

Total Parental Nutrition in High-Risk Preterm Babies

SACHIN THAKUR, NEELAM KLER

Departments of Neonatology & Pediatrics, Sir Ganga Ram Hospita, Rajinder Nagar, New Delhi-110060 India

Abstract: Parental nutrition is used most commonly for preterm babies because of their gut immaturity and their inability to take total feeds directly. TPN includes providing fluids, electrolytes, carbohydrates, proteins, fats, vitamins and trace elements in adequate amounts to maintain growth. Administration of parental nutrition requires regular monitoring for biochemical and catheter related side effects. One needs to know the methodology of parental nutrition administration for its successful execution.

Introduction

Total parental nutrition is required in any baby who is not going to be on full enteral feeds by 5-7 days. Tiny sick babies are born with limited resources and have higher requirements of nutrients per kilogram of body weight often due to respiratory problems, sepsis etc. Most commonly TPN is used for the preterm babies in the nursery as they have feeding intolerance and so need intravenous support. It is also used for any baby with surgical problems, sepsis, persistent pulmonary hypertension, chronic lung disease, etc who is critically ill & whom early feeding is not an option.

TPN includes providing fluids, electrolytes, carbohydrates, proteins, fats, vitamins & trace elements in adequate amounts to maintain growth. Preterm babies have limited energy stores and need to be on IV glucose and proteins as early as possible to prevent protein catabolism.

The TPN calculations for the preterm babies are based on the fetal growth patterns and extrapolations of the requirements in more mature babies. Till 26-28 weeks of gestation fetus has minimal lipid uptake from placenta, has a glucose delivery parallel to energy requirements and amino acid uptake in excess of protein accretion requirements. In NICU the ELBW babies receive lipids in high amounts, glucose often more than in-utero requirements and amino acids in low amounts.

Fluids & Electrolytes

Fluids requirements vary with gestational age, day of life and in different disease states. Full term & preterm babies lose upto 10-15% of birth weight respectively and this is mostly in the ECF component. Weight should be monitored at least once a day (and more often in premies) and babies should be allowed to lose upto 3% of birth weight daily (keeping urine output > 2ml/kg/hr.) till they have achieved the loss of 10-15% of the birth weight as mentioned above.

When and how to start and which increments? : fluids should be started at 60ml/kg/day in full term babies and 80-100 ml/kg/day in preterm babies. Many preterm babies may require initial fluid resuscitation with normal saline 10-20ml/kg (IV albumin is not recommended) over 1-2 hours for poor cardiac output, poor peripheral circulation and accompanying acidosis. Glucose should be started in preterm babies as soon as possible and amino acid drip can be added on day one itself. Sodium Chloride (2-4 meq/kg/day), potassium (1-2meq/kg/day), calcium are usually added after 24 hours of life or after weight loss of 6% of birth weight (approximately 48 hrs).

Fluids are increased by 10-20ml/kg/day (keeping urine output >

Correspondence: Dr. Sachin Thakur E-mail: srt1986@yahoo.com

2ml/kg/day, weight loss at 3% day, and serum Na<150) & serum electrolytes should be monitored daily in the first week. At the end of the 1st week the skin of the premature baby gets keratinized and fluids need not be given at more than 150-160 ml/kg/day.

If hyponatremia develops (Na>150), usually due to excess water loss via skin in premies, then the fluids may have to be increased upto 200ml/kg/day or more. Hyponatremia may develop due to sodium free fluids being given (also due to hypotonic fluids given to mother during delivery & oxytocin use) and adequate sodium correction should be done over 24 hours for sodium values below 130meq/l. Late onset hyponatremia with peripheral edema is seen in growing premies, due to excessive renal Na losses & use of diuretics for chronic lung disease, so requirements of Na may be as high as 8-10 meq/kg/day.

Non oliguric hyperkalemia may be seen in ELBW babies due to increased fractional excretion of Na along with decreased K excretion, decreased GFR & relative aldosterone insensitivity 91). Insulin infusion may be required along with glucose to control K levels.

Special scenarios for fluid adjustments : If a PDA (patent ductus arteriosus) is present then the fluids should be restricted to 100ml/kg/day (and even lower if indomethacin is given) and similar strategy may be employed in hyaline membrane disease (HMD) till diuresis sets in by 48-72 hours.(2)

Babies with NEC (necrotizing enterocolitis - usually in 2nd -3rd week) lose lot of fluids in third spacing and need vigorous resuscitation with Normal Saline. They often develop hyponatremia is hypotonic maintenance fluids are increased to 1.5-2 times the normal. These babies may be given 120-130ml/kg/day of fluids (with 2-4 meq of Na/kg/day) and additional fluids given as Normal Saline infusion every couple of hours (ie Q6-Q8 hours).

