Nutrition, growth and respiratory function in preterm infants with a birth weight less than 1000 grams

Nutrition, tillväxt och respiratorisk funktion hos för tidigt födda barn med en födelsevikt under 1000 gram

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ABSTRACT

Background The survival among infants born preterm is increasing, which is mainly due to great improvements in the field of perinatal and neonatal intensive care. However, postnatal growth restriction, severe morbidities and long-term health outcome still remain a concern.

Aims The objective was to explore the energy and macronutrient intake and growth among extremely low birth weight (ELBW) infants, and to assess whether there is any relationship between respiratory function, nutritional intake and growth.

Method A retrospective cohort study was performed including 77 ELBW infants born between April 1, 2009, and March 31, 2012, treated at the neonatal intensive care unit, Norrland's University Hospital in Sweden. After exclusion, due to morbidities or mortality, 47 infants remained. Daily nutritional intakes and growth were recorded in the software Nutrium. Information regarding respiratory support, fraction of inspired oxygen (FiO₂) and respiratory rate were noted on day 28. The data was statistically analysed using IBM SPSS Statistics version 20.0. Spearman Rank Order Correlations and Kruskal-Wallis Tests were performed.

Results During the study period, z-score for weight, length and head circumference decreased by 1.7, 2.1 and 1.6, respectively. A higher intake of carbohydrates during the first two weeks was correlated with a lower need for supplemental oxygen (FiO₂ > 21 %) on day 28 (p<0.05). A greater decrease in z-score weight and z-score length, respectively, during the first four weeks of life correlated with a greater need for supplemental oxygen (FiO₂ > 21 %) on day 28 (p<0.05).

Conclusion Infants of extremely low birth weight are in need for close monitoring of nutrient provision and growth due to the risk of undernutrition. FiO₂ on day 28 was significantly correlated to carbohydrate intakes. Furthermore, infants with high need of supplemental oxygen showed poor growth in weight and length.
SAMMANFATTNING

**Bakgrund** Överlevnaden ökar bland för tidigt födda barn, vilket främst beror på stora förbättringar inom den perinatale och neonatale intensivvården. Postnatal tillväxthämning, allvarliga sjukdomar och långsiktigt hälsoutfall utgör dock fortfarande ett bekymmer.

**Syfte** Målsättningen med studien var att undersöka intaget av energi och makronutrienter samt tillväxt hos extremt för tidigt födda barn med en födelsevikt under 1000 gram, och att analysera eventuella samband mellan respiratorisk funktion, näringsintag och tillväxt.


**Resultat** Under studieperioden minskade z-score för vikt, längd och huvudomfång med 1.7, 2.1 och 1.6, respektive. Ett högre intag av kolhydrater under de första två veckorna korrelerade med ett lägre behov av extra syrgas (FiO₂ > 21 %) dag 28 (p<0.05). Minskning i z-score vikt och z-score längd under de första fyra levnadsveckorna korrelerade med ett högre behov av extra syrgas (FiO₂ > 21 %) dag 28 (p<0.05).

**Slutsats** Extremt för tidigt födda barns näringstillförsel och tillväxt behöver noggrant följas på grund av risk för undernäring. Fraktion syrgas i inandningsluften under dag 28 korrelerade med kolhydratintaget och barn med ett högt behov av extra syrgas hade en långsam längdtillväxt och viktökning.
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1 BACKGROUND

The survival among extremely preterm infants is increasing, which is mainly due to great improvements in the field of perinatal and neonatal intensive care (1,2). Also, an improvement in the postnatal condition and survival is observed (3). However, severe morbidities and long-term health outcome still remain a concern (4).

Some of the severe morbidities affecting preterm infants are intraventricular haemorrhage, septicaemia, necrotizing enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity and patent ductus arteriosus (4). Morbidity during early postnatal age is of great concern and it can have a negative effect on nutritional supply (5). One example of this is fluid restriction, a commonly used strategy in patients with patent ductus arteriosus. In Sweden, this group of infants were found to have an energy and macronutrient intake below minimal requirements (6). Immature organ systems, affecting the tolerance of feeding, and risks associated with parenteral as well as enteral nutrition, are examples of other conditions known to affect the nutrition of preterm infants (7).

