Feeding issues in preterm infants

A major concern for those taking care of preterm infants is to ensure that nutritional intake meets requirements, thereby ensuring that poor nutrition is not rate limiting on outcome. However, establishment of an adequate intake is difficult during early life in the sick infant. Dietary needs also vary, depending on maturity and nutritional and clinical status. Furthermore, measures of outcome are not widely agreed on. This paper will briefly review some of the principles involved and address some of the practical questions that arise on a day to day basis during nutritional care of these high risk infants.

Determination of nutritional requirements

Recommended dietary intakes are based on needs for maintenance and growth and the assumption that postnatal growth approximates that in utero at the same post conceptional age. However, recommended intakes take time to establish, and, having been established, are commonly interrupted for clinical reasons during the first three to four weeks of life in preterm infants.

Figure 1 illustrates this situation more clearly. Embleton et al compared actual and recommended dietary intake (energy 102 kcal/kg/day; protein 3.0 g/kg/day) in a group of preterm infants (≤34 weeks gestation) during the initial hospital stay. By 7 days of age, infants had developed major deficits in energy (∼400 kcal/kg) and protein (13 g/kg), which were not recovered by the time of discharge from hospital; the more immature the infant the greater the deficit at discharge.

It has therefore been suggested that dietary intake must also meet needs for “catch up” growth. Whether or not this can be accomplished before hospital discharge remains to be determined, but closer attention must be paid to quantifying and minimising these deficits.

Measures of outcome

The relation between diet and growth appears to be clear cut in that inadequate dietary intake can be directly related to poor growth. However, non-dietary factors also affect growth. In the study of Embleton et al, 50% of the variation in growth was related to diet, and 50% was unexplained. This is not surprising given the differences in size, maturity, and nutritional status at birth and the variable clinical course in these infants. Nonetheless, attention must be paid to the confounding effects of non-nutritional factors when interpreting the effects of diet on growth in these infants.

Weight gain and weight for corrected age are valid measures of adequacy of intake. It is recommended that weight gain approximates that of the normal fetus at the same post conceptional age (10–15 g/kg/day). This may be questioned. After birth, preterm infants lose weight and take variable periods to regain birth weight. Achieved weight therefore will always lag behind expected weight at the same post conceptional age; the more immature the infant the greater the deficit. If infants are to catch up, then weight gain must exceed that found in utero, a rate seldom achieved during the initial hospital stay.

Crown-heel length and length gain are the most sensitive indices of adequacy of nutrient intake, but accurate and reproducible measures of crown-heel length are difficult to obtain. Knee-heel length, as determined by knemometry, has therefore been used to assess linear growth in preterm infants. Still, recent data suggest that the relation between knee-heel and crown-heel length is not consistent, and the former is less reproducible than the latter when linear growth is being assessed. Further studies are needed to examine this critical issue more closely.

The relation between diet, brain growth, and behaviour is complex. Studies in term infants show that diet alone may not be adequate in improving behaviour and that attention must be paid to social and environmental factors that deprive infants of normal, parental, emotional, and educative care. Studies in preterm infants have shown that even short periods of dietary manipulation affect behaviour. However, the same studies show that non-nutritional factors also affect behaviour, and it is not easy to disentangle the effects of one from the other. Nonetheless, development is considered by some to be an important end point when long term outcome is assessed in these high risk infants.
WHEN TO FEED

Withholding enteral feeds does not appear to prevent necrotising enterocolitis,\textsuperscript{15} but small amounts of enteral feeds have been shown to stimulate secretion of intestinal polypeptide hormone thought to be important in postnatal intestinal adaptation.\textsuperscript{20} Dunn \textit{et al}\textsuperscript{26} prospectively examined the effects of early (day 3 of life) hypocaloric enteral nutrition (10–20 ml/kg/day) and reported less jaundice, osteopenia of prematurity, and earlier establishment of full enteral feeds with the hypocaloric regimen. Slagle \textit{et al}\textsuperscript{27} also examined the effects of early low volume enteral feed substrate (12 ml/kg/day) on intestinal function and noted improved feeding tolerance and earlier establishment of full enteral nutrition with the hypocaloric regimen. McLure and Newell\textsuperscript{28} have also reported increased intestinal motility in infants receiving minimal enteral nutrition. If withholding feeds does not prevent necrotising enterocolitis, there appears little reason not to begin early hypocaloric enteral feeds in these nutritionally vulnerable infants.

WHAT TO FEED

The initial goal of enteral feeds is to support postnatal intestinal adaptation. Data suggest that tolerance is better\textsuperscript{4} and the incidence of necrotising enterocolitis is lower\textsuperscript{2} with human milk than low birthweight infant formula. Hypocaloric feeds with human milk therefore appear desirable during the first two weeks of life. If human milk is not available, term infant formula may be fed until enteral tolerance has been achieved, at which point a preterm infant formula should be introduced.

As tolerance is established, intake must meet growth needs. Preterm infants fed on human milk gain less weight than those fed on fortified human milk.\textsuperscript{26–29} Preterm infants fed on human milk alone also show poorer growth than those fed on preterm infant formula.\textsuperscript{30–34} These findings are not surprising because of the lower concentrations of protein and minerals in human milk.\textsuperscript{35} The data therefore suggest that preterm infants be fed on fortified human milk, a preterm infant formula, or a combination thereof.

However, fortification of human milk such that intake meets requirements is not clear cut because the protein and mineral content of human milk is not only low but also highly variable.\textsuperscript{35} At the same time, the nutrient content of human milk fortifiers vary. In effect, the degree of fortification needed to sustain adequate growth may vary from day to day. It is worrying that preterm infants fed on current fortification regimens grow less well than those fed on a preterm infant formula.\textsuperscript{36–38} Further studies must examine this critical issue closely.

