GUIDELINE

Parenteral Nutrition

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

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Contents

Aim 2
Risk 2
Background 2
Key points 2
Indications for PN 3
Types of Formulations 4
Starter PN Bags 4
Standard PN Bags 4
Modifications to Standard PN (Non-Standard PN) 4
Composition of PN 5
Protein 5
Glucose 5
Electrolytes and Paediatric Trace Elements (Biomed®) 5
Trace Elements (Biomed) 5
Heparin 5
Lipid Emulsion plus Vitamins 6
Prescribing TPN 6
Administration 7
Precautions 7

Complications of PN 7
Metabolic Complications 7
Complications related to lines used for infusion of PN 8
Monitoring 9
Appendix 1 – Composition of PN 12

Aim

This guideline describes the indications for, and composition of parenteral nutrition (PN), as well as information regarding prescribing, complications and monitoring of infants receiving PN.

Risk

Compliance with this guideline will support the nutritional care of preterm and term infants, promote safe, standardised parenteral nutrition practice and assist in mitigating risks associated with prescribing and providing parenteral nutrition to neonates.

Background

- Parenteral Nutrition (PN) is intravenous nutrition that is administered to assist in meeting the infant's nutritional requirements for growth and development when enteral feeding is withheld or delayed.
- Standard PN is used preferentially at CAHS (KEMH NICU and PCH NICU) for preterm and term infants. Standard PN consists of pre-determined amounts of glucose and amino acids and standard concentrations of electrolytes, trace elements and heparin.
- If clinically indicated, consultants may order Non-Standard PN by making modifications to the concentration of glucose, amino acids, sodium, potassium and/or acid/base balance in the standard PN.
- If clinically indicated, phosphate and calcium can be simultaneously modified in standard amounts only.

Key points

- In **KEMH NICU only**, Preterm Starter PN containing glucose, amino acids, heparin and electrolytes are given on admission as first fluids to preterm infants born < 30 weeks gestation.
    - **<27 weeks gestation**: 5% Glucose; 2.3 g Amino Acids; 50 Units of heparin and standard amounts of electrolytes and trace elements.
    - **>27 weeks - <32 weeks GA**: 8% Glucose; 2.3 g Amino Acids; 50 Units of heparin and standard amounts of electrolytes and trace elements.

- When clinically indicated, preterm and term infants in NICU at PCH and KEMH receive standard PN – see below - Indications for PN
- Preterm STANDARD PN (per 100 mL) contains either 5% glucose (< 27 weeks GA) or 8% glucose (≥ 27 - < 35 weeks GA), 2.7 g amino acids, 50 units of heparin and standard amounts of electrolytes and trace elements.
- Near-Term/Term (≥ 35 weeks GA) STANDARD PN (per 100 mL) contains 12% glucose and 2.3 g of amino acid, 50 units of heparin, standard concentrations of electrolytes and trace elements.
- STANDARD PNs meet age-appropriate nutrient guidelines when infused at a maximum of 140 mL/kg/d.
- SMOF Lipid 20% with vitamins (Final lipid concentration 17%) is available for preterm and term neonates (6 mL SMOF 17% with vitamins = 1 g fat) and should be commenced at 12 ml/kg/d with first order of Starter or Standard PN, increasing in 4 mL/kg/d increments up to 20 mL/kg/d. SMOF lipid batch number and expiry date should be recorded on the Neonatal Parenteral Nutrition form MR 827.01/MR800 prior to infusing.
- Prescribing NON-Standard (customised) PN is discouraged**; NON-standard PN orders must be authorised by a consultant;** the following components can be modified:
    - Glucose, amino acids, sodium, potassium and acetate/chloride balance
    - Phosphate and calcium can be simultaneously reduced from 1.5 to 0.75 mmol/100 mL PN solution (1:1 molar ratio) if hyperphosphatemia (and/or hypercalcaemia) is identified OR simultaneously increased from 1.5 to 2.0 mmol/100 mL PN solution (1:1 molar ratio) if hypophosphatemia (and or hypocalcaemia) is identified.

Indications for PN

- Prematurity < 32 weeks gestation and/or < 1500g.
- Infants < 35 weeks who are unlikely to achieve full enteral feeds by day 5.
- Necrotising enterocolitis (NEC).
- Surgical gastrointestinal tract anomalies (e.g., exomphalos, gastroschisis, tracheo-oesophageal fistula etc.).
- Prolonged NBM due to other surgery e.g. CDH.
- Short bowel syndrome.

