Total Parenteral Nutrition in Neonates

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Parenteral Nutrition (PN) allows us to meet a neonate's requirement for growth and development when their size or condition precludes enteral feeding. Although feeding through the gastrointestinal tract is the preferred route for nutritional management, there are specific conditions where PN as an adjunctive or sole therapy is necessary. In very low birth weight premature infants, due to the immaturity of the gastrointestinal systems, enteral feeding cannot be established in the first few days of life. In critically ill neonates, neonates with protracted diarrhea and neonates who have had major GI surgery, PN can successfully meet the nutritional demands. Parenteral Nutrition solutions, although still evolving, have improved considerably since the early days and complications are now less common when amino acids and lipids are given in a dose of 1-3 g / kg / day. Meticulous attention to asepsis, good nursing care and close biochemical monitoring are absolutely essential for successful PN therapy.

Key words: *Neonate, Parenteral nutrition.*

Total Parenteral Nutrition (TPN) may be defined as provision of nutrition for metabolic requirements and growth through the parenteral route. The concept of parenteral nutrition existed way back in 1660 when oils and wines were given intravenously(1). The importance of protein administration for nitrogen balance, weight gain and general well being was demonstrated as early as 1852 by Bidder and Schimdt(2). In 1966, Dudrick made a major discovery by implanting a catheter in the superior vena cava of beagle puppies(3) and subsequently in an infant with short bowel syndrome and gave parenteral nutrition(4). He summed up the indications for TPN very simply, by saying that it should be given in babies "who cannot eat, should not eat and cannot eat enough."

Parenteral nutrition has become increasingly complex. Careless use due to inadequate understanding or poor supervision, can result in devastating complications like septicemia and metabolic imbalances. To maximize benefits and minimize complications, many medical centers have developed a team approach to parenteral nutrition. However, in the Indian situation, the physician has to take over all the roles of the entire team.

Total Parenteral Nutrition is technically demanding, expensive and has several side effects. Hence, its use is only justified when enteral feeding is impossible. Its duration should be as short as possible and at least partial enteral feeding should be started as early as possible. TPN should only be used in units where (*i*) there is full time medical coverage, (*ii*) trained nursing staff who can be relied upon for proper care of IV lines, (*iii*) facilities to prepare solutions correctly under laminar flow hood (*iv*) appropriate laboratory backup and (*v*) appropriate equipment including infusion pumps. In 1986, we investigated the feasibility of using TPN in neonates and children in a

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developing country like ours, the cost involved, the problems encountered and the means to circumvent these problems(5).

Use of TPN in neonates

The nutritional requirements of extremely low birth weight infants (ELBW) are rarely met with and they lose a lot of weight in the first two weeks of postnatal life. Early use of parenteral nutrition may minimize these losses and improve growth outcomes. Parenteral nutrition solutions have improved markedly from the early days of use in the 1980's and complications are now less common.

In general, five or more days without adequate nutrition in full term neonates or three or more days without nutrition in VLBW infants places them at nutritional risks and would be an indication for prophylactic TPN. TPN is indicated when neonates cannot tolerate enteral feedings or when there is a need to supplement enteral intake.

The indications for TPN are given in *Table I.*

Components of TPN solutions

The infusate should contain the following:-

TABLE I–*Indications for TPN*

1. Gestation <30 weeks and / or birth weight <1000g

2. Gestation >30 weeks, but unlikely to achieve full feeds, due to respiratory distress syndrome, bronchopulmonary dysplasia.

3. Severe intrauterine growth retardation.

4. Necrotising enterocolitis.

5. Gastro-intestinal tract problems like short bowel syndrome, intractable diarrhea.

6. After surgical correction of gastrointestinal malformations like tracheo-esophageal fistula, intestinal obstruction, malrotation with volvulus omphalocoele, gastroschisis.

(1) Protein as crystalline aminoacids.

(2) Fats as lipids.

(3) Carbohydrate as glucose.

(4) Electrolytes–Sodium, potassium, chloride, calcium and magnesium.

(5) Metals/Trace elements–Zinc, copper, manganese, chromium, selenium.

(6) Vitamins A, C, D, E, K, thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, biotin, choline and folic acid.

