Parenteral Nutrition in Very Low Birth Weight Infants in the United Kingdom and Ireland

Abstract:

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Abstract
Parenteral Nutrition (PN) plays an important role in providing nutrients for infants unable to tolerate enteral feeds. The aim of this study was to look at PN prescribing in neonatal units in the United Kingdom (UK) and Ireland, in particular in infants <1.5kg. A postal questionnaire was administered to the 235 neonatal units. The response rate was 179 (76%), of which 136 (76%) used PN. The initial amount of protein prescribed was 0.1 â 2 g/kg/day in 102 units (91%), >2g/kg/day in 4 (4%) and 5 (5%) used no protein. 88 (80%) started lipids with the first PN prescription. Only 5 units (5%) started with >1g/kg/day. The maximum dose of lipids and protein both varied from 2 â >4 g/kg/day. The initial glucose infusion rate was 4 â 8 mg/kg/min. Interestingly only 44% of units started PN in the first 24 hours of age. Hence results show great variation in PN prescribing.

Introduction
Parenteral Nutrition (PN) plays an important role in the provision of nutrients essential for growth and development for infants unable to tolerate feeds by the enteral route. In particular for very low birth weight (VLBW) infants who have poor energy reserves. The use of PN has been shown to improve the survival rates for these infants. [1,2] However, difficulty exists in trying to imitate the intrauterine growth rates and many VLBW infants continue to experience growth restriction. [3] Evidence suggests that nutrition in early life in low birth weight infants (LBW) contributes to their growth and neurodevelopmental outcomes. [4-7] Hence sub-optimal nutrition in the first few weeks of life is a significant risk factor for short and long-term morbidity including short stature and later behavioural and cognitive disorders. [8] There have been concerns regarding the safety of the early introduction of PN, especially the early use of lipids in LBW infants. Previous studies have shown an increase in plasma lipid concentrations in LBW infants receiving lipids, likely due to a reduced clearance rate. [9] Potential adverse effects include increased vascular resistance, bilirubin toxicity, chronic lung disease and sepsis. [1,10] Concerns exist for infants receiving a high intake of protein, associated risks include metabolic acidosis, elevated ammonia levels and an increased future risk of obesity and diabetes. [11]

Recently more aggressive nutritional regimens for PN have been recommended. Research has shown that early, aggressive treatment in VLBW infants leads to improved growth and a reduced risk of nutritional deficiencies at 40 weeks postmenstrual age. [12] The goal is to start very early with protein (within hours of birth) and to advance to a maximum of 4 g/kg/day. [13] Studies have shown that this is not only safe but can lead to a positive nitrogen balance and protein accretion. [5,14-18] The early use of lipids continues to be more controversial. The early use of lipids cannot be recommended in preventing morbidity and mortality in preterm infants. [10] However lipids are important for brain development and if not given within a few days of life can cause deficiencies of essential fatty acids. Recent guidelines recommend the early use of lipid (0.5-1.0g/kg/day within 24-30 hours of life [3], no later than the third day of life [18]) and a maximum dose of 4g/kg/day. [13,19] Despite these recommendations variation in the prescribing of PN continues to exist. Therefore the aim of this study was to look at the current practice of PN prescribing in neonatal units in the United Kingdom (UK) and Ireland, and in particular to determine the amount of amino acids, lipids and glucose prescribed in preterm infants < 1.5kg.

Methods
A postal questionnaire was sent to one Consultant Neonatologist/Paediatrician from each of the 235 neonatal units in the United Kingdom and Ireland as per the 2008 Directory of Critical Care (UK and Northern Ireland) and the Irish Medical Directory 2006-2007 (Republic of Ireland). The questionnaire was distributed in May and June 2008. A deadline for completion and return of the questionnaire was given after which non-responders were contacted by one of the authors and the questionnaire completed via telephone (by a Consultant/Registrar). Units who did not use PN were excluded. The questionnaire was multiple choice format, with the option to write another answer if more appropriate for the unitâ s practice. Requested information included how the PN was prescribed, who was responsible for prescribing and whether the unit had any policy / guidelines to aid its prescription. This was followed by questions regarding the use of PN in infants less than 24 hours of life and in addition the doses of amino acids, lipids and glucose prescribed in infants < 1.5kg. Further information sought included the monitoring of infants on PN and the action taken in relation to sepsis and hyperglycaemia. Data was analysed using PC based StatsDirect software (v.2.6.1).

Results
Questionnaires were completed by 179 of the 235 units giving a response rate of 76%. Of these, 136 respondents (76%) reported the use of PN in their unit. The responsibility for prescribing was in 98% (134) of units with a doctor. A pharmacist, dietician or nurse practitioner (ANNP) assisted in 31% (42) units. 82% (112) had a protocol available to assist PN prescribing. The preferred method of prescribing was the paper â based system with only 9% (12) having an electronic PC system. In the majority of units (61%) the PN is made in their own hospital. Only 21% (28) of respondents reported the ability to order PN at weekends. Less than half (44%) stated that PN is commenced in the first 24 hours of life (Table 1).

