

RPA Newborn Care Protocol Book

Total Parenteral Nutrition

Aims

Total parenteral nutrition (TPN) aims to provide nutritional requirements for optimal growth and maturation of the infant. It is a substitute for enteral feeding in circumstances where the establishment of full enteral feeds will be delayed or inadequate. However, the preferred form of nutrition for the neonate remains breast milk.³⁵

Why is it necessary?

TPN is used to provide nutrition in situations in which establishment of full enteral nutrition is likely to be delayed. The provision of balanced nutrition (carbohydrate, protein and fat) is essential to provide for growth and prevent catabolism. Early TPN with dextrose, amino acids and lipid has been shown to reduce hypoglycaemia, increase plasma amino acid levels³² and increase albumin levels in preterm infants.⁴¹ Studies are few that prove TPN decreases either morbidity or mortality and are now unlikely to be undertaken as it would be deemed unethical to withhold TPN from a control group.

Indications for TPN

- Premature infants <30 weeks gestation and/or <1000g.
- >30 weeks gestation but unlikely to achieve full enteral feeds by day 5.
- Infants at high risk of NEC:³
 - <30 weeks gestation
 - >30 weeks with absent or reversed fetal umbilical artery flow.
 - Infants with perinatal asphyxia
- Necrotising enterocolitis (NEC).
- Gastro-intestinal tract anomalies.

Venous access

Central cannula: Peripherally inserted central catheters (PICC's) should be used preferentially to provide central venous access in neonates receiving prolonged TPN as PICC use results in improved nutrient intake and fewer insertion attempts.^{1, 2}

Umbilical catheters: In neonates, umbilical vessels can be used for TPN.¹ UVC compared to peripheral venous catheter reduces insertion attempts with no increase in risk of infection or necrotising enterocolitis.²⁸ The risk of complication may increase if umbilical venous catheters are being left in place for more than 14 days.^{7, 36} (**See central line policy and UVC policy** – site PICC line before 7 days or by 48 hours if non-ideally sited).

Peripheral cannula: As phlebitis of peripheral veins can be expected when the osmolality of the intravenous solution exceeds 600 mOsm^{1, 20}, peripheral veins should be used for short term venous access and for providing partial nutritional supplementation. Although extravasation injury occurs in up to 10% of infants managed only with peripheral infusion of TPN,² it is unclear if the risk of peripheral TPN is greater than the risk of peripheral crystalloid infusion.

Prescription

Premature infants tolerate TPN from day 1 of post-natal life.^{4, 8, 23}

Parenteral nutrition can be delivered using standardised or individualised bags. There is RCT evidence that most TPN prescriptions can be adequately done using standardised bags.⁴⁴ Because standardised bags are both easier and cheaper, this is the preferred method on this unit. Some babies, particularly if they are very unstable, may need individualised bags and there is a computer program within the database to aid with these

individualised prescriptions. Individualised prescription should only be done after consultation with the consultant on service.

TPN prescribing

Standardised TPN bags have been developed by a NSW working group with substantial consensus agreement from ANZNN. The following bags are available (link **TPN Consensus Group Formulations**):

Volume of fluid

Day 1 60 ml/kg/day

Day 2-3 90 ml/kg/day

Day 4-6 120 ml/kg/day

Day 7 150 ml/kg/day [usually 135 ml/kg/day parenteral nutrition + 18ml/kg/day lipid]

Note: deduct 80% of lipid volume = 15ml/kg/day when lipid is infused at 18ml/kg/day.

Starter Parenteral Nutrition

- Suitable for
 - preterm infants within the first 24-48 hours of life or up to 120 ml/kg/day and
 - term infants with fluid restriction and renal impairment.
- Starter PN is low sodium and potassium free solution that provides good amount of amino acids at less volume.
- Continued usage of these solutions is dependent on the electrolyte status of infant.

