

Supplementary Online Content

Maas C, Mathes M, Bleeker C, et al. Effect of increased enteral protein intake on growth in human milk–fed preterm infants: a randomized clinical trial. *JAMA Pediatrics*. Published online November 21, 2016. doi:10.1001/jamapediatrics.2016.2681

eTable 1. Fortifier composition

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

eTable 1: Fortifier macronutrient composition per 5 g powder

Component	Commercial fortifier (FM 85, Nestlé)	Study fortifier (10.01.DE.INF, Nestlé)
Energy (kcal)	18	22
Protein equivalent (g)	1	1.8
Fat (g)	0.02	0.87
Carbohydrates (g)	3.3	1.8

eTable 2: Characteristics and growth outcomes of infants < 1000 g at birth

	Lower protein	Higher protein	Mean difference (95% CI)	p-value
Number of infants	6	8		
Birth weight [g] median (IQR)	835 (696-936)	945 (833-980)		
Gestational age [weeks] median (IQR)	29.7 (29.1-30.4)	27.6 (27.1-28.4)		
Female sex n (%)	4 (67)	3 (38)		
Birth weight < 10 th percentile for gestational age n (%)	6 (100)	3 (38)		
Length of intervention period [days] median (IQR)	50 (44-59)	57 (54-62)		p=0.12 [*]
Weight gain from birth to the end of intervention ^{††} [g/kg/d] mean (SD)	18.7 (2.3)	16.7 (1.6)	-2.0 (-4.5,0.5)	p=0.11 ⁺
Weight gain during intervention period ^{††} [g/kg/d] mean (SD)	18.9 (3.0)	17.6 (1.9)	-1.4 (-4.6, 1.8)	p=0.35 ⁺
Lower leg longitudinal growth from birth to the end of intervention ^{††} [mm/week] mean (SD)	4.1 (0.9)	3.6 (0.4)	-0.5 (-1.5, 0.4)	p=0.22 ⁺

* : Wilcoxon test

+ : t-test, two-tailed

†† : mean (SD) of individual means

eTable 3: Biochemical analyses

	Lower protein	Higher protein	p-value
Number of samples first analysis	30	24	
Number of samples second analysis	30	27	
Postnatal age [d] first sample	15 (14-16)	15 (14-17)	
Postnatal age [d] second sample	34 (31-39)	35 (32-41)	
Serum urea [mg/dl] first sample	23.9 (17.7-29.6)	30.6 (22.8-37.6)	p=0.03*
Serum urea [mg/dl] second sample	12.9 (11.4-16.3)	19.2 (15-21.9)	p=0.0008*
Serum cystatin c [mg/l] first sample	1.74 (1.67-1.88)	1.71 (1.58-1.89)	p=0.24*
Serum cystatin c [mg/l] second sample	1.65 (1.59-1.71)	1.59 (1.47-1.68)	p=0.24*
Serum albumin [g/dl] first sample	3 (2.7-3)	3 (2.6-3)	p=0.31*
Serum albumin [g/dl] second sample	2.7 (2.7-3)	2.7 (2.7-3)	p=0.35*

Data given as median (interquartile range)

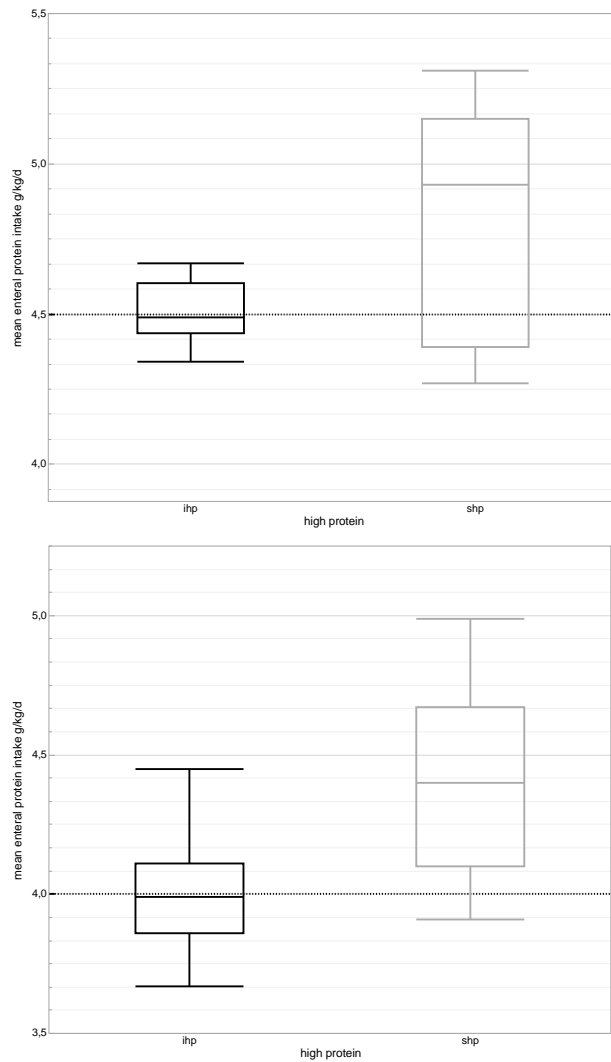
*: Wilcoxon test

eTable 4: Extract of the results of human milk analysis

Week of lactation	Week 2	Week 4	p-value
Protein [g/100 ml] median (range)	1.6 (1.2-2.5)	1.1 (0.9-1.6)	P<0.0001 *
Fat [g/100 ml] median (range)	4.2 (1.9-7.9)	4.3 (2.7-7.1)	p=0.76 *
Energy [kcal/100 ml] median (range)	70 (51-102)	72 (60-95)	p=0.73 *

*: Wilcoxon test

eFigure 1: Mean enteral protein intake during intervention in the high protein group



A Mean enteral protein intake during intervention in the high protein group, Panel **A** in infants weighing < 1500 g and Panel **B** in infants ≥ 1500 g.

ihp: individualized high protein (n=15)

shp: standardized high protein (n=15)

The dotted lines represent targeted protein intakes in individualized supplemented infants. Box-whisker plots are shown, with boxes representing medians and quartiles and whiskers according to the definition of Tukey (extension from the end of the box to the outermost data point that falls within the distance 3rd quartile + 1.5 * (interquartile range) and 1st quartile – 1.5 * (interquartile range)).

Higher variability of protein intake despite individualized supplementation in infants weighing ≥ 1500 g (Panel **B**) compared to infants <1500g is probably caused by temporarily insufficient oral intake after discontinuation of gavage feeding and intermittent cessation of enteral feeds related to inguinal hernia repair.