Optimising nutrition of preterm and term infants in the neonatal intensive care unit

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Abstract

Optimum nutrition leads to improved long-term neurodevelopmental outcomes in both preterm and term infants admitted to the neonatal intensive care (NICU). This review delineates the phases of nutritional management from full parenteral nutrition, transitioning to enteral nutrition and on to full enteral feeds. It describes the essential components of best nutritional care in the neonatal periods and provides practical tips in the management of nutrition in these infants. The authors make recommendations for care based on national and international guidelines and personal expertise of working in a tertiary NICU.

Keywords enteral nutrition; neonatal nutrition; parenteral nutrition

Introduction

Long term outcomes of infants are influenced by nutrition. Despite improvements in the neonatal intensive care which have resulted in improved survival, half of low birth weight babies are still being discharged from the NICU with poor postnatal growth and a quarter with severe growth failure. Optimal postnatal nutrition and growth have wide-ranging benefits such as decreased hospital length of stay and longer-term benefits including improved neurodevelopmental outcome and better socioeconomic status.

Normal neurodevelopmental outcomes following a NICU stay is a key outcome for both the clinical team and parents. The neonatal brain doubles in size from 20 weeks gestation to term, with the brain consuming 60% of available energy. Hence, appropriate nutrition during the neonatal period is required to maximise the opportunity for normal brain growth and development.

Preterm infants are at increased risk of developing significant cumulative nutritional deficits and malnutrition due to negligible energy stores, delays in establishing nutritional support and increased nutritional requirements. Administering optimum parenteral nutrition and initiating early feedings to yield adequate postnatal growth are cornerstones of NICU management.

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Parenteral nutrition

Parenteral nutrition (PN) is a lifeline to premature babies and sick term infants who are unable to tolerate enteral feeding. For most neonates, PN is required for a brief period. Two-thirds of all neonates born under 31 weeks' gestation and started on PN shortly after birth are off all PN by 14 days of age.

PN can provide complete nutrition, which was historically often referred to as total parenteral nutrition (TPN). It is most frequently used when infants cannot be fed enterally. As neonates progress in the NICU, PN is used in conjunction with enteral nutrition (EN) with the PN volume decreasing in a stepwise manner whilst milk feeds are increased correspondingly.

PN is a complex multi-component solution mixed in one bag (3 in 1 bag; carbohydrates, protein, and lipids) or administered as an aqueous (protein and carbohydrate) bag and a separate fat component. PN should be started as soon as possible after birth, and ideally within 8 hours especially in very preterm neonates or when it is likely that enteral feeding is not going to be established soon.

Close monitoring is required before, during and after administration of PN and ideally multidisciplinary team involvement (physician, dietitian, and clinical pharmacist) is recommended in PN ordering.

Both the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the National Institute for Health and Care Excellence (NICE) have recently published guidance on paediatric PN. Recommendations from these guidelines inform the text and tables presented in the review.

Indications for parenteral nutrition

- Preterm infants born less than 30–31 weeks' gestation.
- Infants born later than 30–31 weeks' gestation, where insufficient progress with enteral nutrition is made within 3–5 days.
- Birth weight less than 1250g.
- Any infant unlikely to establish EN due to congenital gut abnormality (e.g. gastroschisis, omphalocele), surgical condition (e.g. gut perforation), necrotising enterocolitis (NEC) or critical illness (e.g. sepsis).
- If enteral feed is stopped start PN, if restarting feeds or insufficient progress with feeds will not occur in 2–3 days.

Neonatal energy requirements

Energy supply needs to meet the nutritional requirements of the neonate. This is a dynamic process as energy requirements will vary depending on the age, clinical status of the neonate and method of feeding (either TPN or mixed PN and EN). Excess energy delivery is not ideal; in the short term it may lead to hyperglycemia and high triglyceride levels, and in the longer term there are increasing concerns regarding developing metabolic syndrome in adult life. Inadequate energy intake is equally unfavorable, resulting in reduced weight gain, delayed wound healing, longer hospital stays and poorer long-term neurodevelopmental outcomes.