Standard Preterm Parenteral Nutrition

- Standard solution for preterm infants after 24-48 hours of age

High Sodium Preterm Parenteral Nutrition

- For hyponatraemic preterm infants.
- Provides Na at 8mmol/kg/day at 135ml/kg/day.

7.5% Dextrose Preterm Parenteral Nutrition

- For hyperglycaemic preterm infants.

Peripheral Preterm Parenteral Nutrition

- For those preterm babies with no long lines – use only if substantial delay expected in insertion of central line – this should be done in consultation with on call Neonatologist.

Term Parenteral Nutrition

- Standard PN solution for term infants.

Lipid

Daily increase in lipid starting at 1 g/kg/day, increasing by 1g/kg/day. Monitor triglyceride levels with each increase. If triglyceride levels >2.8 mmol/L, consider reducing the lipid emulsions by 1 g/kg/day increments but aim to continue at least 0.5g/kg/day to prevent essential fatty acid deficiency.

1 g/kg/day = 6 ml/kg/day

2 g/kg/day = 12 ml/kg/day

3 g/kg/day = 18 ml/kg/day

Transitional Feeds

- Reduce IV lipid by 50% when infant tolerates >50% of total fluid intake as enteral feeds.
- Cease lipids when infant on >75% of total fluid intake as enteral feeds.

Components of TPN

Fluid

Volumes are increased over the first 7 days in line with the **feeding protocol** with the aim of delivering 150 ml/kg/day by day 7.

Day 1	60 ml/kg/day
Day 2-3	90 ml/kg /day
Day 4-6	120 ml/kg /day
Day 7	150 ml/kg /day

Calories

- Babies need at least 100-120 kcal/kg/day to grow.¹³ Some babies will need more than this including growth restricted infants and infants with co-existing disease.¹³
- In preterm infants, at 150 ml/kg/day, total daily calorie delivery will be ~100kcal/kg/day. This will prevent catabolism and provide calories for some but not necessarily optimal growth.

Carbohydrate

- Glucose administration to preterm infants should start at 4-8mg/kg/min (or 5.8g/kg/day to 11.5g/kg/day),¹⁶ and should not exceed 13mg/kg/min (or 18g/kg/day) for full term neonates as this tends to induce net lipogenesis. Starting glucose concentration is 10%.
- Premature infants are often relatively intolerant of glucose infusion resulting in hyperglycaemia and glycosuria (not always with an osmotic diuresis). If this problem arises the options are to reduce glucose intake (use of 7.5% glucose solution) or use of an insulin infusion. The use of an insulin infusion for treatment of hyperglycaemia results significant increases in non-protein energy intake, glucose intake, and short-term weight gain (**see hyperglycaemia guideline**).⁵ The target plasma glucose level should be 5.5 - 9.9 mmol/L.⁹
- Insulin infusion should not be used routinely to prevent hyperglycaemia as this resulted in increased hypoglycaemia and possibly mortality.³⁸

Protein

- **Maximal amino acid / protein intake:** The maximum recommended amino acid intake for preterm infants is 4g/kg/day and 3g/kg/day for full term neonates.¹⁴ Trials show it is possible to achieve positive nitrogen balance from birth onwards as preterm infants are able to tolerate 3.8g/kg/day.^{4, 8, 23, 24, 29, 30, 41, 42} Adverse effects of excess protein include a rise in urea and ammonia and high levels of potentially toxic amino acids such as phenylalanine.
- **Starting amino acid / protein intake:** Amino acid supply should start on the first postnatal day.¹⁴ A minimum amino acid intake of 1.5 g/kg per day is necessary to prevent a negative nitrogen balance. Higher intakes are needed to achieve physiological protein deposition. However, the safety of higher starting doses of amino acids on day 1 has not been adequately assessed with trials demonstrating some infants will develop high blood urea levels at starting amino acid intake of 2g/kg/day.⁸ Trials comparing day 1 amino acid intakes up to 2g/kg/day increasing to up to 4g/kg/day have demonstrated improved growth without harm.^{4, 8, 23, 40, 43}