Fluids

Fluids are a very essential part of parenteral nutrition. Volumes should be increased over the first 7 days depending on electrolytes, hydration and clinical status with the aim of delivering 150 mL/kg/day by the end of a week.

Energy requirements

The most important goal of parenteral nutrition is to provide sufficient energy and nitrogen to prevent catabolism and to achieve a positive nitrogen balance. Preterm infants have very low energy reserves due to low amounts of fat as well as low glycogen reserves in the liver.

The ideal distribution of calories should be 60% carbohydrate, 10-15% proteins and 30% fats(1). A 10% dextrose solution provides 0.34 kcal/mL. A 10% lipid solution provides 0.9 kcal/mL. Although protein is a potential energy substrate, it should be utilized only for tissue growth. Glucose and lipids should provide sufficient calories to avoid protein catabolism. A preterm neonate needs 100-150 kcal/kg/day, whereas a term neonate needs 100-120 kcal/kg/day.

Carbohydrate requirements

Glucose is the most widely used intravenous carbohydrate for neonates because

it is readily available to the brain. A preterm infant, who may have hypothermia and respiratory distress, has a higher glucose demand and hence early administration of glucose is vital(6,7). It is important to balance non-protein calories between carbohydrates and fats. Excess use of glucose would result in lipogenesis, excess production of CO_2 and hyperglycemia, which may produce osmotic diuresis.

Protein requirements

The goal in giving proteins is to limit catabolism and maintain endogenous protein stores, and to provide sufficient energy and protein intake to support growth. In an article entitled "Aggressive nutrition of the VLBW infant," Ziegler, *et al.*(8) state that early administration of PN today is safe and efficacious and no longer fraught with metabolic derangements that had at earlier times made PN a dangerous proposition in VLBW infants. The concept put forth by American Academy of Pediatrics(9) that "nutrition should support postnatal growth that approximates the in utero growth of a normal fetus" should be accepted.

Protein is delivered as a synthetic amino acid solution, which gives 4 kcal/g. These solutions contain 9 essential amino acids and cysteine, tyrosine, taurine and arginine as the semi-essential amino acids. In the absence of an exogenous protein source, a preterm infant will catabolise 1 g/kg/day of their own body protein to meet its metabolic needs. Excess protein administration will cause a rise in blood urea, ammonia and high levels of potentially toxic amino acids such as phenyl-alanine. Paisley and Thureen(10) started amino acids in a dose of 3 g/kg/day within 24 hours in ELBW infants. They showed that higher amino acid doses led to significantly higher protein balance. The experience with

this high dose of amino acids is limited and some caution is warranted.

In our unit, we start amino acids on the second day of life for ELBW infants with 1 g/kg/day and go upto 3 g/kg/day with daily increments of 1 g/kg/day. Some units start smaller doses of amino acids in septic or hemo-dynamically unstable babies. A maximum of 15% calories should be given as proteins.

Lipids

Lipids are a major source of non-protein energy and have a nitrogen sparing effect. It serves as a source of essential fatty acids as well as long chain polyunsaturated fatty acids (LC-PUFA). The importance of LC-PUFA for the development of the brain and retina is well known.

The commercial IV lipid emulsions are aqueous suspensions containing neutral triglycerides derived from soybean, safflower oil, egg yolk to emulsify and glycerine to adjust tonicity. Hydrolysis of triglycerides by hepatic and lipoprotein lipase results in formation of free fatty acids. The free fatty acids circulate and can be used as an energy source or they can enter adipose tissue, where they are re-esterified to form triglycerides(11).

Early use and rapid advancement of lipid emulsions in premature infants should be done cautiously because of a variety of potential complications and toxicities. These are lipid intolerance, increased free bilirubin concentrations, impaired pulmonary function, increased risk for developing chronic lung disease and interference with immune and platelet function. If free fatty acids accumulate, they can displace bilirubin from albumin(12). There has been concern that intravenous lipids induce thrombocytopenia. However, present data does not support this notion(13). Early investigators suggested that intravenous lipid

emulsion impaired neutrophil function, but more recent studies have demonstrated normal immune function(14). There is a theoretical risk involved in giving lipids in a neonate with severe respiratory distress due to fear of pulmonary embolism and PGI_2 formation, which may cause ventilation/perfusion mismatch(15). However, lipids when given as a slow infusion over 24 hours are not associated with worsening of respiratory distress.

