REVIEW ARTICLE

Research issues in parenteral nutrition

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Abstract

Extrauterine growth retardation is a major clinical problem in preterm infants. Aggressive nutritional interventions may play an important role to fight this prevalent problem. Parenteral nutrition is almost indispensable part of aggressive nutritional approach in neonates, because of certain limitations of enteral route during first few days of life. Formidable research work done in developed world has resolved certain important issues like dosage regimens. However, still we need to resolve quite a few unanswered queries. This is especially true for Indian context where we deal with a different population of neonates than the developed world. In this article we will discuss both the resolved and unresolved issues regarding neonatal parenteral nutrition and the research priorities for us.

Key words: growth, neonate, nutrition, parenteral

Introduction

Extrauterine growth retardation is a major clinical problem in preterm infants[1,2]. Recently it has become clear that small infants, especially very low birth weight (VLBW) babies, have special nutrition needs in early life. This underlines the importance of nutritional interventions immediately after birth. The limitations of enteral route during early life in preterm babies, makes PN essential component of nutritional management. However, the results of surveys conducted to assess nutritional practices in NICUs, indicate that the nutritional practices are variable, especially pertaining to PN[3]. The situation in India is quite serious. There is a lack of scientific approach towards PN in India, which is reflected by the limited research evidence from India[4-12]. However, there has been a lot of research done in the field of neonatal parenteral nutrition (PN), in the developed world. In this article we will review certain known facts about PN, issues with uncertainty and the researchable issues.

What is known on this topic

Indications

All level II and level III units should have the facility for PN. These units should provide space for preparation and dispensing PN. PN is necessary in neonates admitted to NICU with following problems[13-16].

1. Prematurity <28 weeks gestation and/or <1000 grams
2. Prematurity <32 weeks gestation and/or <1500 grams who are unable to achieve reasonable enteral feeds by day 3.
3. Infants >32 weeks and/or >1500 grams who are unlikely to achieve at least 50% enteral feeds by day 5.
4. NEC.
5. Surgically correctable gastrointestinal tract anomalies (exomphalus, gastroschisis, atresia of intestine, volvulus etc).
6. Short bowel syndrome.

PN should be started at the earliest in eligible preterm neonates and neonates with surgical problems. Once the enteral nutrition is tolerated and baby takes 75-80% of the expected fluid volume by enteral route, PN can be stopped.

Dosing regimens

(a) Energy: Minimal energy needs are met by 50-60 kCal/kg/day.[17] On parenteral nutrition energy needs for growth for preterm and term neonates are 110-120 kCal/kg/day and 90-100 kCal/kg/day, respectively. Energy is necessary for protein utilization and 30-40 kCal/kg/day are required for utilization of one gram of aminoacids. The reasonable goal for energy accretion in preterm neonates is 25 kCal/kg/day, which is fetal energy accretion rate in third trimester.[18]

(b) Dextrose: Dextrose is started on day 1. The dose of dextrose is calculated as glucose infusion rate (GIR). Recommended GIR in preterm neonates on day 1 is between 4 to 8 mg/kg/min.[19] It is increased daily by 1-

2 mg/kg/min till normoglycemia (blood sugar level between 45 to 150 mg/dl) is maintained. For babies on PN, minimum blood glucose desired is 60 mg/dl. Maximum GIR for preterm and term is 12 mg/kg/min and 13 mg/kg/min, respectively.[19,20] Glucose intake should cover 60-75% of non-protein calories(NPC). Insulin use should be restricted to conditions where reasonable adaptation of GIR does not control marked hyperglycemia[21].

(c) Amino acids (AA): Proteins are major structure and functional components of cells of body. Preterm infants without AA supplement excrete around 0.6 – 1.1 g/ kg / day protein.[27-30] Preterm neonates tolerate amino acid supplementation on day 1 of life and positive effects on protein metabolism are seen.[14,15,22,23-25] It has been shown in newer studies that newborns tolerate 3.5 g/ kg / d amino acids on first postnatal day.[15] Positive nitrogen balance is achieved at AA administration of 2.3 – 2.65 g/kg/d.[22,24] Preterm babies can tolerate amino acid supplementation upto 3.9 g/kg/d.[26]

For proper protein accretion 30 NPC per gram of amino acid are required. While prescribing amino acids, nitrogen energy ratio or calorie nitrogen ratio should be calculated and maintained between 150 and 250.

(d) Lipids: Lipid is energy dense source needed for cell metabolism and proper brain development. Generally lipid intake of 25 – 40% of NPC is recommended in fully parenterally fed neonate for maximal oxidation.[27] Lipid provides essential fatty acids(EFA) like linoleic and linolenic acid. In preterm neonates, lipids can be started on day 1 of life.[15] Preterm neonates tolerate upto 3 g/kg/d of continuous lipid supply.[15, 28, 29] However, in ELBW babies, this should be strictly monitored.[30] Before initiation and prior to every increment of lipids serum levels of triglycerides should be checked and confirmed to be <200 mg/dl.

Lipid infusion can be given in patients with hyperbilirubinemia and thrombocytopenia.[31,32] It does not increase risk of bacterial sepsis[31,32] and it is not associated with increased sepsis related mortality[33] Carnitine is administered in neonates with TPN more than 4 weeks (50 – 100 mg/kg/d).[34]

(e) Vitamins: Parenteral vitamins are usually supplied as a mixture of different vitamins. Vitamins should be added to lipid emulsion to increase stability and reduce peroxide formation.[35,36] Vitamin induced peroxide load can be reduced by shielding of tubing from light exposure.[37] Except vitamin K, all vitamins should be supplemented daily. Adult MVI is the only preparation available in our country. It contains benzoic acid as stabilizer which is not recommended for neonates and should be used with caution. The dose of adult MVI is 0.5 ml/kg. It is added on day 1.

