Clinical Nutrition ESPEN 10 (2015) e234–e241

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Computer-aided nutrition – Effects on nutrition and growth in preterm infants <32 weeks of gestation

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ARTICLE INFO

Article history:
Received 8 May 2014
Accepted 21 September 2015

Keywords:
Infant
Premature
Nutrition
Computer
Growth
Outcome

SUMMARY

Background & aims: Preterm infants are often discharged from the NICU with suboptimal growth. The aim of our intervention study was to determine if a computer-aided nutrition calculation program could help to optimise the nutrition and secondary improve the growth of preterm infants.

Methods: Intake of macro- and micronutrients and anthropometric data was collected in 78 preterm infants with GA ≤32+0 from birth to postnatal week 7. The nutrition of 43 preterm infants was ordinated with help of the program Nutrium™ (IG). Before the introduction of the program 35 consecutive preterm infants served as control group (CG). Their data were collected in retrospect.

Results: Amino acid, carbohydrate, fluid intake and total energy intake were statistically different at all time points. Fatty acid intake was statistically different expect for week 2 and 4. Similar differences were found for magnesium, calcium and phosphorus, zinc, copper and selenium. In contrast vitamin intake was higher in the control group.

At birth there were no differences between the groups with respect to anthropometric data. Weight, length and head circumference (HC) SDS decreased in both groups from birth to day 28 of life (CG −1.2 SDS; −1.2 SDS; −0.8 SDS vs IG −0.9 SDS; −0.8 SDS; −0.4 SDS). The infants in the CG showed until discharge a partial catch-up but remained below birth SDS for weight and length (−0.5 SDS; −0.9 SDS). In the IG, infants reached birth values for weight and length (−0.1 SDS; 0 SDS). For HC both groups showed similar values at the time point for birth and discharge (CG +0.3 SDS vs IG +0.5 SDS).

Conclusion: By using a computer-aided nutrition calculation program better postnatal growth was achieved. Nutritional intake was increased in respect to nearly all micro- and macronutrients. There were no adverse effects. In contrast there was a tendency of decreased incidence of BPD, infection rate and PDA.

1. Introduction

There is a growing body of evidence that under- and malnutrition, as well as poor growth during critical periods of human development, influence health later in life [1]. As preterm infants require intricate nutritional support in order to multiply their weight, as expected, during their hospital stay, they are vulnerable to nutritional deficits. Extrauterine growth restriction is a common problem in neonatal intensive care units (NICU), especially for the sickest infants [2]. Poor growth is linked to short and long term complications including bronchopulmonary dysplasia (BPD) [3,4], retinopathy of prematurity (ROP) [5], poor neurodevelopmental

Abbreviations: AA, amino acids; B, birth; BPD, bronchopulmonary dysplasia; CG, control group; CH, carbohydrates; CPAP, continuous positive airway pressure; D, discharge; DOL, day of life; FA, fatty acids; GA, gestational age; IG, intervention group; IVH, intra ventricular haemorrhage; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; PMA, post-menstrual age; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity; SDS, standard deviation score.

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http://dx.doi.org/10.1016/j.clnesp.2015.09.002

outcomes [6,7], low bone mass later in life [8] and adult diseases such as diabetes, coronary heart disease and premature death [1]. Nutritional guidelines for preterm infants have been published by various societies [9,10] and publishing groups [11,12]. Adherence to these guidelines during the first weeks of life can be both difficult and sometimes contradictory. The prescriber has to take into account the gestational age, weight, chronological age, enteral feeding tolerance, intestinal absorption capacity, different types of enteral formulas and early or mature breast milk and so forth. Although many NICUs calculate nutritional needs manually or by using simple computer programs such as EXCEL™ (Microsoft Corporation, Redmond, USA), more advanced nutrition calculation programs are now available. The program Nutrium™ (Nutrium AB, Umeå, Sweden) gives real-time feedback on the adherence of all macro- and mircronutrients prescribed in respect to existing recommendations. The aim of the present study was to investigate if the use of such a program results in nutritional intake closer to the guidelines stated for preterm infants, and if this may lead to improved growth for the infants.

2. Materials and methods

The study was performed at the Swedish Level II neonatal care unit (NICU) at the Mälar Hospital, Sörmland. Since June 2009 the Nutrium™ software package was used on a daily base to prescribe parenteral and enteral nutrition for infants treated at the NICU. Nutrium™ software is an interactive, multi user, graphical front-end, computer-aided nutrition calculation program written in JAVA (Oracle Inc, California, USA) that runs in every Web browser with encrypted client-server-communication. In general all data were encrypted and stored on the Nutrium™-server. After composing all nutrition products the order was digitally signed and printed out for clinical use. The nurses documented daily in retrospect the received nutrition and fluids in a second form (intake summary). All statistical analyses were based on these intake summaries.

Eligible for inclusion were all infants born at gestational age (GA) less than 32 + 0 weeks. Infants nursed at a different hospital for more than 10 days were excluded. Nutrition and growth data for infants treated before introducing the Nutrium™ software were collected retrospectively from January 2008 to May 2009 and served as a control group (CG). Infants treated at the NICU between June 2009 and December 2010 after the introduction of Nutrium™ served as the intervention group (IG). The overall nutrition strategy was not changed during the study period, implying that all infants were started on parenteral nutrition and received small amounts of enteral nutrition stared on day 1 based on the neonatologist clinical decision. The enteral feeding was started using donated breast milk or preterm formula if donated breast milk was refused by the parents. There were no major changes in nutrition products used during the study period.

Nutrition in the control group was calculated based on schemes for enteral/parenteral nutrition, vitamin and iron supplementation. Fortification of breast milk was based on the neonatologist's decision.