Controversy exists about the role of long chain polyunsaturated fatty acids in feeding the preterm infant. The long chain polyunsaturated fatty acids arachidonic acid and docosahexanoic acid are critical for eicosanoid synthesis and cell membrane, retinal, and brain function. However, the synthesis of arachidonic acid and docosahexanoic acid may be limited in the preterm infant, and formula supplementation has been suggested.\textsuperscript{39} Some studies have suggested a benefit,\textsuperscript{40} others a transient effect,\textsuperscript{41} others no effect,\textsuperscript{42} and some an adverse effect on growth.\textsuperscript{43,44} A recent summary report suggests that further data are needed before final recommendations can be made.\textsuperscript{45}

HOW TO FEED

Nasogastric versus orogastric enteral feeds

The narrowest point of the airway is the anterior nasal valve, located just behind the nose. Nasal resistance accounts for ∼40% of total airway resistance in neonates.\textsuperscript{46} Passage of a size 5 French nasogastric tube increases airway resistance in preterm infants by 30–50%,\textsuperscript{47,48} and, presumably, the work of breathing.

Greenspan \textit{et al}\textsuperscript{49} examined pulmonary function in normal neonates with nasogastric and orogastric tubes. Infants with nasogastric tubes had diminished minute ventilation and respiratory rate and increased pulmonary resistance, resistive work of breathing, and peak transpulmonary pressure. The authors concluded that “neonates demonstrate significant pulmonary compromise with nasogastric placement”\textsuperscript{50}.

Van Someren \textit{et al}\textsuperscript{39} also examined the effects of nasogastric and orogastric tube placement on respiratory function in preterm infants. An increased incidence of periodic breathing and central apnoea were noted with nasogastric tube placement. These data therefore do not support the routine use of nasogastric tubes in preterm infants who are at risk for apnoea and/or those with respiratory problems such as chronic lung disease of prematurity.

Continuous versus bolus enteral feeds

Enteral feeding stimulates an enterohormonal surge. Data from Aynsley-Green \textit{et al}\textsuperscript{51} suggested that surges in insulin, gastrin, and gastric inhibitory peptide are less with continuous than with bolus feeds. However, preprandial hormone levels were higher with continuous feeds,\textsuperscript{60} but the significance of these findings are not entirely clear.

Toce \textit{et al}\textsuperscript{61} compared growth with feeding related complications in preterm infants randomised to continuous or bolus enteral feeds. Weight gain was greater (+ 3–6 g/kg/day) and the incidence of apnoea tended to be less with continuous enteral feeds. Silvestre \textit{et al}\textsuperscript{62} was unable to show any differences in growth or incidence of apnoea between continuously fed and bolus fed infants. However, infants withdrawn from the study because of feeding related problems (recurrent apnoea and bradycardias, abdominal distension, and increased gastric residues) were all bolus fed.\textsuperscript{63}

Studies in term\textsuperscript{52,53} and preterm\textsuperscript{14–18,55} infants consistently document falls in oxygenation after feeding. The reasons for this are not entirely clear. Patel \textit{et al}\textsuperscript{64} were unable to show any changes in respiratory function. Others have shown decreased functional residual capacity\textsuperscript{56} and/or decreased lung volumes.\textsuperscript{57} Blondheim \textit{et al}\textsuperscript{12} have also reported increased pulmonary resistance and reduced tidal
Nutrition after discharge from hospital

Postnatal growth retardation appears inevitable during the initial hospital stay, with preterm infants weighing significantly less than term infants at discharge. After discharge, little catch up growth occurs, and infants remain small throughout infancy and childhood. Despite these observations, limited attention has been paid to nutrition in these infants after discharge.

In one study, preterm infants (< 1850 g; n = 32) were fed on either a standard term infant or nutrient enriched formula after hospital discharge; weight gain and linear growth were greater with the nutrient enriched formula. In another study, infants (n < 1750 g; n = 129) were fed on a standard term or preterm infant formula after discharge from hospital; weight, length, and head growth were greater with the preterm infant formula. Increased weight gain and head growth reflected increased lean body mass, suggesting that the preterm formula more closely met protein requirements. However, questions remain about these studies.

In the study of Lucas et al., no differences were detected in nutrient intake between the groups, making differences in growth difficult to explain. In that of Cooke et al., better growth was related to increased protein intake, but, at identical nutrient intakes, boys fed the preterm infant formula grew faster and accreted more lean mass than girls fed the preterm infant formula. This is surprising but suggests that factors other than nutrition may be important determinants of growth in preterm boys and girls.

Nonetheless, both studies suggest that “normal” preterm infants benefit from nutritional intervention after hospital discharge. Clear cut recommendations are difficult because nutritional status, and therefore needs, vary. In both trials, formula with a protein/energy ratio of 2.8 g/100 kcal was fed until term, 6,29 or 9 months corrected age.29 Feeding until term had no long term effects on growth.29 It therefore appears to be logical to feed formula with a similar protein/energy ratio until between 3 and 9 months corrected age, but nutritional status must be closely monitored during and after nutritional intervention.

Conclusion

Feeding practices in preterm infants vary widely between and within special care baby units. In the past, this was understandable because feeding was more art than science and practices largely reflected anecdotal experience. This is no longer the case, and the results of randomised controlled trials now provide a “template” on which nutrition support can be based. The results of any randomised trial may be questioned and the effects of intervention may differ depending on patient population. Nonetheless, which ever approach is taken within a given unit it must be consistent enough that outcome can be audited and practice can be adapted to meet the particular needs of infants and practice.
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