Both 10% and 20% formulations are available. When lipids are exposed to light, they form potentially toxic lipid hydro-peroxides. Hence lipid syringes and tubing should be covered by wrapping it in foil or carbon paper if foil is not available(16). It should be given by a separate line (*Fig.1*). Due to their isotonicity, they can be given through the peripheral line. The tolerance for lipids in extremely premature infants is often poor and hence triglyceride levels should be monitored closely. The dose of lipids may be reduced following acute episodes of sepsis, respiratory distress, thrombocytopenia and severe hyper-bilirubinemia.

In our unit, we usually start lipids on the third day of life in ELBW infants when the most acute phase of respiratory distress or other life threatening events is controlled. We start with 1 g/kg/day and go upto 3 g/kg/ day with increments of 1 g/kg/day. At present 20% lipid emulsion is preferred over 10%, because the higher phospholipid content of the 10% solution impedes plasma triglyceride clearance, resulting in higher triglyceride and plasma cholesterol concentration. Advantages of lipid emulsions over concentrated glucose solutions include their isotonicity and greater energy density, the latter meaning that less volume is required per calorie. This is particularly true for 20% lipid, because it leads to a more normal pattern of plasma lipids in ELBW infants. We use 10% lipid solutions because 20% lipid solutions are available only in 250 mL bottles and not in 100 mL bottles. Not only is the cost more, but there is a lot of wastage of the lipid solution since ELBW babies need such a small quantity. There is really no credible evidence of adverse effects when IV lipids emulsions are used properly. Proper use includes slow infusion rates (<150 mg/kg/hr) and avoidance of unduly high doses *i.e.,* >3g/kg/day.

Minerals

Sodium, potassium, chloride, calcium, magnesium and phosphorus levels need to be closely monitored and the infusate needs to be prescribed accordingly.

Trace elements

Trace elements like zinc, copper, manganese, selenium, fluorine and iodine are provided in some of the TPN solutions available abroad. However, the Indian TPN
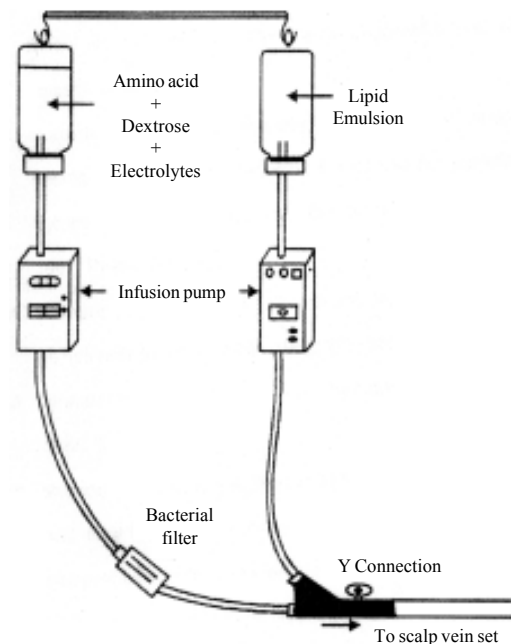

Fig. 1. TPN infusion assembly.

solutions do not contain these trace elements. Neonates on long term TPN may develop trace element deficiencies and it is recommended that their levels should be checked(17). In general we use only short term TPN and hence do not add trace elements.

Vitamins

The daily requirements for both water and fat-soluble vitamins can be provided in TPN. The dose of Pediatric Multi vitamin Infusion is 1 mL/kg/day, with an absolute maximum of 5 mL/day. This should be added to the dextrose-electrolyte solution.

Other additions

Heparin may be added to the TPN solutions in 0.5-1 unit per ml to decrease the risk of thrombosis. Use of heparin is recommended in neonates where small lumen central lines are used. Its use is contraindicated in neonates with evidence of coagulopathy.

Table II shows the calculation of TPN step by step.

Illustrative case (For TPN calculation)

A 5-day-old neonate, with gestational age of 28 weeks and birth weight of 900 g with respiratory distress on a ventilator, on TPN since day one.