The nutritional need of the preterm is related to growth and development (8). The supply of energy and nutrients should provide the quantity and quality to enable a growth rate similar to that of a foetus (7,8). Normal foetal nutrition has been considered a guide in the assessment of nutrient supply for infants born prematurely (9). During pregnancy the foetus use glucose and amino acids as main substrates for energy, protein synthesis and growth, while fatty acids are mainly used as structural components in cell membranes and for energy storage (10).

According to the Swedish national guidelines on nutrition for preterm infants of extremely low gestational age (ELGA) there are two main assessments: the infants nutrition must be insured, avoiding negative effects of starvation, and the need for daily individual nutrition prescriptions, which should be based on calculations of energy- and nutrient intakes (7). The current national recommendations are based on European Society for Paediatric Gastroenterology, Hepatology, and Nutrition, Committee on Nutrition (11) and guidelines according Tsang et al (12). According to the Swedish national recommendations, the goal is to reach full dose nutrition on day four at the latest (7).

Human milk, preferably mother’s own and if not available, donor human milk, is the recommended source of enteral nutrition until an age corresponding to 34 weeks gestational age (7). If neither mother’s own milk nor donor human milk is available, preterm formula can be used. The enteral nutrition should be gradually increased, aiming to reach total enteral nutrition at 14 days postnatal age. To ensure optimal energy and macronutrient intakes, regular breast milk analysis and individual fortification using human milk fortifiers is recommended.

The severity of illness might influence the feeding of extremely low birth weight (ELBW) infants (13). In a study of 1366 ELBW infants (birth weight less than 1000 g), where days of mechanical ventilation during the first week of life was used to define illness, researchers found that the less critically ill infants received significantly more total nutritional support and higher total energy intake compared to the more critically ill infants. Enteral nutrition support was initiated significantly later among the more critically ill infants and they were also significantly older when enteral nutrition exceeded 110 kcal/kg/day compared to the less critically ill infants. The prevalence of feeding interruptions for at least 24 hours was also significantly higher among the more critically ill infants. This finding was accompanied by a
significantly slower rate of weight gain and a higher incidence of moderate and severe bronchopulmonary dysplasia, intraventricular haemorrhage and late-onset sepsis. The length of hospital stay was also significantly longer in this group. The researchers found that the total daily energy intake during the first week mediates the influence of critical illness on the risk of later growth and adverse outcomes.

In Sweden, a retrospective study was recently performed to explore associations between energy and macronutrient intakes and early growth in extremely low gestational age infants born during 2004-2007 (14). The infants in the study received energy and macronutrients well below the recommended and, consequently, showed severe growth restriction.

Postnatal growth restriction is a serious, but common, problem among preterm infants (15). Low birth weights and gestational age are significantly associated with postnatal growth restriction. Other factors independently associated with postnatal growth restriction are history of necrotizing enterocolitis, need for respiratory support at 28 days postnatal age, administration of postnatal steroids and male gender. Postnatal administration of corticosteroids is associated with a decrease in the rate of weight gain and head growth (14,16) as well with a reduction in length gain (14). Despite concurrent illness, nutrient intake alone is an independent predictor of growth.

Infants born with a birth weight below 1500 g are in need of long periods of hospital care before discharge to home (11). In many neonatal units in Europe, discharge to home occur around 35-36 weeks postconceptional age, if the ELBW infant is stable.

Respiratory illness is associated with an increase in metabolic rate and, consequently, higher energy requirements (17). On the other hand, energy expenditure is reported to be lower among preterm infants on nasal continuous airway pressure than spontaneously breathing infants (18). However, little is known about the associations between energy and macronutrient intake, growth and respiratory function in ELBW infants.

2 AIMS

The objective of this study was to explore the nutritional intake and growth among ELBW infants, and to assess whether there is any relationship between respiratory function, nutritional intake and growth in this group of infants. The specific aims were to investigate correlations between fraction of inspired oxygen (FiO₂) and respiratory rate on day 28 and energy- and macronutrient intake and to investigate correlations between fraction of inspired oxygen (FiO₂) and respiratory rate on day 28 and growth (weight, length and head circumference).

