:

- Vomiting and diarrhoea.
- Infection.
- Raised CK (may be related to the ingestion of fat or an inadequate calorie intake).
- Growth spurt.

6.0 MANAGEMENT:

6.1. Acute Management

a. If vomiting and/or diarrhoea are present, IV glucose must be started. Nasogastric feeding is instigated if IV treatment is not indicated.
b. Discontinue fat exchanges & restrict protein intake.
c. **Do not give intravenous lipids.**
d. Extra calories are required to prevent catabolism. Calories are given as high carbohydrate drinks to provide energy or, if administered intravenously, as glucose.
e. Electrolyte balance is monitored (sodium & potassium supplemented into IV fluids).
f. Intake and output is strictly monitored, recorded and reported to Metabolic Consultant. The large volume of fluid that is necessary to meet calorie intake may necessitate administration of IV diuretics.

6.2. On-going Management

a. The success of treatment is assessed by improvement in the clinical status and reduction of CK to normal level. Creatinine kinase can therefore be used to monitor the child's treatment.
b. Specialised diet plans are resumed following recovery, in consultation with the Metabolic Consultant and Dietitian.
c. Give adequate calories to suppress catabolism and support growth, development and energy needs.
d. Echocardiograph and Liver ultrasounds will be performed as part of an annual assessment to assist with treatment monitoring.
e. Dietary restriction of fat also restricts intake of essential fatty acids. Docosahexaenoic acid (DHA), an essential fatty acid, is supplemented as it improves visual acuity, especially in patients who have LCHAD deficiency (Gillingham et al, 2005).
f. Parental education with regard to recognising early signs of illness, fasting times between feeds and treatment plans.

7.0 NURSING MANAGEMENT OF CHILDREN WITH FATTY ACID OXIDATION DEFECT.

ACTION	RATIONALE
7.1. EMERGENCY ASSESSMENT - Complete patient assessment on admission and document vital signs in Paediatric Early Warning System (PEWS) chart. Escalate care as indicated by clinical judgment and PEWS score. - Frequency of monitoring will be dictated by child's condition (i.e. 2-4 hourly during initial presentation and acute illness).	
a. **A**irway	Airway patency may be compromised due to altered Glasgow Coma Scale. Due to hypoglycaemia, the brain does not receive adequate amounts of energy (i.e. glucose) resulting in altered state of consciousness. Seizure activity due to hypoglycaemia may also compromise airway patency.
b. **B**reathing (Respiratory rate, effort, oxygen requirements).	Tachypnoea, increased respiratory effort, reduced oxygen levels and increased CO_2 levels may indicate • Infection • Underlying respiratory Illness • Metabolic Acidosis • Fluid overload

ACTION	RATIONALE
c. **C**irculation (Pulse, blood pressure, capillary refill time, patient colour).	• Cardiomyopathy Patients with LCHAD may present with a cardiomyopathy (Wajner and Amaral, 2016). Tachycardia may indicate • Infection • Acidosis • Fluid overload • Dehydration • Cardiomyopathy Patients with cardiomyopathy may also present with bradycardia or an irregular heart rhythm (Tril et al. 2019). Hypertension may indicate fluid overload, stress or pain. Hypotension may indicate dehydration or hypovolemic shock.
d. Include Capillary Refill Time assessment as per PEWS. - Observe colour and peripheral perfusion of skin.	To identify hydration status and nutritional status and presence of hypovolemic shock. Observe for pallor, cool clammy skin, decreased central capillary refill time, mottled extremities, dry mucous membranes and sunken eyes (Schub & Karakashian, 2017).

ACTION	RATIONALE
e. **D**isability (level of consciousness and neurological status).	
- Assess and record baseline neurological status using **Glasgow Coma Scale**, and continue to reassess regularly especially during further episodes of acute illness.	Low availability of brain substrates (glucose and ketones) and the potential toxicity of the accumulating fatty acids and derivatives were hypothesised to lead to disruption of brain energy functions and the development of encephalopathy (Wajner and Amaral 2016).
- Observe for and report poor feeding, ataxia, history of falling, lethargy, vomiting, irritability, altered level of consciousness, muscle weakness, soreness of limbs, seizures and confusion.	Risk of encephalopathy due to metabolic crisis (may be mild to severe). Muscle weakness may cause ataxia and instability while walking. Seizures may occur due to hypoglycaemia.
- Check with parents regarding child's usual behaviour.	
f. **E**xposure to ensure full examination (whilst respecting the child's dignity and ensuring body temperature conservation) looking for rashes and signs of altered skin integrity etc.	

