NURSING GUIDELINES FOR THE MANAGEMENT OF CHILDREN WITH PROPIONIC ACIDURIA
Revision: 1

Policy ☐ Procedure ☐ Protocol ☐ Guideline ☑

Document Approval / Sign-off			
AUTHOR/TITLE:	Louise Perris, Clinical Education Facilitator, NCIMD.		
SIGNATURE:		**DATE:**	
APPROVED BY:	Maria O'Regan, Clinical Nurse Manager III, NCIMD.		
SIGNATURE:		**DATE:**	
RATIFIED BY:	Professor Ahmad Monavari, Clinical Lead of NCIMD (National Centre for Inherited Metabolic Disorders).		
SIGNATURE:		**DATE:**	

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1.0 STATEMENT:

The objectives in preparation of Nursing Guidelines for Management of Inherited Metabolic Disorders (IMD) are 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 Propionic Aciduria or suspected of having Propionic Academia.

3.0 DEFINITION:

Propionic aciduria is a rare autosomal recessive metabolic disorder (Quintero et al. 2018). It occurs as the result of a deficiency in the enzyme propionyl Co-A carboxylase, or an abnormal metabolism of biotin, its co-enzyme (Haijes et al. 2019). Consequently, a defect in the protein breakdown pathway occurs, affecting four amino acids, namely: Isoleucine, methionine, threonine and valine.

These amino acids are the primary source of propionic acid (approx. 50%). Propionic acid may also be produced by anaerobic fermentation in the gut and by beta-oxidation of odd-chain fatty acids (approx. 50%).

3.1 PREVALENCE

Propionic aciduria is rare with an incidence of 1 in 100,000- 150,000 (Tuncel et al. 2018).

4.0 PRESENTATION:

Children with a severe enzyme defect usually present in the neonatal period. The following signs and symptoms may be present:

4.1 Severe form:

- Poor suck reflex / poor feeding
- Vomiting and anorexia
- Lethargy
- Truncal hypotonia
- **Metabolic acidosis with increased anion gap**
- Ketosis (excessive ketones in urine or point of care ketone test)
- Hyperammonaemia
- Seizures
- Coma

4.2 Less severe form, varying degrees of the following:

- Refusal to eat
- Vomiting and failure to thrive
- Lethargy
- Dehydration
- **Metabolic acidosis with increased anion gap**
- Ketosis
- Hyperammonaemia

4.3 Further complications:

- Hypotonia

- Dehydration
- Hypoglycaemia / hyperglycaemia
- Hyperlactataemia
- Hypocalcaemia
- Anaemia, Neutropenia & Thrombocytopenia (Ogier de Baulny et al, 2012)

5.0 DIAGNOSIS:

Diagnosis is made on the following;

- Clinical presentation
- Acylcarnitines - increased propionyl carnitine (C_3)
- Analysis of urine organic acids is diagnostic – find increased 3-hydroxypropionate, methylcitrate and propionylglycine
- Serum amino acids – Increased glycine & alanine (Zschocke & Hoffmann, 2011).
- Skin biopsy – may be performed to determine enzyme activity
- Mutation analysis of genes involved.

Other siblings in the family will be tested and any future births will be considered "high risk". Prenatal diagnosis is possible and families should be referred for genetic counselling.

6.0 MANAGEMENT:

6.1 Emergency Management:

a. **Stop natural protein intake** (infant formula / breast feeding / food products which are sources of protein) temporarily (max. 48 hours).
b. **Ensure adequate calorie intake** to prevent catabolism and promote anabolism.
c. Administration of L-Carnitine – this is excreted in urine bound to organic acids.
d. Administration of Metronidazole (antibiotic) - used to clear gut bacteria as gut bacteria produce propionic acid (Ogier de Baulny et al, 2012).
e. Administration of intravenous glucose and lipids in order to minimise ammonia production from endogenous protein breakdown. **Condition specific** IV amino acid mixture may also be required if available.

f. Administration of Carglumic acid or other scavenger drugs may be recommended for hyperammonaemia.
g. Haemodialysis or haemofiltration may be required on initial presentation and on subsequent admissions, where ammonia and acid levels are grossly elevated, to reduce levels rapidly.
h. If patient is unconscious or has low Glasgow Coma Scale (GCS) score, intubation and assisted ventilation may be required.

