

TEMPLE STREET CHILDREN'S UNIVERSITY HOSPITAL		DOCUMENT REF NO:	PP-CLIN-NUR-110
TITLE:	Nursing Guidelines for the Management of Children with Propionic Aciduria	REVISION NO:	1
LEAD AUTHOR:	Eilish O'Connell	EFFECTIVE FROM:	16.03.2017
APPROVED BY:	Clinical Director NCIMD	REVIEW DATE:	15.03.2019
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**TITLE: NURSING GUIDELINES FOR THE MANAGEMENT OF CHILDREN
WITH PROPIONIC ACIDURIA**

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1. PURPOSE:

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. DEFINITIONS:

Propionic acidaemia is a rare autosomal recessive metabolic disorder (Davidson, 1992). It occurs as the result of a deficiency in the enzyme propionyl Co-A carboxylase, or an abnormal metabolism of biotin, its co-enzyme (Ogier de Baulny et al, 2012). Consequently, a defect in the protein breakdown pathway occurs, affecting four amino acids, namely:

- Isoleucine
- Methionine
- Threonine
- 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%).

2.1 PREVALENCE

Propionic acidaemia is rare with an incidence of 1 in 100,000 (Ogier de Baulny et al, 2012).

3. PRESENTATION:

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

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Severe form:

- Poor suck reflex/poor feeding
- Vomiting
- Anorexia
- Lethargy
- Truncal hypotonia
- Metabolic acidosis with increased anion gap.
- Ketonuria
- Hyperammonaemia
- Seizures
- Coma
- Exaggerated deep tendon reflexes
- Clonus

Less severe form:

- Refusal to eat
- Vomiting
- Lethargy
- Dehydration
- Metabolic acidosis with increased anion gap.
- Ketonuria
- Hyperammonaemia

Further complications:

- Hypotonia
- Dehydration
- Hypoglycaemia / hyperglycaemia
- Hyperlactataemia
- Respiratory Alkalosis due to hyperammonaemia
- Hypocalcaemia
- Hyperglycinaemia
- Neutropaenia & Thrombocytopaenia (Ogier de Baulny et al, 2012)

4. DIAGNOSIS:

Diagnosis is made on the following;

- Clinical presentation
- Acylcarnitines - increased propionyl carnitine (C3)

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- Analysis of urine organic acids – increased 3-hydroxypropionate, methylcitrate and propionylglycine.
- Serum amino acids – Increased glycine & alanine
(Zschocke & Hoffmann, 2011).
- Skin biopsy – to detect decreased amounts of enzyme activity.
- Mutation analysis

Other siblings in the family will be tested and any future births will be considered “high risk”. Prenatal diagnosis is possible by chorionic villi sampling in the first trimester or direct measurement of metabolites in amniotic fluid in 2nd trimester (Ogier de Baulny et al, 2012).

4. MANAGEMENT:

4.1 Emergency Treatment:

- a. **Stop natural protein intake** (infant formula / breast feeding / food products which are sources of protein).
- b. **Ensure adequate calorie intake** to prevent catabolism and promote anabolism.
- c. Administration of Carnitine – this is essential for the transport of fats across the mitochondria, but is lost in urine bound to organic acids when amino acidopathies occur.
- d. Metronidazole (antibiotic) - used to clear gut bacteria, as they produce propionic acid (Ogier de Baulny et al, 2012).
- e. Administration of intravenous glucose, lipids and **condition specific** IV amino acid mixture in order to minimize ammonia production from endogenous protein breakdown.
- f. Administration of Carglumic acid may be recommended for hyperammonaemia.
- g. Haemodialysis or haemofiltration may be recommended on initial presentation and on subsequent admissions, where ammonia levels are grossly elevated, to reduce levels rapidly.

4.2 After initial treatment for acidosis, long-term treatment consists of:

- a. Small 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, sugars, fats and specially manufactured low-protein foods.
- d. Administration of vitamin and mineral supplements.
- e. Biotin administration – it is the co-factor to the enzyme propionyl Co-A carboxylase (Ogier De Baulny et al, 2005).
- f. Long term metronidazole treatment (as directed by metabolic consultant)
- g. Long term administration of L-carnitine.
- h. Liver transplant may be an option for patients with PA.

