# Supplemental Table 1 Hematological and biochemical parameters on day 7

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Lipid type | Conventional lipid | Conventional lipid | Conventional lipid | Study lipid | Study lipid | P-value  |
| Amino acid and lipid group | Standard amino acids | Standard amino acids plus lipids | High amino acids plus lipids | Standard amino acids plus lipids | High amino acids plus lipids |  |
|  | N = 48 | N = 24 | N = 24 | N = 25 | N = 23 |  |
| Platelet count (\*109/L) | 247.1 ± 127.4 | 225.0 ± 141.4 | 216.9 ± 95.3 | 235.7 ± 124.8 | 254.2 ± 109.4 | 0.866 |
| Glucose (mmol/L) | 5.9 ± 1.6 | 6.0 ± 2.8 | 6.7 ± 2.9 | 6.0 ± 2.1 | 5.8 ± 2.2 | 0.668 |
| pH | 7.29 ± 0.08 | 7.31 ± 0.05 | 7.27 ± 0.06 | 7.29 ± 0.05 | 7.29 ± 0.04 | 0.374 |
| Base excess (mmol/L) | -4.21 ± 2.26 | -2.55 ± 2.46 | -4.41 ± 3.13 | -3.86 ± 2.46 | -3.67 ± 2.27 | 0.117 |
| Bicarbonate (mmol/L) | 22.16 ± 1.99 | 23.53 ± 2.46 | 22.23 ± 2.96 | 22.81 ± 2.85 | 22.59 ± 2.49 | 0.299 |
| Sodium (mmol/L) | 134.8 ± 4.7 | 133.8 ± 4.8 | 133.4 ± 5.1 | 134.5 ± 4.3 | 135.7 ± 4.0 | 0.479 |
| Potassium (mmol/L) | 4.37 ± 0.78 | 4.18 ± 0.71 | 4.07 ± 0.51 | 4.60 ± 0.72 | 4.52 ± 0.74 | 0.084 |
| Urea (mmol/L) | 5.67 ± 2.77 | 6.26 ± 2.11 | 7.65 ± 2.38 | 6.00 ± 1.67  | 7.67 ± 3.17 | 0.018\*\* |
| Triacylglycerol (mmol/L) | 1.82 ± 0.88 | 2.30 ± 1.75 | 1.96 ± 1.49 | 1.91 ± 1.11 | 1.95 ± 0.82 | 0.738 |
| Albumin (g/L) | 30.59 ± 5.24 | 28.13 ± 5.33 | 29.25 ± 3.97 | 29.47 ± 4.39 | 30.25 ± 5.73 | 0.558 |
| Bilirubin, total (µmol/L) | 90 ± 31 | 93 ± 28 | 86 ± 27 | 84 ± 29 | 77 ± 27 | 0.408 |
| Bilirubin, direct (µmol/L) | 3.1 ± 5.1 | 3.8 ± 3.8 | 2.1 ± 2.9 | 1.7 ± 1.2 | 3.1 ± 4.0 | 0.529 |
| ASAT (U/L) | 23.84 ± 11.51 | 24.31 ± 10.50 | 23.68 ± 9.66 | 40.00 ± 31.04 | 29.19 ± 14.50 | 0.016\*\* |
| ALAT (U/L) | 6.00 ± 2.08 | 6.44 ± 2.66 | 7.84 ± 8.37 | 8.67 ± 6.73 | 7.43 ± 3.88 | 0.448 |
| Cholesterol (mmol/L)\* | 2.64 ± 0.79 | 2.83 ± 0.65 | 3.01 ± 0.96 | 3.02 ± 0.62 | 3.17 ± 0.80 | 0.165 |

The conventional lipid was the purely soybean oil lipid emulsion, the study lipid was the multicomponent lipid emulsion.Infants in the standard amino acid group received only glucose and 2.4 g amino acids.kg-1.d-1; parenteral lipids were started from the second day of life onwards. Infants in the standard amino acids plus lipid group received glucose, 2.4 g amino acids.kg-1.d-1, and parenteral lipids from birth onwards. Infants in the high amino acids plus lipid group received glucose, 3.6 g amino acids.kg-1.d-1, and parenteral lipids from birth onwards. Results were partly published in Vlaardingerbroek et al. (J Pediatr 2013; 163(3):638-44.e5).

The data are presented as the means ± SD; the P-values are based on ANOVA.

ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase.

\* Measured on day 4

\*\* ANOVA post-hoc comparison: all P-values > 0.05 between groups.