Amino acids
95% of units commenced amino acids in the initial PN prescription. The starting dose of amino acids was between 0.1-2g/kg/day in 91% of units. 4% reported a starting dose of >2g/kg/day and 5% did not use any protein in the first PN prescription. The maximum dose of protein varied widely from 2 - >4 g/kg/day. Interestingly, 24% (33 respondents) were unsure of the maximum dose used. The preferred daily increase in the dose of amino acids was 0.5-1g/kg/day (60% respondents). 24% (33 respondents) were unsure or gave no reply. 23% of units (30) did not perform any blood tests to monitor amino acid intake. Of the units who did, the most frequent test used was blood urea, performed in 76% (100) units. 5 units (4%) performed amino acid profiles (Table 2).

Lipids
Lipids were started in the first PN prescription in 80% of units. The majority of respondents stated a starting dose of between 0.1-1g/kg/day. 5 units used a higher initial dose of >1g/kg/day. In 81% of units the dose of lipids was increased daily by 0.5-1g/kg/day. 18% (24 respondents) were unsure of the exact daily increase. As with amino acids, the maximum dose of lipids varied from 2 - >4g/kg/day. (Table 3) The most common blood test performed to monitor infants on lipids was triglyceride levels, 59% (77) of units. 42% (55) however did not perform any blood monitoring. Great variation existed in the action taken if infants receiving lipids became septic. 31% (39 units) discontinued the lipids, 47% (60 units) continued at the same rate and 18% (22 units) reduced the lipid dose. In the remaining units the action varied and sometimes a combination of the above was used.

Glucose
The initial glucose infusion rate ranged from 4-8 mg/kg/min. There was great variation in the frequency of blood glucose monitoring with a range of 2-24 hourly. The most common frequency reported was 4-6 hourly (31%), followed by >6-8 hourly (18%). A number of respondents stated that the blood glucose was checked whenever a blood gas was performed. If the blood glucose of an infant on PN was rising the level at which action was taken in order to reduce it varied from 10 to 15 mmol/l. Action taken included the prescription of insulin, reduction of the glucose infusion dose or both. Respondents who used insulin on their unit stated various indications for its commencement e.g. the presence of glycosuria or three consecutively elevated glucose levels.

Discussion

The results of our study show that variation in PN prescribing still exists between neonatal units in the UK and Ireland. What is surprising is that only 44% of units commence PN in the first 24 hours of life despite the current recommendation of early, aggressive nutritional regimens in VLBW infants.[3,13] 79% of respondents also stated that they were unable to order PN at weekends. Hans et al carried out a survey of nutritional practices in the neonatal intensive care units in North America in 2006.[20] In their study 55% of units used PN in the first 24 hours of life, compared to 44% in our study. 46% in their study used an electronic system to order PN but in ours the paper based system remained the method of choice (91% units). Recent studies have shown that the electronic method of prescribing is more accurate and effective.[13,21] One study revealed that nearly half of the medical errors that occurred with the paper based method could have been prevented with an electronic system.[22] The electronic method has also been shown to improve both the nutrient content of the PN solution and the early postnatal outcome.[21] The range for the maximum dose of amino acids prescribed in infants <1.5 kg of 2-4g/kg/day was similar in both studies. Hence some units are using a dose lower than the 3g/kg/day needed to produce protein accretion.3 76% of units measured blood urea nitrogen (BUN) as part of the monitoring of amino acid intake. However research looking at BUN as a marker of amino acid intolerance in infants less than 1250g showed that there was no correlation between the amino acid intake and BUN concentration in these infants.[23]

Our study revealed great variation in the amount of lipid prescribed in VLBW infants. Not all units commenced lipids in the first PN prescription even though evidence exists to show that omission can lead to fatty acid deficiency within a few days of life in these premature infants.[13] The maximum dose also varied with a range of 2 - >4g/kg/day. 42% of units did not perform any blood monitoring of lipids. Recent guidelines recommend the monitoring of serum/plasma triglycerides for those receiving lipids, in particular those at risk of hyperlipidaemia e.g. extremely low birth weight infants or those with sepsis.[13] There was no consensus between units on what action should be taken if an infant on lipids became septic. This may reflect the lack of published data in this area and the need to vary the action depending on the individual infantâ s case. Our study showed that the initial glucose infusion rate of 4-8mg/kg/min used by all units complied with that stated in recent recommendations.[13] There was no agreement however between the units on the frequency of blood sugar monitoring. A large range existed of 2-24 hourly. Not all units used insulin to treat hyperglycaemia.

The response rate for our study was good at 76%, however there are limitations. The results of the questionnaire can only show what respondents aim to prescribe. We have no way of knowing what is actually prescribed. Also, the PN prescribed for extremely low birth weight infants may differ from that prescribed for VLBW infants however this was not addressed in our study. In conclusion, discrepancy exists between neonatal units with regards to the doses of PN prescribed in VLBW infants. Less than 50% of units commence PN in the first 24 hours of life despite the recognized morbidity with sub optimal nutrition. The starting dose of amino acids seems to be more â semi-aggressiveâ in most units and the maximum dose varies widely from a possible suboptimal dose on one hand to a possible detrimentally high dose on the other. The maximum dose of lipids is also variable. In accordance with current guidelines we would recommend that in VLBW infants PN is started within the first 24 hours of life with at least 1.5g/kg/day of amino acids. Our study also highlights the need for further studies to determine a consensus on the doses of amino acids and lipids required to give optimal growth and development in these VLBW infants.

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