Recommended daily nutrient provision for term and preterm infants

Nutrient provision per day	Preterm Infants		Term Infants	
	ESPGHAN	NICE	ESPGHAN	NICE
Energy (kcal/kg)	90–120	75–120	75–85	75–120

ESPGHAN 2018: European society of paediatric gastroenterology, hepatology, and nutrition; NICE 2020: National Institute of Clinical Excellence.

Table 1

Energy is obtained from the macronutrients such as protein, carbohydrate, and lipid. Energy requirements increase in the first few days after birth and typically coincide with the incremental increase in intravenous fluid provision post-delivery with onset of diuresis following contraction of extra cellular fluid space, which occurs in normal postnatal adaptation. PN should initially provide 40–60 kcal/kg/day and build up to maintenance requirements over 3–4 days. Infants who have previously received nutrition and have had a short interruption in their intake can be initiated at maintenance requirements.

Neonates on PN receiving no enteral nutrition have energy requirements typically 10–30% lower than those receiving enteral feeds due to a reduction in diet-induced thermogenesis, fecal energy loss and splanchnic blood flow.

Recommended daily amino acid provision for term and preterm infants

Amino acid provision per 24 h (g/kg)	Preterm Infants		Term Infants	
	ESPGHAN	NICE	ESPGHAN	NICE
Day 1	>1.5	1.5–2	1.5	1–2
Days 2–3	2.5–3.5		3	
Day 4		3–4		2.5–3

Table 2

Recommended daily lipid provision for term and preterm infants

Nutrient provision per 24 h	Preterm Infants		Term Infants	
	ESPGHAN	NICE	ESPGHAN	NICE
Lipid (g/kg)	Up to 4	3–4	Up to 4	3–4

Table 4

Practical tips:

How to calculate energy intake in PN?

Example:

1 kg preterm (GA 28 weeks) is on 120ml/kg of PN containing; 3g/kg of Protein, Glucose 12g/kg and 3g/kg of lipid.

Protein = 4kcal/g, Glucose = 4kcal/g, and Lipid = 10 kcal/g.

Therefore, this neonate is receiving (3x4) + (12x4) + (3x10) = 90kcal/kg/day.

For term neonates the ESPGHAN 2018 guidelines recommend 75–85 kcal/kg/day (see Table 1). Previously, the ESPGHAN 2005 guidelines recommended 90–100 kcal/kg/day for term infants. This reduction is due to concerns regarding global obesity and overnutrition. The energy recommendations for preterm and very low birthweight babies have remained the same (see Table 1).

Constituents of parenteral nutrition

Amino acids (protein): protein is provided as amino acids in PN; and the terms are used interchangeably in this review. PN formulations contain essential and non-essential amino acids. While amino acids can be used as an energy source, their provision should be prioritised for structural and functional constituents in

Practical tips:

Note difference in maximum protein requirements for preterm and term infants.

It can be confusing when documents state protein, nitrogen and/or amino acids. Choose one and try to remain consistent.

1g Nitrogen = 6.25g Protein = 7.5g free amino acids.

Recommended daily glucose provision for term and preterm infants

Nutrient provision per 24 h	Preterm Infants		Term Infants	
	ESPGHAN	NICE	ESPGHAN	NICE
Day 1				
Glucose (g/kg)	5.8–11.54–8	6–9	3.6–7.2	6–9
GIR [mg/kg/min]	[4–8]	[4.2–6.3]	[2.5–5]	[4.2–6.3]
Day 2 onwards				
Glucose (g/kg)	11.5–14.4 (max of 17.3)	9–16	7.2–6.9 (max of 17.3)	9–16
GIR [mg/kg/min]	[8–10] [max of 12]	[6.3–11.1]	[5–10] [max of 12]	[6.3–11.1]

Table 3

the body and for growth. An energy supply of 20–30 kcal non-nitrogen energy per gram of amino acid (or 30–40 kcal total energy per gram of amino acid) is widely recommended to allow for optimal protein utilization (see Practical tips above).

The minimum protein intake needed to prevent protein breakdown and a negative nitrogen balance after birth is 1.5g/kg/day. It is recommended to start amino acids on day one and increase to maximum levels over 2–3 days (see Table 2).