Types of Formulations

Starter PN Bags

- **Preterm Starter PN is available at KEMH only and prescribed as first fluids on day 1 of life.**
- Two Preterm Starter PN formulations with differing glucose concentrations are available for different gestational age groups; each Preterm Starter PN Solution also contains heparin (50 units per 100 mL), and standard amounts of electrolytes (Appendix 1).

Standard PN Bags

- Three Standard PN formulations are available in the NICU's at KEMH and PCH.
- The glucose, amino acids, electrolytes and trace elements in each Standard PN formulation are designed to meet the nutritional requirements of infants of different gestational age groups when infused at a maximum volume of 140 mL/kg/d (Appendix 1).

Modifications to Standard PN (Non-Standard PN)

- If clinically indicated, NON-Standard PN can be ordered under Consultant authorisation and medical order.
    - One or more of the following components of Standard PN can be modified: amino acids, glucose, potassium, sodium and/or acetate-chloride balance components;
- If hyper- or hypophosphataemia (and/or hyper- or hypocalcaemia) is identified, phosphate and calcium can be simultaneously increased or reduced under consultant authorisation and medical order in standard amounts
    - Preterm reduced from 1.5 mmol/100 mL to 0.75 mmol/100 m or increased from 1.5 mmol/100 mL to 2 mmol/100 mL
    - Term reduced from 0.90 mmol/100 mL to 0.75 mmol/100 mL or increased from 0.90 mmol/100 mL to 1.5 mmol/100 mL
    - **Note** - for solubility issues, both calcium and phosphate MUST be simultaneously modified to maintain a 1:1 molar ratio.
- Any other modifications to PN **must** be requested by the Consultant in direct consultation with Pharmacy.
- Clinical situations in which Non-standard PN solutions may be considered include fluid restriction, metabolic disorder, protein restriction, electrolyte abnormalities, hyperphosphataemia, hypercalcaemia, refeeding syndrome (phosphate <1.4 mmol) and renal failure.

Composition of PN

Protein

- Crystalline amino acids are the building blocks for protein in PN solutions. Primene 10% contains essential amino acids that mimic amino acids in the umbilical cord in the last trimester of pregnancy.
- In the absence of exogenous protein, a preterm infant will catabolise 1g/kg/day of their own body protein to meet their metabolic needs. Therefore, the prompt introduction of glucose and amino acids via PN may support an early positive nitrogen balance for the infant.
- Each 1g of amino acid provides 0.1515g Nitrogen, equivalent to approximately 0.94g protein and 15.9kJ or 3.8kcal of energy.
- Infants at KEMH will receive 1.7g protein/kg/d within the first 24 hours of life when Starter PN is infused at 80 mL/kg/d.
- Preterm infants will receive 3.5 g protein/kg/d and near term/term infants will receive 3.0 g protein/kg/day when gestational age-appropriate Standard PN is infused at recommended maximum infusion rates of 140 mL/kg/d.

Glucose

- Rate of glucose oxidation in appropriate for gestational age preterm infants is 6-8mg/kg/min (8.6-11.5g/kg/d).
- In term infants after surgery, or infants on long term PN, the maximal rate of glucose oxidations is estimated to be about 12mg/kg/min (17.2g/kg/d).
- The upper rate of glucose administration is determined by glucose oxidative capacity for energy production and glycogen deposition and is influenced by gestational age and clinical presentation.
- Each 1g of glucose provides 3.8kcal, equivalent to 15.9kJ of energy.

Electrolytes and Paediatric Trace Elements (Biomed®)

- Electrolytes are added in varying standard amounts depending on the type of PN. See Appendix 1

Trace Elements (Biomed)

- Trace elements (Biomed ®) are added in standard amounts to Standard PN (Appendix 1)

Heparin

- All PN formulations contain heparin (50 units /100 mL) to reduce risk of catheter occlusion. There is no significant difference in the duration of catheter patency, risk of thrombosis, catheter related sepsis or extension of intraventricular haemorrhage with the addition of Heparin.

Lipid Emulsion plus Vitamins

- Lipid Emulsion with Vitamins is an isotonic fat emulsion containing refined soya oil (30%), medium chain triglycerides (30%), refined olive oil (25%), and fish oil (15%). It is rich in omega-3 acids, glycerol, purified egg phospholipids, all-rac-α-tocolpherol, sodium hydroxide, sodium oleate and water.
- Water (Soluvit N Infant®) and fat (Vitalipid N Infant®) soluble vitamins are added to the SMOF 20% lipid emulsion.
- One pre-filled 25 mL syringe of SMOF 20% fat emulsion with vitamins contains 18.75 mL of SMOF fat emulsion, 1.25 mL Soluvit N Infant® and 5 mL Vitalipid N Infant®.
- Final fat content of SMOF emulsion with vitamins is 17%.
- 6 mL of SMOF emulsion with vitamins contains 1g fat and provides 10 kcal of energy, equivalent to ~42kJ.
- Lipid emulsion with vitamins should be
    - Started at 12mL/kg/d (g fat/kg/d) on day 1 of PN with Starter PN and infused over 20 hours (0.6mL/kg/hr)
    - Increased by 4mL/kg/day each day to a maximum of 20mL/kg/day. Infuse over 20 hours. Rate/hr not to exceed 1mL/kg/hour

Lipid volume is NOT included in the total fluid intake.