**Supplemental Table 2 Neonatal outcomes**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Lipid type | Conventional lipid | Conventional lipid | Conventional lipid | Study lipid | Study lipid | P-value  |
| Amino acid and lipid group | Standard amino acids | Standard amino acids plus lipids | High amino acids plus lipids | Standard amino acids plus lipids | High amino acids plus lipids |  |
|  | N = 48 | N = 24 | N = 24 | N = 25 | N = 23 |  |
| PDA, pharmacologically or surgically treated, n (%) | 17 (35%) | 12 (50%) | 11 (46%) | 9 (36%) | 10 (43%) | 0.741 |
| IRDS, n (%) | 36 (75%) | 17 (71%) | 15 (63%) | 21 (84%) | 18 (78%) | 0.514 |
| Mechanical ventilation, days | 9.1 ± 11.4 | 11.9 ± 12.6 | 12.4 ± 12.9 | 8.2 ± 11.7 | 9.0 ± 9.9 | 0.683 |
| BPD, n (%)  | 16 (33%) | 7 (29%) | 9 (38%) | 4 (16%) | 7 (30%) | 0.570 |
| NEC ≥ grade 2, n (%) | 2 (4%) | 2 (8%) | 0 | 2 (8%) | 1 (4%) | 0.659 |
| Late onset sepsis, n (%) | 8 (17%) | 11 (46%) | 9 (38%) | 6 (24%) | 7 (30%) | 0.100 |
| IVH ≥ grade 3, n (%) | 1 (2%) | 0  | 1 (4%) | 2 (8%) | 2 (9%) | 0.455 |
| PVL, n (%) | 1 (2%) | 0 | 0 | 0 | 0 | 1.000 |
| ROP ≥ grade 3, n (%) | 2 (4%) | 0 | 2 (8%) | 0 | 0 | 0.300 |
| Repeated failure on OAE hearing test, n (%) | 3 (6%) | 0 | 2 (8%) | 2 (8%) | 1 (4%) | 0.674 |
| Length of hospital stay, days | 91.0 ± 39.9 | 87.5 ± 28.0 | 100.2 ± 38.1 | 84.4 ± 30.4 | 89.7 ± 22.6 | 0.663 |
| Mortality, n (%) | 5 (10%) | 4 (17%) | 4 (17%) | 6 (24%) | 3 (13%) | 0.651 |

The conventional lipid was the purely soybean oil lipid emulsion, the study lipid was the multicomponent lipid emulsion.Infants in the standard amino acid group received only glucose and 2.4 g amino acids.kg-1.d-1; parenteral lipids were started from the second day of life onwards. Infants in the standard amino acids plus lipid group received glucose, 2.4 g amino acids.kg-1.d-1, and parenteral lipids from birth onwards. Infants in the high amino acids plus lipid group received glucose, 3.6 g amino acids.kg-1.d-1, and parenteral lipids from birth onwards. Results were partly published in Vlaardingerbroek et al. (J Pediatr 2013; 163(3):638-44.e5).

The data are presented as the means ± SD or median (IQR), unless otherwise indicated. The P-values are based on ANOVA or Chi-square, as appropriate.

PDA: patent ductus arteriosus; IRDS: infant respiratory distress syndrome; BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; IVH: intraventricular hemorrhage; PVL: periventricular leukomalacia; ROP: retinopathy of prematurity; OAE: otoacoustic emission.

**Supplemental Table 3 Growth during the hospital stay**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Lipid type | Conventional lipid | Conventional lipid | Conventional lipid | Study lipid | Study lipid | P-value  |
| Amino acid and lipid group | Standard amino acids | Standard amino acids plus lipids | High amino acids plus lipids | Standard amino acids plus lipids | High amino acids plus lipids |  |
|  | N = 48 | N = 24 | N = 24 | N = 25 | N = 23 |  |
| Regain birth weight, d | 8.5 ± 4.2 | 8.9 ± 4.1 | 8.5 ± 5.0 | 7.1 ± 4.2 | 8.5 ± 6.1 | 0.733 |
|  |  |  |  |  |  |  |
| Weight gain, g.kg-1.d-1 |  |  |  |  |  |  |
|  | First 28 days | 13.1 ± 5.7 | 12.7 ± 5.2 | 11.0 ± 4.4 | 14.0 ± 4.1 | 13.6 ± 6.9 | 0.649 |
|  | Discharge\* | 25.8 ± 8.1 | 24.2 ± 5.5 | 24.8 ± 6.6 | 25.9 ± 4.9 | 29.2 ± 7.4 | 0.439 |
|  |  |  |  |  |  |  |  |
| Head circumference gain, mm/wk |  |  |  |  |  |  |
|  | First 28 days | 6.6 ± 3.7 | 6.0 ± 3.2 | 5.6 ± 2.0 | 5.6 ± 2.7 | 6.1 ± 2.9 | 0.419 |
|  | Discharge | 8.3 ± 1.3 | 8.0 ± 1.6 | 8.0 ± 1.1 | 8.3 ± 1.3 | 8.7 ± 1.4 | 0.699 |