Glucose: carbohydrate is the main source of energy in our diets. Carbohydrate is provided as Dextrose (D glucose) in PN. During the last trimester, the fetus receives a glucose infusion rate (GIR) of 4–5mg/kg/minute via the placenta. Glucose supply on day 1 is recommended to provide a minimum of 4mg/kg/minute (5.8g/kg/day) to mimic the supply *in utero*. The glucose concentration can be incremented over 2–3 days or longer as tolerated (see Table 3).

Practical tips:

If hyperglycaemia develops, reduce GIR to minimum of 4mg/kg/min and watch for osmotic diuresis. Urine dipstick helps monitor glucose tolerance. Insulin should be last resort as significant risk of hypoglycaemia.

How to calculate GIR?

If PN is being given continuously over 24 hours, there is a quick way to calculate GIR: Glucose (g/kg/day) ÷ 1.44 = GIR (mg/kg/minute).

Example:

1 kg preterm (GA 28 weeks) is on 120ml/kg of PN containing Glucose of 12g/kg/day.

12 g/kg/day ÷ 1.44 = 8.3 mg/kg/minute.

Close monitoring of glucose tolerance is essential; it is recommended not to exceed a glucose supply of 12 mg/kg/minute (17.3g/kg/day) as excessive glucose can result in hyperglycemia, liver steatosis and increased triglyceride levels (see monitoring section). Higher concentrations of glucose are associated with better weight gain but may cause hyperglycemia. If the hyperglycemia is complicated by dehydration secondary to an osmotic diuresis, reduce the GIR to the minimum and monitor glucosuria before considering insulin.

Lipids: lipids are an essential part of PN, they are energy dense and help preserve maximum protein utilisation. Lipids, given as intravenous lipids emulsions (ILEs), contain free fatty acids, triglycerides, and glycerol. Lipids yield weight for weight more than twice the number of calories compared with glucose and protein. Fat alone yields 9kcal/g, however in 20% solutions the glycerol content in the ILE increases the energy content to 10kcal/g.

Essential fatty acids (EFA) are necessary for normal brain development and brain cell differentiation. EFA deficiency can occur in as little as 3 days in preterm infants who do not receive sufficient lipids. This is particularly important and time-critical in preterm infants where the brain mass doubles in size from 20 weeks gestation to term. Starting lipids on day one is safe and lipids should be increased to a maximum of 3–4g/kg/day in the preterm and term newborn (see Table 4).

Historically, there have been concerns linking ILEs with sepsis, however, the evidence is mixed. Overall, the nutritional benefit of giving lipid outweigh the potential concerns, and there is insufficient evidence to support withholding lipids when treating for sepsis or critical illness. Careful monitoring of serum triglycerides can help determine tolerance of lipid infusions (see monitoring section).

First generation ILEs contained only soya bean oil (SO), second generation ILEs introduced additional olive oil or medium chain triglycerides (MCT) and the latest generation ILEs also contain fish oil.

Practical tips:

Intravenous lipid emulsions (ILEs) vary in composition.

Intralipid 20%: soybean oil (100%). Can be used in short-term PN.

Lipofundin 20%: soybean oil (50%) and medium-chain triglycerides –MCT (50%). Can be used in short-term PN.

SMOF lipid 20%: soybean oil (30%), MCT (30%), olive oil (25%) and fish oil (15%). For long-term PN and infants with extensive GI malformations/surgery.

Omegaven 10%: fish oil (100%). Reserved for short-term or intermittent use in liver cholestasis and IFALD.

PN dependency of more than 60 days is associated with intestinal failure associated liver disease (IFALD). This was historically known as parenteral nutrition associated liver disease (PNALD). ILEs play a role in this process; soybean oil contains pro-inflammatory phytosterols which may contribute to liver dysfunction. There is evidence that a pure soybean based ILE is more likely to promote liver cholestasis. Composite ILEs which contain less soya bean oil are recommended as first choice over pure soybean oil ILEs, and close monitoring of conjugated bilirubin levels is required.

Carnitine: carnitine is an important component of lipid metabolism, as it facilitates the transportation of long-chain fatty acids into mitochondria. Carnitine is found in breast milk and infant formulas, but not in PN. It is suggested to screen for carnitine and consider carnitine supplementation in patients receiving PN for more than 4 weeks.