3 METHOD

3.1 Choice of method

A retrospective cohort study was performed to investigate the energy and macronutrient intake, growth and respiratory function during the first four weeks of life in ELBW infants. During March 2012-March 2013 data were obtained from infants' hospital records.
3.2 Subjects
The study included ELBW infants born between April 1, 2009, and March 31, 2012 and treated in Umeå, Sweden within their first seven days of life at the neonatal intensive care unit, Norrland's University Hospital. Infants born at other hospitals and transported to Norrland's University Hospital within their first week of life were included given that nutritional and medical information was obtained. A total number of 77 prematurely born infants with a birth weight less than 1000 g were included in the study. Infants who died within the first four weeks of life were excluded from the study. Other exclusion criterions were severe morbidities affecting nutritional intake or growth, such as necrotizing enterocolitis, hydrocephalus, gastrointestinal perforation, extensive abdominal surgery and congenital anomalies. A final number of 47 infants were included in the study (Figure 1).

![Figure 1. Included and excluded infants. 1ELBW, extremely low birth weight (<1000g). 2Necrotizing enterocolitis, n = 6; Gastrointestinal perforation, n = 4; Hydrocephalus, n = 4; Congenital anomalies, n = 1.](image)

3.3 Data collection
Daily total enteral and parenteral nutritional intakes, including infusions and blood products were retrospectively retrieved and recorded in a software called Nutrium (www.nutrium.se). Any administration of glucocorticosteroids was also noted. Breast milk analyses were performed at Eurofins Steins Laboratory AB, Jönköping, Sweden, using mid-infrared spectrophotometry analysis (MilkoScan 4000, FOSS, Denmark). If an infant was transferred to another hospital before 28 days postnatal age, medical records were ordered from other hospitals to attain at least four weeks of complete information of nutritional intake and anthropometric measurements.

3.3.1 Nutritional data
Nutritional intakes were recorded the first 28 days of life. Both enteral and parenteral intakes including blood products and infusions, were included in the nutritional assessment. A diluted amino acid solution were used to flush the infants' umbilical artery catheters, why the amount
of flush solutions also were included in the nutritional assessment. Energy intake were calculated in kcal/kg/d and macronutrients (protein, carbohydrates and fat) in g/kg/d. Macronutrient analyses of human milk, both mother’s milk and donor human milk, were collected and used in the nutrition assessment when available. Otherwise, the average content of macronutrients, based on the analysed human milk samples, were used in the nutrition assessment. Other enteral and parenteral intakes where calculated using product-specific data on nutritional content.

3.3.2 Growth data
All available data on weight, length and head circumference were recorded from birth until hospital discharge. Since the anthropometric measurements were not available for every seventh day, interpolation technique were used to calculate growth data for day 7, 14, 21 and 28. Standard deviation score (z-score) for weight, length and head circumference were calculated by using a Swedish growth reference (19). The difference in z-score, delta z-score (Δ z-score), was calculated as the difference between birth z-score and z-score at 28 days of postnatal age. Small for gestational age (SGA) was defined as a birth weight of two or more z-score below normal growth curve. Appropriate for gestational (AGA) age was defined as a birth weight within two z-score below or above normal growth curve.

3.3.3 Respiratory data
To determine the respiratory function, information regarding respiratory support, fraction of inspired oxygen (FiO₂) and respiratory rate were noted for each study participant on day 28. The oxygen saturation target ranged from 86 to 92 %. The lowest recorded value of FiO₂ and respiratory rate, respectively, which lasted for at least one hour, was chosen on day 28. The number of days infants received mechanical ventilation and nasal continuous positive airway pressure (nCPAP) during the first four weeks of life, were also recorded.

3.4 Statistical analysis
The data was statistically analysed using IBM SPSS Statistics version 20.0. The significance level was set at p<0.05. Preliminary analyses of linearity, normality and homoscedasticity were performed. The continuous variables that were normally distributed are presented as mean and standard deviation (SD), otherwise median, quartile one (Q₁) and quartile three (Q₃) are presented.