Hepoxic Ischemic Encephalopathic babies may require vigorous resuscitation with N Saline 10-30ml/kg for shock/acidosis and may also require inotropic support to maintain good tissue perfusion. Restriction of IV fluids may be required (in view of risk of SIADH) but adequate intravascular volume should be maintained, as these babies are prone to PPHN (persistent pulmonary hypertension).

Infants with chronic lung disease have high calorie requirements but at the same time their fluids need to be restricted to 150ml/kg/day. Diuretics may need to be added to decrease pulmonary edema and fluid retention and oral Na-K supplements may be needed to offset the renal losses.(3)

Thus fluid & electrolyte management should be individualized for each baby after daily evaluation of Cardiovascular, Respiratory status, weight change, peripheral edema, urine output, serum Na & K and the underlying pathology.

Amino Acids :

The amino acid composition in the TPN is derived from the amino acid composition of the cord blood, from blood values of breast fed babies and still the ideal composition is unknown. Preterm babies on glucose-only fluids lose 1% of protein stores per day & thus amino acids need to be added to IV fluids from Day One of life. Usually 1-1.5gm/kg/day of parenteral protein is adequate to prevent protein catabolism and 3-4g/kg/day is sufficient to equal protein accretion rates of fetus in ELBW babies (4,5). In fetus 50% of amino acids are used for energy production and part of the amino acids in TPN are also oxidized for energy production. For 1 gm of protein accretion 10 calories/kg/day needs to be added to the RMR (resting metabolic rate = 40-50 cal/kg/day). Thus for an Amino acid intake of 2gm/kg/day (for nitrogen retention) minimum calories required are 50-60 cal/kg/day. Usually this energy can be met with glucose infusion rates of 8-10mg/kg/min.

Amino acids are usually started @ 1gm/kg/day from Day 1 and then increased incrementally upto 3-4g/kg/day in next 3-4 days, though there is no evidence to suggest increasing the proteins faster is detrimental or not tolerated well by ELBW babies.

Protein intake of >4gm/kg/day is not usually recommended and in TPN induced cholestasis & babies in stress (sepsis, surgery, NEC etc) proteins are limited to 2.5 gm/kg/day.

Acidosis, hyper-ammonemia were seen in TPNs in 1980s due to poor utilization of the Amino Acids but with improved crystalline amino acids in TPNs since 1990s these complications are not seen. In the fetus, high amino acid oxidation for energy utilization leads to high BUN, and a rising BUN in ELBW premie may not be a sign of amino acid intolerance, rather it maybe an indication of amino acid oxidation. Thus acidosis, ammonia and azotemia are poor markers to reflect amino acid intolerance.

Carbohydrates :

Glucose is the primary source of energy for brain. Premies have high glucose requirement as they have large metabolically active organs like heart, liver, kidney and brain compared to their body weight. Endogenous glucose production in premies is 4-7 mg/kg/min the endogenous production cannot be completely suppressed with insulin infusion unlike in full term babies and adults. Glucose infusion should be started at 6mg/kg/min and increased gradually to 12mg/kg/min keeping serum glucose below 180 mg/dl when glycosuria may develop leading to polyuria and dehydration. Twenty to eighty percent of ELBW babies develop hyperglycemia due to hepatic & peripheral tissue insuli resistance and this may limit the amount of glucose that can be infused(6). Maximal oxidative capacity for glucose in babies is 12-13mg/kg/min and beyond this rate the glucose is converted to fat in an energy inefficient process leading to increased CO₂ production (especially @ 16-18mg/kg/min.)⁷. For treating *hyperglycemia*

- decrease glucose infusion rates or use hypotonic solutions of as low as D 2.5% till serum glucose is below 150mg/dl (only for transient hyperglycemia)
- start IV amino acids from Day of Life One (as they enhance endogenous insulin secretion)
- start insulin infusion if the blood sugar is more than 200-250 mg/dl especially with urinary spill over and osmotic diuresis. (this may also help in weight gain in ELBW babies though development of lactic acidosis remains a concern.)

As the preterm baby has minimal glycogen stores before 28 weeks of gestation any serum glucose below 40mg/dl needs to be treated with 2ml/kg IV push of D10 W accompanied with an increase in the baseline glucose infusion rate.