In the intervention group, the nutrition was ordinated using the Nutrium™ software with the primary intention of following recommendations issued by Tsang et al. as closely as possible [11].

Tsang et al. differentiate day of life (DOL)0 (first 24 h), transitional phase (time between DOL0 and the time full enteral feeds are reached) and stable growing phase (time, when full enteral feeds are established). Every phase has different recommendations for enteral and parenteral intake. In addition recommendations differentiate by weight (ELBW < 1000 g and VLBW 1000–1500 g).

The program calculates daily for every nutrient the recommended range based on GA, weight, DOL and the ratio between enteral and parenteral intake. The program displays the ordination in relation to the recommendation in real-time (Fig. 1). The ordination can be adjusted until it conforms with the recommended intake.

Neonatal data including use of antenatal steroids, gestational age, gender, infection, ventilator use, surfactant supplementation, days on CPAP, length of oxygen requirement, use of antibiotics, length of hospitalization, number of transfusions, secondary morbidities such as bronchopulmonary dysplasia (BPD), Retinopathy of prematurity (ROP) (grade III or IV), intra-ventricular haemorrhage (IVH), periventricular leukomalacia (PVL), patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC) (Bell's stage two or three) and nutrition data as days of parenteral nutrition, days needed to regain birth weight and days to enteral toleration of 150 ml/kg/day

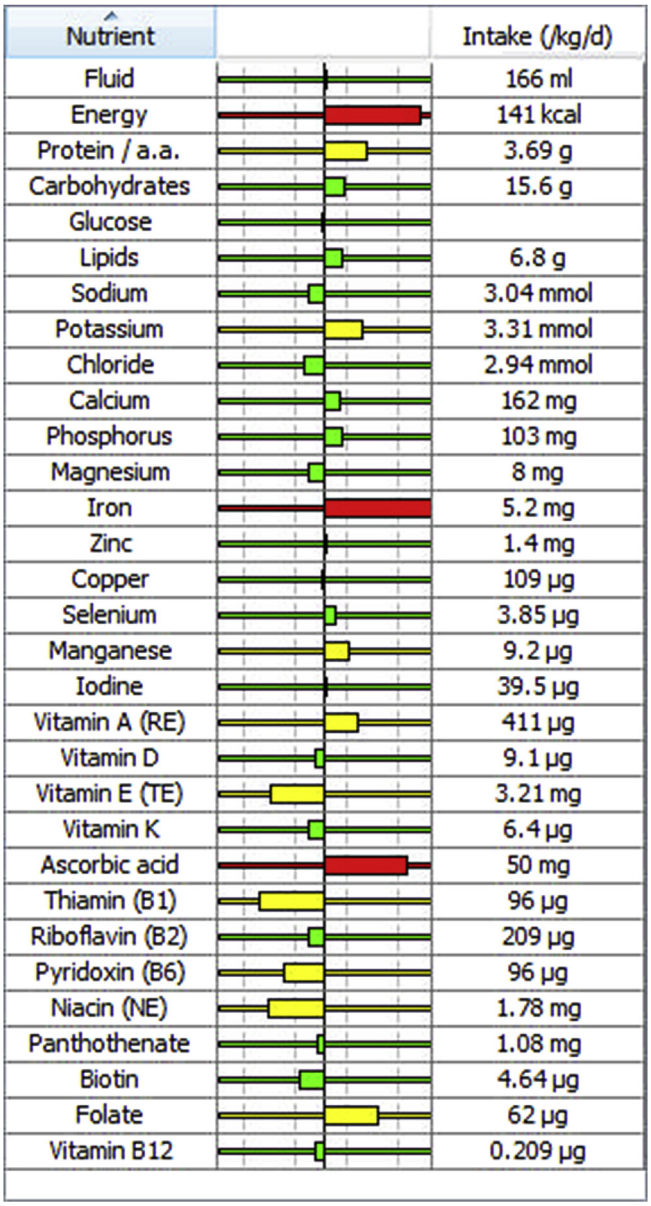

Fig. 1. Graphical feedback displayed by the Nutrium™ software while composing and calculating nutrition. Bars to the left imply less and to right more than recommended. Green means OK, yellow means slightly above/below and red means far outside the recommendations. Used with permission.

Table 1
Patient characteristics for control group and intervention group.

Groups	Control		Intervention		p
n	35		43		
Female gender	13	(37.1%)	16	(37.2%)	
GA (weeks)	29.52	(±2.00)	29.85	(±1.67)	0.44
SGA	11	(31.4%)	7	(16.3%)	0.19
Antenatal steroids	33	(97.1%)	31	(75.6%)	0.03
CPAP (days)	13.66	(±19.12)	15.14	(±20.16)	0.74
Oxygen (days)	18.38	(±32.14)	18.79	(±31.86)	0.96
Surfactant	13	(37.1%)	14	(32.6%)	0.85
Respirator treatment	15	(42.9%)	17	(39.5%)	0.95
Transfusion	1.91	(±2.29)	1	(±1.57)	0.04
Infection	19	(54.3%)	22	(51.2%)	0.96
Antibiotic treatment	22	(62.9%)	33	(76.7%)	0.28
BPD	10	(28.6%)	9	(20.9%)	
ROP	0	(0%)	0	(0%)	
IVH grade >3	0	(0%)	0	(0%)	
NEC	0	(0%)	0	(0%)	
PVL	0	(0%)	0	(0%)	
PDA	8	(23.5%)	7	(16.3%)	
PDA treatment	0	(0%)	4	(9.3%)	

were collected retrospectively from the charts. Differences between groups were analysed by the use of the Wilcoxon rank sum test with continuity correction for numerical values and Chi square test for nominal values.

