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Concentrated parenteral nutrition solutions and central venous catheter complications in preterm infants

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ABSTRACT

Standardised, concentrated neonatal parenteral nutrition (PN) regimens can overcome early nutritional deficits in very preterm infants. A PN regimen with increased macronutrient content (standardised, concentrated, added macronutrients parenteral (SCAMP)) has been shown to improve early head growth in a randomised controlled trial. Line complications including late onset sepsis were secondary outcomes of this study. Infants were started on standardised, concentrated PN at birth and randomised at 2–5 days to either switch to SCAMP or remain on control PN. Central venous catheter (CVC), blood culture (BC) and inflammatory marker data were collected for the 28-day intervention period. 150 infants were randomised with mean (SD) birth weight (g) of 900 (158) versus 884 (183) in SCAMP (n=74) and control (n=76) groups, respectively. There were no differences in CVC use/type or duration or in positive/negative BC with/without associated C reactive protein rise in SCAMP versus control groups. Increasing the macronutrient content of a standardised, concentrated neonatal PN regimen does not increase CVC complication rates.

Trial registration number ISRCTN 76597892.

BACKGROUND

Early postnatal growth failure is well recognised in very preterm infants (VPIs) and is associated with early nutritional deficits. This period of suboptimal nutrition coincides with the period of parenteral nutrition (PN) dependency. We have shown that protein and energy intakes in the first 2 weeks of life can be increased using a standardised, concentrated PN regimen.[1] Other observational studies using a similar approach have provided further evidence for growth benefits.[2] We have reported improved head growth[1] in a randomised controlled trial (RCT) that compared a control, standardised, concentrated PN regimen with one where macronutrient content had been increased (the standardised, concentrated, added macronutrients parenteral (SCAMP) nutrition regimen). A recent RCT in VPI investigated the growth benefits for increased protein/energy intake in the first few days of life but was stopped because of a higher incidence of late onset sepsis (LOS) in the intervention group.[3] There are few data from the preterm population describing central venous catheter (CVC) complication rates with concentrated PN. It is not known whether increasing osmolality and lipid/glucose content to SCAMP regimen levels reduces the duration of line life or increases sepsis rates due to CVC occlusion, thrombophlebitis and infection. We aimed to compare line life and infection rates during first 28 days of life in VPI randomised to receive SCAMP nutrition or the original standardised, concentrated PN regimen (control).

METHODS

The study (ISRCTN: 76597892) received ethical and regulatory approval and is described in detail with the published primary outcome.[1] Eligible infants were born <29 weeks of gestation, weighed <1200 g and were admitted to the Neonatal Intensive Care Unit at Liverpool Women's Hospital (LWH) within 48 h of birth. This was a single centre, parallel group, RCT with blinding of caregivers, parents and outcome assessors. For patient safety reasons, the dispensing pharmacist was not blinded. Randomisation was required within 120 h.

The control regimen comprised the standardised, concentrated neonatal PN regimen used in current clinical practice (10% glucose, 2.8 g/kg/day protein/lipid) with an estimated osmolality of 855 mosmol/L water (aqueous bag 1120 mosmol/L water). All study infants received the control PN regimen as soon after birth as possible. After parental consent, VPIs (birth weight <1200 g; gestation <29 weeks) were randomised to either start SCAMP or continue receiving the control regimen. The SCAMP regimen (12% glucose, 3.8 g/kg/day protein/lipid) had an estimated osmolality of 1025 mosmol/L water (aqueous bag 1270 mosmol/L water). The regimens have been described in detail previously.[1] There were no differences in the micronutrients, vitamins or electrolytes provided by the two regimens.

All infants received clinical care in accordance with LWH PN protocols including fluid management, introducing, increasing and stopping enteral feeds, biochemical monitoring, insulin-treated hyperglycaemia, hypertriglyceridaemia and the monitoring, investigation and treatment of LOS. Double lumen umbilical venous catheters (UVCs) are the CVC of choice at birth and to be used for 14 days maximum. They are replaced with a percutaneous CVC (PCVC) should the infants remain PN dependent. PN via peripheral cannulae is avoided if possible (and then for no more than 24 h). The study intervention continued until 28 completed days of life. PN was discontinued once enteral feeds exceeded 75% total. The transition from PN to enteral feeds has been described previously[1] and involved the preferential use of expressed or donor breast milk, which remained unfortified until 150 mL/kg/day enteral feeds.