Lipid

- Lipid is provided as ClinOleic 20%.^{10, 21, 22}
- In order to prevent EFA deficiency a minimum linoleic acid intake of 0.25 g/kg per day should be given to preterm infants and 0.1 g/kg per day to term infants and older children.¹⁵
- **Starting lipid intake:** There is no evidence that early versus late introduction of lipid changes neonatal outcomes.³⁷

- **Increasing lipid intake:** There is no evidence that gradual increments in the infusion rate of lipids improve fat tolerance. If lipid infusion is increased in increments of 0.5 to 1 g/kg/day, it is possible to monitor for hypertriglyceridaemia.
- **Maximal lipid intake:** Parenteral lipid intake should usually be limited to a maximum of 3–4 g/kg per day (0.13–0.17 g/kg per hour) in infants.^{6, 15}
- **Titrating lipid:** If triglyceride levels reach beyond 250 mg/dl (2.8 mmol/L), consider reducing the lipid emulsions by 1 g/kg/day increments but aim to continue at least 0.5g/kg/day to prevent essential fatty acid deficiency.
- Heparin does not improve utilisation of intravenous lipids and should not be given with lipid infusion on a routine basis, unless indicated for other reasons.
- **Thrombocytopenia:** In patients with severe unexplained thrombocytopenia serum triglyceride concentrations should be monitored and a reduction of parenteral lipid dosage be considered.¹⁵
- **Pulmonary function.** In the presence of severe pulmonary hypertension, higher concentrations of lipid (>2g/kg/day) should be avoided. There are reports of increased pulmonary vascular resistance of a dose and time dependent nature which suggest lipid may aggravate pulmonary hypertension in susceptible individuals.³⁴
- **Kernicteris:** In the presence of jaundice requiring phototherapy, higher concentrations of lipid (>2g/kg/day) should be avoided. Lipid itself does not displace bilirubin, but the liberated free fatty acids displace bilirubin from albumin. Whilst early introduction of lipid has not been shown to increase clinically significant jaundice,³⁷ infants receiving early aggressive TPN including 3g/kg/day lipid had higher serum bilirubin levels.²³ Some Units use the free fatty acid to albumin ratio as a guide with a value <0.6 taken as safe.
- **Sepsis.** There is insufficient evidence to recommend changes to lipid infusion during sepsis. Consider monitoring triglyceride levels. Systematic review of trials of early introduction of lipids for preterm infants found no difference in rates of sepsis.³⁷
- **Free radical formation:** Lipid peroxidation of the polyunsaturated fatty acids occurs if they are exposed to light, accelerated by phototherapy. Covering with silver foil, using opaque tubing, or the addition of ascorbate prevents oxidation.²⁵⁻²⁷

Acetate

An RCT found that an anion regimen where the first 3 mmol was provided as chloride, the next 6 mmol as acetate, and thereafter as chloride again reduces metabolic acidosis and hyperchloraemia.³³

Minerals

Premature infants require high intakes of Ca and P to mimic fetal accretion rates. Use of calcium gluconate 75mg/kg/day and inorganic phosphate 45mg/kg/day (glucose-1-phosphate) increases solubility and resulted in increased Ca and P retention and reduced PTH.¹¹ However, there is concern regarding precipitation of Ca and P in TPN solutions preventing higher amounts being delivered. Low AA concentrations and high temperatures (in infusion tubing in the infant humidicrib) are significant risk factors for the precipitation of the insoluble dibasic calcium phosphate that may be fatal upon intravenous infusion. The AA concentration of the TPN formula should not be less than 15 g/L (and ideally >30 g/L) when high intakes of calcium (15 mmol/L) and phosphate (16.6 mmol/L) are prescribed.³⁹

Trace element syringes:

Trace elements are recommended with long term TPN. However, precise requirements for individual nutrients remain a matter of debate.¹²

TPN solutions may be contaminated with aluminium and chromium.