Lipids :

Preterm babies have minimal fat stores and develop Essential Fatty Acid deficiency within 72 hours if not given intralipid (IL) infusions. Lipids can be started from Day 1-2 & EFA deficiency can be prevented with a IL dose as low as 0.5gm/kg/day (8). Routinely lipids are increased by 1gm/kg/day to reach a maximum of 3gm/kg/day though no evidence exists to show that lipids are tolerated better when the dose is gradually increased daily. Lipids in the blood stream are cleared via. (a) lipoprotein lipase in the endothelium, (b) hepatic lipase, (c) lecithin cholesterol acyltransferase.

The activity of all these enzymes remains low in preterm babies and activity of (a) & (b) can be induced with low dose heparin (usually running in the central line). Currently available IL are of soybean + safflower oil and a 20% solution given over 24 hours infusion is ideal (as the clearance of IL depends on rate of infusion/min). Triglyceride levels should be monitored initially 2-3 times per week and then weekly and levels below 150-200mg/dl are acceptable.

Lipids are known to increase pulmonary pressures and thus need to be used cautiously in RDS & PPHN. Infusion rates > 0.025mg/kg/hr (1.5gm/kg/day) have shown to worsen pulmonary vascular resistance in multiple studies(9). Concerns of lipid deposition in the lungs of preterm infants have been allayed in recent studies which found lipid deposition in lungs artifactual(10). In ELBW babies with bilirubin levels of 10-12mg/dl the intralipids should be restricted to 2gm/kg/day (with serum albumin of at least 2.5 gm/dl.) due to concern of bilirubin displacement by free fatty acids. In stress due to sepsis, surgery the lipid intake should be restricted to 2gm/kg/day as the ability to utilize lipids is diminished.

Medium Chain Triglyceride - Intralipid preparations are in trial presently and have the theoretical advantage of (1) improved lipid oxidation (2) carnitine independent oxidation (3) low risk of displacing bilirubin bound to albumin.

Carnitine is required for oxidation of fatty acids. Current TPNs do not have carnitine in them and at present there is no recommendation to add carnitine in IV fluids.

Calories :

Calorie requirement of preterm babies on TPN for maintaining existing weight is 50 cal/kg/day (60 cal/kg/day for enteral feeds) and 100 cal/kg/day for growth (120 cal/kg/day for enteral feeds). Protein calories (4 cal/gm) are included in the calculations through all protein calories are not available for energy expenditure. Carbohydrates and lipids are the main source of energy and provide 3.4 cal/gm and 9 cal/gm respectively. In enteral feeds the ratio of carbohydrate to fat calories should be 65/35 with EFA providing 3-5% of the total caloric intake and MCTs not providing more than 40% of the fat derived calories. By 2 weeks of age all the ELBW babies should regain their birth weight, and then grow by 15-20 gm/kg/day if receiving adequate amount TPN and enteral feeds. In babies with BPD the energy requirements are higher but giving more than 160-180 cal/kg/day is not of benefit.

Vitamins & Trace Elements :

Vitamin supplementation should start as soon as protein is added to the TPN. Water soluble vitamins act as co-enzymes in carbohydrate and protein metabolism and cannot be stored in the body (except vitamin B12). Vitamin D requirements are 160-400IU/kg/day though studies have shown even 30IU/kg/per day to be effective in preventing osteopenia of prematurity (11). Vitamin A (requirement 1670 IU/kg/day) is usually low in commercially available IV multivitamin preparations and intramuscular injections

of Vit A may be used to reduce the incidence of Chronic Lung Disease (IM x 3 per week). MVI (NBZ Pharma Ltd.) has 1000 IU of Vit.A and 100IU of Vit.D per ml along with the other fat soluble and water-soluble vitamins. A dose of 1.5ml/kg/day in IV fluids is adequate to meet the daily requirements.

Trace elements like Zn, Cu, Se, Iodine, Manganese, and Chromium should be added to the TPN as their deficiency states may aggravate the metabolic problems. Cececel (Core Healthcare Ltd.) manufactures three types of trace element solutions of which Cececel-4 has Chromium, Copper, Manganese and Zinc. Cececel-5 has Se in addition to the 4 elements and Cececel 7 has Iodine & Molybdenum in addition to the trace elements in Cececel 5. A dose of 0.05 ml/kg/day meets the daily requirements.

Minerals : The accretion rate for Calcium is 120-150mg/kg/day in the 3rd trimester and 75-85 mg/kg/day for Phosphorus. The Ca/P ratio in TPN should be 1.7/1 for accretion rates of 90%. When EBM is well tolerated HMF (Ca fortifier) should be added to oral feeds, as breast milk is inadequate in Ca for the growing premie. If preterm formula is being used exclusively then Ca supplementation is not required.