Non-parametric tests were performed, since the data did not meet the requirements of parametric tests. To evaluate correlations between energy and macronutrient intakes, Δ z-score for weight, length and head circumference and FiO₂ and respiratory rate, Spearman Rank Order Correlation analyses were performed (bivariate analyses). Kruskal-Wallis Tests were performed to evaluate the effects of respiratory support on energy and macronutrient intakes on day 28.

3.5 Ethical considerations
The study is based on medical records and was approved by the Regional Ethical Review Board, Umeå University (Dnr 2012-458-31M). The retrospectively collected data were treated confidentially and the ethical principles stated in the Declaration of Helsinki were respected.
4 RESULTS
Of the 47 included infants (Figure 1), 24 were girls and 23 were boys. The gestational age ranged from 22.4 to 30 weeks. Infant characteristics are shown in Table 1.

Table 1. Characteristics of the 47 Swedish extremely low birth weight infants at birth

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Median</th>
<th>Q1</th>
<th>Q3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (week)</td>
<td>47</td>
<td>25.3</td>
<td>24</td>
<td>26.6</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>47</td>
<td>728</td>
<td>531</td>
<td>822</td>
</tr>
<tr>
<td>Birth length (cm)</td>
<td>46</td>
<td>32</td>
<td>29.8</td>
<td>34</td>
</tr>
<tr>
<td>Birth head circumference (cm)</td>
<td>46</td>
<td>22.7</td>
<td>21.3</td>
<td>24</td>
</tr>
</tbody>
</table>

1Quartile one, 2quartile three

The number of infants born small for gestational age was 14 (29.8 %), while the rest of the infants (n = 33) were born appropriate for gestational age. During the four week study period, 33 infants (70.2 %) received postnatal steroids.

4.1 Energy and macronutrient intakes
During the period from birth to 28 days postnatal age, mean intakes of energy and macronutrients increased (Table 2).

Table 2. Intake of energy and macronutrients during the first four weeks of life in 47 Swedish extremely low birth weight infants.

<table>
<thead>
<tr>
<th>Energy and nutrients</th>
<th>Week 1 *</th>
<th>Week 2 *</th>
<th>Week 3 *</th>
<th>Week 4 *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal/kg/d)*</td>
<td>81 (12)</td>
<td>113 (14.4)</td>
<td>119 (14.9)</td>
<td>129 (19)</td>
</tr>
<tr>
<td>Energy from EN**</td>
<td>25 (12)</td>
<td>69 (31)</td>
<td>94 (30)</td>
<td>112 (37)</td>
</tr>
<tr>
<td>Energy from PN**</td>
<td>56 (15)</td>
<td>44 (20)</td>
<td>25 (19)</td>
<td>18 (24)</td>
</tr>
<tr>
<td>Protein (g/kg/d)**</td>
<td>3.4 (0.6)</td>
<td>3.6 (0.5)</td>
<td>3.6 (0.4)</td>
<td>3.7 (0.5)</td>
</tr>
<tr>
<td>Fat (g/kg/d)**</td>
<td>2.3 (1.0)</td>
<td>4.0 (1.3)</td>
<td>5.1 (1.1)</td>
<td>5.7 (1.5)</td>
</tr>
<tr>
<td>Carbohydrates (g/kg/d)**</td>
<td>11.6 (1.4)</td>
<td>14.0 (1.8)</td>
<td>14.4 (2.0)</td>
<td>15.3 (2.0)</td>
</tr>
</tbody>
</table>

*Numbers are mean (SD), **Energy calculated as kcal per kilo and day, ***enteral nutrition, ****parenteral nutrition

4.2 Growth
Birth data are presented in Table 1. Table 3 shows weekly data on weight, length and head circumference during the first four weeks of life. From birth to day seven, a decrease in weight was observed. Thereafter weight slowly increased during the study period.

Table 3. Interpolated mean and SD of weight, length and head circumference the first four weeks of life in 47 Swedish extremely low birth weight infants.