Daily intake summaries during the first seven weeks of life were recorded using the Nutrium™ software. Macro- and micronutrient data were exported for each infant on a daily basis for the first 49 days of life as total and enteral intake.

Anthropometric measures (weight, length and head circumference) were collected at birth (B), day 28 of life (DOL28), post menstrual age (PMA) of 36 weeks (GA36) and at discharge (D).

Analysis of nutrition data included all macro- and micronutrients per kilogram per day grouped by postnatal weeks for the control and the intervention group. The mean and standard deviation were computed for each group. Differences between the control and the intervention group with respect to nutrition data were compared using the Welch's Two Sample t-test.

All growth data were calculated as standard deviation scores (Z-score) using the growth charts by Niklasson [13]. Differences in growth data were compared between groups at B, DOL28, GA36 and D using the Welch's Two Sample t-test.

P-values <0.05 were considered statistically significant. All calculations were performed using the R-Statistical-Software Version 3.1.2 (A Language and Environment for Statistical Computing, Vienna, Austria).

The study was approved by the regional research ethical committee in Stockholm.

3. Results

For the three year period from January 2008 to December 2010, 78 infants were included, 35 in the CG and 43 in the IG. Antenatal steroids, postnatal patient characteristics and major morbidities are shown in Table 1. In the IG less infants were born SGA (IG 16.3% vs. CG 31.4%, p = 0.19), less mothers were treated with antenatal steroids (75.6% vs. 97.1%, p = 0.03) and infants needed fewer blood transfusions (mean = 1.0 vs. 1.9, p = 0.04). Time of discharge was

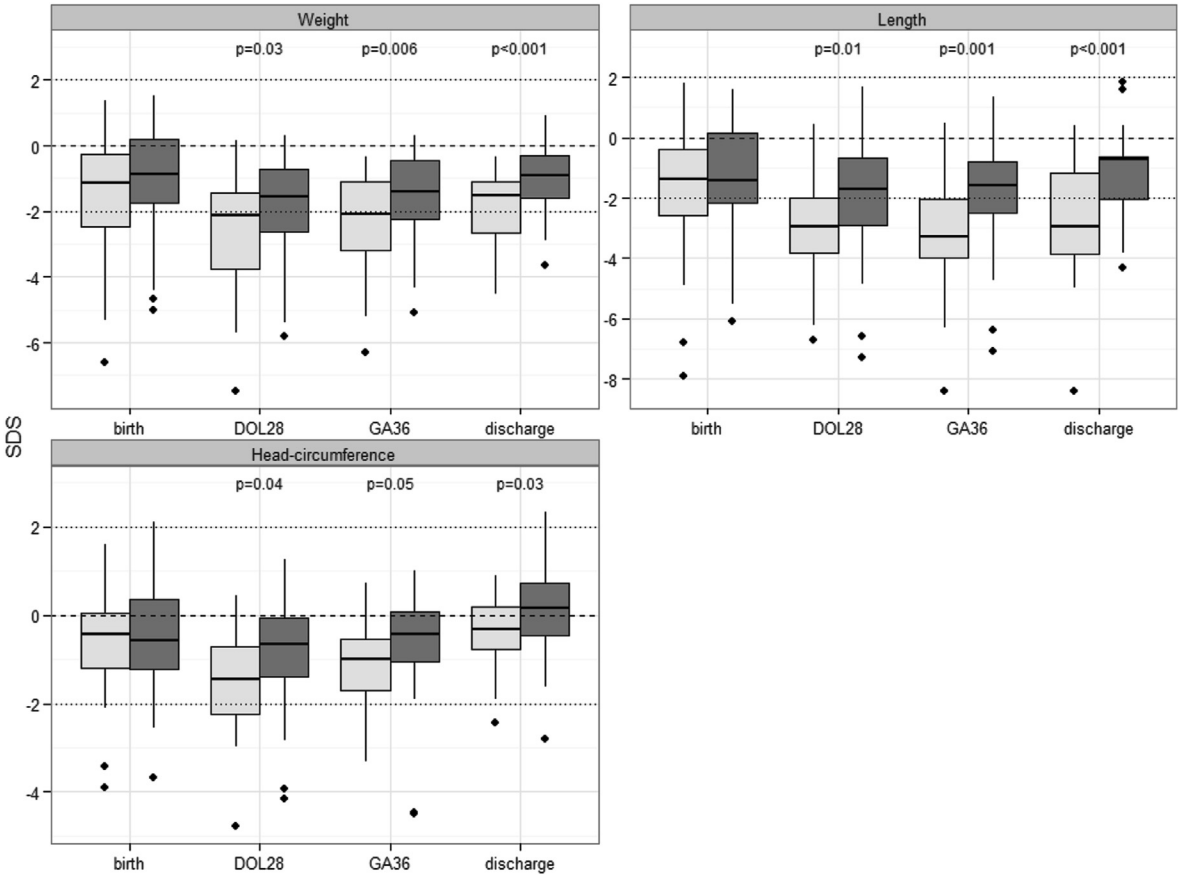

Fig. 2. Postnatal growth. Weight, length and head circumference in both groups (control group = light grey, intervention group = dark grey) shown as SDS. SDS was calculated using the growth charts by Niklasson et al. (DOL28 = day 28 of life, GA 36 = Post menstrual age of 36 + 0 weeks).

not statistically different (IG 41.2 ± 3.3 weeks of gestation vs CG 40.4 ± 2.8, p = 0.4).