Patient data were collected from the electronic patient record. Daily nutritional intake and estimated mean daily osmolality from PN infusion

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data were collected for days 1–28 along with blood culture (BC) and inflammatory marker data. LOS was defined as a positive BC after 72 h of postnatal age. A LOS-related C reactive protein (CRP) rise was defined as >20 mmol/L in the 24 h before BC or 48 h after BC. Daily CVC data (type, location and reason for removal) were recorded. Data analysis was performed in 28-day survivors. The study was powered according to the primary outcome (early head growth) with CVC complications as a planned secondary outcome analysis.

RESULTS

One hundred and fifty infants were randomised with mean (SD) birth weight (g) and gestation (weeks): 900 (158) versus 884 (183) and 26.8 (1.3) versus 26.6 (1.4) in SCAMP (n=74) and control (n=76) groups, respectively. The incidence of early onset sepsis (<72 h) was 6% in SCAMP versus 3% control infants. Randomisation occurred at a median (IQR) postnatal age of 70 (46–94) versus 67 (47–93) h in SCAMP and control groups, respectively. There were 1243 CVC days (489 UVC; 697 PCVC; 57 other) in the SCAMP group and 1255 CVC days (545 UVC; 605 PCVC; 105 other) in the control group. The survival curves for UVC and PCVC are compared in figure 1 with no differences in line duration identified between the groups. There were no differences in positive or negative BC with or without associated CRP rise when comparing SCAMP and control groups (table 1). The CVC-associated infection rate was 18.5 of 1000 and 23.9 of 1000 CVC days in SCAMP and control groups, respectively. The majority of positive BCs were coagulase negative staphylococcus (CoNS). The number of non-CoNS cultures was similar in both groups, although there was a preponderance of infants with Gram-negative organisms in the SCAMP group and Gram-positive organisms in the control group (table 1).

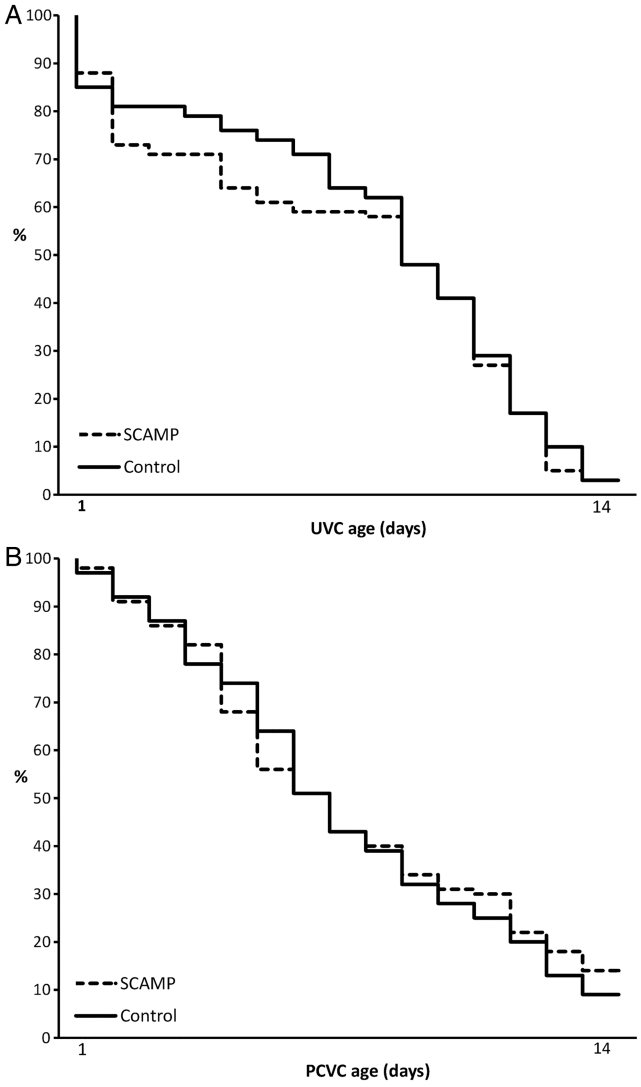

Figure 1 Survival curves for the duration of central venous catheter placement in days and stratified according to line type: (A) umbilical venous catheter (UVC) or (B) percutaneous central venous catheter (PCVC). SCAMP, standardised, concentrated, added macronutrients parenteral.