<table>
<thead>
<tr>
<th>Growth</th>
<th>Week 1 Mean (SD)</th>
<th>Week 2 Mean (SD)</th>
<th>Week 3 Mean (SD)</th>
<th>Week 4 Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (g)</td>
<td>667 (138)</td>
<td>786 (157)</td>
<td>867 (187)</td>
<td>963 (236)</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>32 (2.7)</td>
<td>33 (2.7)</td>
<td>34 (2.8)</td>
<td>35 (2.8)</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>23 (1.6)</td>
<td>23 (1.6)</td>
<td>24 (1.7)</td>
<td>25 (24.6)</td>
</tr>
</tbody>
</table>

During the first 28 days of life, growth failure was observed. Weight decreased with 1.7 z-score, length with 2.1 z-score and head circumference with 1.6 z-score (Figure 2). From birth to day seven, weight decreased from -1.5 to -2.7 z-score and length decreased from -1.9 to -2.8 z-score. Head circumference changed from -0.8 to -1.6 z-score during the first week of life.
4.3 Respiratory function

During the first 28 days of life, the infants required mechanical ventilation on average 14.5 days (median 15 days) of the 28 days studied. The average time in nCPAP was 12.5 days (median 12 days). The number of infants who received respiratory support at 28 days postnatal age was: nasal continuous airway pressure (n=19), biphasic positive airway pressure (n=13), conventional mechanical ventilation (n=5), high frequency ventilation (n=8) and no respiratory support (n=2). Table 4 gives additional information regarding respiratory function on day 28.

Table 4. Fraction of inspired oxygen and respiratory rate at 28 days postnatal age in 47 Swedish extremely low birth weight infants.

<table>
<thead>
<tr>
<th> </th>
<th>n</th>
<th>Median</th>
<th>Q1</th>
<th>Q3</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiO2 Respiratory rate</td>
<td>47</td>
<td>39</td>
<td>25</td>
<td>50</td>
</tr>
</tbody>
</table>

1Quartile one, 3quartile three. Infants receiving high frequency ventilation not included (n=8). FiO2: fraction of inspired oxygen

4.4 Correlations between respiratory function and nutritional intake

A higher intake of carbohydrates during week one and week two was correlated with a lower need for supplemental oxygen (FiO2 > 21 %), to meet the targets for oxygen saturation on day 28 (Table 5).

Table 5. Correlations between mean energy and macronutrient intakes during the first four weeks of life and respiratory rate and FiO2 at 28 days postnatal age in 47 Swedish extremely low birth weight infants.

<table>
<thead>
<tr>
<th> </th>
<th>Respiratory rate at 28 days postnatal age (n=39)1</th>
<th>FiO2 at 28 days postnatal age (n=47)1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>Week 2</td>
<td>Week 3</td>
</tr>
<tr>
<td>Energy (kcal/kg/d)</td>
<td>-0.129</td>
<td>-0.276</td>
</tr>
<tr>
<td>Carbohydrates (g/kg/d)</td>
<td>-0.010</td>
<td>-0.185</td>
</tr>
<tr>
<td>Protein (g/kg/d)</td>
<td>-0.186</td>
<td>-0.231</td>
</tr>
<tr>
<td>Fat (g/kg/d)</td>
<td>-0.0186</td>
<td>-0.230</td>
</tr>
</tbody>
</table>

1Spearman rank order correlation coefficient; * p < 0.05
Energy and macronutrient intakes on day 28 were not correlated with any type of respiratory support on day 28 (data not shown).

4.5 Correlations between respiratory function and growth

A greater decrease in z-score weight and z-score length, respectively, during the first four weeks of life correlated with a greater need for supplemental oxygen (FiO₂ > 21 %), to meet the targets for oxygen saturation on day 28 (Table 6).

Table 6. Correlations between changes in growth (delta z-scores for weight, length and head circumference) during the first four weeks of life and respiratory rate and FiO₂ at 28 days postnatal age in 47 Swedish extremely low birth weight infants.