Prescribing TPN

- **ALL** Starter and Standard PN and Intravenous Lipid orders are written on the neonatal parenteral nutrition orders form MR827.01 / MR800 which also incorporates a Quick Reference Guide to assist with correct prescribing of PN.
- At KEMH only, Starter PN can be used as replacement PN while awaiting a new pharmacy-supplied PN order. Starter PN is prescribed on the neonatal parenteral nutrition orders form MR827.01 / MR800, but if unavailable when the replacement PN is required, the Neonatal Parenteral Fluid Chart (MR725) can be used.

Standard PN must be prescribed whenever possible.

See above for Types of Formulations

- Standard PN
- Non-Standard PN

Administration

- PN can be administered through peripheral or central lines. If glucose concentration exceeds 12.5%, administer via a central vein catheter or PICC line.
- If a prolonged period of PN is anticipated, i.e. greater than 5-7 days, insertion of a percutaneous central venous catheter may be considered. Aseptic technique in preparation and administration of the TPN is essential.

Precautions

- Hyperkalaemia - **use caution when prescribing potassium in renal impairment or persisting hypotension with poor urine output**.
- Toxicity - Due to accumulation of certain amino acids should be considered in an infant becoming unwell and acidotic on PN. Serum and urinary amino acids should be measured.
- Fatty acids. Due to fatty acids being precursors of prostaglandin synthesis, potential adverse effects on pro/anti-coagulation homeostasis and pulmonary vascular tone are theoretically possible.

Complications of PN

Metabolic Complications

- **Hyperglycaemia**
  - Maximum glucose oxidation in preterm infants is 8.3mg/kg/min or 12g/kg/d. The upper rate of glucose administration is determined by glucose oxidative capacity for energy production and glycogen deposition and is influenced by gestational age and clinical condition.
  - Glucose administration may range from 7-12mg/kg/min. Hyperglycaemia is common after preterm birth, possibly related to surges in catecholamines; decrease in insulin production; and insulin resistance.
  - Hyperglycaemia is associated with death, IVH and sepsis.
  - Excessive glucose intakes may increase carbon dioxide production and exacerbate chronic lung disease. Insulin is not recommended as offers no clinical benefit and infusion is associated with risk of hypoglycaemia and associated morbidity (Beardsall 2008).
- **Excess protein**
  - Adverse effects of excess protein include a rise in urea and ammonia, as well as a metabolic acidosis.
  - The addition of a buffer (base), acetate, can reduce metabolic acidosis.
    - In one RCT the partial replacement of chloride by acetate in the amino acid solution resulted in an improved pH, a reduction in both

bicarbonate and colloid use, with no adverse effect on ventilation requirements compared to the group receiving standard PN (Peters et al 1997).

- There are 2 mmol of acetate and 2.01 mmol of chloride in 100 mL of Standard Preterm PN and 2.6 mmol of acetate and 2.54 mmol of chloride in 100 mL of Standard Near Term/Term PN.
- If sodium is ordered as acetate, then the acetate chloride balance can be altered. More acetate can be used if more sodium is prescribed.

- **Cholestasis**
  - associated with administration of TPN for >2 weeks.
  - The exact cause is unknown. It is thought to be due to either hepatotoxicity of the infusiate or to the lack of hepatic stimulation in the absence of enteral feeds. Studies in older children, have shown that the infusion of fish oil may reverse the cholestasis associated with parenteral nutrition.
- **Refeeding syndrome (RF)**
  - a potentially serious cluster of electrolyte disturbances that can occur after a period of poor nutrition (such as occurs with placental insufficiency or inadequate intravenous energy and protein intake for several days after birth). The precipitating factors are the sudden supply of IV amino acids and glucose following a period of poor nutrition.
  - Close monitoring of PN bloods is recommended.