There were no differences between the groups in duration of parenteral nutrition (IG 11.8 ± 7.8 days vs CG 10.7 ± 8.2 days, p = 0.57), in days needed to regain birth weight (IG 11.7 ± 5.1 days vs CG 12.2 ± 3.5 days, p = 0.64) and days needed to tolerate 150 ml/kg/day oral intake (IG 11.0 ± 4.8 vs CG 10.9 ± 7.8, p = 0.57). Ten infants in the CG and 26 infants in the IG demonstrated catch-up weight gain to their birth SDS. Catch-up time to birth SDS did not differ between the groups (IG 51.0 days ± 34.4 vs. CG 50.9 days ± 14.7, p = 0.99).

No significant differences in growth parameter-SDS were observed between the groups at B. From B to DOL28, mean weight SDS decreased in both groups but less in the IG. At DOL28 the mean weight in the IG was 0.8 SD higher than in the CG (p = 0.04) and this difference increased to 0.9 SD at D (p = 0.004).

Differences in length were more pronounced. In the IG, mean length SDS decreased from −1.2 SDS at birth to a minimum of −2.0 at DOL28 and increased to −1.2 SDS at time of discharge. In the CG, mean length SDS dropped from −1.8 SDS at birth to −3.0 at DOL28 but did not recover into the normal range at D (−2.7 SDS).

In the IG, mean head circumference SDS showed a drop of 0.4 SD at DOL28 and ultimately an increase from birth (−0.5 SDS) to discharge (+0.1 SDS). In the CG, mean head circumference SDS decreased from −0.4 to −1.4 between B and DOL28, before recovering to −0.4 SDS at D (Fig. 2).

During the first postnatal week, the intake of all macronutrients and the total energy intake were significantly higher in the IG. During week 2–7, the daily intake of amino acids (AA), carbohydrates (CH) and total calories were significantly higher in the IG, while the fatty acids (FA) intake was not significantly different between groups. Infants in the IG received in average 27.4 ml/kg/day more fluids during the first week of life compared to infants in CG. (140.8 ± 37.0 ml vs. 113.5 ± 37.9) (Fig. 3).

The intake of sodium and chloride was slightly lower in the IG compared to CG. The infants in the IG had a higher intake of potassium, calcium, phosphorus and magnesium compared to CG. The infants in the IG received twice as much magnesium as infants in the CG between week two and week five (Fig. 4). In the IG infants received significantly less iron during week two to four but equal amount of iron during week one and week five to seven (Fig. 5). During all seven weeks the infants in the intervention group had a higher intake of zinc, copper and selenium (Fig. 5).

Analysis of the daily vitamin intake showed that infants in the IG had significantly lower intake of vitamins A, D and B1. Both groups had equal amounts of vitamins E, K and C intake (Fig. 6).

After the second week of life, all infants in both groups received more than 89% of their daily intake enterally (week 1: IG 41% vs. CG 46%; week 2: IG 57% vs. CG 83%; week 3: IG 94% vs. CG 89%).

The amount of macronutrients ingested through the enteral route during the first week of life was similar in both groups. However, infants in the intervention group received significantly more amino and fatty acids through the parenteral route (AA: IG 1.76 ± 0.99 g/kg/day vs. CG 0.57 ± 0.67 (p < 0.0001), FA: IG 0.93 ± 0.62 g/kg/day vs. CG 0.33 ± 0.40 (p < 0.0001)). The parental intake of carbohydrates was also higher in the IG compared to the CG (IG 5.69 ± 2.82 g/kg/day vs. CG 4.93 ± 3.03 (p = 0.0002)). Accordingly, the infants in the IG received significantly more total carbohydrates, fatty and amino acids due to an enhanced parenteral intake during the first week of life.