Vitamins: vitamins are essential micronutrients for energy and protein metabolism and for growth and development. There is limited evidence on the daily requirements of vitamins that are required. Fat soluble Vitamins (A, D, E and K) are at risk of being deficient in preterm and low birth weight infants due to insufficient fat stores and deficiency in transport proteins.

Vitamin A is important for vison, epithelial cells including the respiratory tract and overall growth and development. Vitamin D has a major role in calcium and phosphate regulation and plays a crucial role in bone health. Vitamin E is a powerful antioxidant and Vitamin K plays a major role in coagulation pathways. Essential roles in various functions played by water soluble vitamins (B, C, folic acid) are also recognised. It is considered safe and appropriate to provide vitamins in PN daily, from day one.

Practical tips:

Some micronutrients are photo-sensitive, hence it is recommended to cover PN bags and use validated light-protected tubing.

In divided PN preparations (i.e. lipids separate from aqueous solution) vitamins preparations are typically added to ILEs, and trace elements are added to the aqueous component. This improves micronutrient stability.

In babies requiring long-term PN, careful monitoring of iron status (FBC, ferritin) is required, and where possible, enteral supplementation should be attempted before considering parenteral iron infusions.

Trace elements (particularly copper and manganese) can be toxic if cholestasis is present — avoid or decrease dose.

Iron and trace elements: iron is an essential micronutrient required to prevent anemia and iron deficiency and deficiency is associated with impaired neurological development. Iron is not routinely added to PN due to an increased risk of sepsis and iron overload. Usually iron is started in oral form after 3 weeks and once enteral feeds have been established.

Important trace elements are zinc, copper, iodine, selenium, manganese, molybdenum and chromium. These elements are important in enzymatic activity, antioxidant properties and essential for metabolism.

Fluids and electrolytes: incremental intravenous fluid is given during the first few days of life for preterm and term infants. The rationale for incremental increase is to allow for initial post-natal diuresis and weight loss, and adaption of immature renal function. Therefore, in the first few days the volume of fluid to prescribe PN is limited by whether the diuresis has started and if fluids can be increased. Once the total fluid intake (TFI) can be increased, incrementally escalate the TFI up to 150–180 mL/kg reaching a steady state of PN fluid to deliver the necessary macro and micronutrients.

Important electrolytes while prescribing PN are sodium, potassium, calcium, phosphate, and magnesium. For post-natal diuresis to occur, sodium and potassium intake is limited initially. Once diuresis starts, sodium and potassium can be started. It is important to note that electrolytes are essential for energy metabolism, and prolonged limited electrolyte supply alongside increasing macronutrient provision in the PN can result in electrolyte deficiencies (increasingly referred to as "neonatal refeeding syndrome").

Practical tips:

Weight, urine output, fluid balance can be monitored daily to assess PN fluid volume. Loss of weight, urine output >4ml/kg/hr in preterm and > 2ml/kg/hr in term and a negative balance suggests an incremental increase in fluid is required.

If chloride levels are high; acetate salts can be used such as sodium acetate instead of sodium chloride.

Preterm infants can be at risk of renal tubule immaturity and can become sodium depleted quickly which can result in poor growth. Hence, early supplementation of sodium when diuresis starts and aiming for normal serum sodium levels is essential. Chloride intake runs in parallel with sodium; excess administration of chloride can result in metabolic acidosis.

Calcium, phosphate, and magnesium are required for bone health and early calcium and phosphates are needed for bone mineral accretion.

Standardised vs. individualised PN

PN solutions can be made bespoke each day for each individual or can be standardised solutions. In most instances, the benefits of standardised PN outweigh the benefits of individualised PN. These benefits are highlighted by the 2010 PN audit by National Confidential Enquiry into Patient Outcome and Death (NCEPOD). Individualised PN was associated with more delays in initiating PN, inconsistencies in prescribing and increased risk of prescribing errors. Standardised PN can also reduce financial cost as the bags are often mass-produced and have a longer shelf-life compared to customised bags. Despite these advantages in standardised PN, some neonates with complex requirements will still require individualised PN prescriptions.

Monitoring

Monitoring of biochemical and anthropometric parameters is essential to ensure that PN is tolerated and is providing optimal nutritional support and growth. Some parameters may need to be monitored more frequently during times of intolerance or critical illness e.g. serum glucose may be tested 3–4 hourly for infants experiencing hypo/hyperglycemia.