(f) Minerals: Sodium, Potassium and Chloride are essential minerals for survival. In VLBW infants, sodium intake should be restricted during first phase of fluid balance to reduce risk of bronchopulmonary dysplasia.[38] Till 6% weight loss has occurred sodium should not be added to PN. Potassium should not be added till diuresis sets in. Sodium and potassium are added to PN usually from day 3 onwards, depending on serum levels. Calcium, Phosphate and Magnesium should be added from day 1.

Calculation and Preparation of PN

Manual calculation is a demanding job, needs training and confirmation before execution of order. Automating of the process of writing repetitive tasks and tedious calculations should be aimed at, as PN prescription error rate is 27.9% and it can be reduced by interactive computerized PN worksheet.[39,40] Software for PN calculation are now available. These softwares are accurate, validated and reduce errors of compounding. They can be of use to keep track of patient's nutritional status.

PN can be prepared by pediatricians, neonatologists, pediatric residents, nursing staff and nutritionists, who are trained for PN preparation. A strict sterile aseptic technique is essential for preparation and administration of the PN. Use of Laminar flow is desirable with surgical scrubbing during preparation and administration. These applications reduce PN related complications.[5]

Administration of PN

TPN can be administered through peripheral or central lines (umbilical or central venous route). Use of peripheral line is safer when PN is needed for less than 10 days.[41]

PICC is inserted to avoid phlebitis when:[42]

1. Concentrations of > 12.5% glucose are needed.
2. Osmolarity of solution is >900 mOsm.
3. Prolonged period of TPN is anticipated.

The position of the tip of the catheter needs to be in a large vessel preferably the superior or inferior vena cava outside the heart with position confirmed by x-ray prior to use. Single lumen central lines are preferred over multiple lumen catheters due to less risk of sepsis[43]. PN lines should be handled minimally and with all aseptic techniques. PICC use reduces number of catheters inserted and has not been associated with increased risk of infection [44]. Heparin should be added to the PN when PICC is the route of delivery. Photo

Table 2. Research issues in parenteral nutrition

Subjects	Role of aggressive PN in Indian VLBW babies	Safety and tolerance of newer lipid preparations
Settings	Level III NICUs	Level III NICUs
Study design	Double blind randomized controlled trial	Double blind randomized controlled trial
Inclusion criteria	VLBW neonates with conditions not allowing aggressive enteral feeding	VLBW neonates with conditions not allowing aggressive enteral feeding
Main outcome variable	Nitrogen retention	Incidence of cholestasis
Secondary outcome variables	Tolerance, anthropometric outcomes	Anthropometric outcomes
Adverse outcomes	Sepsis, mortality	Sepsis, mortality

protection of PN reduces peroxide load on the newborn.[45] Photo protection of PN reduces incidence of BPD.[46]

Monitoring during PN

Metabolic and sepsis related complications are most common. Catheter related problems and calculation errors need continuous vigilance. Certain problems like cholestasis are seen with prolonged PN. Clinical assessment for hydration status is very important. Weight should be checked daily. Blood sugar should be checked twice daily initially and later on once daily. The target blood sugar level is more than 60 mg/dl. Serum electrolyte needs daily check during first few days followed by twice weekly later on. Blood gas analysis should be done initially depending on babies hemodynamic status. Once hemodynamically stable it needs check once in 48 to 72 hours. Blood Urea Nitrogen and Creatinine is checked once in 48 to 72 hours initially, then once in a week. When lipid emulsion is started base line triglyceride level is documented and it is rechecked with each 1 g/kg increment in dose. Later on it needs once a week checking. Cut off for triglyceride is 250 mg/dl. Complete Blood Count is done once a week and whenever required. It tells about the hemoglobin status and infection.

Gaps in knowledge

Though a lot of research has been done, quite a few questions are unanswered. We are listing a few of them below:

1. As most of the work is done on appropriate for gestational age (AGA) babies, evidence about small for gestational age (SGA) babies is weak. This is an important issue for us, because SGA babies comprise a big proportion of our NICU admissions.
2. Newer lipid preparations seem to be better tolerated in adult population. This should be tried in neonatal population.
3. Effect of PN administration on easily measured parameters like weight gain, hospitalization days needs to be assessed.
4. The impact of aggressive PN on risk of metabolic syndrome.
5. Effect of PN on long term development of preterm babies should be identified.

Researchable issues

Very limited research is done about neonatal PN in India. We cater a population with higher proportion of SGA babies. The Indian babies carry the 'thifty phenotype' (thin, fat babies). This makes Indian babies different from babies from developed world. Hence we need to produce even the baseline evidence about the tolerance of PN by Indian neonates. We have to define aggressive PN for Indian context. We have briefly summarized the research issues in table 2.

Conclusion

With the rapid progress of Indian neonatology in most of the fields, PN needs to be developed on war footing. The lack of sufficient evidence from Indian population, urges for a serious and planned research in near future.

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Newborn Week 2010

15th – 21st November 2010

Theme: **Improving care of LBW babies**

This is to request all state branches to observe this year's Newborn Week with commitment towards reducing morbidity and mortality related to Low birth weight. Please organize activities with the theme **"Improving care of LBW babies"**. Each branch and its members are requested to conduct workshops related to care of low birth weight babies for all categories of health personnel including birth attendants, midwives, nursing personnel, medical students and serving as well as practicing physicians. All the state and city branches of NNF are requested to compile the work and activities done during Newborn week for poster presentation to be put up during the Annual convention at Chennai in 2011.