Paediatric parenteral nutrition

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This second article in our special feature considers the nutritional requirements of infants and children, and looks at how parenteral nutrition can provide the necessary nutrients for those unable to tolerate enteral feeding

Adequate nutrition is essential for the survival and growth of infants and children. Growth of the foetus, infant or child, is impaired by nutrient deficiency. The critical period for development is during the first few years of life, and so malnutrition in this period can have a profound effect, with stunting of growth.[1] "Catch up" growth may be exhibited when more liberal feeding occurs.[2]

Neuronal development is maximal during the third trimester of pregnancy and throughout the first two years of life. Even modest energy deprivation during periods of rapid brain growth and differentiation is thought to lead to adverse neuronal development.[3]

Nutritional requirements differ according to age. Unlike in adults, endogenous nutrient reserves are limited in the young paediatric population and can be rapidly depleted by the metabolic stresses from surgical procedures or disease. Poor nutrition

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leads to immunosuppression, impaired tissue and muscle function, reduced respiratory and cardiac reserve, and impaired growth.[4] Chronically ill paediatric patients with congenital heart defects, or gastrointestinal or respiratory disease, are particularly at risk of malnutrition.

Parenteral nutrition is indicated for infants and children who are unable to tolerate adequate enteral feeding to sustain their nutritional requirements. The therapeutic goal is to maintain nutritional status and achieve balanced somatic growth. Somatic growth spurts occur in early infancy and adolescence. A preterm infant of 1kg has reserves that will sustain it through four days of starvation, whereas a term infant (4kg) has reserves that will sustain it for 30 days.[5] Older children do not require parenteral nutrition unless malnutrition is anticipated for more than five or seven days.[6]

Optimal use of parenteral nutrition has resulted in higher survival of critically ill infants. Also, improvements in techniques for artificial nutrition have led to an improved quality of life for long-term parenteral nutrition patients. Indications for

parenteral nutrition are shown in Panel 1, p59.

ENERGY REQUIREMENTS

Energy is required for the maintenance of homeostasis and new tissue synthesis. Energy requirements are increased when the body is under catabolic stress, fever or sepsis, or if there is failure to thrive.[7] An adequate energy substrate is necessary to ensure proper utilisation of protein. The principle sources of calories in parenteral nutrition formulations are carbohydrates and lipids. Glucose and lipids are increased in a step-wise approach, as tolerated. For effective nitrogen utilisation, the nitrogen to kcal ratio should be between 150 and 250kcal per gram of nitrogen.[3,8-10] If the energy intake is insufficient, the nitrogen is used for calories; with excessive intake, the energy is deposited as fat, which may have long-term consequences.

The World Health Organization recommends that, where possible, energy requirements should be based on measures of expenditure, rather than intake. The energy

Panel 1: Indications for parenteral nutrition

- Prematurity
- Congenital defects, eg, gastroschisis (defect within the abdominal wall) or tracheoesophageal fistula
- Abdominal surgery, eg, for malrotation (failure of the intestinal tract to rotate during embryonic development)
- Chronic intestinal pseudo-obstruction
- Autoimmune enteropathy, severe diarrhoea or microvillus atrophy
- Short bowel syndrome
- Pancreatitis
- Respiratory distress syndrome
- Post chemotherapy complications, such as inflammation of mucous membrane surfaces

requirements for premature infants are higher than for older infants and children (see Table 1). Premature infants require sufficient calories to promote growth, matching *in utero* growth rates. They have elevated metabolic rates because they possess a high percentage of metabolically active tissue, with low carbohydrate and lipid stores, high evaporative losses and immature gastrointestinal systems.

To achieve appropriate utilisation of energy substrate, carbohydrates and lipids are used in conjunction, at a maximum of 18g/kg/day (12.5mg/kg/min).[11-13] Maximal oxidative capacity has been shown with such daily doses, although recent guidelines from the United States recommend up to 14mg/kg/min in premature infants.[6]

FLUID REQUIREMENTS

Parenteral nutrition typically has not been used in the first 72 hours of life because of rapid changes in fluid and electrolyte balance. However, current practice is moving towards a more aggressive approach, with parenteral nutrition starting on day one or two of life, where clinically possible.[6,14-15] In the first week of life, between 6 and 10 per cent of body weight is lost as the extracellular compartment contracts, and this confers respiratory benefit.