6.2 After initial treatment for acidosis, long-term treatment may consist of:

a. Low protein diet with measured amounts of natural protein.
b. A special amino acid mixture containing all amino acids essential for growth **excluding** Isoleucine, Methionine, Threonine and Valine.
c. 'Free foods' (i.e. non-protein) e.g. fruit, vegetables and specially manufactured low-protein foods.
d. Long term administration of L-carnitine.
e. Administration of vitamin and mineral supplements may be required.
f. Metronidazole treatment (as directed by metabolic consultant)
g. Liver transplant may be a treatment option for some patients with PA.

7.0 NURSING MANAGEMENT OF THE PATIENT WITH PROPIONIC ACIDURIA

ACTION	RATIONALE
7.1 EMERGENCY ASSESSMENT - Complete full patient assessment on admission and document vital signs in PEWS record. - Escalate care as indicated by clinical judgment and PEWS score. - Ascertain if parent (s) have any particular concern and score accordingly. - Frequency of monitoring will be dictated by patient's condition (i.e. 2-4 hourly during initial presentation and acute illnesses.	Frequent observation ensures early detection of deterioration and allows for monitoring of progress as condition improves.
a. AIRWAY - Seek emergency medical intervention if signs of airway compromise e.g respiratory distress, reduced SpO_2, absent cough, gag etc.	Decompensation in PA, manifesting as decreased consciousness can be life threatening and indicates a severe clinical condition (Fujisawa et al. 2013). Airway patency may be compromised with reduced GCS.
b. BREATHING - Monitor respiratory rate, respiratory effort and oxygen requirements as per PEWS. - Monitor oxygen saturation levels if concerned and report abnormalities to medical team.	Tachypnoea, increased respiratory effort, reduced oxygen levels and increased CO_2 levels may indicate; • Infection • Underlying respiratory Illness • Acidosis - can have metabolic acidosis with an increased anion gap (Ogier de Baulny et. al. 2012) • Fluid overload. Respiratory depression may occur if level of consciousness decreases in the presence of raised intracranial pressure.

ACTION	RATIONALE
c. OXYGEN SATURATION When using pulse oxymetry, ensure frequent rotation of the probe position (particularly in neonates).	Low oxygen saturation may be present with acidosis or when patient is shocked. Failure to change position of probe may result in burning of the skin.
d. CIRCULATION - Monitor **pulse** (rate, volume and strength).	Tachycardia may indicate • Infection • Acidosis • Fluid overload • Dehydration
- Assess central capillary refill time CRT and document in PEWS. - Continue to reassess regularly if > 2 seconds.	Decreased peripheral perfusion, decreased central capillary refill time, pallor and skin that is cool to touch may indicate hypovolemic shock (Standl et al. 2018).
- **Record and Monitor Blood Pressure.** - Report abnormalities in vital signs to the metabolic team.	Check baseline. Frequency of monitoring as indicated by condition and status of patient. Hypertension may indicate stress, fluid overload or pain. Can be hypotensive with hypovolemic shock or dehydration.
e. DISABILITY: (Level of consciousness and neurological status). - Assess and record baseline neurological status using **Glasgow Coma Scale**, and continue to record especially during further episodes of acute illness.	Risk of encephalopathy secondary to hyperammonaemia.

ACTION	RATIONALE
- Monitor GCS 4 hourly or as condition indicates. - Report altered level of consciousness or any deterioration to the metabolic team.	
- Observe for signs of muscle weakness and for signs of seizure activity. - Record seizure type, duration and intervention and record seizure activity in nursing notes.	Severe forms of acidaemia and/or hyperammonaemia can produce seizures and coma.
- Report any abnormal movements for patient to the medical team. If ambulant, observe for ataxia and dystonia and report to medical team. - Check with parent(s) regarding patient's usual behaviour.	Children presenting following a cerebral insult caused by an intercurrent illness may exhibit dystonia and a high-pitched cry.
f. EXPOSURE To ensure full examination (whilst respecting the child's dignity and ensuring body temperature conservation).	
g. TEMPERATURE - Monitor temperature 4 hourly or more frequently if indicated.	Pyrexia may indicate presence of infection.
- Consider in conjunction with other signs such as tachycardia and delayed central capillary refill time.	Hypothermia may suggest catabolism and need for increased calorie intake. Normothermia must be maintained because hypothermia with shivering may trigger neurologic crisis by increasing catabolism (Ituk et al. 2013). Hypothermia may indicate overwhelming infection (Goldstein et al. 2005).
- Follow Sepsis 6 protocol in PEWS chart.	
- The following should be performed, blood cultures, F.B.C., U+E, LFTs, ammonia, blood gas, serum amino acids, and urine for culture and sensitivity.	