Practical tips:

Suggested monitoring frequency of electrolytes, biochemistry, trace elements and growth parameters.

Frequency	Parameter
Daily until stable, then at least weekly	Body weight. Serum urea, creatinine, sodium, potassium, calcium, phosphate, magnesium, glucose, triglycerides.
Weekly	Body length, head circumference. Liver function tests (including conjugated bilirubin), Urinary sodium (GI stoma patients).
Monthly	Serum trace elements (zinc, selenium, copper, manganese), ferritin, vitamin D.

Intravenous access

Where possible, administer PN through a central venous catheter (CVC). PN can be infused peripherally, however this is associated with increased risk of extravasation and phlebitis due to the

acidic and hypertonic nature of PN. Additionally, it is widely recommended that the glucose concentration and osmolarity of peripheral PN cannot exceed 12.5% and 900 mOsm/L respectively, which will compromise nutrient provision.

In the NICU, peripherally inserted central catheters (PICC) are routinely used and generally preferred to tunneled surgical central lines (e.g. Broviac central catheter), due to limited positional sites and the need for sedation and ventilation at insertion. Surgical central lines are commonly reserved for infants with poor peripheral access. It is not recommended to infuse PN with other infusions in the same lumen, and interrupting PN infusions for other infusions increases the risk of infection and hypoglycemia. Ideally use double or triple lumen catheters, as one lumen can be dedicated to PN.

Complications of PN

Infection: infants receiving PN are at risk of central line associated bloodstream infections (CLABSI). Regular screening of clinical status (e.g. temperature, respiration), and biochemical parameters (e.g. CRP, FBC) is warranted and any changes should first be considered as potential CLABSI until proven otherwise. Prompt identification of the microorganism is essential to help narrow antibiotic therapy (for the benefit of antibiotic stewardship) and to determine whether the CVC should be removed. Units should have guidelines in place to standardise care of CVC lines.

CVC occlusion: occlusions can occur due to thrombosis, mechanical issues, or precipitation of PN. The latter is typically due to PN being infused with other medications, hence the importance of one lumen dedicated to PN. Medications should not be routinely added to PN, and fibrinolytic blocks are recommended when lumens are not in use to help prevent thrombosis.

Liver cholestasis: most cases of liver cholestasis seen with long term PN are reversible. The pathogenesis of IFALD (described earlier in lipid section) is not fully understood but is considered multi-factorial with PN as one of the associations. Underlying diagnosis, sepsis, surgery, medication, malnutrition, and the absence of enteral feeding can all contribute to the development of IFALD.

The management of liver cholestasis includes starting and maintaining trophic EN, avoiding glucose intakes >12mg/kg/minute, ursodeoxycholic acid, using reduced dose of composite ILE dose while ensuring enough EFA delivery and short-term use of pure fish oil ILEs and consider cyclical PN in infants >4kg. Cycling PN involves gradually reducing the PN infusion time from 24 to 12–18 hours each day. This is dependent on enteral intake and the infant's ability to maintain normal serum glucose levels when off PN.

Metabolic bone disease: preterm infants are already at increased risk of osteopenia, and PN is a compounding factor. Regular monitoring of relevant biochemical analysis (calcium, phosphate, magnesium, alkaline phosphatase and vitamin D) and urinalysis is recommended with supplementation of electrolytes and vitamin D if required.

Transitioning from PN to EN

While titrating PN down and increasing milk feeds, an energy and protein-deficit state often occurs, as the same volume of enteral nutrition usually has less calories than the same volume of PN solution.

If possible, we suggest that total fluid intake should be increased to 180 ml/kg/day; this should allow for maximum energy and calorie provision. At the bedside, aqueous PN is titrated down milliliter for milliliter as enteral feed is advanced; lipid infusions are titrated by the PN prescribers to provide a daily sequential stepdown of lipids as aqueous PN is reduced.

Enteral nutrition

Enteral feeding on the NICU has multiple advantages; the promotion of gastrointestinal motility, mucosal structure, function, and enzymatic activity as well as decreasing the occurrence of sepsis related to bacterial translocation and liver cholestasis.

