

## **Additional File**

This appendix has been provided by the authors to give readers additional information about their work.

**Supplement to: The efficacy and safety of peripheral intravenous parenteral nutrition and lipids vs 10% glucose in preterm infants born 30 to 33 weeks' gestation: a randomised controlled trial.**

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**Supplementary Table 1. Baseline characteristics**

<b>Variable</b>	<b>P-PN (n=42)</b>	<b>Control (n=50)</b>
<b>Maternal</b>		
Caesarean section in labor	9 (21)	5 (10)
Caesarean section, no labor	19 (45)	30 (60)
Antenatal steroids – complete course	19 (45)	22 (44)
<b>Infant characteristics</b>		
<i>Birth order</i>		
Singleton	18 (43)	32 (64)
First of a multiple	9 (21)	11 (22)
Second of a multiple	14 (33)	5 (10)
Third of a multiple	1 (2)	2 (4)
<i>Apgar score</i>		
At 1 minute, median (IQR), (n=41/50)	7 (6 - 9)	7 (6 - 8)
<i>Temperature</i>		
On admission, mean, SD	36.4 (0.5)	36.4 (0.5)
Admission temperature $\leq 36.5^{\circ}\text{C}$	20 (48)	28 (45)
Admission temperature $\geq 36.5^{\circ}\text{C}$ to $\leq 37.4^{\circ}\text{C}$	21 (50)	21 (42)
Admission temperature $> 37.4^{\circ}\text{C}$	1 (2)	1 (2)
<i>Baseline biochemistry</i>		
Blood urea nitrogen, mmol/L, mean (SD) (n=37/42)	4.6 (1.5)	4.5 (1.6)
Albumin, g/L, mean (SD) (n=41/41)	24.6 (3.2)	25.4 (3.0)
Triglyceride, mmol/L, median (IQR) (n=40/42)	0.6 (0.5-0.6)	0.6 (0.4-0.7)
pH, mean (SD) (n=42/47)	7.4 (0.0)	7.4 (0.1)
Base excess, mean (SD) (n=42/47)	-1.8 (1.7)	-2.3 (2.3)
Blood glucose level, mmol/L, mean (SD) (n=42/47)	4.8 (1.1)	4.4 (1.4)

Data are presented as n (%) unless otherwise indicated

**Supplementary Table 2. Parenteral and enteral intake over 21 day study period**

<b>Outcome</b>	<b>P-PN (n=42)</b>	<b>Control (n=50)</b>	<b>Adjusted mean difference<sup>a</sup> (95% CI)</b>	<b>P<sup>a</sup></b>
<b>Week 1</b>				
<b><i>Parenteral</i></b>				
Protein (g/kg/d)	1.1 (0.4)	0.0 (0.1)	1.10 (1.0, 1.2)	<0.0001
Lipid (g/kg/d)	1.1 (0.3)	0.0 (0.2)	1.1 (1.0, 1.2)	<0.0001
Energy (kcal/kg/d) <sup>b</sup>	29.3 (9.5)	18.5 (6.6)	1.6 (1.4, 1.9) <sup>c</sup>	<0.0001
<b><i>Enteral<sup>d</sup></i></b>				
Protein (g/kg/d) (n=41/50)	1.0 (0.5)	1.0 (0.5)	0.0 (-0.2, 0.2)	0.9
Lipid (g/kg/d) (n=41/50)	2.2 (0.9)	2.4 (0.8)	-0.1 (-0.5, 0.2)	0.5
Energy (kcal/kg/d) <sup>b</sup> (n=41/50)	41.2 (16.5)	42.8 (15.1)	0.9 (0.7, 1.2) <sup>c</sup>	0.4
<b>Week 2<sup>e</sup></b>				
<b><i>Enteral<sup>d</sup></i></b>				
Protein (g/kg/d) (n=40/47)	3.3 (0.6)	3.4 (0.5)	-0.1 (-0.3, 0.2)	0.5
Lipid (g/kg/d) (n=40/47)	6.4 (0.9)	6.7 (0.6)	-0.3 (-0.7, 0.0)	0.09
Energy (kcal/kg/d) <sup>b</sup> (n=40/47)	124.5 (16.8)	129.5 (11.7)	1.0 (0.9, 1.0) <sup>c</sup>	0.08
<b>Week 3<sup>f</sup></b>				
<b><i>Enteral intake</i></b>				
Protein (g/kg/d) (n=37/43)	3.6 (0.4)	3.5 (0.5)	0.1 (-0.1, 0.3)	0.3
Lipid (g/kg/d) (n=37/43)	6.7 (1.0)	6.7 (1.0)	0.0 (-0.3, 0.4)	0.9
Energy (kcal/kg/d) (n=37/43)	133.5 (15.2)	132.1 (10.4)	1.0 (1.0, 1.1)	0.7

Data are presented as mean (SD)