Patients with cholestatic jaundice should be closely monitored for copper toxicity.

Patients with renal impairment may not be able to excrete selenium, molybdenum, zinc and chromium.

Trace elements Zinc, Selenium and Iodine are added to TPN infusion bags at the following rates:

- Zinc – 440 µg/kg/day at 135 ml/kg/day
- Selenium – 2.7 µg/kg /day at 135 ml/kg/day
- Iodine – 1.08 µg/kg /day at 135 ml/kg/day.

For infants on TPN >7 days, additional an additional NSW Neonatal Trace Element syringe at 1 ml/kg daily will provide:

- Copper 20 µg/ml
- Chromium 0.1 µg
- Manganese 1 µg/ml
- Molybdenum 1 µg/ml

If on long term TPN (>2 weeks duration) perform trace element assays and adjust dose as required.

1. Cholestatic liver disease: conjugated bilirubin > 34 µmol/L reduce trace elements to twice weekly. Avoid giving copper and manganese. If receiving enteral nutrition, discontinue trace elements.
2. Persistent diarrhoea and gastrointestinal loss: Increase Zinc.

Filtration

Filtration is aimed at filtering out particulate matter including mineral precipitates and microbes from infusates. It is recommended that TPN admixtures should be administered through a terminal filter.¹⁷ However, limited RCT data has not yet demonstrated a benefit from this practice.¹⁸

Duration of infusion

Parenteral solution and lipid are to be infused over 48 hours.

Parenteral nutrition solution: there is no significant difference in bacterial or fungal colonisation of infusate or neonatal sepsis in infants receiving 24 or 48 hour infusions of parenteral nutrition solution.¹⁹

Lipid infusion: fungal contamination may be increased in infants receiving lipid infusion for 24 hours compared to 48 hours.¹⁹ Microbial contamination of infusion sets was significantly more frequent with 72- than with 24-hour set changes in neonates receiving lipid solutions. This may be associated with an increased mortality rate.³¹

Monitoring

TPN administration requires careful clinical and laboratory monitoring. Adequate growth is best determined by linear growth as weight gain can reflect an increase in total body water rather than tissue accretion. In addition to routine observations the following are required for short term TPN use.

Routine TPN Biochemistry Orders

Test	First 3 Days	Thereafter
UEC (Na, K, Cl, HCO ₃ , urea)	Daily	Monday/Thursday
Ca, PO ₄ , bilirubin, albumin	Baseline	Monday
FBC	Baseline	Monday
Triglyceride	With each increase	Monday / When ill
Clinical		
Blood glucose level	4-6hrly	Twice a day once stable

Key Points

	Level of evidence	Grade of recommendation
Early TPN with dextrose, amino acids and lipid has been shown to reduce hypoglycaemia, increase plasma amino acid levels and increase albumin levels in preterm infants.	1b ^{32, 41}	B
Trials comparing day 1 amino acid intakes up to 2g/kg/day increasing to up to final intake 4g/kg/day have demonstrated improved nitrogen balance without harm.	1a ^{16-18, 23, 24}	A
The use of an insulin infusion for treatment of hyperglycaemia results significant increases in non-protein energy intake, glucose intake, and short-term weight gain (<i>see hyperglycaemia guideline</i>).	1a ⁵	B
Parenteral nutrition can be delivered using standardised or individualised bags. There is RCT evidence that most TPN prescriptions can be adequately done using standardised bags.	1b ⁴⁴	B
Peripherally inserted central catheters (PICC's) should be used preferentially to provide central venous access in neonates receiving prolonged TPN.	1a ^{1, 2}	A
Parenteral nutrition solution may be infused over 48 hours with no increase risk of infection.	1b ¹⁹	B
Lipid infusion may be infused over 48 hours.	1b ^{19, 31}	B

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