Step I: Total fluids 150 mL/kg = 135 mL

Step II: Aminoacid (10%) 3 g/kg/day = 27 mL

TABLE II– *Step for Calculation of TPN*

Step I:	Calculate total fluid intake
Step II:	Amino acids: 1-3 g / kg / day
Step III:	Lipids: 1-3 g / kg / day
Step IV:	Supplementation
	• Sodium: 3 meq / kg / day
	1 mL of concentrated Ringer lactate = 3 meq
	• Potassium: 2 meq / kg / day
	1 mL of Potassium chloride = 2 meq
	• Calcium: 2 meq /kg /day
	1 mL of Calcium gluconate = 0.45 meq
	• Magnesium 0.3 meq / kg / day
	1 mL of 50% of Magsulph = 4 meq
	• Multivitamin infusion – 1 mL / kg
Step V:	Calculate dextrose infusion
Step VI:	Calculate Calorie Nitrogen Ratio (CNR)
	$\dfrac{\text{Carbohydrate Calories} + \text{Fat calories} \times 6.25 \ (\text{constant})}{\text{Aminoacids in gm}}$
	This ratio should be between 100-200 cal / g
Step VII	Add heparin 1 unit /mL

Source: Protocol of KEM Hospital, Pune.

Step III: Lipids (10%) 3 g/kg/day = 27 mL

Step IV: Supplementation

(1) Sodium 3 meq/kg/day = 2.7 meq
Conc. Ringer lactate = 0.9 mL

(2) Potassium 2 meq/kg/day = 1.8 meq
Potassium chloride = 0.9 mL

(3) Calcium 2 meq/kg/day = 1.8 meq
Calcium gluconate 10% = 4 mL

(4) Magnesium 0.3 meq/kg/d = 0.27 meq
50% Magnesium sulphate = 0.07 mL

(5) MVI 1 mL/kg/day
MVI solution = 0.9 mL

Step V: Dextrose Infusion: 6 mg/kg/min = 7.8 g/24hours

Total fluids – Total additives
(Step II, III, IV)

$135 - 60.77 = 74.23$ mL

This can be given as 10% dextrose

70 mL $= 7000$ mg

50% dextrose $= 1.6$ mL $= 800$mg

Distilled water $= 2.63$mL $= 0$ mg

Step VI: Calculation of Caloric Nitrogen Ratio

Total carbohydrate calories + Total fat calories $\times 6.25 \div$ Amino acid (g)

$$\frac{(7.8 \times 3.4) + (2.7 \times 9) \times 6.25}{2.7}$$

CNR $= 117.63$ cal/g

Step VII: Add heparin 1 unit/mL = 135 units

Note: If the baby is unstable, calculations may have to be done every 12 hours instead of every 24 hours.

TPN preparation

All the TPN bottles are kept in laminar flow hood and ultraviolet rays are switched on. Two hours later, the ultraviolet rays are switched off. The doctor or nurse scrubs and puts on a gown, cap and mask and gloves and mixes the solutions as per calculation inside the laminar flow hood. If ultraviolet rays are not switched off during mixing, the personnel may get conjunctival irritation. They then connect the bottles to the IV set under strict aseptic precautions. The TPN assembly is shown in *Fig.1*. The bottles along with the tubing are changed every 24 hours.

Peripheral versus central venous access

PN is delivered by peripheral or central vein access, depending on the concentration of dextrose and consequent osmolarity of the solution. The maximum concentration of dextrose for peripheral venous access is 12.5%. A dextrose concentration greater than 12.5% has an acidic pH and can be irritating to the peripheral veins. In addition to dextrose, electrolytes and minerals added to the solution increase the osmolarity of the solution. Short term TPN for less than 3 days can be given via the peripheral line.

Hypertonic solutions must be administered via a central venous catheter to prevent peripheral vein inflammation and thrombosis. There are no restraints on the osmolarity of central PN because of its high flow rate, infusion into a large vessel and the type of catheter used for infusion. PN can be given through the umbilical vein.

Route of administration

TPN should be delivered whenever possible through central lines. Usually, a percutaneous central line is placed with the position of the tip of the catheter confirmed by *X*-ray. The amino acid solution is attached to a burette with a suitable bacterial filter in line

with a Y connector to which the lipid infusion is attached (*Fig.1*). A strict aseptic technique in preparation and administration of TPN is mandatory. Breakage of the central line through which TPN is administered should be avoided. Drugs should be given through a separate IV line.