Minimal enteral nutrition

Minimal enteral nutrition (MEN) also called trophic feeding is defined as small volumes of milk $\leq$ 24 ml/kg/day. The main purpose of MEN is to stimulate and provide nutrition to the gut mucosa and is not intended to contribute substantially to nutrition. MEN should be started in all infants on day one, but this will depend on the underlying diagnosis, general clinical state of the infant and whether breast milk is available. If enteral feeding is not possible in the first few days after delivery, colostrum to provide mouth care is suggested. Trophic feeds are usually given every 2 hours in preterm infants and every 3 hours in term infants.

Feeding route

Preterm infants (typically less that 32–33 weeks gestation) and critically ill infants will require an orogastric or nasogastric tube. Bolus feeding via gravity at a frequency of every 2–3 hours (depending on the size and gestation of the infant) is considered optimal. Compared with continuous feeds, bolus feeding is associated with bowel opening and bile duct contraction resulting in improved feed tolerance and weight gain. Continuous feeding may be useful in some neonates e.g. post gut resection, severe gastro-oesophageal reflux disease (GORD) and high output stomas. Infants receiving jejunal feeding require continuous feeding due to reduced luminal capacity of the jejunum.

Rate to advance feeds

A large multi-center RCT (The Speed of Increasing milk Feeds SIFT trial) showed no significant difference in survival or NEC rates when comparing slow advancement of feeding (18mL/kg/day) with faster advancement (30mL/kg/day). However, infants fed in faster increments reached full milk feeds earlier at 7 days, compared with 10 days in the slower increment groups. This can impact length of dependency on PN and length of stay. Extremely premature and low birth weight infants may not tolerate faster increments.