Complications related to lines used for infusion of PN

- **Malposition**
  - Could potentially lead to a fatal complication of pericardial tamponade due to central line being positioned in the right atrium, and a subsequent pericardial effusion of TPN.
  - Measurement of the estimated distance of insertion of central lines is essential as is an X-ray before the infusion commences.
  - During insertion the lines should aspirate blood freely at the length at which they are to be inserted. This is to ensure the line is sitting in a large vessel. (See CVAD Bundle).
- **Sepsis**
  - Infants requiring long term parenteral nutrition are at risk of line sepsis. Follow CVAD guidelines.
  - Minimised by maintaining strict sterility of the line during and after insertion (see CVAD Bundle).
  - In adults, sepsis induces profound changes in both energy and protein metabolism. Several neonatal studies have documented glucose and lipid

intolerance in neonates with sepsis but the single study of protein metabolism in neonates with sepsis did not demonstrate either increased protein requirements or significant protein intolerance. PN may be reduced during the acute phase of an episode of sepsis.

  - Optimal infusions of glucose, amino acids and lipids should be reinstated as soon as the infant improves, and parameters are stable.

- **Catheter tip thrombi**
- **Thrombophlebitis**
  - related to infusion of PN via peripheral lines
  - Requires close observation of infusion sites
- **Extravasation** into the soft tissue, with resulting tissue necrosis.

Monitoring

Biochemical and anthropometric monitoring for infants commenced on PN includes:

- Daily blood gas in the first week, and as clinically indicated thereafter.
- UEC, Phosphate, Calcium and Magnesium on days 3, 7 and 14 after commencing PN.
- Bone bloods (Calcium, Phosphate, Magnesium, ALP and Vitamin D) on day 28. Consideration should be given to performing bone bloods earlier, in cases of prolonged TPN use.
- If prolonged TPN, fortnightly liver function tests.
- If CVL, consider twice weekly CRP for catheter-related sepsis.
- Weight daily or alternate days; and head circumference weekly. Length at admission and discharge
- Urinary sodium weekly for surgical infants with fluid losses (i.e. intestinal stoma)

Related CAHS internal policies, procedures and guidelines
Neonatal Clinical Guidelines • CVAD: Central Venous Access Device Bundle Neonatal Medication Monographs • Lipid Emulsion with Vitamins

References and related external legislation, policies, and guidelines

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Appendix 1 – Composition of PN

		STARTER PN (KEMH NICU ONLY)		STANDARD PN (KEMH / PCH NICUs)		
		Starter A	Starter B	Preterm A	Preterm B	Near/Term
Gestational age (week)		$<26^{+6}$	≤32	$<26^{+6}$	≤34+6	$\geq 35^{+0}$
mL/Kg						
Maximum target volume		80	80	140	140	140
Per 100mL PN Bag						
Glucose	%	5	8	5	8	12
Amino acid	g	2.3	2.3	2.7	2.7	2.3
Heparin	Units	50	50	50	50	50
Sodium	mmol	3	3	4	4	4
Potassium	mmol	2	2	2	2	2
Magnesium	mmol	0.25	0.25	0.25	0.25	0.25
Calcium	mmol	1.50	1.50	1.50	1.50	0.90
Phosphate	mmol	1.50	1.50	1.50	1.50	0.90
Acetate	mmol	1.2	1.2	2	2	2.6
Chloride	mmol	1.2	1.2	2.01	2.01	2.54
Zinc	µg			296	296	296
Manganese	µg			0.74	0.74	0.74
Copper	µg			14.8	14.8	14.8
Molybdenum	µg			1	1	1
Iodine	µg			0.74	0.74	0.74
Selenium	µg			5.2	5.2	5.2
SMOF LIPID EMULSION						
Per kg						
SMOF Lipid	g	2		3	3	3
Vitamin A	IU (µg)	541 (162)		812 (244)	812 (244)	812 (244)
Vitamin D	IU (µg)	94 (2.4)		141 (3.5)	141 (3.5)	141 (3.5)
Vitamin E	IU (µg)	1.5 (1.5)		2.3 (2.3)	2.3 (2.3)	2.3 (2.3)
Vitamin K	µg	27		71	71	71
Ascorbate	mg	6.6		10	10	10
Thiamine	mg	0.18		0.27	0.27	0.27
Riboflavin	mg	0.29		0.43	0.43	0.43
Nicotinamide	mg	2.35		3.53	3.53	3.53
Pyridoxine	mg	0.29		0.4	0.4	0.4
Biotin	µg	3.53		5.3	5.3	5.3
Pantothenate	mg	0.97		1.5	1.5	1.5
Folate	µg	23.53		35	35	35
Vitamin B12	µg	0.29		0.44	0.44	0.44