Feeding the preterm infant

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Abstract. The sick preterm infant has special nutritional needs, and the provision of appropriate nutrition is now recognised as an important part of the increasingly intensive management of this population. “Optimal” nutrition is difficult to define for an individual infant, but prospective randomised studies have shown that the early diet given to preterm infants can have a major impact on their neurological development and growth, with the best outcomes for those receiving either a preterm formula or maternal milk fortified with a range of nutrients. In contrast, diets suitable for term infants do not meet the needs of small preterm infants, either in the short or longer term, and should not be used. This article reviews the nutritional needs of the preterm infant and outlines the strategies commonly used in this area of neonatal intensive care.

Key words: Preterm infant – Nutrition – Formula – Human milk

Introduction

At birth, the supply of all nutrients from the placenta ceases. For the infant born at term, adaptive mechanisms maintain homeostasis by utilising the large stores of all nutrients accumulated during the third trimester to ensure a smooth transition to the process of enteral nutrition. In contrast, the preterm infant has little in the way of nutrient reserves, is growing more rapidly than the infant born at term and is likely to enter a catabolic state because of intercurrent illness.

Meeting the special nutritional needs of this population is a problem that has exercised the minds of both scientists and paediatricians; in particular, the important questions of what and how the preterm infant should be fed have been addressed in a multiplicity of studies. The majority have been short term and have provided information on immediate tolerance and serious adverse consequences of feeding and feeding methods [effects on infection rates, incidence of necrotising enterocolitis (NEC), hypoglycaemia, chronic lung disease, metabolic bone disease], short-term growth rates (which may influence the duration of hospitalisation) and the biochemical response to different diets. More recently, longer-term studies have addressed the influence of early nutrition on long-term growth, development and health.

General considerations

Initial management in many centres is dictated by the infant’s clinical condition. The commonest disease of prematurity is the respiratory distress syndrome and the prescription of fluids and electrolytes in these infants, particularly the more immature (<28 weeks' gestation), may change several times during the first 48 h. For this reason in particular, few United Kingdom neonatal intensive care units consider the provision of total parenteral nutrition as a priority during this early period. From 48 h onwards, however, the metabolic milieu is often stable enough to permit the introduction of parenteral nutrition.

Parenteral feeding

Intravenous feeding is used frequently in preterm infants, although no prospective randomised studies have shown that it is of proven benefit. The ethos of providing this treatment varies according to patient – for most, support is short term and the expectation is that enteral feeding will commence within the foreseeable future. In cases where longer-term parenteral feeding is anticipated (gut surgery in particular), management is directed more at providing for all needs, rather than just “bridging the gap”.

Target intakes for infants receiving short-term intravenous feeding are 3 g/kg per day of protein, up to 3 g/kg per day of fat emulsion and 10–15 g/kg per day of dextrose so that there is sufficient energy (80–90 kcal/kg per day) to ensure full utilisation of protein [1, 2]. Parenteral intake of
energy and amino acids at these levels are compatible with intrauterine rates of nitrogen retention and weight gain. Essential fatty acid deficiency can be prevented by the administration of just 0.5 g/kg per day of lipid emulsion. Mineral intakes approaching the in utero accretion rates (calcium 3.5 mmol/kg per day, phosphate 2.5 mmol/kg per day) can be achieved by using organic phosphorus compounds, such as sodium glycerol phosphate, in combination with either calcium chloride or gluconate. Vitamins are administered admixed with lipid emulsion to protect the more vulnerable components against light-trace element-induced degradation. The volume of the added vitamin solution can be varied to provide more or less as required, but the ratios of the concentrations of each remain constant. Trace elements are admixed with the amino acid/dextrose part of the regime [3].

More than with enteral feeding, the potential for adverse effects is significant. Catheter-related complications, including migration (typically causing hydrothorax or pericardial effusion) and venous thrombosis, have been reported. Infection is common, typically with Staphylococcus epidermidis.