The conventional lipid was the purely soybean oil lipid emulsion, the study lipid was the multicomponent lipid emulsion.Infants in the standard amino acid group received only glucose and 2.4 g amino acids.kg-1.d-1; parenteral lipids were started from the second day of life onwards. Infants in the standard amino acids plus lipid group received glucose, 2.4 g amino acids.kg-1.d-1, and parenteral lipids from birth onwards. Infants in the high amino acids plus lipid group received glucose, 3.6 g amino acids.kg-1.d-1, and parenteral lipids from birth onwards. Results were partly published in Vlaardingerbroek et al. (J Pediatr 2013; 163(3):638-44.e5).

The data are presented as the means ± SD; the P-values are based on ANOVA.

\* The growth data were measured until discharge home or postmenstrual age of 40 weeks, whichever event came first.

**Supplemental Table 4 Mean nutritional intake from birth to day 14 of life**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Study group** | **Control group** | **P-value** |
|  | **Total****N = 41** | **Total****N = 41** |  |
| Parenteral glucose intake (mg.kg-1.min-1) | 4.2 ± 0.9 | 4.2 ± 1.1 | 0.713 |
| Parenteral amino acid intake (g.kg-1.d-1) | 1.9 ± 0.4 | 2.0 ± 0.4 | 0.244 |
| Parenteral lipid intake (g.kg-1.d-1) | 1.8 ± 0.4 | 2.1 ± 0.5 | 0.032 |
| Enteral intake (mL.kg-1.d-1) | 55.6 ± 23.7 | 48.9 ± 24.3 | 0.211 |
| Parenteral + enteral non-protein energy intake (kcal.kg-1.d-1) | 89.9 ± 12.8 | 87.8 ± 13.6 | 0.479 |
| Cumulative parenteral lipid load (g/kg) | 25.2 ± 6.4 | 27.6 ± 8.9 | 0.557 |

The data are presented as the means ± SD.