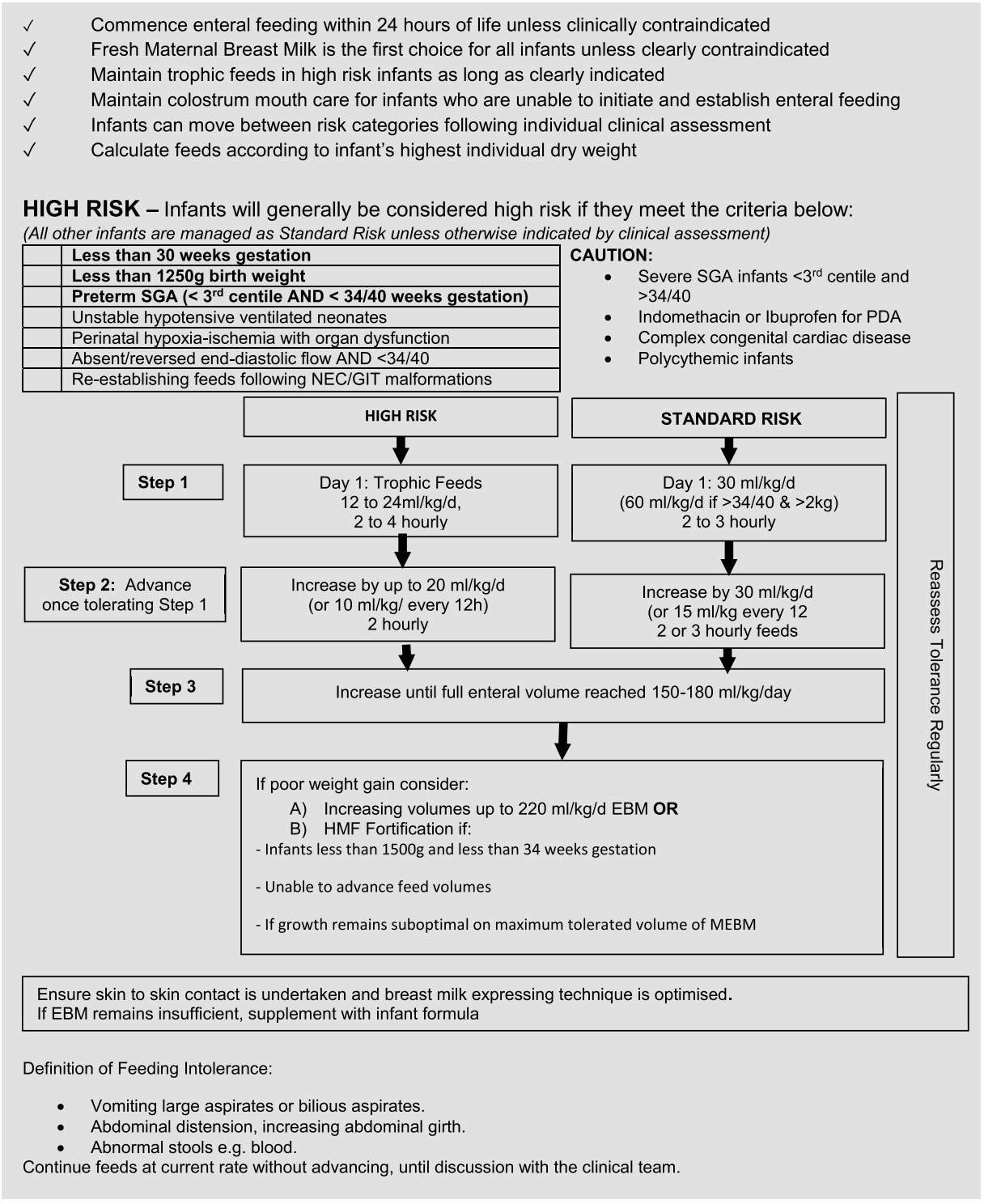

Figure 1 Initiating and advancing enteral feeds algorithm. Adapted from East of England Clinical Guidelines – Feeding of preterm infants on neonatal unit. http://www.nnuh.nhs.uk/publication/download/enteral-feeding-of-preterm-infants-regional-network-document/

The feeding algorithm shown in Figure 1 is a modification of the original East of England Neonatal Network guideline, which has now been adopted in several areas of the UK.

Breast milk

Human breast milk or maternal expressed breast milk (MEBM) remains the gold standard and the first choice of milk for all infants, including preterm infants. The benefits of breast milk are well known; reduced risk of NEC, sepsis, retinopathy of prematurity, hospital readmission and improved neurodevelopmental outcome. However, there is a nutritional shortfall in breast milk compared with preterm formula milks i.e. less energy, protein, and sodium. This shortfall is significant especially in VLBW and ELBW infants due to their higher calorie requirements; they are unable to get adequate nutrition for optimum growth on mature breast milk alone. Fortification of breast milk with human milk fortifier is therefore recommended in this population. Preterm neonates fed formula milk achieve greater weight gain than those receiving breast milk alone. Although breast fed preterm infants seem to grow at lower centiles there is some evidence that their long-term outcomes may be better.

Human milk fortification (HMF): there is no consensus on when to add breast milk fortifier. Some units wait until full feeds, others start adding when enteral feeds are around 50ml/kg/day. Multicomponent bovine-based HMF, which contains a blend of macronutrients and micronutrients typically increases the average energy density of breastmilk from 0.7 kcal/mL to 0.8 kcal/mL and protein from 1.3 g per 100ml, to 2.3 g per 100mL. Some NICU's may have access to breastmilk analysers, allowing fortification by adjusting individual nutrients. Human milk based multicomponent HMF is also increasing in popularity and availability globally, due to the accumulating evidence for exclusive human milk diets in the prevention of NEC and early mortality. However, it comes at significant financial cost, which will likely limit its accessibility for many babies.

HMF should be considered in the following infants while on MEBM.

- Birthweight <1500g and <34 weeks' gestation.
- Fluid restrictions secondary to significant concerns regarding fluid overload e.g. cardiac abnormality, chronic lung disease (CLD).
- If growth remains suboptimal despite maximal tolerated volume of MEBM (see "Anthropometric parameters" section).

Donor breast milk: donor breast milk (DBM) processed in milk banks is usually provided by mothers of term infants with excess milk. Studies have shown that DBM reduces NEC rates but has worse short-term growth outcomes. In preterm babies at high risk of NEC without available MEBM, DBM is a good choice of milk feed. However, DBM has a lower calorie and protein count compared with MEBM. Many units use DBM with breast milk fortifiers because exclusive DBM feeding without fortification will result in a nutritional shortfall. When breast milk fortifiers are added to DBM, growth appears to improve. Access to DBM is variable as milk banks are not present in every country.