<table>
<thead>
<tr>
<th></th>
<th>Respiratory rate at 28 days postnatal age</th>
<th>FiO₂ at 28 days postnatal age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ z-score weight (n=47)</td>
<td>0.167</td>
<td>-0.303*</td>
</tr>
<tr>
<td>Δ z-score length (n=40)</td>
<td>-0.74</td>
<td>-0.521**</td>
</tr>
<tr>
<td>Δ z-score head circumference (n=39)</td>
<td>-0.117</td>
<td>-0.262</td>
</tr>
</tbody>
</table>

Δ z-score, delta z-score

*Spearman rank order correlation coefficient; *p < 0.05, **p < 0.01

5 DISCUSSION

5.1 Method evaluation

This retrospective cohort study was performed to explore nutritional intake and growth and to evaluate the correlations between respiratory function, energy and macronutrient intakes and growth, respectively. There are several methodological issues worth considering before interpreting the results.

The study has many strengths, such as the extensive retrospective collection of data on all enteral and parenteral fluids as well as regularly measured values of weight, length and head circumference throughout the study period. Nutrient intakes were carefully calculated from all applied liquids using the software Nutrium (www.nutrium.se). Calculations of energy and macronutrient intakes from breast milk were based on analyses of energy and macronutrients in mother’s own milk and in donor human milk.

Extremely low birth weight infants are a vulnerable group to study, due to their general immaturity and risk of postnatal complications during their first weeks of life. A small number of infants were included in the final analyses, caused by an extensive exclusion due to severe morbidity or mortality. Extrapolation of the results to the entire population is thereby difficult. Confounding factors, such as medical treatment and gestational age, could have affected the results, but was not investigated in this study. Other limitations include limited reliability of growth measurements as well as the retrospective collection of nutritional data.

The validity is considered high for the specific variables entered in the analysis. The validity is considered low when it comes to any specific respiratory disease, due to the limited number of variables and no information on medical conditions.

In this study, non-parametric tests were performed since the data did not meet the assumptions of parametric tests, but also because of a small sample size. Non-parametric tests are less sensitive than parametric tests, but they are preferred when the data does not meet the requirements of parametric tests.
5.2 Results discussion

The extremely low birth weight infants in this study showed severe postnatal growth failure and they received less energy and macronutrients than recommended, according to the Swedish nutritional guidelines (7). These findings are similar to those reported in the national population-based study on extremely low gestational age infants (14).

The infants in this study received respiratory support. Respiratory diseases, both acute and chronic, are very common in preterm neonates (12). A consequence of acute respiratory problems (respiratory distress syndrome, pneumonia, and aspiration) is increased energy metabolism. To meet the higher energy needs, additional supply of carbohydrates and fat are mainly used. During carbohydrate metabolism, oxygen consumption and carbon dioxide production rise, leading to an increase in respiratory work. Because of this, a high carbohydrate intake (>12.5 mg/kg/min) may be harmful. Fat has a lower respiratory quotient than carbohydrates and higher energy density and therefore considered as a good source of energy.

The mean carbohydrate intake during the first week was 11.6 g/kg/d and during the second week 14.0 g/kg/d. This is in accordance with the Swedish national recommendations for ELGA infants (7) as well as the nutritional guidelines for ELBW infants (12). In this study, fraction of inspired oxygen on day 28 was shown to be significantly correlated to mean carbohydrate intake during the first two weeks of life (Table 5). The correlation was negative, which implies that a higher intake of carbohydrates was correlated with a decrease in the need for supplemental oxygen to meet the targets for oxygen saturation. More studies are needed to examine this correlation closer.

In this study, the infants showed severe growth failure and no catch-up growth was seen during the first four weeks of life. The lack of catch-up growth is assumed to be associated with a nutritional intake below recommended, since energy intake and weight gain are shown to be significantly correlated (19). Energy and protein intake are positively correlated with weight, length and head circumference, even after adjusting for severity of illness (14). Stoltz Sjöström et al. found that some weight and head circumference catch-up growth were initiated at 28 days postnatal age, while catch-up growth in length was observed after 42 days of postnatal age.

According to current nutritional guidelines, few infants received the recommended intake of energy, protein and fat during the first week of life. In the guidelines from the European Society of Paediatric Gastroenterology and Nutrition on nutrition and feeding of preterm infants, no specific recommendations for ELBW infants are provided, except for protein needs (8). This, because of lack of scientific data in the field. According to the guidelines for these infants, a protein intake of 4.0-4.5g/kg/d is recommended. The mean protein intake, which ranged from 3.4 to 3.7 gram/kg/day during the four-week study period was below this recommendation, which is assumed to have influenced the growth rate among the study participants. Correlations between protein intake and growth was not analysed in this study, though it would have been interesting since previous studies have found relationships between them (14). Low energy intake, fluid restriction and a low protein content in parenteral nutrition products are other possible explanations to this finding.