Monitoring protocol for parenteral nutrition

Meticulous monitoring is necessary not only to detect complications, but to document clinical benefit(18). Most septic and metabolic complications can be prevented or detected before they cause serious consequences, if the monitoring protocol is followed rigidly. Monitoring should be more frequent in the initial stages. Once a steady metabolic stage has been achieved, monitoring can be reduced to once a week. *Table III* gives the monitoring protocol of neonates on PN in our hospital. It is essential to develop micromethod systems for biochemical monitoring of infants. In the absence of these, blood sampling volumes should be carefully recorded and replenished. Adjustment of daily electrolytes, nutrients and fluid orders are based on biochemical monitoring.

Complications

Sepsis is the most common and serious complication of TPN in India. In 1986, we reported an incidence of 52% of sepsis in 36 patients given TPN(5). But twenty years later, our sepsis rate has gone down considerably with the use of laminar flow hood for preparation and training of nurses in strict aseptic techniques. *Table IV* summarizes TPN related complications.

Dextrose related complications

Hypo and hyperglycemia are more common in neonates than older children and hence blood glucose should be monitored closely. Dextrose infusion should be cut down if hyperglycemia occurs. Treatment of hyperglycemia is initiated with insulin if blood glucose is above 200 mg/dL despite reducing the dextrose infusion below 5 mg/kg/min. Insulin can be started in a dose of 0.05-0.1U/kg/hr(19). Adjust insulin infusion rate by 0.05 U/kg/hr to keep glucose levels to 150-200 mg%. Discontinue when levels drop to <100 mg% and monitor glucose every 4 hours once target level is achieved. Before starting insulin, rule out other causes of hyperglycemia like

TABLE III–*TPN Monitoring Schedule*

Parameter	Frequency
Laboratory measurement	
Serum electrolytes	3-4 times / week initially, then weekly
Blood urea	3 times / week initially, then weekly
Calcium, magnesium, phosphorus	3 times / week initially, then weekly
Glucose	2 times / day
Urine glucose	Daily
Protein	Weekly
Liver function tests	Weekly
Hematocrit	Weekly
Serum triglycerides	4 hours after a dose increase initially, then weekly
Physical assessment	
Weight	Daily
Intake / output	Daily
Inspection of catheter insertion site (for swelling, redness, extravasation)	Daily
Anthropometric measurements	Weekly
Growth curves	Weekly

Source: Protocol of KEM Hospital, Pune.

TABLE IV–*Complications of TPN*

Sepsis	–
Dextrose-related	Hyperglycemia, Hypoglycemia
Protein-related	Azotemia, Metabolic acidosis
Lipid-related	Hyperlipidemia, Hyperbilirubinemia
Cholestasis	
Trace element deficiency (long-term TPN use)	
Catheter related complications	Dislodgement, Infection.
Hematological	Thrombocytopenia, platelet dysfunction, eosinophilia.

sepsis, intraventricular hemorrhage, steroids.

Protein related complications

If BUN is raised twice above the normal value, fluids may have to be increased or protein may have to be cut down(6).

Lipid related complications

Hyperlipidemia and hyperbilirubinemia may occur in neonates. Lipids may have to be cut down or stopped completely(20). PaO_2 may be lowered due to changes in pulmonary microcirculation, especially in neonates with RDS. Lipids will have to be stopped if there is severe sepsis. Severe sepsis is defined as sepsis with organ dysfunction associated with hypotension and need for inotropes.

Hepatic effects

Liver disease due to PN is a well-recognized iatrogenic entity, also called PN associated cholestasis. PN associated cholestasis is defined as onset of hyper-bilirubinemia within 2 weeks of starting PN(21). Thureen, *et al.* have stipulated that a direct bilirubin >2 mg/dL may be called cholestatic jaundice(22). There may be hepatomegaly, mild elevation of conjugated bilirubin, alkaline phosphatase and trans-aminases. Liver function generally normalizes within 1-4 months of stopping PN; but in some cases, prolonged liver dysfunction and even fibrosis has been reported(23).