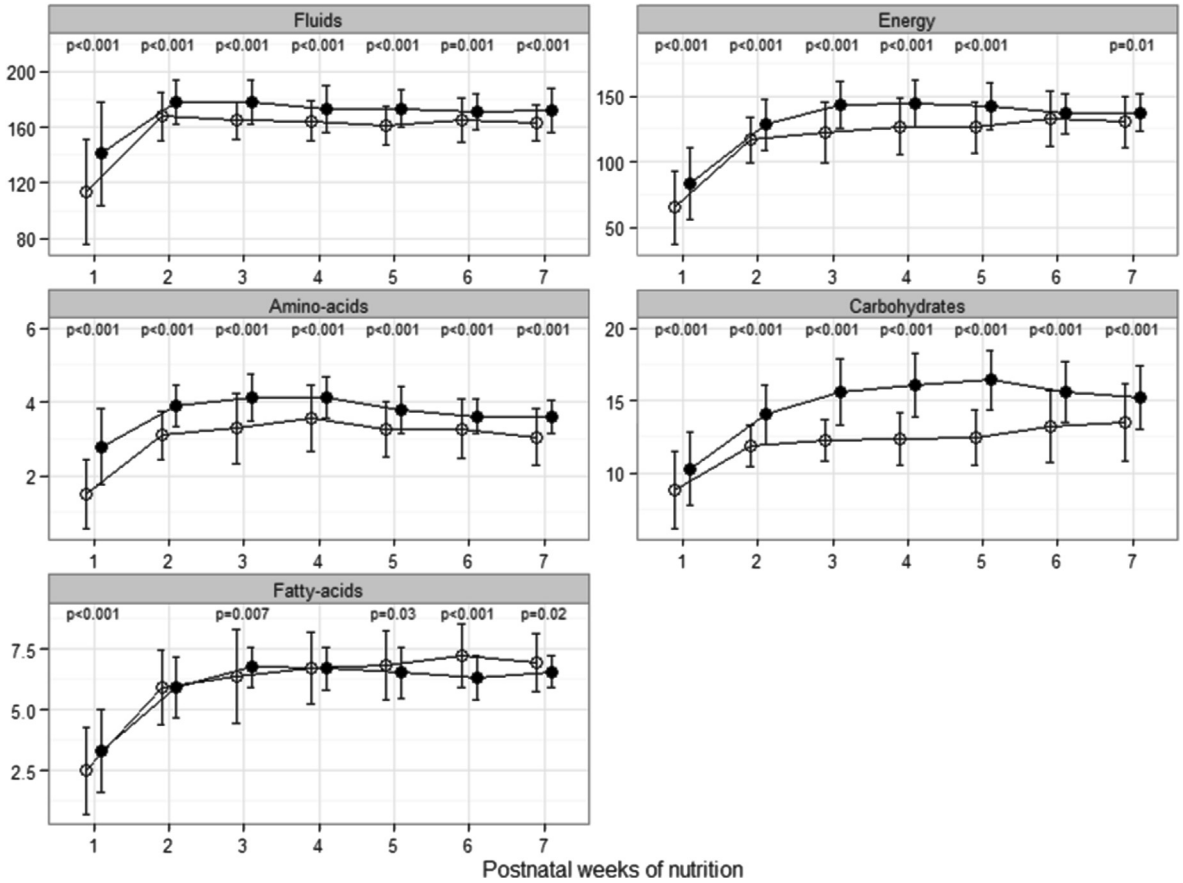

Fig. 3. Macronutrients. Intake of macronutrients during the first seven weeks of life [mean and SD] in control group (transparent dots) and intervention group (black dots). Fluids are shown as ml/kg/day, energy as kcal/kg/day, amino acids, carbohydrates and fatty acids as g/kg/day.

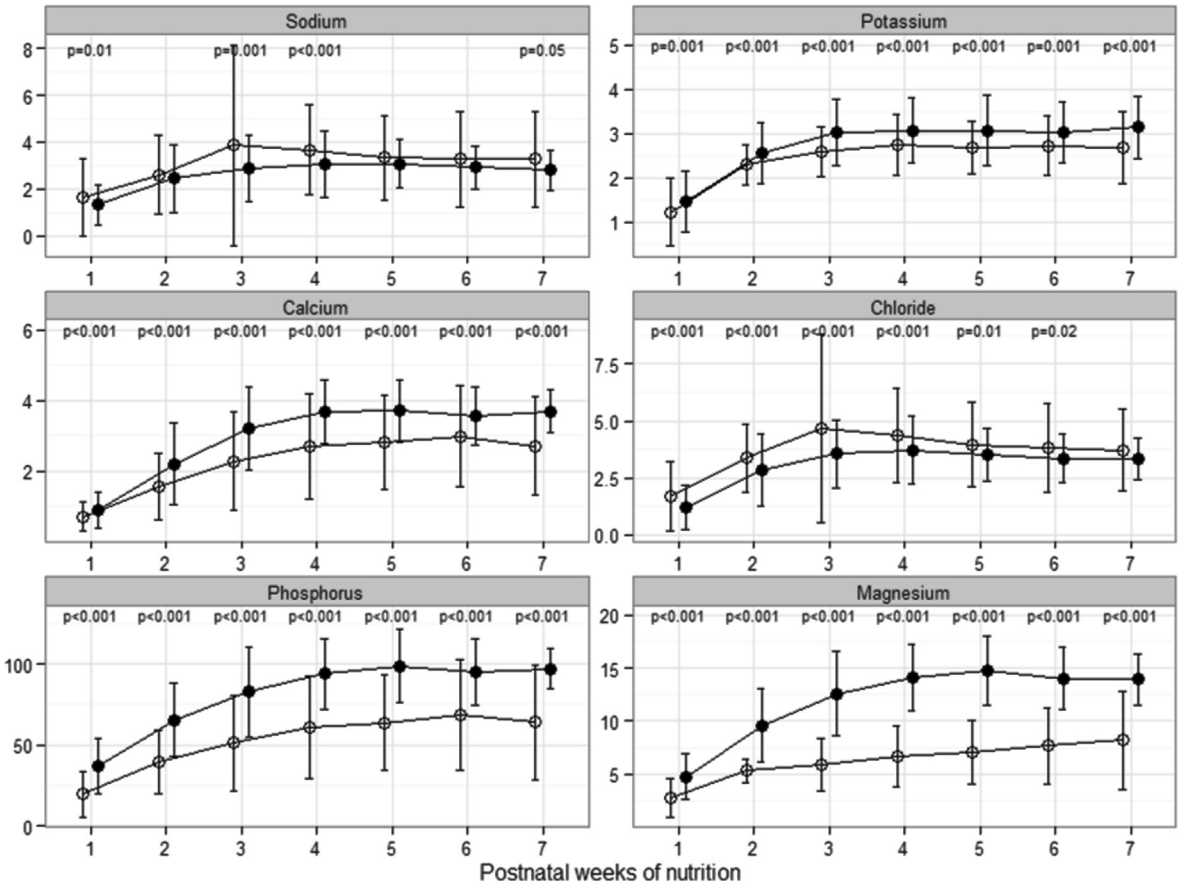

Fig. 4. Electrolytes. Intake of electrolytes (mean and SD) in control group (transparent dots) and intervention group (black dots) during the first seven weeks of nutrition. Sodium, potassium, calcium and chloride are plotted as mmol/kg/day and phosphorus and magnesium as mg/kg/day.