Preparation of TPN in NICU :

Commonly available amino acid solution in India is Aminoven Infant 10% (Fresenius Kabi India) which has 10gm of amino acids per 100ml. Ivelip 20% (Baxter) is the lipid solution used in NICU, which has 20 gm of lipids per 100ml. Start with glucose infusion rates (GIR) of 6mg/kg/min and the goal is to increase GIR by 1-2mg/kg/min every day to reach at least 50-60 cal/kg/day within 2-3 days to prevent protein catabolism. Add insulin for persistent hyperglycemia and add amino acids (1.5gm/kg/day and increase to 3.5 gms/kg/day over next 3-4 days) & intralipids (1gm/kg/day from Day 2 and increase by 1gm/kg/day to maximum of 3gm/kg/day).

Calculate the total volume required per day, deduct the volume for intralipids and feeds. Calculate the GIR and the total glucose required per day in 24 hours and then use a combination of D10% & D25% to make the required glucose concentration.

For a 1kg preterm baby :

Day 1 Start with: Total volume of fluids 90ml/kg/day
Protein at 1.5gm/kg/day 15ml of Aminovin
Glucose infusion rate (GIR) at 6mg/kg.min 75 ml/day

8640mg glucose per day (8.6 gm)
i.e. 7.5ml D25% (1875mg)

+
67.5ml D10% (6750mg)

This will be a D9.5% TPN when amino acids and the glucose solutions are finally mixed.

D10% solution has 10gm glucose/100ml or 100mg/ml
D25% solution has 25gm glucose/100ml or 250mg/ml
N Saline has 0.154meq/l & 3% saline has 0.514meq/l

Calories :Glucose-29cals (8.6gmsx3.4cals/gm)
Proteins-06cals (1.5gmsx4cals/gm)
Total 35 cals

Day 2 Total volume of fluids 100ml/kg/day
Increase proteins to 2.5gm/kg/day 25ml of Aminovin
Add 2meq/kg of Na & 1 meq/kg 05ml of 20% IL
of K to 24 hr fluids Start Intralipid
1gm/kg/day
Increase GIR to 8mg/kg/day (if no 70ml
hyperglycemia)

11520mg glucose per day (11.5 gm)
i.e. 25ml of D25% (7500mg)

+
40ml of D10% (4000mg)

Calories : Glucose - 39cals (11.5gm x 3.4cals/gm)
Proteins - 10cals (2.5gm x 4 cals/gm)
Intralipid - 9 cals (1gm x 9 cals/gm)

Total Calories 60 cals

This will be a D12% TPN when the amino acids and glucose solutions are finally mixed. (nitrogen retention starts if the calories are at least 60 cal/kg/day with 2gm/kg of protein intake. Volume for saline not used here to simplify the calculation).

10% Calcium gluconate can be given 150-200mg/kg/day from Day 1 via a separate IV line either as a continuous drip over 24 hours or as Q6 hr infusions. It should not be added to TPN with sodium bicarbonate as it may precipitate.

Peripheral IV lines can be used for providing TPN if the requirement is for less than a week and intralipid solutions Y-ed into the TPN line help in decreasing the complication of IV line infiltration. For TPN lasting longer than 7 days a central line must be placed in the form of PICC line for a Broviac. Heparin in TPN, whether via peripheral or central line (35-150 units per day) helps in preventing hypertriglyceridemia and decreases complication of clotting in IV lines.)

Complications of TPN

Electrolyte imbalances, hypo & hyperglycemia, hypertriglyceridemia, vitamin and trace element excess and deficiencies (management as discussed above), metabolic bone disease are some of the complications of TPN. Prolonged TPN use is associated with cholestatic jaundice with elevation of direct bilirubin and liver enzymes. The exact cause is not known but proportions of amino acids in TPN, high glucose intake and some trace elements, sepsis, hemodynamic instability have been implicated. The longer the use of TPN and the more premature and sick the baby, higher is the incidence of cholestasis (with 90% of babies on TPN for >90 days having cholestasis)

Metabolic acidosis is a complication in preterm babies on TPN as the amino acids are in the form of chloride salts & due to renal losses of bicarbonate. TPN solutions buffered to base excess of 12mmol/L with hydroxide and acetate salts of sodium & potassium help in decreasing the TPN associated acidosis and also improve calcium and phosphorus retention.

Monitoring

Electrolytes Na, K, Cl, Ca, bilirubin, BUN & creatinine should be monitored daily for the initial 3-4 days and then 2 times per week (Preterm baby will need closer bilirubin monitoring as needed clinically). Triglycerides should be monitored daily for the first 3-4 days when the lipids are being increased and then once a week. Weight should be monitored daily along with a strict intake-output chart. Serum protein, albumin, SGOT, SGPT, bilirubin & alkaline phosphatase are done on day 4-5 and then every 2 weeks.