Fluid requirements are related to calorie expenditure, and can be calculated using a formula for body weight (see Panel 2, p60). Fluid intake, insensible losses (eg, while undergoing phototherapy), abnormal fluid losses (eg, diarrhoea or vomiting), urine output and intravenous drugs will need to be taken into account when calculating fluid requirements. Fluid balance and hydration status can be monitored by regularly weighing the young patient.

PROTEIN REQUIREMENTS

Amino acids are essential for growth and formation of new tissue, plasma proteins, enzymes and blood cells. There are 20 amino acids used by the body for tissue growth. Eight are essential and must be supplied in the diet, and the remaining 12 are non-essential and require synthesis by the body. The essential amino acids should account for 40 per cent of the total nitrogen provided by parenteral nutrition. Histidine,

Table 1: Estimated nutritional requirements

Age (years)	Fluid (ml/kg/day)	Energy (kcal/kg/day)	Nitrogen (g/kg/day)
Preterm	150–200	120–130	0.48–0.64
0–1	100–150	90–120	0.34–0.46
1–6	80–100	70–100	0.22–0.38
6–12	75–80	50–70	0.20–0.33
12–18	50–75	30–60	0.16–0.20

Panel 2: Daily maintenance fluid requirements

- **Body weight less than 10kg**
  10ml/kg fluids per day
- **Body weight between 11 and 20kg**
  1,000ml per day + 50ml/kg for each kg above 10kg
- **Body weight greater than 20kg**
  1,500ml per day + 20ml/kg for each kg above 20kg

cysteine, taurine and tyrosine are "conditionally essential" in neonates up to the age of six months because they have a reduced capacity to synthesise certain amino acids and have immature enzyme systems.[16] Growth may be compromised in the absence of these amino acids.

Cysteine synthesis relies on the activity of cystathionase, which is found at low levels in neonates. Taurine is required for the development of the central nervous system and also for retinal and cardiac muscle. However, the lack of taurine in parenteral nutrition substrates may be a factor in the development of cholestasis as taurine is used to conjugate bile acids.[17]

Amino acid preparations contain a mixture of crystalline, branched chain amino acids, eg, proline and glycine, and aromatic amino acids. The nitrogen source is based on either breast milk (Vaminolact) or cord blood amino acid profiles (Primene) for premature babies or infants, and on egg protein profile for older children (Vamin 9). Vamin 9 is not used in neonates or infants under six months of age because of the risk of potential neurotoxicity from high blood levels of phenylalanine and tyrosine.[18,19]

Protein requirements are high in premature infants where the goal is to achieve postnatal growth approximating to that of a normal foetus. The brain accounts for almost 70 per cent of the basal metabolic rate in a neonate, and approximately 50 per cent at one year of age.

CARBOHYDRATES

Carbohydrate is normally provided in parenteral nutrition formulations as glucose, which is readily used by all body tissues. Between 40 and 45 per cent of the calories provided by parenteral nutrition should be from carbohydrate sources. Carbohydrate intolerance is not uncommon in infants because they have low glycogen reserves in the liver and a diminished capacity for gluconeogenesis.[20] Carbohydrate, as the sole source of energy, will lead to steatosis, increased carbon dioxide production and essential fatty acid deficiency. The upper carbohydrate intake is dependent on the infant's maximal carbohydrate oxidation capacity.

Parenteral nutrition can be administered over less than 24 hours in older children, but must be tapered over one or two hours to prevent rebound hypoglycaemia. Blood glucose measurements should be checked 15 to 60 minutes after discontinuation of a parenteral feed.

LIPID REQUIREMENTS

Lipids provide between 35 and 40 per cent of the total non-nitrogen calories in parenteral nutrition. Lipids may be decreased in sepsis or if bilirubin levels exceed 200mmol/L because lipoprotein lipase activity is reduced. Free fatty acids displace bilirubin from albumin, which may lead to the risk of kernicterus (nuclear jaundice). However, kernicterus is rare in clinical practice, unless the ratio of free fatty acids to albumin exceeds six.[9]

Lipids provide essential polyunsaturated fatty acids, which are important for visual and cognitive function in later life.[21] Lipids are incorporated into the structural components of cell and plasma membranes and are used for prostaglandin synthesis and platelet function.[22] Between 0.5-1g/kg/day of lipid is required to prevent essential fatty acid deficiency in infants and children.