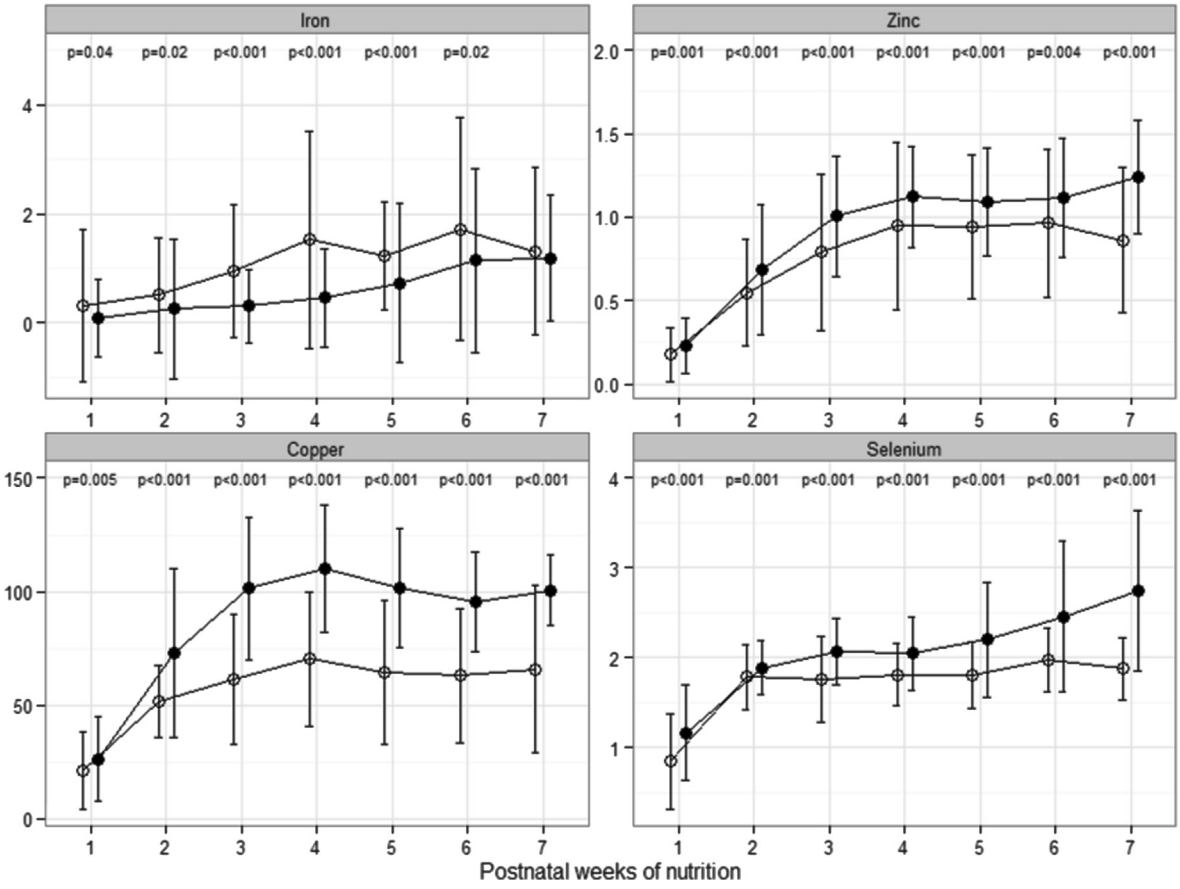

Fig. 5. Micronutrients. Intake of micronutrients (mean and SD) in control group (transparent dots) and intervention group (black dots) during the first seven weeks of nutrition. Iron and zinc are plotted as mg/kg/day, copper and selenium as microg/kg/day.