Weaning From TPN

As the oral feeds are increased the TPN rate should be decreased proportionately and the glucose concentration brought down to D10%. This makes administration simpler as the need to recalculate TPN daily is avoided. Feeds are usually initiated as trophic feeds (5-10ml/kg/day via oro-gastric tube, EBM preferentially) by 1-2 days of life and increased by 10-20 ml/kg/day or more rapidly as

tolerated. EBM should be fortified with HMF.

(human milk fortifier) once full feeds are well tolerated and MCT oil can be added to improve the caloric content. By 32 weeks feeds can be given via spoon or directly from breast. Lactodex-HMF (Raptakos, Brett & Co Ltd) has a 2gm sachet with 730 IU Vit. A, 250 IU of Vit. D, & other water and fat-soluble vitamins. It also has 50mg of Calcium along with trace elements like copper, magnesium, manganese & zinc. It also has 0.2gm of protein, 0.1gm of fat and provides 6.5 calories per sachet. Adding 1 sachet per 50ml of EBM meets all the vitamin and calcium requirements of a growing premie.

If the preterm baby is going to be on exclusive preterm formula then calcium & vitamins need not be added, as they are adequate in the preterm formula. Iron supplementation will be required in all premies from about 8-10 weeks of age whether on EBM or on preterm formula. The maximum catch-up growth for the minerals in the preterm baby is from 40 weeks to 52 weeks of age and they therefore should be on preterm formula or EBM_HMF for at least 3-6 months to meet their energy and mineral needs.

Full term babies on formula or breast milk do not require any vitamin or iron supplementation till at least 6 months of age (may need Vit D supplementation if on breast milk exclusively).

Thus TPN is essential to maintain the protein stores and provide calories to the newborn infant. Early initiation of TPN on Day One with a smooth transition to intermittent enteral feeds helps to put the preterm baby on the road to optimal catch-up growth and improved neuro-developmental outcome.

References

1. Shaffer SG, Kilbrida HW, Hayen LK, et al: Hyperkalemia in very low birth weight infants. *J Pediatr* 1992;**121**:275.
2. Gersony WM, Peckham GJ, Ellison RC, et al: Effects of indomethacin in premature infants with patent ductus arteriosus: Results of a national collaborative study. *J Pediatr* 1983;**102**:895.
3. Kurzner SI, Garg M, Bautista B, et al: Growth failure in BPD: Elevated metabolic rates and pulmonary mechanics. *J Pediatr* 1988;**112**:73.
4. Ziegler EE: Protein in premature feeding. *Nutrition* 1994;**10**:69.
5. Zlotkin SH, Bryan MH, Anderson GH: Intravenous nitrogen and energy intakes required to duplicate in utero nitrogen accretion in prematurely born human infants. *J Pediatr* 1981;**99**:115.
6. Louik C, Mitchell AA, Epstein MF, et al: Risk factors for neonatal hyperglycemia associated with 10% dextrose infusion. *Am J Dis Child* 1985;**139**:783.
7. Jones MO, Pierro A, Hammond P, et al: Glucose utilization in the surgical newborn infant receiving total parenteral nutrition. *J Pediatr Surg* 1993;**28**:1121.
8. Cook RJ, Yeh YY, Gibson D, et al: Soybean oil emulsion administration during parenteral nutrition in the preterm infant: Effect on essential fatty acid, lipid and glucose metabolism. *J Pediatr* 1987;**111**:767.
9. Hertel J, Tystrup I, Anderson EE: Intravascular fat accumulation after intralipid infusion in the very low-birth-weight infant. *J Pediatr* 1982;**100**:975.
10. Prasertan W, Phillipos EZ, Van Aerde JE, et al: Pulmonary vascular resistance during lipid infusion in neonates. *Arch Dis Child* 1996;**74**:F95.
11. Koo WWK, Tsang RC, Succop P, et al: Minimal vitamin D and high calcium and phosphorus needs of preterm infants receiving parenteral nutrition. *J Pediatr Gastroenterol Nutr* 1989;**8**:225.

THE UNIVERSITY OF HONG KONG

Interested in Postgraduate Training in Dentistry?

Faculty of Dentistry, University of Hong Kong offers a wide range of high quality postgraduate programmes (1 to 3 years; *Language: English*) provided by a devoted team of internationally recognized and experienced teachers.

Please visit our website

<http://www.FacDentHKU.org>

for further information and application forms.