ACTION	RATIONALE
g. **Temperature**	Pyrexia may indicate the presence of infection. Follow Sepsis 6 protocol in PEWS chart. The following should be performed, blood cultures, F.B.C., U+E, LFTS, CRP and blood gas (including lactate) – standard for sepsis. Urine should be sent for culture and sensitivity. Hypothermia may suggest the need for more calories. However, it may be an indicator for infection in the neonate.
- Provide periods of rest between nursing care procedures.	Minimises stress due to excessive handling.
7.2. INVESTIGATIONS:	
a. **BLOOD GLUCOSE :** - Monitor blood glucose & lactate on admission, and if normal, four hourly thereafter.	Hypoglycaemia is a late finding with acute illness (Morris & Spiekerkoetter, 2012), which can result in coma as ketones are not being produced to serve as fuel for the brain. Hyperglycaemia may indicate stress. It may also occur secondary to increased calories or high dose intravenous glucose. Consider the need for insulin (refer to Medical Guidelines). Doses appropriate for patients with Insulin Dependent Diabetes are not appropriate for these patients as the pancreatic gland is usually functioning normally.
b. **KETONES:**	Ketones indicate fat catabolism. Ketones rare as fat cannot be utilised for energy.
c. **URINALYSIS:** - Carry out urinalysis on all urine produced during acute episodes.	**Positive glucose** may be due to high glucose intake. This is **NOT** an indication that glucose infusions may be reduced or terminated. An insulin infusion may be necessary to promote anabolism, prevent catabolism and prevent hyperglycaemia. Notify team / doctor on call and refer to Medical Guidelines for Management of Children with Metabolic Disorder.

ACTION	RATIONALE
	Positive ketones rarely occur as fat cannot be utilised for energy. **Positive protein** may be due to the presence of blood, or infection.
- Observe the Urine appearance / colour.	Presence of myoglobin. Dark red / brown in colour - Disintegration of striated muscle fibres (Rhabdomyolysis). Contact laboratory reception if sample requested as specimen will need to be transported to external laboratory.
d. BLOOD SAMPLING: - As directed by the metabolic team. - FBC, U&E, LFTs, Bone profile, Venous blood gas, CK, Glucose and lactate, ammonia, serum amino acids, and acylcarnitine profile are bloods routinely required. Additional blood sampling as directed by the metabolic team.	Individuals with a FAOD are at risk for dehydration and electrolyte imbalance during periods of recurrent vomiting, diarrhoea and/ or reduced intake of nutrients and fluids. Electrolyte balance is monitored (sodium & potassium supplemented into IV fluids). Raised CK (may be related to the ingestion of fat or an inadequate calorie intake). The success of treatment is assessed by improvement in the clinical status and reduction of CK to normal level. Creatinine kinase can therefore be used to monitor the patient's treatment.
7.3 DIET: - Withhold fat exchanges until otherwise instructed if child is a known patient.	To prevent toxicity.
- Avoid long periods of fasting (adhere to instructions given by Metabolic Consultant).	To prevent any period of fasting which would require the use of fatty acids as fuel.

ACTION	RATIONALE
- Administer calorie rich feeds orally or via nasogastric tube. - 2-4 hourly feeds or continuous feeding may be required when unwell. - **In event of vomiting, diarrhoea or inability to take / tolerate feeds orally, intravenous administration of glucose will be necessary.** - **DO NOT ADMINISTER LIPIDS TO PATIENTS WITH FAT OXIDATION DEFECTS.** - Liaise with Dietetic team for information on Fat Exchanges, Free foods etc.	To ensure adequate calories are provided To prevent catabolism, lipolysis and hypoglycaemia.
7.4. MEDICATIONS: - Paracetamol is not recommended for use in patients with Fatty Acid Oxidation defects. - Walnut Oil - DHA - Antiemetic	Paracetamol is metabolised in the liver (Malar and Bai, 2012). Contains essential fatty acids. Essential fatty acid – assists in maintaining visual acuity. Maybe be required to treat vomiting – administered as per metabolic consultant

ACTION	RATIONALE
7.5. ONGOING MULTI-DISCIPLINARY / FOLLOW UP CARE:	
- Emergency Letter for local Emergency Department in event of illness.	To ensure appropriate management is instigated and delay avoided**.**
- Medical / Nursing / Dietetic Teams	
- Psychology	To assess effects of chronic illness on the family unit and relationships within the Unit and to provide support**.**
- Social Work	
- Cardiology	
- Ophthalmology	Many patients with Long Chain FAOD have poor eyesight which worsens with age. It is thought that this may be due to restriction of essential fatty acids (due to diet restriction).

8.0 MONITORING, AUDIT & EVALUATION:

This procedure shall be reviewed and updated at least every three years by the Clinical Nurse Education Facilitator, NCIMD in order to determine its effectiveness and appropriateness. It shall be assessed and amended as necessary during this period to reflect any changes in best practice, law, substantial organisational change and professional or academic change.

9.0 KEY STAKEHOLDERS

The following Key Stakeholders were consulted in the review of this document:

Professor Ahmad Monavari, Clinical Lead of NCIMD (National Centre for Inherited Metabolic Disorders).	Signature: _____ Date: _____
Professor Ellen Crushell, Consultant Paediatrician with Special Interest in Inherited Metabolic Disorders.	Signature: _____ Date: _____
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Susan Keane, Clinical Practice Facilitator	Signature: _____ Date: _____

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