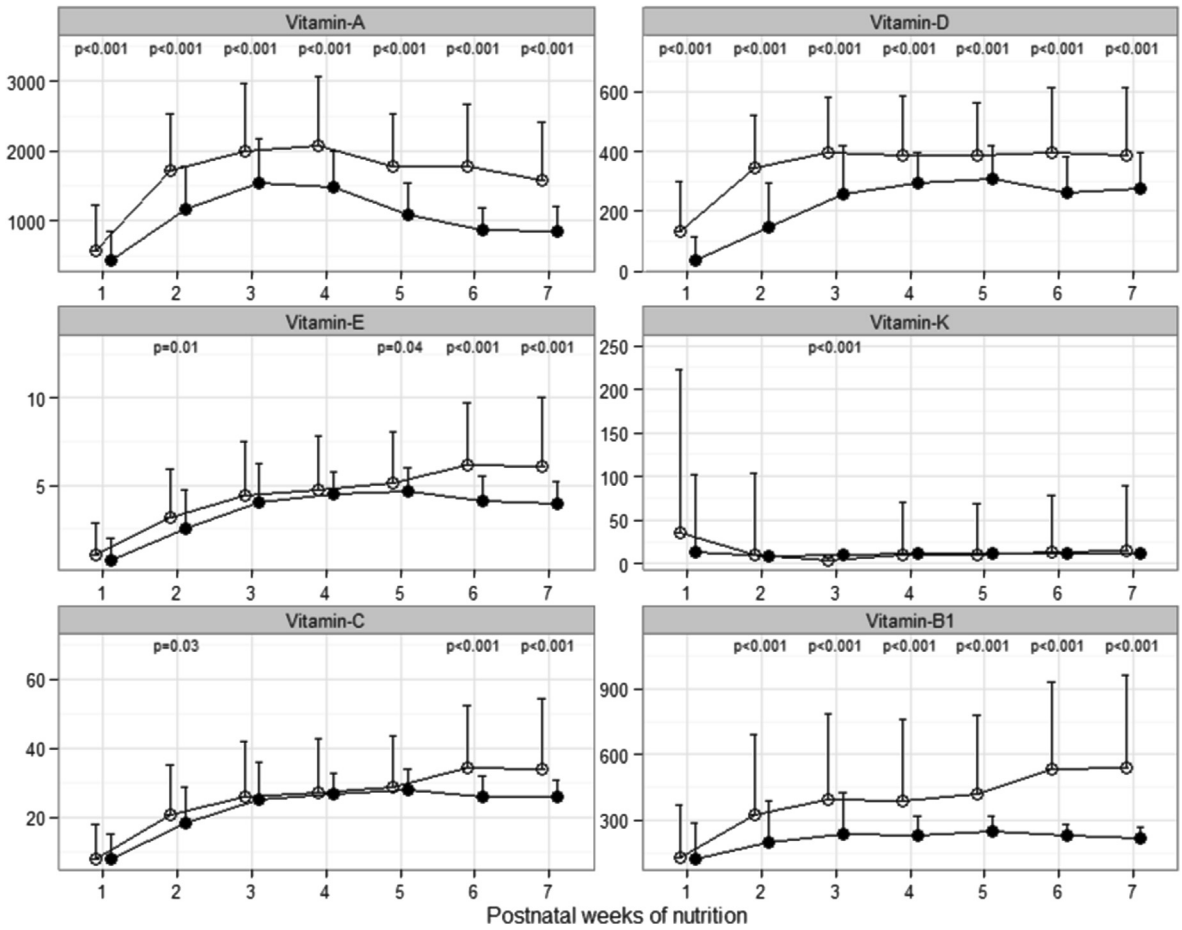

Fig. 6. Vitamins. Intake of vitamins [mean + SD] in control group (transparent dots) and intervention group (black dots) during the first seven weeks of nutrition. Vitamin-A and D are plotted as IU/kg/day, vitamin-E and C as mg/kg/day and vitamin-K and B1 as μg/kg/day.

From week 2 of life infants in the IG received significantly more amino acids and carbohydrates enterally (Fig. 7).

In contrast to the AA and CH intake which was mostly administered parenterally during the first week of life, FA were given mainly enterally with nearly equal amounts in both groups (control group 84.2% vs intervention group 65.1% ($p = 0.38$). From week two to seven infants in both groups received more or less all FA enterally with only small differences between the groups (Fig. 7).

4. Discussion

The results of this study show that by using a computer-aided nutrition calculation program it was possible to offer nutrition that complied better with the established guidelines. Furthermore, in the IG, growth pattern were more in agreement with the expected intrauterine growth.

Our intervention group showed symmetrical growth in terms of weight for length. Infants in the CG lost 1.2 SD in length during the first 4 weeks of life, while infants in the IG lost only 0.8 SD. Infants in the CG hardly showed any catch-up growth between DOL28 and discharge (SDS −3.0 at DOL28 to −2.7 at discharge). In contrast children in the IG showed a catch-up from a SDS of −2.0 at DOL28 to −1.2 at discharge. Only a small part of this difference can be explained by differences in nutrition after DOL28. As expected, the main differences between the groups were seen in the parenteral nutrition during the transition phase after birth. During the first week of life AA (<2 g/kg/d) and energy intake (<80 kcal/kg/d) in the CG were below recommendations. In contrast in the IG the intakes reached recommended levels (3 g/kg/d AA and 90 kcal/kg/d energy intake). Protein-energy malnutrition is a known cause of growth retardation, smaller brain size, obesity later in life and impaired neuro-cognitive function [7,14]. An intake of 2.3–3.5 g/kg/day is recommended to promote protein accretion [11]. A higher protein intake is associated with better growth [7,15].

As glucose was traditionally used as first line parenteral nutrient in preterm infants we only observed a small difference in the carbohydrate amounts administered parenterally in both groups. Considering both the enteral and parenteral glucose intake, infants in the IG received significantly more carbohydrates during all seven weeks of nutrition.

The infants in the IG had a three-fold higher parenteral fat intake during the first week of life, while enteral intake did not differ significantly between the two groups.

As the enteral fat is provided by breast milk, the amount of enteral feeding is guided by enteral tolerance and as this is a proven practice in Sweden there were no differences between both groups. The increased parenteral fat delivery in the IG was due to the determination to meet recommendations guided by the computer-aided nutrition program. This higher intake was achieved by an increase of the standard TPN. During stable growth a slightly higher fluid intake in the IG resulted in a higher intake of macronutrients with the exception of fat. From fifth week onwards fat intake was higher in the CG. Explanation for the higher intake of FA was the practice to supplement enteral feeds with maize or rapeseed oil if growth was believed to be suboptimal. Our results are conform to data from Collins et al., showing an optimized growth in all