Formula feeds

There are several types of formula feeds used in the NICU and in the immediate post NICU discharge period: preterm formula/low birth weight formula, post discharge preterm formula, standard term formula, high energy term formula, extensively hydrolysed (with or without and MCT), amino acid based and disease specific e.g. renal and metabolic conditions. It is important for clinicians and dietitians working in the NICU to have a sound overview of the milk choices available.

When breast milk is unavailable the first choice for a preterm neonate under 1700g, is a low birth weight formula, and as weight increases to 1800–2000g and/or at discharge, this can be changed to a post-discharge preterm formula.

At around 40 weeks' corrected gestational age, a term high energy formula may be useful in infants who have a restricted fluid intake despite a high calorie requirement e.g. cardiac conditions or babies with chronic lung disease. Extensively hydrolysed formulas may be used when intolerance to cow's milk protein is suspected; milks containing MCT oil with low osmolality, are preferred for infants post gastrointestinal surgery. Use amino acid-based formulas in infants who do not tolerate extensively hydrolysed formulas.

Probiotics

Probiotics are bacteria that are considered favourable in the human gut microbiome. Probiotics have been demonstrated to help prevent NEC, sepsis and reduce mortality rates. Multiple studies have been conducted to try and determine the optimal strains and doses to be given to premature infants. While some RCTs have shown promising results, this has yet to be translated into strong results through meta-analysis.

An ESPGHAN working group has produced a weak conditional recommendation for the use of *L.rhamnosus GG* or a mix of *B.infantis, B.lactis* and *Str.thermophilus* to reduce NEC rates in preterm infants.

Monitoring

Frequent and accurate anthropometric measurements of weight, length and head circumference are essential for monitoring growth and for early detection of malnutrition. Preterm infants should be weighed daily until growth is established, then twice weekly. Term infants can be weighed twice weekly. Weekly length and head circumference measurements are recommended for all infants.

It is also important that relevant growth charts are used for infants, depending on their gestation and diagnosis. Preterm growth charts revised by Fenton and colleagues in 2013, can be used for infants born < 37 weeks gestation. Once 50 weeks gestation is reached, the WHO growth standards (2006) charts can be used for preterm infants and term infants from birth. There are a limited number of validated growth charts for specific genetic disorders (e.g. trisomy 21) that should be used once these infants have a corrected age of 40 weeks.

The aim of optimal nutritional support is for appropriate growth, but opinions can vary on what optimal growth is. As well as following growth chart trends, the following approximated intrauterine growth rates can be used:

- Corrected <33 weeks' gestation: 15–22 g/kg/day
- Corrected 33–37 weeks' gestation: 10–15 g/kg/day

- Corrected >37 weeks' gestation or term: 25–35 g/day

If growth is suboptimal, causes related to increased nutritional requirements (e.g. cardiac abnormalities, CLD) or increased losses (vomiting, high stoma output) should be investigated, and attempts to increase nutrient provision made. This should be done gradually and incrementally with input from a specialist dietitian to reduce the risk of overfeeding and worsening of symptoms.

Feed tolerance

Careful and routine clinical assessment of feed tolerance is essential to prevent unnecessary restrictions of enteral feeds. Gastric residual volumes and colour of gastric aspirates may indicate a certain level of gut maturity, however they should not be used solely to limit enteral feed advancements.

Preterm infants have immature gut motility, so a degree of gastric aspirates, emesis and gastroesophageal reflux is common. These symptoms should resolve over time as the infant matures, and the urge to intervene with feed manipulation and/or medication should be limited unless there are significant complications associated with the episodes (e.g. aspiration, respiratory tract infections, and profound apneas). Bilious aspirates/vomiting are abnormal and may indicate gut obstruction which requires further assessment and surgical review.

Summary

There is increased awareness and acknowledgment that long term neurodevelopmental outcome of neonates is dependent on good nutrition. Each neonatal unit must have a robust and intensive detail orientated approach to monitoring nutrition and growth. Ensuring that excellent nutrition provision and demanding that appropriate growth is an essential part in everyday decision making and management plan of every infant on the NICU, will yield the best neonatal outcomes. ◆

FURTHER READING

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