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Original Article

Effect of a neonatal standard aqueous parenteral nutrition formulation on aseptic unit capacity planning☆,☆☆

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SUMMARY

Background & Aims: The manufacture of parenteral nutrition (PN) by pharmacy aseptic units in the UK requires a stated capacity plan. Standard PN formulations maximise manufacturing capacity but reduce the flexibility. The unique nutritional needs of preterm infants leads to frequent individualised PN prescription. We evaluated the effect of the neonatal standard aqueous PN (SaqPN) formulation on aseptic unit capacity planning by: - measuring SaqPN usage during routine neonatal prescribing practice – identifying factors that continued to require individualised PN prescription.
Methods: A 2-year prospective audit collected demographic, biochemical and diagnostic details from patient records. PN prescription information was collected from pharmacy records.
Results: A total of 145 infants, median (range) gestation 28 (23–40) weeks and birth weight 1100 (480–4040) g received 2157 days of parenteral nutrition. The standard aqueous PN formulation was used on 2016 (93%) parenteral nutrition days. Individualised aqueous PN prescriptions were required in 22 infants median (range) gestation 26 (23–36) and birthweight 730 (480–3700) g for period of 3 (1–42) days. The proportion of individualised prescriptions increased with decreasing birthweight, reached 18% in the 500–750 g birthweight group and usually resulted from recognised complications of prematurity.
Conclusions: Most neonates can be managed with this standard aqueous PN formulation. Pharmacy aseptic units' neonatal PN manufacturing capacity can be increased using this standard formulation.

1. Introduction

Mandatory standards developed for safe aseptic dispensing for NHS patients[1,2] have had a major impact on pharmacy aseptic units throughout the UK. Aseptic dispensing, aseptic preparation and aseptic manufacture are terms that relate to prescriptions used within 24 h, within 7 days and beyond 7 days respectively. In order to provide an aseptic manufacturing service, a Manufacturers Specials Licence is required from the Department of Health and the pharmacy aseptic unit is subject to Medical and Healthcare products Regulatory Agency (MHRA) audit. These units must have a stated capacity plan in order to maintain their manufacturers licence. This ensures that the activity level of the unit does not exceed the point at which quality and safety standards would be compromised whatever the clinical demand.

In teaching hospitals and other large centres with multiple tertiary specialties the workload of aseptic units is complex and increasing. However, clinical demand must be managed within the stated capacity plan. This has particular implications for the manufacture of parenteral nutrition (PN) bags. Individual PN prescription requires a bag to be manufactured from it's basic components. This requires more resources than prescription of a standard PN formulation[3,4] that is batch manufactured (but allows some additional electrolyte supplementation). The PN manufacturing capacity of an aseptic unit can effectively be increased by increasing the proportion of standard PN bag presciptions.

The neonatal intensive care unit (NICU) population is dominated by extremely preterm infants many of whom require prolonged PN. The need for growth combined with the heterogeneity and clinical instability of this population frequently requires individualised PN prescription.[5,6] Indeed, early studies demonstrated better patient

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outcomes with individualised compared to standard PN regimes.[7] The introduction of aseptic unit capacity planning necessitates an urgent review of the role of individualised versus standard PN formulations in the NICU population.

The need for individualised neonatal PN prescription is largely driven by rapid and frequent changes in fluid and electrolyte requirements rather than nutritional considerations. Thus, the formulation of the aqueous PN component is critical to any standard neonatal PN regimen. Typical neonatal PN protocols allow for a gradual introduction of the aqueous nutritional components (protein and glucose) over the first 3–7 days.[8] More recent evidence indicates that more rapid introduction of protein is well tolerated[9,10] confirming that glucose is the only aqueous nutritional component likely to lead to metabolic disturbance.[8] The design of a standard neonatal aqueous PN formulation needs to focus on electrolyte and glucose content.

We developed a standard aqueous PN (SaqPN) formulation to replace individualised aqueous PN (IaqPN) bag prescriptions whenever daily neonatal PN fluid, electrolyte and metabolic requirements. We introduced and evaluated this formulation with the following aims:

1. To measure standard and individualised aqPN bag usage while maintaining the same neonatal PN prescribing protocol
2. To identify the type of infant who continued to need the IaqPN formulation
3. To calculate the effects of SaqPN usage on aseptic unit capacity planning.