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5. NURSING MANAGEMENT OF THE PATIENT WITH PROPIONIC ACIDURIA

ACTION	RATIONALE
<p>1. GENERAL OBSERVATIONS</p> <p>SKIN Assess and record</p> <ul style="list-style-type: none"> • Colour / perfusion / temperature • Integrity <p>Assess nappy area at each nappy change. Keep skin clean and dry.</p> <p>HAIR</p> <ul style="list-style-type: none"> • Assess integrity and condition of hair (dry / brittle / alopecia) 	<p>Cool, pale skin and capillary refill greater than 2 seconds may indicate shock / stress.</p> <p>Skin break-down and desquamation of cells is common with protein deficiency.</p> <p>Dry, brittle hair and alopecia are signs of protein or zinc deficiency.</p>
<p>2. NEUROLOGICAL STATUS</p> <p>Assess and record using Glasgow Coma Scale, especially during further episodes of acute illness.</p>	<p>Severe forms of acidaemia and/or Hyperammonaemia can produce seizures and coma.</p>
<p>3. HEIGHT AND WEIGHT (recorded on centile chart)</p>	<p>Accurate records are necessary for drug, fluid, calorie and protein prescription.</p>
<p>4. VITAL SIGNS</p> <p>Record 2-4 hourly or more frequently as indicated by the condition of the patient. (Paediatric Early Warning Score (PEWS) is used in TSCUH) Any abnormalities should be reported immediately to medical staff.</p> <ul style="list-style-type: none"> • TEMPERATURE (consider route and method) • PULSE 	<p>Frequent observation ensures early detection of deterioration and allows for monitoring of progress as condition improves.</p> <p>Pyrexia may indicate underlying infection. Hypothermia may indicate catabolism (Both of the above indicate the need for an increased calorie intake).</p> <p>Tachycardia occurs with: -Acidosis -Infection -Fluid overload</p>

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ACTION	RATIONALE
<ul style="list-style-type: none"> RESPIRATORY RATE BLOOD PRESSURE OXYGEN SATURATION When using pulse oxymetry, ensure frequent rotation of the probe position (particularly in neonates). 	<p>-Dehydration</p> <p>Tachypnoea may indicate</p> <ul style="list-style-type: none"> -Acidosis -Infection -Fluid overload <p>Respiratory depression may occur if level of consciousness decreases. Check baseline. Frequency of monitoring as indicated by condition and status of patient. Hypertension may indicate stress, overload or pain. Hypotension may indicate shock or dehydration.</p> <p>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.</p>
<p>5. URINE</p> <ul style="list-style-type: none"> Organic Acids Frequency according to stability of condition, and doctors' requests. 5-10 mls urine is required. <p>A universal container must be used and the sample frozen until transport to the laboratory.</p> <p>Urinalysis</p> <ul style="list-style-type: none"> Glucose Ketones Protein (send MSU) Specific Gravity pH 	<p>Detects and measures abnormal amounts of propionate and respective metabolites.</p> <p>May be positive when using high volumes of dextrose concentration. Consider need for insulin. (Refer to Medical Guidelines Handbook on Metabolic conditions). Present with catabolism of fat. Present with urinary tract infection. Indication of hydration status (dehydration is a frequent finding in patients with PA). Indication of acid / base balance.</p>
<p>5. BLOOD GLUCOSE</p> <p>Record baseline glucose level on admission. Condition determines need for on-going monitoring.</p>	<p>Elevation in blood glucose may occur when using high concentrations of dextrose, or during stress. Hypoglycaemia may occur if patient is vomiting or has diarrhoea.</p>

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ACTION	RATIONALE
<p>6. BLOOD TESTS</p> <ul style="list-style-type: none"> Full blood count Assess need for reverse barrier nursing. Urea + Electrolytes Liver Function Tests Blood Cultures Quantitative Amino Acids Blood gas Ammonia Acylcarnitine profile 	<p>Raised white cells indicate infection (bacterial / viral). Identifies neutropenia - Propionic acid interferes with the maturation of white blood cells (Harris, 1988).</p> <p>To monitor electrolyte balance.</p> <p>Liver enzyme levels rise when unwell.</p> <p>If infection is suspected.</p> <p>Checks level of isoleucine, methionine, threonine, valine, glycine and other essential amino acids.</p> <p>Baseline if well. If acidotic/ alkalotic, more frequent monitoring will be required.</p> <p>Hyperammonaemia is a constant finding in the initial presentation and during acute episodes of decompensation (Ogier de Baulny et al, 2012)</p> <p>Demonstrates increased levels of propionyl carnitine.</p>
<p>7. LIVER Size checked daily by doctor as an in-patient and on each outpatient visit.</p>	<p>Hepatomegaly may occur due to fat deposits or secondary to stress, i.e. infection (Ogier de Baulny et al, 1990)</p>
<p>8. MEDICATIONS</p> <ul style="list-style-type: none"> Carnitine (100mgs/Kg/day) Check total and free carnitine levels as directed by Metabolic consultant. Biotin (co-factor) Metronidazole 	<p>Dose may be increased during times of illness, as increased levels of carnitine are lost in the urine (Harris, 1988). Diarrhoea is common if large doses are being administered orally/enterally (Leonard, 1995)</p> <p>Enhances enzyme activity where enzyme is not</p>