<sup>a</sup> Adjusted for sex and gestational age at birth

<sup>b</sup> Log-transformed due to heterogeneous residual variance

<b>Outcome</b>	<b>P-PN (n=42)</b>	<b>Control (n=50)</b>	<b>Adjusted mean difference<sup>a</sup> (95% CI)</b>	<b>P<sup>a</sup></b>
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<sup>c</sup> Effects are ratio of geometric means

<sup>d</sup> Intake data not collected because of transfer to another hospital or discharge home: PPN – Transferred week 1 n=1, week 2 n=1, week 3 n=1; Discharged home week 3 n=2; Control - Transferred week 2 n=2, week 3 n=1; Discharged home week 2 n=1, week 3 n=3;

<sup>e</sup> Data not reported for parenteral intake as 7 infants in P-PN and 6 infants in control had parenteral intake in week 2

<sup>f</sup> No infants had parenteral intake in week 3

**Supplementary Table 3. Clinical outcomes**

Outcome	P-PN (n=42)	Control (n=50)	P-value <sup>a</sup>
	N (%)	N (%)	
Oxygen at discharge home	0 (0.0)	2 (4.0)	0.5
Intraventricular haemorrhage	1 (2.4)	0 (0.0)	0.5
Necrotising enterocolitis	0 (0.0)	1 (2.0)	1.0

<sup>a</sup> Due to low counts, groups compared using Fisher's exact test

**Supplementary Table 4. Peripheral intravenous cannulae**

Outcome	P-PN (n=42)	Control (n=50)	Adjusted effect (95% CI) <sup>a</sup>	P-value <sup>a</sup>
Length of time peripheral IV required (days), mean, SD	5.9 (1.9)	5.7 (1.3)	1.0 (0.9, 1.2) <sup>b</sup>	0.5
Peripheral IV infiltration <sup>c</sup> , n,%	24 (57)	32 (64)	0.8 (0.3, 1.8) <sup>d</sup>	0.5
Peripheral cannula, number required, mean, SD	2.1 (1.1)	2.2 (0.9)	1.1 (0.9, 1.3) <sup>b</sup>	0.3

<sup>a</sup> Adjusted for sex and gestational age at birth

<sup>b</sup> Ratio of means (95% CI)

<sup>c</sup> IV classification stage  $\geq 1$  (Montgomery LA, Hanrahan K, Kottman K et al. Guideline for IV infiltrations in pediatric patients. *Pediatric Nursing*. 1999;25(2):167-180.)

<sup>d</sup> Odds ratio (95% CI)

**Supplementary Table 5. Mean biochemical measures by day of life and overall**

Outcome	Day	P-PN (n=42)		Control (n=50)		P <sup>a</sup> (interaction)	Adjusted mean difference <sup>a</sup> (95% CI)	P <sup>a</sup>
		n	Mean (SD)	n	Mean (SD)			
Blood Urea Nitrogen, mmol/L	2	39	5.3 (1.8)	43	4.0 (2.0)		1.2 (0.7, 1.7)	<0.0001
	4	39	5.4 (1.6)	45	2.6 (1.5)		2.7 (2.1, 3.2)	<0.0001
	7	32	4.7 (2.0)	43	3.6 (1.8)		1.1 (0.2, 2.0)	0.02
	14	27	5.0 (1.3)	36	4.7 (1.6)		0.3 (-0.4, 0.9)	0.5
	21	20	4.1 (1.2)	30	3.7 (1.0)		0.5 (-0.2, 1.3)	0.1
	Overall			5.0 (1.7)		3.7 (1.8)	<0.0001	
Albumin, g/L	2	41	25.1 (3.1)	44	25.9 (3.2)			
	4	41	26.8 (3.8)	45	26.8 (3.1)			
	7	37	27.8 (2.5)	46	27.9 (2.6)			
	14	32	27.6 (1.9)	37	27.5 (2.1)			
	21	24	26.7 (1.7)	33	26.9 (1.9)			
	Overall			26.7 (3.0)		27.0 (2.7)	0.1	0.2 (-0.5, 0.8)
Triglyceride <sup>b</sup> , mmol/L	2	40	1.0 (0.4)	46	0.6 (0.5) <sup>c</sup>		1.7 (1.4, 2.0)	<0.0001
	4	41	1.1 (0.3)	46	0.8 (0.3) <sup>c</sup>		1.4 (1.2, 1.6)	<0.0001
	7	36	1.0 (0.3)	46	1.2 (0.4) <sup>c</sup>		0.9 (0.7, 1.0)	0.02
	14	32	0.7 (0.2)	38	0.8 (0.3) <sup>c</sup>		0.9 (0.8, 1.0)	0.05
	21	24	0.7 (0.3)	33	0.8 (0.3) <sup>c</sup>		0.9 (0.8, 1.1)	0.4
	Overall			0.9 (0.3)		0.9 (0.4) <sup>c</sup>	<0.0001	
pH	2	42	7.4 (0.1)	49	7.4 (0.0)			
	4	41	7.4 (0.0)	48	7.4 (0.0)			
	7	37	7.4 (0.0)	46	7.4 (0.0)			
	14	32	7.4 (0.0)	38	7.4 (0.0)			
	21	27	7.4 (0.0)	33	7.4 (0.0)			
	Overall			7.4 (0.0)		7.4 (0.0)	0.07	-0.0 (-0.0, 0.0)
Base Excess	2	42	-2.1 (2.1)	49	-2.2 (1.7)			

