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MERITS AND DEMRITS OF TPN (TOTAL PARENTERAL NUTRITION)

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ABSTRACT

Total parental nutrition is an important step towards providing nutritional requirements for optimal growth and maturation of an infant the provision of balanced nutrition (carbohyrates, protin, fats) is essential to provide for growth and prevention of catabolism. This review articls enlightens the usefulness and risks of TPN, so as to come across a conclusion whether TPN is is a successful concept or needs to be improved improved in some aspects. This article also focuses on the uses of TPN in various deseases an also possibilities of reducing risk in emergency cases

KEYWORD: TPN (Total Parental Nutrition), infant, carb, protin, fats, infusion, cancer.

What is TPN

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.

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 levels and increase albumin levels in preterm infants. 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:<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.
- **Umbilical catheters:** In neonates, umbilical vessels can be used for TPN.[1] UVC compared to peripheralvenous catheter reduces insertion attempts with no increase in risk of infection or necrotisingenterocolitis. The risk of complication may increases if umbilical venous catheters are being left in place for more than 14 days.(*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 mOsm1, 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] 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. 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 (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
- ✓ **[At 150ml/Kg/day total, this will be made of 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 (see formulation)
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. Commence as soon as central line access obtained.

Standard Preterm Parenteral Nutrition
(see formulation)
Standard solution for preterm infants after 24-48 hours of age.

High Sodium Preterm Parenteral Nutrition
(see formulation)
For hyponatraemic preterm infants.
Provides Na at 8mmol/kg/day at 135ml/kg/day.

7.5% Dextrose Preterm Parenteral Nutrition
(see formulation)
For hyperglycaemic preterm infants.

Peripheral Preterm Parenteral Nutrition
(see formulation)
For those preterm babies with no long lines Â– use only if substantial delay expected in insertion of central line Â– this should be done in consultation with on call Neonatologist.

Term Parenteral Nutrition (see formulation)
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 100ml/kg/day of enteral feed. Cease lipids when infant tolerates 120ml/kg/day of 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. Some babies will need more than this including growth restricted infants and infants with co-existing disease. 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). The target plasma glucose level should be 5.5 - 9.9 mmol/L. Insulin infusion should not be used routinely to prevent hyperglycaemia as this resulted in increased hypoglycaemia and possibly mortality.

- ➢ **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. Trials show it is possible to achieve positive nitrogen balance

from birth onwards as preterm infants are able to tolerate 3.8g/kg/day. 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. 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.[1]

➢ **Lipid**

Lipid is provided as ClinOleic 20%. 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.[1]

- ✓ **Starting lipid intake:** There is no evidence that early versus late introduction of lipid changes neonatal outcomes.
- ✓ **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 3Â–4 g/kg per day (0.13Â–0.17 g/kg per hour) in infants.
- ✓ **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.
- ✓ **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.
- ✓ **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, infants receiving early aggressive TPN including 3g/kg/day lipid had higher serum bilirubin levels. 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.
- ✓ **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.

✓ **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.

✓ **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-l-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.

✓ **Vitamins**

Vitamins are supplied in the in lipid emulsion (soluvit N and vitalipid). The table below shows the amount of vitamins supplied to infants through the proposed lipid emulsion run at 3g/kg/day.

Prolonged parenteral nutrition

Infants (e.g. post surgical infants) who are exclusively on PN for long periods (>4 weeks) may be at risk of other trace element deficiency such as copper and manganese. There are 2 additional PN solutions supplied by Baxter (Standard Preterm PN + TE and Standard Term PN+TE) that contain copper and manganese for these particular group of infants.

Monitoring trace elements

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

1. Cholestatic liver disease: conjugated bilirubin > 34 Aμmol/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. However, limited RCT data has not yet demonstrated a benefit from this practice.[1]

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.
- ✓ **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.

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.

Key Point	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.	32, 41 1b	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.	1a5	A
The use of an insulin infusion for treatment of hyperglycaemia results significant increases in nonprotein energy intake, glucose intake, and short-term weight gain (see hyperglycaemia guideline).	1a5	B
Parenteral nutrition can be delivered using standardised or individualised bags. There is RCT evidence that most TPN prescriptions can be adequately done usin standardised bags.	1b44	B
Peripherally inserted central catheters (PICCÂ's) should be used preferentially to provide central venous access in neonates receiving prolonged TPN.	1a1, 2	A
Parenteral nutrition solution may be infused over 48 hours with no increase risk of infection.	1b19	B
Lipid infusion may be infused over 48 hours.	1b19, 31	B

Complication Metabolic
The most common metabolic complications of PN are hyperglycemia and hypoglycemia. Limiting the amount of dextrose to less than 300 g/day can reduce the risk for hyperglycemia. Hypoglycemia is generally caused by sudden cessation of TPN solutions. To prevent hypoglycemia, PN should be decreased to half rate for 1 hour and then discontinued.

Refeeding syndrome is a severe alteration of electrolyte balance caused by a rapid increase in nutrient intake in malnourished patients; it is a less common but more serious complication. Limiting the amount of calories, particularly dextrose to start, can reduce the risk of refeeding syndrome. Fluid status, potassium, phosphorus, and magnesium status need to be checked and corrected until stable at full PN rate. PN should be increased gradually over 2 to 3 days. Other metabolic disturbances associated with long-term parenteral nutrition are metabolic bone disease such as osteomalica and osteoporosis. Hepatic disease, biliary disease, and renal disease (such as decreased glomerular filtration rate) have been noted in patients on long-term parenteral nutrition, as well as gastrointestinal disturbances, including gastroparesis. Cholestasis, gallbladder stasis, and cholelithiasis are gallbladder-related potential complications of PN administration. Patients with short-bowel syndrome are particularly at risk for gallstone formation. If possible, a transition from parenteral to enteral nutrition can stimulate the gallbladder, which can help avoid gallbladder-related complications. Otherwise, the use of cyclic PN, carbohydrate restrictions, and avoidance of overfeeding will help minimize possible side effects.