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ACTION	RATIONALE
<ul style="list-style-type: none"> Vitamin and mineral supplements Sodium Bicarbonate may be prescribed during initial diagnosis and subsequent acute admissions to correct acidosis. Carbamylglutamate & Sodium Benzoate Analgesia / Anti-pyretic Therapy Paracetamol is not recommended. 	<p>completely absent.</p> <p>Decreases propionate production in the gut. Approx. 20% of propionate acid is produced by the gut (Leonard, 1995). Value of long-term therapy must be considered as side effects occur (e.g. altered bowel flora).</p> <p>Corrects hyperammonaemia and hyperglycinaemia and has been used for long term management (Ogier de Baulny et al, 2005). Paracetamol is metabolised in the Liver (Higgins, 1996). Non steroidal anti-inflammatory medications can be used</p>
<p>9. DIET</p> <ul style="list-style-type: none"> NATURAL PROTEIN (1 gram equals one exchange) SYNTHETIC PROTEIN Supplemented amino acid mixture, omitting those amino acids that are metabolised by propionyl- Co-A. Carbohydrate and fat. Consider method of feeding, i.e. oral / nasogastric / gastrostomy. <p>Liaise with dietetic team regarding education of parents and family. Provide weaning lists etc.</p> <p>UNWELL REGIME</p> <p>According to the instructions of a Consultant physician:</p>	<p>Usually limited to the estimated minimum required for normal growth and development.</p> <p>Necessary to replace amino acids and vitamins which would otherwise be deficient as the result of restricting natural protein.</p> <p>Needed to meet calorie demands to prevent catabolism.</p> <p>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 (Harris, 1988; Leonard, 1995).</p> <p>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.</p> <p>Each child will have his/her individual "Unwell Plan"</p>

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ACTION	RATIONALE
<ul style="list-style-type: none"> Protein may be omitted or reduced. Calorie requirements may be increased by 20% of normal daily requirements. Intravenous Dextrose and lipids may be required. Check intravenous site at least half hourly if administering Dextrose 10% or every 15 minutes if using 12.5% <p>INTAKE AND OUTPUT</p> <ul style="list-style-type: none"> Record intake and output, i.e. vomiting /diarrhoea (observe colour, amount and consistency). Document if sweating excessively. Record calorie intake. 	<p>- Prevent toxicity.</p> <p>Reduces risk of catabolism.</p> <p>Extravasation can result in dextrose burns.</p> <p>Detects dehydration or overload.</p> <p>Insensible loss must be estimated to ensure adequate fluids are given.</p> <p>Ensures adequate calorie intake.</p>
<p>10. MULTIDISCIPLINARY FOLLOW UP</p> <ul style="list-style-type: none"> Metabolic Clinic for medical, dietetic and nursing support. Blood testing at each OPD visit e.g amino acids Psychology & Medical Social Work Speech & Language Therapy Genetic counselling Implications for future pregnancies 	<p>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.</p> <p>Oral aversions have been known to occur in patients who require prolonged use of the Nasogastric / Percutaneous Endoscopic Gastrostomy (PEG) route.</p> <p>25% risk of occurrence in other pregnancies to same partners.</p>

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6. REVIEW:

This procedure shall be reviewed and updated at least every two 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. KEY STAKEHOLDERS

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

NAME	TITLE
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Ms. Caroline O' Connor	Nursing Quality, Practice & Research Co-ordinator (Lead Author – Original Nursing Guidelines)

8. REFERENCES:

Propionic Acidaemia

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