ACTION	RATIONALE
h. SKIN - Assess and document skin colour, peripheral perfusion, temperature and skin integrity. - Assess nappy area at each nappy change. - Keep skin clean and dry.	Pallor and decreased peripheral perfusion may indicate shock / stress. Skin breakdown (nappy rash etc.) and desquamation of cells in a previously d1iagnosed child may indicate protein deficiency and need to slowly re-commence / increase protein intake. Protein deficiency may result from restriction of protein / frequent intercurrent illness
i. HAIR - Assess if coarse / brittle / alopecia.	Dry, brittle hair and alopecia are signs of protein or zinc deficiency.
j. HEIGHT AND WEIGHT - Ensure accurate height and weight are recorded on centile chart.	Accurate records are necessary for drug, fluid, calorie and protein prescription.
7.2 INVESTIGATIONS	
a. BLOOD **Full blood count** - Assess need for reverse barrier nursing.	Raised white cells indicate infection (bacterial / viral). Identifies neutropenia - Propionic acid interferes with the maturation of white blood cells (Critelli et al. 2018).
Urea + Electrolytes	To monitor electrolyte balance.
Liver Function Tests	Liver enzyme levels rise when unwell.
Blood Cultures	If infection is suspected.
Quantitative Amino Acids	To check level of isoleucine, methionine, threonine, valine, glycine and other essential amino acids.

ACTION	RATIONALE
Blood gas	Baseline if well. If acidotic / alkalotic, more frequent monitoring will be required.
Ammonia	Hyperammonaemia is a constant finding in the initial presentation and during acute episodes of decompensation (Haberle et al. 2018) Ammonia, acid-base balance and anion gap are important biochemical parameters to identify a metabolic decompensation, and to estimate its severity (Zwickler et al. 2014).
Acylcarnitine profile	Demonstrates increased levels of propionyl carnitine.
Blood glucose - Record baseline glucose level on admission. Condition determines need for on-going monitoring.	Elevation in blood glucose may occur when using high concentrations of IV Glucose or during stress. Hypoglycaemia may occur if patient is vomiting or has diarrhoea.
Blood ketones - Check ketones on admission and 4-6 hourly when unwell.	To establish if patient is in catabolism phase.
b. URINE **Organic Acids** - Frequency according to stability of condition, and doctor's requests. - **5-10 mls of urine** is required. - A universal container must be used and the sample frozen until transport to the laboratory.	Detects and measures abnormal amounts of propionate and respective metabolites.
Urinalysis - **Monitor Urinalysis.**	

ACTION	RATIONALE
○ Glucose	May be positive when using high volumes of glucose concentration. Consider need for insulin. (Refer to Medical Guidelines Handbook on Metabolic conditions).
○ Ketones	Ketonuria is a common finding and indicates catabolism of fat – prompt action is required. Present if catabolic / ketoacidosis.
○ Protein (send MSU)	Present with urinary tract infection.
○ Specific Gravity	Specific gravity - Indication of level of hydration (dehydration is a frequent finding in patients with PA). Increased specific gravity occurs in case of dehydration. Decreased specific gravity occurs in patients with renal failure or after excessive fluid intake.
○ pH	Elevated urine pH and blood results indicating metabolic acidosis may suggest renal tubular acidosis with increased bicarbonate losses (tubulopathy).
7.3 MEDICATIONS **a. Carnitine (100mgs/Kg/day)** - Check total and free carnitine levels as directed by Metabolic consultant.	Dose may be increased during times of illness, as increased levels of carnitine are lost in the urine. Diarrhoea is common if large doses are being administered orally/enterally.
b. **Biotin** (co-factor)	Enhances enzyme activity where enzyme is not completely absent.
c. Metronidazole	Decreases propionate production in the gut (Grunert et al. 2013). Approx. 20% of propionate acid is produced by the gut. Value of long-term therapy must be considered as side effects occur (e.g. altered bowel flora).
d. Vitamin and mineral supplements	