# Supplemental Table 5 Plasma triacylglycerol content

|  |  |  |
| --- | --- | --- |
|  | Day 6 | Day 14 |
| Fatty acid | Study groupN = 10 | Control groupN = 11 | Study groupN = 10 | Control groupN = 11 |
| 10:0 | 0.81 (0.51 – 1.95) | 0.59 (0.28 – 1.20) | 0.77 (0.50 – 1.26) | 0.83 (0.52 – 0.99) |
| 12:0 | 1.19 (0.69 – 3.85) | 1.26 (0.32 – 2.41) | 4.57 (2.36 – 7.64) | 4.00 (3.76 – 5.06) |
| 14:0 | 1.88 (1.69 – 4.71) | 2.29 (0.61 – 5.14) | 5.43 (4.21 – 7.24) | 5.59 (4.15 – 5.79) |
| 16:0 | 18.85 (16.58 – 21.89) | 18.12 (15.58 – 21.33) | 26.42 (23.19 – 28.70) | 26.03 (24.48 – 27.79) |
| 18:0 | 3.60 (2.82 – 4.17) | 3.49 (3.13 – 3.98) | 2.86 (2.39 – 2.97) | 2.76 (2.28 – 3.26) |
| 20:0 | 0.20 (0.15 – 0.26) | 0.20 (0.15 – 0.28) | 0.13 (0.10 – 0.15) | 0.14 (0.08 – 0.21) |
| 22:0 | 0.17 (0.12 – 0.26) | 0.17 (0.14 – 0.22) | 0.11 (0.09 – 0.15) | 0.13 (0.06 – 0.17) |
| 24:0 | 0.07 (0.06 – 0.09) | 0.08 (0.05 – 0.11) | 0.06 (0.04 – 0.09) | 0.08 (0.05 – 0.12) |
| 14:1 | 0.15 (0.10 – 0.23) | 0.11 (0.08 – 0.30) | 0.18 (0.14 – 0.27) | 0.23 (0.17 – 0.28) |
| 18:3n3 | 1.69 (1.19 – 1.93) | 1.97 (0.50 – 3.36) | 1.20 (0.65 – 1.44) | 0.65 (0.48 – 0.74) |
| 20:3n3 | 0 (0 – 0.06) | 0 (0 – 0.04) | 0 (0 – 0) | 0 (0 – 0) |
| 20:5n3 | 1.35 (0.89 – 1.62) | 0.16 (0.10 – 0.18)\* | 0.37 (0.26 – 0.89) | 0.17 (0.13 – 0.27)\* |
| 22:6n3 | 1.85 (1.38 – 2.69) | 0.32 (0.24 – 0.52)\* | 1.03 (0.79 – 1.39) | 0.37 (0.32 – 0.46)\* |
| 18:2n6 | 22.02 (17.44 – 24.02) | 34.37 (20.11 – 43.57) | 12.79 (9.31 – 18.01) | 10.99 (9.63 – 12.86) |
| 18:3n6 | 0.36 (0.26 – 0.53) | 0.46 (0.38 – 0.59) | 0.37 (0.26 – 0.45) | 0.50 (0.43 – 0.63) |
| 20:2n6 | 0.24 (0.21 – 0.27) | 0.39 (0.25 – 0.45)\* | 0.22 (0.19 – 0.31) | 0.24 (0.19 – 0.28) |
| 20:3n6 | 0.62 (0.51 – 0.71) | 0.63 (0.54 – 1.03) | 0.65 (0.52 – 0.73) | 0.66 (0.51 – 0.84) |
| 20:4n6 | 0.92 (0.69 – 1.22) | 1.11 (0.80 – 1.65) | 1.16 (0.95 – 1.42) | 1.12 (0.83 – 1.33) |
| 22:2n6 | 0.10 (0.02 – 0.20) | 0.13 (0.04 – 0.37) | 0.08 (0.02 – 0.14) | 0.07 (0.07 – 0.12) |
| 22:4n6 | 0.27 (0.20 – 0.74) | 0.27 (0.18 – 0.48) | 0.23 (0.19 – 0.44) | 0.23 (0.19 – 0.38) |
| 16:1n7 | 2.62 (2.30 – 4.61) | 1.62 (1.17 – 3.56) | 5.24 (4.02 – 6.17) | 6.38 (5.65 – 9.50) |
| 18:1n7 | 2.03 (1.67 – 2.48) | 1.76 (1.53 – 1.93) | 2.37 (0.44 – 2.80) | 2.72 (2.48 – 2.89) |
| 18:1n9 | 35.27 (28.58 – 36.53) | 29.55 (25.17 – 33.89) | 31.96 (30.27 – 34.88) | 32.99 (29.70 – 40.06) |
| 20:1n9 | 0.30 (0.28 – 0.34) | 0.28 (0.18 – 0.36) | 0.25 (0.22 – 0.27) | 0.25 (0.19 – 0.30) |
| 22:1n9 | 0.03 (0 – 0.28) | 0 (0 – 0) | 0.10 (0 – 0.28) | 0.03 (0 – 0.35) |
| 24:1n9 | 0.02 (0 – 0.23) | 0.03 (0 – 0.18) | 0.17 (0 – 0.31) | 0.15 (0 – 0.25) |

The study group received the multicomponent lipid emulsion, the control group the purely soybean oil lipid emulsion.

The data are presented in mol% as median; interquartile ranges in parentheses.

\* Significant difference (Mann-Whitney U test, P < 0.05) between the study group and the control group.