Parenteral nutrition is associated with GI atrophy. The lack of enteral stimulation causes villus hypoplasia, colonic mucosal atrophy, decreased gastric function, impaired gastrointestinal immunity, bacterial overgrowth, and bacterial translocation. A reduction in mass of both the small and large intestine has been associated with PN. Reduced stimulation by gastric hormones and inadequate pancreatic and gallbladder secretions contribute to PN-associated gastrointestinal

atrophy. Enteral feedings should be initiated if feasible. Beneficial effects have been seen in animal models with enteral administration in amounts as small as 10% to 25% of total caloric requirements.

PN provides postoperative nutrition support for patients who have had intestinal resections. These patients often receive long-term PN, particularly when less than 150 cm of small bowel is remaining after resection. This group of patients is prone to a high volume of acidic gastric secretions, depending on the length of bowel resected. Gastric hypersecretion can lead to peptic ulcers and hemorrhagic gastritis. Histamine, H2 receptor antagonists, cimetidine (Tagamet, generics), ranitidine (Zantac, generics), and famotidine (Pepcid, generics) are used to reduce gastric output and prevent ulcers after extensive small bowel resections. These medications can be added to the PN solution and administered over a 24-hour period.

- ✓ **Infectious** The vascular access devices can be the source of infectious complications. These complications are typically associated with endogenous flora, contamination of the catheter hub, seeding of the device from a distant site, and contamination of the PN solution.
- ✓ **Mechanical** Venous thrombosis is noted in patients receiving long-term PN. Catheter occlusion may also occur during long-term PN administration. Nutrition.[2]

PN in Patients with Advanced Cancer

The use of PN and home PN in patients with advanced cancer remains controversial. The ASPEN guidelines state: "The palliative use of nutrition support in cancer patients is rarely indicated." However, for patients with cancer and their families, severe anorexia and resultant weight loss produce great anxiety and stress. Parenteral nutrition, home PN in particular, can provide some sense of relief that the patient is receiving some nutrition. It cannot reverse cancer-related cachexia because cachexia is mediated by chronic disease inflammatory factors. A recent study revealed that home PN adminstration seems to relieve anxiety because patients are receiving attention from health care aides. PN serves as a palliative measure for certain advanced cancer patients. Palliative care promotes symptom management and quality of life for terminal patients. A patient with a terminal cancer may no longer be a candidate for treatment; however, the patient may have weeks, perhaps months, to live. Several studies on survival rates of patients with advanced cancer noted extended survival improved for patients on home PN. One study of ovarian cancer patients with short bowel obstruction treated for 75 days showed improvement with home PN vs pre-home PN rates. Another study of cancer patients with GI obstruction revealed a longer survival rate, up to 1 year, and improved quality of life after cessation of active therapies.

In the palliative setting, PN can extend survival; however, it is associated with risks such as line infections, fluid and electrolyte imbalances, and liver and pancreatic issues. There are general guidelines suggested for the use of PN in patients with advanced cancer. First, standard oral diet or enteral nutrition is always the preferred form of nutrition. PN should only be used in patients with a nonfunctioning GI tract, if death will occur from starvation earlier than it would from disease progression, and the patient has a life expectancy of at least 2 to 3 months. Finally, parenteral nutrition improves quality of life for the patient in the last part of life. PN administration to patients with advanced cancer presents ethical and moral considerations that should be carefully considered when deciding on the care plan for cancer patients in the final stages of life.[2]

Discontinuing Parenteral Nutrition

PN may be stopped when the infant is tolerating ≥100-120 cc/kg of enteral feedings or is receiving ≤25 cc/kg/d of PN. The rate of dextrose administration should be tapered to prevent rebound hypoglycemia. Chemstrips should be done q6h. Newborns need a slower tapering than older children and require continued monitoring of glucose after the solution has been stopped. Lipids may be stopped without tapering. If the PN catheter clots or infiltrates, start another IV with dextrose concentration ≤12.5% depending on the current glucose concentration. The "Starter TPN" may also be used to maintain protein intake until a new bag arrives.[3]

Advantages

- Does not requires a functioning GIT.
- All of the nutrition enters the systemic circulation.

Disadvantages

- Problems associated with the line: pneumothorax, haemothorax, neurovascular damage, thoracic duct injury, thrombosis, air embolus, thrombophlebitis.
- metabolic disturbances: hyponatraemia, hypernatraemia, hypokalaemia, hyperkalaemia, hyperglycaemia, hyperchloraemia, trace element and folate deficiency, linoleic acid deficiency, Hepatic dysfunction
- More expensive than enteral nutrition.
- Can cause GIT atrophy.
- Need for regular monitoring of: weight, U&E's, LFTs, Mg+, Ca+, PO4G Zn+and nitrogen balance.

CONCLUSION

As we see above detail information about the parentrals regarding there components, there administration routes, metabolic complications, advancement of TPN in cancer patients also depending on all information coclusion s TPN are very good nutrition suppliers but as we consider there disadvantages metabolic complication like hyponatraemia, hypernatraemia, hypokalaemia, hyperkalaemia, hyperglycaemia, hyperchloraemia, trace element and folate deficiency, linoleic acid deficiency,

Hepatic dysfunction, complications related to neonates, again the cost criteria if we can overcome these complications one by one definetly use TPN in all category of diseases will increase.

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