A variety of biochemical disturbances have been documented. Hyperaminoacidaemia occurs when energy intake is inadequate for the amount of protein given, but is not associated with long-term developmental problems [4]. Hypercholesterolaemia and hypertriglyceridaemia have been reported in infants receiving fat emulsions (more often with the 10% rather than 20% form of Intralipid) [5, 6]. There is little information available as yet regarding the new 30% Intralipid solution in newborns. Of greater concern are the prospective studies of Hammerman and Aramburo [7] and retrospective studies of Cooke [8], which suggest that the use of intravenous fat emulsion is associated with chronic lung disease in the preterm infant. Hyper- and hypoglycaemia are common and usually dealt with by altering glucose intake and giving insulin or glucagon where such alterations are ineffective. Average intakes of glucose are 7–10 mg/kg per min; more than 12 mg/kg per min implies hyperinsulinism. Hypophosphataemia (plasma phosphorus < 1.8 mmol/l – a clear difference from the value expected in the adult population) has been common because of the poor solubility of inorganic calcium and phosphorus salts; the introduction of organic phosphorus salts should ameliorate this situation [9]. Trace element deficiency (particularly of the ultratrace elements such as selenium) is common despite supplementation, and may be a significant problem when parenteral nutrition continues long term, as in some surgical units [3]. Aluminium contamination of intravenous feeding solutions remains a concern; the components which are most heavily contaminated are the calcium and phosphorus salts [10, 11]. Calcium chloride should be used in preference to calcium gluconate for infants with renal insufficiency, as this will reduce the aluminium intake by 75%.

Parenteral nutrition should only be undertaken in units familiar with these common complications, and preferably where there is regular individual review by a nutrition team. A computerised prescribing system incorporating guidelines for those undertaking the prescription, often junior doctors with limited previous experience, is invaluable.

**Enteral feeding**

**Which diet is best for premature babies?**

It is now widely recognised that preterm infants have special nutritional needs and that those infants who receive suboptimal early nutrition are at increased risk of problems in later life. The following discussion of the nutritional needs of the preterm infant assumes that the desired outcomes are optimisation of the potential for long-term growth, neurological development and bodily health without increased risk of morbidity in the short term.

Prospective randomised controlled studies of the effect of early diet on later growth and development for infants born prematurely, which compared "term" and "preterm" formula either as sole diet or as supplement to maternal milk, have shown a 6-point advantage on the Bayley scales of infant development at 18 months post term for infants receiving the preterm formula [12]. For infants previously malnourished and therefore growth retarded at birth, this difference increased to 16 points in favour of those receiving the preterm formula. Most infant feed manufacturers now produce preterm formula which is nutrient- and energy-dense in comparison with term formula (Table 1).

In comparison with unsupplemented human milk, a number of studies have documented increased short-term rates of weight gain and linear growth and reduced incidence of metabolic bone disease for infants fed preterm formula [13–16]. Nevertheless, there is evidence that breast milk, particularly fresh unpasteurised milk from the infant’s own mother, has a range of beneficial effects both in the short and longer term.

In the short term it has been suggested that the early use of human milk as part of the infant’s intake, rather than intake of formula alone, is associated with a reduced risk of the devastating neonatal disease of NEC. Of 926 infants in a recent study, 51 developed NEC, and in stringently confirmed cases NEC was six times more common in infants fed formula alone than in those who received human milk alone [17]. The early use of human milk as opposed to formula is associated with better feed tolerance, as judged by the length of time taken to achieve full enteral nutrition [18].

In the longer term, biochemical evidence of metabolic bone disease during the period of hospitalisation (raised plasma alkaline phosphatase activity) was associated with reduced length at 18 months in one study; feeding with human milk was independently associated with a further reduction in length then, but in addition most of the infants with high plasma alkaline phosphatase activities were fed human milk [13].

The possibility that early diet could influence later neurological development is a key issue in neonatal nutrition. In a large prospective double blind controlled study, preterm infants fed donated pasteurised breast milk had a small disadvantage in developmental quotient at 9 months post term compared with infants fed preterm formula [19], although this difference had disappeared by 18 months (Lucas et al., personal communication). In a contemporaneous non-randomised study, infants fed their own mo-