Several overlapping mechanisms may contribute to PN associated liver disease(24). These include prolonged duration of PN therapy, sepsis, low serum albumin, excessive caloric load, enteral fasting, nutritional deficiencies of taurine, choline, carnitine, phytosterol, manganese, oxidative stress and hormonal factors like elevated insulin/glucagon ratio, gut hormones and biliary stasis.

Simple interventions such as minimizing the duration of therapy, prevention and early detection and treatment of sepsis and choosing enteral over parenteral nutrition whenever possible, will minimize liver injury.

Ursodeoxycholic acid (UDCA) is used in the therapy of cholestasis. It has been postu-lated that UDCA increases the hydrophilic non-hepatotoxic bile acid pool, decreases hepato-cyte display of histocompatibility antigens and gives direct cytoprotection(25). UDCA is available as Tab Udiliv (300 mg) and the dose is 20-30 mg/kg/day.

Electrolyte and trace element deficiencies

Careful monitoring of fluid losses is essential to avoid electrolyte deficiencies. Most of the trace element deficiencies are due to improper supplementation and monitoring in long term TPN(26). Adequate levels of calcium may be hindered by incompatibility with other electrolytes, especially phosphorus. L-cysteine, which is present in the amino acid solution improves the solubility of both calcium and phosphorus.

Catheter related complications

These may be either technical or infectious in nature. Proper placement of the catheter with strict aseptic technique may reduce these complications. Peripherally inserted central catheters have a lower incidence of infection(19).

Hematologic effects

Thrombocytopenia, eosinophilia and hemolysis can occur following lipid administration. Thrombocytopenia and platelet dysfunction are believed to be dose related (30). Maximum lipid administration of 2-3 g/kg/day or temporary discontinuation of lipids would result in normal platelet count and function(14).

Cost of TPN

On an average, the cost of the TPN infusate with additives is around Rs. 700-800/day in our unit. Commercially available TPN solutions with prices are given in *Table V*.

Cost saving should not be done by economizing on disposables, biochemical monitoring and infusion pumps. Laminar flow hood for mixing solutions is a must. Cost can be reduced by sharing the bottles between two patients, if two patients are receiving TPN at the same time.

Transition to enteral feedings

While parenteral nutrition provides the neonate with nutrients to sustain life and promote growth, its use can have negative physiologic effects on the gastrointestinal tract(22). Enteral starvation results in decreased secretion of gastrointestinal hormones, atrophy of gastric mucosa, decreased Immunoglobulin A production, a decline in gastrointestinal motility and an increase in the incidence of intestinal ulceration. These effects result in a decline in the digestive and absorptive capabilities of the GI tract and a loss of protective effects, increasing the risk for systemic bacterial infections. To minimize these effects, enteral feeding should be started as soon as possible. In our unit, we start small trophic feedings (small volume feeding given at the same rate for at least 5 days) as early as possible.

For many neonates, parenteral nutrition is a life saving intervention, providing energy for growth and tissue repair when the gastrointestinal tract cannot be used. This is especially true for preterm and extremely low birth weight neonates. Familiarity with the nutritional requirements, complications and methods of monitoring parenteral nutrition will help minimize the risks to this population.

Newer Perspectives

Manganese

The recognition that manganese is an essential trace element has led to its incorporation into parenteral solutions. A study in children on long term TPN showed increased signal intensity on T_1 weighted images of the basal ganglia on MRI(27). Hence, manganese supplementation in neonates with long term PN needs further appraisal(28).

Glutamine

Glutamine supplementation has been recommended to prevent morbidity and mortality in preterm infants. The available data from good quality randomized controlled trials suggest that glutamine supplementation does not confer clinically significant benefits for preterm infants(29).