Outcome	Day	P-PN (n=42)		Control (n=50)		P <sup>a</sup> (interaction)	Adjusted mean difference <sup>a</sup> (95% CI)	P <sup>a</sup>
		n	Mean (SD)	n	Mean (SD)			
	4	41	-2.6 (2.2)	48	-2.7 (1.8)			
	7	37	-0.7 (2.0)	46	-1.1 (2.6)			
	14	32	1.6 (1.8)	38	0.9 (2.0)			
	21	27	1.9 (1.7)	33	1.1 (1.8)			
	Overall		-0.7 (2.7)		-1.0 (2.5)	0.4	0.2 (-0.2, 0.7)	0.3
Blood glucose level, mmol/L	2	42	4.4 (1.2)	49	4.6 (1.1)			
	4	42	5.1 (1.0)	48	5.5 (1.4)			
	7	38	5.4 (1.1)	47	5.3 (1.2)			
	14	32	5.3 (1.0)	38	5.3 (0.8)			
	21	27	5.0 (0.8)	33	5.0 (1.1)			
	Overall		5.0 (1.1)		5.1 (1.2)	0.5	-0.0 (-0.3, 0.2)	0.8

<sup>a</sup> adjusted for sex, gestational age at birth and corresponding baseline measure

<sup>b</sup> log-transformed due to heterogeneous residual variance

<sup>c</sup> effects are ratio of geometric means

**Supplementary Table 6. Biochemical measures outside normal clinical parameters<sup>a</sup>**

Outcome	Day	P-PN (n=42)	Control (n=50)	P-value <sup>b</sup>
		N (%)	N (%)	
High blood urea nitrogen (>14.3 mmol/L) <sup>c</sup>	2	0 (0.0)	0 (0.0)	
	4	0 (0.0)	0 (0.0)	
	7	0 (0.0)	0 (0.0)	
	14	0 (0.0)	0 (0.0)	
	21	0 (0.0)	0 (0.0)	
	Overall	0 (0.0)	0 (0.0)	
Low serum albumin (<18 g/L) <sup>c</sup>	2	2 (4.8)	0 (0.0)	
	4	1 (2.4)	0 (0.0)	
	7	0 (0.0)	0 (0.0)	
	14	0 (0.0)	0 (0.0)	
	21	0 (0.0)	0 (0.0)	
	Overall	2 (4.8)	0 (0.0)	
Hypertriglyceridemia (>2.25 mmol/L) <sup>d</sup>	2	1 (2.4)	1 (2.0) <sup>f</sup>	
	4	0 (0.0)	0 (0.0)	
	7	1 (2.4)	1 (2.0) <sup>f</sup>	
	14	0 (0.0)	0 (0.0)	
	21	0 (0.0)	0 (0.0)	
	Overall	2 (4.8)	2 (4.0)	
Hyperglycemia (>8.3 mmol/L) <sup>c</sup>	2	1 (2.4)	0 (0.0)	
	4	0 (0.0)	1 (2.0)	
	7	1 (2.4)	2 (4.0)	
	14	1 (2.4)	0 (0.0)	
	21	0 (0.0)	0 (0.0)	
	Overall	2 (4.8)	3 (6.0)	



<b>Outcome</b>	<b>Day</b>	<b>P-PN (n=42) N (%)</b>	<b>Control (n=50) N (%)</b>	<b>P-value<sup>b</sup></b>
Metabolic acidosis (pH <7.25 and/or Base Excess <-5) <sup>c</sup>	2	3 (7.1)	2 (4.0)	
	4	4 (9.5)	2 (4.0)	
	7	0 (0.0)	3 (6.0)	
	14	0 (0.0)	0 (0.0)	
	21	0 (0.0)	0 (0.0)	
	<b>Overall</b>	<b>7 (16.7)</b>	<b>6 (12.0)</b>	<b>0.6</b>

<sup>a</sup> Only descriptive summary shown due to low counts

<sup>b</sup> from Fisher's exact test

<sup>c</sup> cut-off limits as used in: Osborn DA, Schindler T, Jones LJ, Sinn JKH, Bolisetty S. Higher versus lower amino acid intake in parenteral nutrition for newborn infants. Cochrane Database of Systematic Reviews. 2018; Issue 3. Art. No.: CD005949. DOI: 10.1002/14651858.CD005949.pub2.

<sup>d</sup> limit as used in: Kapoor V, Malviya MN, Soll R. Lipid emulsions for parenterally fed preterm infants. Cochrane Database of Systematic Reviews. 2019; Issue 6. Art. No.: CD013163. DOI: 10.1002/14651858.CD013163.pub2.

<sup>e</sup> no P-value obtained since no participant in the study had a high blood urea nitrogen

<sup>f</sup> Infant did not receive intravenous SMOFlipid