# Supplemental Table 6 Plasma phospholipid content

|  |  |  |
| --- | --- | --- |
|  | Day 6 | Day 14 |
| Fatty acid | Study groupN = 10 | Control groupN = 11 | Study groupN = 10 | Control groupN = 11 |
| 10:0 | 0.25 (0.09 – 0.58) | 0.57 (0.41 – 0.68) | 0.37 (0.15 – 0.72) | 0.40 (0.11 – 0.83) |
| 12:0 | 0.17 (0.05 – 0.25) | 0.15 (0.10 – 0.23) | 0.14 (0.11 – 0.34) | 0.13 (0.11 – 0.17) |
| 14:0 | 0.41 (0.39 – 0.58) | 0.36 (0.29 – 0.63) | 0.81 (0.52 – 0.92) | 0.89 (0.73 – 1.03) |
| 16:0 | 31.78 ( 30.46 – 33.07) | 30.85 (30.12 – 33.94) | 30.92 (27.68 – 32.06) | 32.36 (31.54 – 32.90) |
| 18:0 | 12.43 (12.01 – 13.62) | 13.37 (12.57 – 14.20) | 12.84 (11.86 – 13.60) | 12.20 (11.69 – 12.61) |
| 20:0 | 0.46 (0.43 – 0.49) | 0.47 (0.39 – 0.56) | 0.56 (0.51 – 0.60) | 0.54 (0.43 – 0.55) |
| 22:0 | 0.66 (0.63 – 0.77) | 0.75 (0.57 – 0.83) | 0.72 (0.62 – 0.75) | 0.67 (0.66 – 0.69) |
| 24:0 | 0.46 (0.42 – 0.54) | 0.44 (0.28 – 0.55) | 0.46 (0.42 – 0.49) | 0.41 (0.40 – 0.44) |
| 14:1 | 0.10 (0.07 – 0.13) | 0.09 (0.08 – 0.11) | 0.09 (0.06 – 0.11) | 0.07 (0.05 – 0.11) |
| 18:3n3 | 0.14 (0.09 – 0.18) | 0.18 (0.08 – 0.21) | 0.13 (0.10 – 0.18) | 0.09 (0.07 – 0.12) |
| 20:3n3 | 0 (0 – 0.05) | 0 (0 – 0) | 0 (0 – 0) | 0 (0 – 0.04) |
| 20:5n3 | 1.41 (1.23 – 1.69) | 0.26 (0.19 – 0.36)\* | 1.04 (0.91 – 1.89) | 0.58 (0.46 – 0.76)\* |
| 22:6n3 | 2.53 (1.98 – 2.83) | 2.14 (2.02 – 2.31) | 2.76 (2.46 – 2.92) | 2.16 (1.78 – 2.19)\* |
| 18:2n6 | 16.75 (14.64 – 17.53) | 21.44 (18.18 – 22.19)\* | 17.51 (16.48 – 18.59) | 15.62 (15.14 – 17.69) |
| 18:3n6 | 0.17 (0.11 – 0.21) | 0.16 (0.11 – 0.22) | 0.24 (0.12 – 0.28) | 0.29 (0.26 – 0.35) |
| 20:2n6 | 0.28 (0.21 – 0.70)\* | 0.43 ( 0.37 – 0.51) | 0.42 (0.32 – 2.55) | 0.43 (0.31 – 0.48) |
| 20:3n6 | 1.65 (1.34 – 1.96) | 1.55 (1.21 – 2.15) | 3.51 (2.76 – 3.66) | 3.47 (2.88 – 4.17) |
| 20:4n6 | 8.12 (7.56 – 9.37) | 9.65 (7.78 – 11.18) | 8.28 (7.13 – 10.87) | 9.68 (9.49 – 9.95) |
| 22:2n6 | 0.06 (0.04 – 0.31) | 0.08 (0.05 – 0.10) | 0.09 (0.06 – 1.47) | 0.07 (0.07 – 0.08) |
| 22:4n6 | 0.27 (0.24 – 0.29) | 0.30 (0.27 – 0.32) | 0.23 (0.22 – 0.25) | 0.26 (0.24 – 0.36) |
| 16:1n7 | 0.81 (0.72 – 1.09) | 0.60 (0.47 – 0.69)\* | 0.94 (0.82 – 1.28) | 1.62 (1.17 – 2.22)\* |
| 18:1n7 | 2.07 (1.95 – 2.46) | 2.23 (1.72 – 2.36) | 2.30 (2.13 – 2.85) | 2.73 (2.45 – 3.02) |
| 18:1n9 | 16.23 (15.92 – 16.89) | 13.81 (12.75 – 14.52)\* | 11.00 (9.21 – 13.21) | 12.53 (10.85 – 13.20) |
| 20:1n9 | 0.18 (0.15 – 0.22) | 0.23 (0.13 – 0.26) | 0.28 (0.21 – 0.36) | 0.24 (0.22 – 0.38) |
| 22:1n9 | 0.06 (0.05 – 0.07) | 0.06 (0.04 – 0.08) | 0.08 (0.06 – 0.12) | 0.10 (0.07 – 0.13) |
| 24:1n9 | 1.88 (1.78 – 2.05) | 1.34 (0.95 – 1.91)\* | 2.24 (2.06 – 2.36) | 1.89 (1.79 – 2.05)\* |

The study group received the multicomponent lipid emulsion, the control group the purely soybean oil lipid emulsion.

The data are presented in mol% as median; interquartile ranges in parentheses.

\* Significant difference (Mann-Whitney U test, P < 0.05) between the study group and the control group.