Carnitine

Carnitine is essential for the oxidation of long chain fatty acids. It is required to transport these fatty acids across the inner mitochondrial membrane to their site of oxidation with the

TABLE V–*Commercially available TPN Solutions in India*

Name of solution	Concentration	Manufacturer	Bottle	Cost
Aminoven (Amino acid)	6%	F. Kabi	100 mL	Rs. 220
Aminoven (Amino acid)	10%	F. Kabi	100 mL	Rs. 280
Primene (Amino acid)	10%	Baxter	100 mL	Rs. 288
Intralipid (Lipid)	10%	F. Kabi	100 mL	Rs. 255
Intralipid (Lipid)	20%	F. Kabi	250 mL	Rs. 520
Additives				
Conc. Ringer lactate	–	T.Walker	20 mL	Rs. 20
Multi Vitamin Infusion (Adult)	–	NBZ Pharma	10 mL	Rs. 11
Calcium Gluconate	10%	Biostan	10 mL	Rs. 12
Kesol (Pottassion Chloride)	15%	Eisen Pharma	10 mL	Rs. 12
Mag. Sulph	50%	Ravi Pharma	2 mL	Rs. 8
Heparin		Gland Pharma	5 mL	Rs. 21

mitochondrial matrix. The preterm has low plasma and tissue concentrations of carnitine and decreased capacity to synthesize carnitine, hence carnitine supplementation may have some role in ELBW infants on long term PN. Carnitine is available as injection Carnitor and the dose is 10 mg/kg/day. However, this issue needs to be confirmed by more studies(30).

Lipid preparations

Currently available lipid preparations contain triglycerides derived from soyabean oil and safflower oil. European trials are evaluating medium-chain triglyceride intravenous lipid preparations(19). These may have an improved rate of oxidation, less chances of displacement of bilirubin from albumin and more carnitine content.

Early initiation of enteral feeding

There is no clear evidence to show that early initiation of enteral feeding in a parenterally fed ELBW infant is better than late initiation of enteral feeding according to the Cochrane database(31). Needless to say that there is plenty of evidence to show that enteral feeding is always preferred over parenteral nutrition, whenever possible. Among infants given trophic feeding, there was an overall reduction in days to full feeding and total hospital stay compared to infants given no enteral intake(32). In our unit, we start small trophic feeds as early as possible.

Use of standardized versus individualized PN solutionsm

Many centres abroad are now opting for standard or stock preparations than going through the laborious process of mixing the

solutions. Yeung, *et al.* studied standardized versus individualized PN solutions for neonates <33 weeks gestation. They found no significant clinical and statistical differences in newborn infants in both the groups. However, the cost of PN went down by 30% when standardized solutions were used(33). These solutions are presently not available in India.

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REFERENCES

1. Grant JP. Handbook of Total Parenteral Nutrition. W.B. Saunders Co., Philadelphia. 1980; 1.

2. Bidder F, Schmidt C. Die Verdauungssaefte und der Stoffwechsel. Leipsig, 1852.

3. Dudrick SJ, Vars SM, Rhodes JE. Growth of puppies receiving all nutritional requirements by vein. Forschritte der parenteralen Ernahrung, Symposium dev International Society of Parenteral Nutrition. Munich, 1967, Pallas Verlage: 2.

4. Wilmore DW, Dudrick SJ. Growth and development of an infant receiving all nutrients by vein. JAMA 1968; 203: 860-861.

5. Chaudhari S, Vaidya UV. Total Parenteral Nutrition in India. Indian J Pediatr 1988; 55: 935-940.

6. Murdock N, Crighton A, Nelson LM, Forsyth JS. Low birthweight infants and total parenteral nutrition immediately after birth. II. Randomised study of biochemical tolerance of intravenous glucose, amino acids, and lipid. Arch Dis Child Fetal Neonatal 1995; 73: F8-12.

7. Lipsky CL, Spear ML, Recent Advances in Parenteral nutrition. Clin Perinatol. 1995; 22: 141-155.

8. Ziegler EE, Thureen PJ, Carlson SJ. Aggressive nutrition of the very low birth weight infant. Clin Perinatol 2002; 29: 225-244.

9. Committee on nutrition. American Academy of Pediatrics. Nutritional needs of LBW infants. Pediatrics 1985;75: 976-986.

10. Paisley JE, Thureen PJ, Baron KA. Safety and efficacy of low versus high parenteral amino acid intakes in ELBW neonates immediately after birth. Ped Res 2000; 47: 293A.

11. Adamkin DH, Radmacher PG. The use of lipids in pediatric Parenteral nutrition. *In:* Baker BB, Baker RD, Davis A, eds. Pediatric Parenteral Nutrition, New York: Chapman & Hall 1997; 109-127.

