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## 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  $GA \leq 32+0$  from birth to postnatal week 7. The nutrition of 43 preterm infants was ordinated with help of the program Nutrium<sup>TM</sup> (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.

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# 1. Introduction

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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

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*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.

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<sup>TM</sup> (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<sup>™</sup> software package was used on a daily base to prescribe parenteral and enteral nutrition for infants treated at the NICU. Nutrium<sup>™</sup> software is an interactive, multi user, graphical frontend, 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<sup>™</sup>-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<sup>™</sup> 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<sup>™</sup> 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<sup>™</sup> 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

Nutrient			Intake (/kg/d)
Fluid			166 ml
Energy		-	141 kcal
Protein / a.a.			3.69 g
Carbohydrates			15.6 g
Glucose			
Lipids			6.8 g
Sodium			3.04 mmol
Potassium			3.31 mmol
Chloride			2.94 mmol
Calcium			162 mg
Phosphorus			103 mg
Magnesium			8 mg
Iron			5.2 mg
Zinc			1.4 mg
Copper			109 µg
Selenium			3.85 µg
Manganese			9.2 µg
Iodine			39.5 µg
Vitamin A (RE)			411 µg
Vitamin D			9.1 µg
Vitamin E (TE)			3.21 mg
Vitamin K			6.4 µg
Ascorbic acid		_	50 mg
Thiamin (B1)			96 µg
Riboflavin (B2)			209 µg
Pyridoxin (B6)			96 µg
Niacin (NE)			1.78 mg
Panthothenate	+++		1.08 mg
Biotin			4.64 µg
Folate			62 µg
Vitamin B12		1 1	0.209 µg

Fig. 1. Graphical feedback displayed by the Nutrium<sup>™</sup> 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.

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