ACTION	RATIONALE
e. Sodium Bicarbonate may be prescribed during initial diagnosis and subsequent acute admissions.	To correct acidosis.
f. Carbamylglutamate +/- Sodium Benzoate	Corrects hyperammonaemia and hyperglycinaemia and has been used for long term management (Almasi et al. 2019).
g. Analgesia / Anti-pyretic Therapy - Paracetamol is not recommended.	Paracetamol is metabolised in the liver (Malar and Bai, 2012). Non-steroidal anti-inflammatory medications can be used
7.4. DIET **a. NATURAL PROTEIN** (1 gram equals one exchange)	Usually limited to the estimated minimum required for normal growth and development.
b. SYNTHETIC PROTEIN Supplemented **amino acid** m**ixture**, omitting those amino acids that are metabolised by propionyl- Co-A.	Necessary to replace amino acids and vitamins which would otherwise be deficient as the result of restricting natural protein.
c. CARBOHYDRATE AND FAT.	Needed to meet calorie demands to prevent catabolism.
- Consider method of feeding, i.e. oral / nasogastric / gastrostomy.	Feeding problems are extremely common and to ensure a good nutritional state, it is almost invariably necessary to give feeds via nasogastric or gastrostomy tubes at some stage (Baumgartner et al 2014.)
- Liaise with dietetic team regarding education of parents and family. - Provide weaning lists etc.	Provide resource material for reference. Long-term diet treatment is aimed at preventing accumulation of toxic metabolites while maintaining normal development, nutritional status and preventing catabolism.

ACTION	RATIONALE
UNWELL REGIME According to the instructions of a Consultant physician: - Protein may be omitted or reduced. - Calorie requirements may be increased by 20% of normal daily requirements. Intravenous glucose and lipids may be required. - Check intravenous site at least half hourly if administering Glucose 10% or every 15 minutes if using 12.5% **INTAKE AND OUTPUT** - Record intake and output, i.e. vomiting /diarrhoea (observe colour, amount and consistency). - Document if sweating excessively. - Record calorie intake.	Each child will have his/her individual "Unwell Plan". Prevent toxicity. Reduces risk of catabolism. Extravasation can result in dextrose burns. Detects dehydration or fluid overload. Insensible loss must be estimated to ensure adequate fluids are given. Ensures adequate calorie intake.
7.5 MULTIDISCIPLINARY FOLLOW UP a. Metabolic Clinic for medical, dietetic and nursing support. b. **Blood testing** at each OPD visit e.g. amino acids c. **Psychology** & **Medical Social Work** **d. Speech & Language Therapy**	 Chronic illness may have adverse effects on the family unit and relationships within the family. Psychologist and Social Worker input are necessary to assess coping mechanisms and difficulties with diet etc. The Medical Social worker can help to ensure that appropriate entitlements and services are accessed. Oral aversions have been known to occur in patients who require prolonged use of the Nasogastric / Percutaneous Endoscopic Gastrostomy (PEG) route.

ACTION	RATIONALE
e. Genetic counselling Implications for future pregnancies	25% risk of occurrence in other pregnancies to same partners.
f. **Play therapist**	To help the child master and cope with anxieties and feelings and to use play to prepare child for hospital procedures.

8.0 MONITORING, AUDIT & EVALUATION:

This procedure shall be reviewed and updated at least every three years by the Clinical 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.

7.0 KEY STAKEHOLDERS

The following Key Stakeholders were consulted/involved in the development of this document:

Professor Ellen Crushell, Consultant Paediatrician with Special Interest in Inherited Metabolic Disorders.	Signature: _____ Date: _____
Dr. Joanne Hughes, Consultant Paediatrician with Special Interest in Inherited Metabolic Disorders.	Signature: _____ Date: _____
Professor Ina Knerr, Consultant Paediatrician with Special Interest in Inherited Metabolic Disorders.	Signature: _____ Date: _____
Dr. Ritma Boruah, Locum Consultant Paediatrician.	Signature: _____ Date: _____
Caroline O' Connor, Nursing Quality, Practice and Research Co-ordinator. (Lead Author – Original Metabolic Nursing Guidelines)	Signature: _____ Date: _____
Susan Keane, Clinical Practice Facilitator.	Signature: _____ Date: _____

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