Another important aspect to consider is the energy expenditure. Studies have shown that energy expenditure in preterm infants is correlated to energy intake (18,20) and weight gain (20). Energy intake has a greater impact on energy expenditure, compared to weight gain.
Differences in energy expenditure between spontaneously breathing infants and infants on nasal continuous positive airway pressure have previously been investigated. Infants on nasal CPAP had lower energy expenditure compared to spontaneously breathing infants during postnatal week one (18), while energy expenditure was higher in infants requiring mechanical ventilation (17). However, less critically ill infants are more likely to receive more total nutritional support and higher total energy intake compared to the more critically ill infants (13). It cannot be ruled out that this may have influenced the result of the present study.

In this group of infants, different respiratory supports were used during the postnatal period studied and fraction of inspired oxygen and respiratory rate on day 28 were studied as variables of respiratory function. A greater decrease in z-score weight and z-score length, respectively, during the first four weeks of life was correlated to a greater need for supplemental oxygen to meet the targets for oxygen saturation on day 28. Growth restriction, possibly caused by energy- and macronutrient deprivation, can be assumed to have affected the respiratory function. Different types of respiratory support, energy expenditure and its effect on growth is not studied here, but would be interesting in further research in the field.

Early nutrition is considered important avoiding negative nitrogen balance as well as providing sufficient amounts of energy (21). Early nutrition is also reported to have favourable effects in preterm infants with respiratory distress syndrome, such as shorter duration of parenteral nutrition and fewer days of mechanical ventilation (22). The total daily energy intake during the first week of life is shown to mediate the influence of critical illness on the risk of later growth and adverse outcomes among ELBW infants (13).

5.3 Societal perspectives
Having a preterm baby is a challenging experience for the family. At seven years corrected age, parents of preterm infants born before 30 weeks gestational age were found to have significantly higher levels of parenting stress and poorer family functioning, compared to infants born term (23). Also, reporting of depression and anxiety symptoms were more common among parents of preterm infants, than parents of infants born term. These families are in need for effective support throughout early childhood, to possibly diminish the difficulties these families and parents may experience.

5.4 Gender perspectives
Previous studies have found that preterm males are more likely to develop neonatal morbidities or die within the early postnatal period compared to their female counterparts (24). Among moderately preterm infants, with a gestational age ranging from 30 to 34 weeks, male gender was found to be a risk factor for transient tachypnoea of the newborn and respiratory distress syndrome (25). Preterm male infants, born before 29 weeks gestational age, were found to receive significantly more frequently mechanical ventilation and surfactant during their first six postnatal hours, compared to their female counterparts (26). Also, a significantly higher proportion of male infants, compared to females, contracted chronic lung disease during their first week of life. There is no evident explanation to the differences in morbidity between preterm males and females, but one possible cause could be gender differences in physiological responses during neonatal care. Gender differences were not investigated in this study, however, this can be assumed as a potential confounding factor for the results in this study.
6 CONCLUSION
The essential findings from this study were the low intakes of energy and macronutrients and the severe growth failure during the first 28 days of life. Therefore, infants of extremely low birth weight are in need for close monitoring of nutrient provision as well as growth due to the risk of undernutrition. A higher intake of carbohydrates during week one and week two was correlated with a lower need for supplemental oxygen (FiO₂ > 21 %), while a greater decrease in z-score weight and z-score length, respectively, during the first four weeks of life was correlated with a greater need for supplemental oxygen (FiO₂ > 21 %), to meet the targets for oxygen saturation on day 28.

7 PROFESSIONAL RELEVANCE
Since this group of infants are at risk of having too low intake of energy and macronutrients which are associated with growth restriction, the dietitian plays a key role for the infants care. Since growth restriction in length and weight was shown to be correlated with a greater need for supplemental oxygen, having a dietitian on the ward may improve their respiratory function as well.

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9 REFERENCES