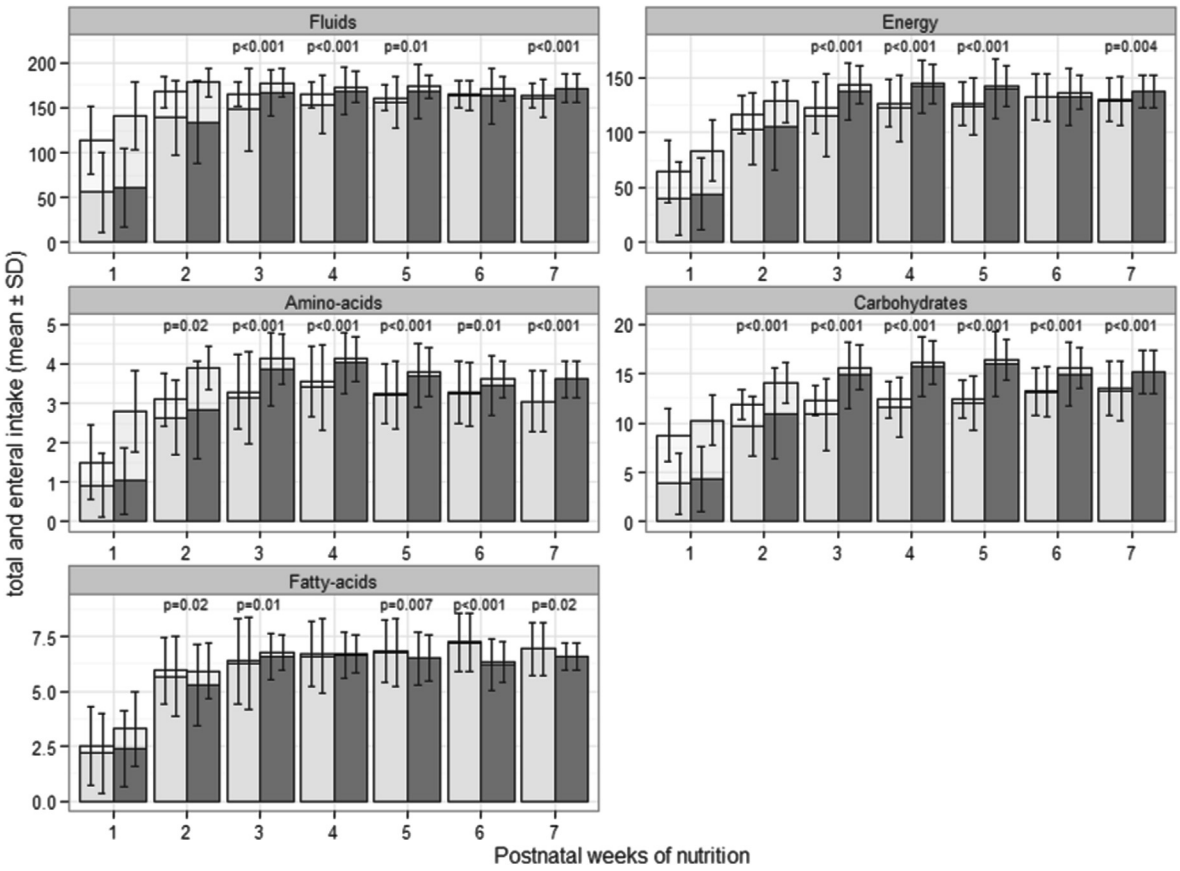

Fig. 7. Macronutrients: Enteral vs parenteral intake. Intake of macronutrients plotted as total intake (mean ± SD) and enteral intake (mean ± SD) for control group (light grey) and intervention group (dark grey). Fluids are shown as ml/kg/day, energy as kcal/kg/day, and amino acids, carbohydrates and fatty acids as g/kg/day.

anthropometric parameters in infants when protein was dosed in the optimal range and carbohydrate intake was increased. In that study fat intake was even negatively associated with growth in infants born before 33 weeks of gestation [16].

Calcium and phosphorus intake was significantly higher in infants in the IG during the hospital stay. In the first two weeks we did not reach the recommended intake of Calcium (2.5–5.5 mmol/kg/day [11]) in either of the groups. Infants in the CG received just above the lower recommended level of calcium from the fourth week of life and onwards. The same intake pattern was seen for phosphorus. The limited calcium and phosphorus intake amongst the infants in the CG was due to a less consistent fortification of breast milk. The limited calcium and phosphorus intake may have further impaired growth of infants in the CG.

The intake of copper was more than 40% higher per week in the IG during week 2–7. Zinc and selenium intake were significantly higher during all 7 weeks. This was mainly achieved by more intensive fortification of the breast milk with the objective to meet recent recommendations, as previous studies has indicated that these three micronutrients could have particular impact on the developing limbic system [17].

In contrast infants in the IG received less iron, which was due to the decreased transfusion rate and a pause in iron supplementation after transfusions to decrease the risk of iron overload with its associated risk for development of BPD and ROP [18].

As infants in the CG received vitamin supplementation by a standardized protocol in combination with breast milk fortification, their intake was slightly above the recommended levels. When using the computer-aided nutrition calculation program the vitamin intake was held within the recommended range.

In the IG there were fewer infants with PDA but significantly more that received treatment for PDA closure. The higher fluid intake in the IG seemed not to have increased the risk for PDA.

When using a software that display recommended nutritional intakes for varies variables in real-time and gives you color coded feedback (red, yellow, green) when prescribing adequate nutritional intake it is impossible to distinguish whether solely the use of the software or an increased awareness of nutrition in whole has the greatest impact on the prescribed nutrition and furthermore the improved growth.

Our study is limited by the low number of infants in both groups and the slightly higher number of SGA infants in the CG and the fact that we have not collected serial blood samples on key elements of growth and nutrition. Therefor we can only speculate that different intakes of macro and micronutrients have resulted in deficiencies and therefor impaired growth. Further studies are needed to evaluate the impact of improved growth on long-term complications such as impaired growth potential, risk for obesity, the metabolic syndrome and cardiovascular diseases.

Statement of authorship

The author's responsibilities were as follows: DW and AB designed and conducted the research; FA provided essential methodological help; DW analysed the data and performed the statistical analyses; DW, AB and FA wrote the paper; and DW, AB and FA reviewed and approved the final content. All authors have read and approved the manuscript, and all qualify for authorship.

Funding source

No external funding was received for this study.

Conflict of interest

The authors have no conflicts of interest to disclose.

Acknowledgement

We would like to thank all infants and their parents who participated in the study. Furthermore, we would like to thank our colleagues and all the nursing staff working on the NICU at the Mälarsjukhus hospital during the study helping us to optimise nutrition for our small patients.

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