12. Thiesson SH, Jacobsen J, Brodersen R. Displacement of albumin bound bilirubin fatty acids. Acta Pediatr 1972; 61: 285-287.

13. Spear ML, Cohen AR, Pereira GR. Effect of fat infusions on platelet concentration in premature infants. J Parent Enter Nutr 1990; 14: 165-168.

14. Herson VC, Block C, Eisenfeld L, Maderazo EG, Krause PJ. Effects of intravenous fat infusion on neonatal neutrophil platelet function. J Parent Enter Nutr 1989;13: 620-622.

15. Hageman JR, McCulloh K, Gora P. Intralipid alteration in pulmonary prostaglandin metabolism and gas exchange. Crit Care Med 1983; 10: 794-798.

16. Neuzil J, Darlow BA, Inder TE, Sluis KB. Oxidation of Parenteral lipid emulsion by ambient and phototherapy lights: Potential toxicity of routine parenteral feeding. J Pediatr 1995; 126: 785-790.

17. Solomons NW, Ruz M. Essential and beneficial trace elements in pediatric Parenteral nutrition. *In:* Baker BB, Baker RD, Davis A, eds. Pediatric Parenteral Nutrition. New York: Chapman & Hall, 1997; 175-196.

18. Davis A. Initiation, monitoring, and complications of pediatric parenteral nutrition. *In:* Baker BB, Baker RD, Davis A, eds. Pediatric Parenteral Nutrition. New York: Chapman & Hall. 1997; 212-237.

19. Acra SA, Rollins C. Principles and Guidelines for Parenteral nutrition in children. Pediatr Ann 1999; 28: 13-120.

20. Helbock HJ, Ames BN. Use of intravenous

lipids in neonates J Ped 1995; 126 : 747-750.

21. Postuma R, Trevenen C. Liver disease in infants receiving total parenteral nutrition. Pediatrics 1979; 64: 342-347.

22. Thureen PJ, William WH. Intravenous nutrition and postnatal growth of the micropremie. Clin Perinatol 2000; 27: 49-64.

23. Moss R, Das J, Raffensperger J. Total parenteral associated cholestasis: Clinical and histopathologic correlation. J Pediatr Surg 1993; 28: 1270-1274.

24. Kwan A, George J. Liver disease due to parenteral nutrition. Clin Liver Dis 2004; 8: 893-913.

25. Levine A, Maayan P, Shamir R, Sulkes J, Sirotta L. Parenteral nutrition – associated cholestasis in preterm neonates: evaluation of urodeoxycholic acid treatment. J Pediatr Endocrinol Metab 1999;12: 549-553.

26. Jospe N, Forbes G. Fluids and electrolytes-Clinical aspects. Pediatr Rev 1996; 17: 395-403.

27. Fell JM, Reynolds AP, Meadows N, Khan K, long SG, Quaghebeur G *et al.* Manganese toxicity in children receiving long term parenteral nutrition. Lancet 1996; 347: 1992-1996.

28. Fok TF, Chui KK, Cheung R, Ng PC, Cheung KL, Hjelm M. Manganese intake and cholestatic jaundice in neonates receiving parenteral nutrition: a randomized controlled study. Acta Pediatr 2001; 90:1009-1015.

29. Tubman TRJ, Thompson SW, McGuire W. Glutamine supplementation to prevent morbidity and mortality in preterm infants. The Cochrane Database Syst Rev 2005; (1): CD001457.

30. Cairns PA, Stalker DJ. Carnitine supplementation of parenterally fed neonates. The Cochrane Database Syst Rev 2000; (4), CD000950.

31. Kennedy KA, Tyson JE. Early versus delayed initiation of progressive enteral feedings for parenterally fed low birth weight or preterm infants. Cochrane Database Syst Rev 2000; (1): CD001970.

32. Tyson JE, Kennedy KA. Trophic feedings for parenterally fed infants. Cochrane Database Syst Rev 2005; (3): CD000504.

33. Yeung MY, Smyth JP, Maheshwari R, Shah S. Evaluation of standardized versus individualized total parenteral nutrition regime for neonates less than 33 weeks gestation. J Paediatr Child Health 2003; 39: 613-617.