The lipid emulsions currently available are isotonic and are suitable for parenteral administration because of their low osmolarity. Lipids are an important component of parenteral nutrition as a source of energy dense calories, providing 2kcal/ml. Intralipid 20 per cent is the most commonly used lipid source. It is a soya bean oil, containing long chain triglycerides emulsified with egg yolk phospholipids. Soya bean 10 per cent emulsions are not recommended because they have a high phospholipid to triglyceride ratio, which can lead to elevated plasma triglycerides and hyperphospholipidaemia. Olive oil preparations (Clinoleic) are currently used, however, and these combine 20 per cent soya bean oil with 80 per cent olive oil.

Carnitine, a quaternary amino acid, is important in the oxidation of long chain fatty acids. A lack of carnitine in parenteral nutrition substrates compared with breast milk may be an aetiological factor in the inability of premature infants to utilise parenteral lipids. Medium chain triglycerides are more rapidly cleared from the circulation and are not carnitine dependent.

Newer lipid substrates that combine soya bean oil, olive oil and omega-3 fish oils are in development. Omega-3 enriched emulsions contain arachidonic acid and docosahexaenoic acid, which are important for the development of the brain and retina.

ELECTROLYTES

Electrolytes are added to parenteral nutrition regimens according to the patient's individual requirements, based on blood chemistry. Differences in body water composition and immature renal function are two factors that make a neonate more susceptible than older children or adults to dehydration and electrolyte imbalances. In comparison with adults, water accounts for a much larger percentage of body weight in neonates, with approximately 80 per cent being extracellular fluid.

Sodium is restricted during the first few days after birth to allow contraction of extracellular fluid.

Panel 3: Parameters to be monitored

- **Initial monitoring**
  Full blood count and plasma levels of sodium, potassium, urea, calcium, magnesium, phosphate, bilirubin, albumin, alanine transaminase, alkaline phosphatase and blood glucose (for long-term parenteral nutrition, plasma levels of copper, zinc, selenium and vitamins A and E should be monitored in addition to urinary sodium and potassium)
- **Continued monitoring (weekly)**
  Urea and electrolytes, calcium, magnesium, phosphate, bilirubin, alanine transaminase and albumin
- **Continued monitoring (monthly)**
  Zinc, copper, selenium and vitamins A and E

Renal immaturity in premature infants results in an inability to concentrate urine, and the concomitant use of diuretics leads to increased sodium requirements. Sodium is usually given at a dose of 3–4mmol/kg/day in premature infants and 2mmol/kg/day in older children. Potassium is also given, at a dose of 2–3mmol/kg/day. There is evidence of sodium depletion in patients failing to thrive, especially if urinary sodium falls below 10mmol/L. Parenteral nutrition is also supplemented with calcium and organic phosphate.

Requirements for vitamins and trace elements are based on recommendations given by the American Society for Clinical Nutrition.[23] Vitlipid, Solivito and Peditrace are all given at a dose of 1ml/kg/day, with a maximum daily dose of 10ml. Acid-base imbalance is prevented by administering acetate to patients with acidosis and replacing chloride loads of more than 3mmol/kg.[24]

Monitoring serum electrolytes will indicate the nutritional requirements of an individual and will show any nutritional deficiencies. Growth can be measured by weight, height and mid arm circumference. Some parameters that can be monitored are shown in Panel 3, but these should be used as a guide only and local practice should be followed.

The complications arising from parenteral nutrition are either metabolic or mechanical. Cholestasis is a common complication of long-term artificial feeding and is often associated with sepsis, lack of enteral feeding and excess energy. Cyclical parenteral nutrition and trophic feeding may reduce this complication.[25–27] Minimal enteral or trophic feeding of 1–10ml/h (dependent on age of child) is recommended to maintain intestinal mucosa integrity, reduce bacterial translocation and prevent biliary cholestasis. Cyclical parenteral nutrition involves the parenteral nutrition being infused over a shorter period of time (12–16 hours overnight).

Catheter-related sepsis is the most frequently seen complication and *Staphylococcus epidermis*, *Staphylococcus aureus*, enterococci and *Candida albicans* are the common causative organisms. Treatment is with antibiotics.

Summary

Nutritional requirements alter according to age and disease state. Parenteral nutrition is a safe and effective supportive treatment, when used with adequate monitoring.

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