2. Methods

A standard aqueous PN (SaqPN) formulation was developed by the Royal Free Hospital pharmacy aseptic unit (Table 1). The composition is based on recommended requirements,[11] local neonatal network experience[12] and our own data. Although described as "standard", an SaqPN bag can be supplemented with certain electrolytes up to a maximum shown in Table 1. Although electrolytes can be added, the unsupplemented SaqPN bag still has to be useable in most patients to allow PN to be started out side normal working hours. Thus our SaqPN formulation contains electrolytes at the low end of the range of normal neonatal requirements. This compromise between being usable but flexible was designed to optimise use of the SaqPN formulation in clinical practice. The SaqPN has advantages for aseptic unit capacity planning because the capacity plan allows for the manufacture of 2 SaqPN bags for 1 IaqPN bag. This is based on time saved by bulk manufacture of SaqPN bags (improving stock control) and the much shorter time taken to modify the SaqPN bag with electrolyte supplements when compared to complete IaqPN bag manufacture from original components.

IaqPN bags are still required when one or more of the components required are outside the figure or range given in Table 1 (eg a glucose concentration other than 15 g per 150 ml or potassium concentration outside the range 2.0–6.8 mmol per 150 ml). The decision to use an IaqPN bag was made by the pharmacy aseptic unit when the daily neonatal PN prescription has been completed by the neonatal medical team.

A prospective audit of aqueous PN prescription was performed on the Royal Free Hospital NICU April 2000–April 2002 following the introduction of the SaqPN formulation. The lipid PN component is effectively already a standard formulation, does not affect fluid and electrolyte prescription and administration and was not studied. The audit compares SaqPN usage against the previous standard (100% neonatal aqueous PN bags prescribed and administered as IaqPN). The NICU PN protocol (that includes regular biochemical and growth monitoring[11]) was used to prescribe daily PN requirements and remained unchanged following the introduction of the SaqPN formulation. The medical teams were unaware that SaqPN had been introduced. Pharmacy provided SaqPN bags where the daily prescription allowed. Where electrolyte (or glucose) requirements were outside the range achievable with SaqPN, IaqPN was provided. The neonatal PN protocol introduces PN within 24 h of birth in all infants unlikely to tolerate enteral feeding. SaqPN is introduced at 60 ml kg^{-1} day^{-1} on day 1, increasing by 30 ml kg^{-1} day^{-1} until the maximum rate of 150 ml kg^{-1} day^{-1} is reached on day 4. This rate of increase may vary according the needs of the individual patient. The maximum protein and glucose intake are achieved at 150 ml kg^{-1} day^{-1}(Table 1). Glucose intake is modified by adjusting total fluid volume or (if infants fluid balance requirements do not allow this) by modifying dextrose concentration. The latter requires IaqPN. Hyperglycaemia is managed with insulin according to a sliding scale protocol. Lipid is administered in a separate infusion starting at 0.5 g/kg/day and increasing by 0.5 g increments until a maximum of 3 g/kg/day is reached (15 ml/kg/day). The intravenous lipid infusion rate is not altered with changing fluid balance and therefore unaffected by the introduction of SaqPN bags.

Data were collected from the individual patients daily PN prescription charts. Where IaqPN prescription was required, the reasons for IaqPN prescription were obtained from the patient record including biochemical results. The PN prescription did not change with the introduction of the SaqPN formulation.

3. Results

During the study period, a total of 145 infants, median (range) gestation 28 (23–40) weeks and birth weight 1100 (480–4040) g received 2157 days of PN. The median (range) duration of PN for each infant was 20 (2–95) days. The SaqPN formulation was used on 2016 (93%) PN days. The duration of PN for individual patients increased with decreasing birthweight (Table 2). The median of 6 PN days for infants of >1500 g suggested a need to review prescribing practice in this group.

Table 1
Concentration of standard aqueous parenteral nutrition (SaqPN) components per 150 ml and the maximum supplementation of electrolytes within SaqPN regimen.

Component	Standard	Maximum
Glucose (g)	15	–
Amino acids (g)	2.8	–
Non-protein calories (kcal)	89	–
Sodium (mmol)	2.25	12.0
Potassium (mmol)	2.0	6.8
Calcium (mmol)	0.9	1.8
Magnesium (mmol)	0.15	
Phosphate (mmol))	1.13	1.9

Table 2
Birth weight and individualised aqueous parenteral nutrition (IaqPN) requirements.

Birthweight (g)	N	Total PN days	Total PN days median (range)	IaqPN days (%)
<500	5	125	23 (9–53)	5 (4)
501–750	26	574	19 (4–73)	103 (18)
751–1000	30	504	14 (2–44)	25 (5)
1001–1250	38	444	12 (3–30)	5 (1)
1251–1500	17	174	9 (3–24)	0
>1500	29	336	6 (3–95)	3 (1)
Total	145	2157	20 (2–95)	141 (7)