DISCUSSION

Our study found that increasing the macronutrient content and osmolality of a standardised, concentrated neonatal PN regimen did not affect line usage or line life. This suggests that the difference in osmolality between SCAMP and control regimens is insufficient to affect factors likely to influence line life such as thrombophlebitis, catheter occlusion or CVC-LOS associated with neonatal PN. Recent RCT evidence indicates that where PN infused via a *peripheral* venous cannula in paediatric clinical practice, 1000 mOsm/L is an important threshold associated with increased complication rates.[4] Our data provide reassurance that a similar threshold does not exist for neonatal PN via a CVC.

Table 1 Comparison between standardised, concentrated, added macronutrients parenteral (SCAMP) and control groups (28-day survivors): blood cultures (BCs), BC with C reactive protein (CRP) rise and central venous catheter (CVC)-related BC organisms

Criteria	SCAMP (n=66)	Control (n=69)	SCAMP (n=66)	Control (n=69)	p Value
BCs	**Number of cultures**		**Number of infants**		
All	110	129	53 (80%)	61 (88%)	0.24
All negative	81	89	48 (73%)	53 (77%)	0.69
All positive	29	40	20 (30%)	29 (42%)	0.21
All CVC-related positive	23	30	17 (26%)	24 (35%)	0.27
BC with CRP rise	**Number of BC with CRP rise**		**Number of infants**		
Negative BC	19	20	17 (26%)	16 (23%)	0.84
Positive BC	13	24	11 (17%)	19 (28%)	0.15
All CVC-related positive BC	11	22	10 (15%)	18 (26%)	0.14
Organisms (CVC related)	**Number of cultures**		**Number of infants**		
CoNS	14	22	11 (17%)	19 (28%)	0.15
All non-CoNS bacterial	7	9	6 (9%)	9 (13%)	0.59
Staphylococcus aureus	2	6	2	6	
Other Gram positive	0	2	0	2	
Escherichia coli	4	0	3	0	
Other Gram negative	1	1	1	1	
Candida	2	0	1	0	

The p values result from comparisons of number of infants with at least one BC meeting the criteria described in the first column.
CoNS, coagulase negative staphylococcus.

The study did not find any clinically or statistically significant differences in bacteraemia between the groups. Establishing true rates of neonatal LOS using routine clinical and laboratory markers of infection has important limitations and is a weakness of this study. However, by comparing total BC rates (performing a BC indicates clinical signs to suggest that infection is present), all positive BC and CVC-related BC together with associated raised inflammatory markers (plasma CRP levels), the risk of failing to identify a difference in LOS due to false-positive or false-negative BC is reduced. The uneven distribution of Gram-negative and Gram-positive non-CoNS organisms in our study was difficult to interpret, given the small numbers involved.

Hyperglycaemia[5] and intravenous lipid[6] have both been associated with an increased risk of neonatal infection. However, routine biochemical monitoring and PN management protocols limit metabolic complications resulting from increased intravenous glucose or lipid intake. Moltu *et al*[3] speculated that immunosuppression due to hypophosphataemia in the first few days of life may have contributed to the increased VPI infection rates associated with enhanced early macronutrient intake. Our PN protocol includes standardised supplementary electrolyte infusions to allow rapid correction of electrolyte derangements. Moltu's study achieved much higher macronutrient intakes in the first week of life than our study and the statistically significantly lower birth weight in the intervention group makes the findings of this shortened study difficult to interpret.

CONCLUSION

Increasing the osmolality and macronutrient content of a standardised, concentrated neonatal PN regimen in one arm of an RCT was not associated with increased CVC complication rates.

Contributors TW developed the secondary outcome analysis plan, collated data and performed the secondary analysis and helped draft the initial manuscript. CM developed the original concept and designed the study, co-ordinated data analysis and drafted the initial manuscript. PM performed data collection and made study design modifications. MAT was involved in study design, data analysis and all authors approved the final manuscript as submitted.

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Competing interests None.

Patient consent Obtained.

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