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NUTRITION OF THE PRETERM INFANT

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Abstract. Nutrition is of great importance for the preterm infant. It is not only essential for survival, but also makes provision for rapid development of many organs outside the uterus which process normally takes place in the third trimester of pregnancy. It is for future life essential that all factors that might influence the development are as optimal as possible, including nutrition. However, there might also be an upper limit to the intake of some ingredients in the neonatal period. The rate of growth of the preterm infant is five times higher compared to term infants and the breast of the mother delivering preterm might yet be ready to produce the optimal composition of milk. Preterm infants receiving mothers milk only are known to show a lower gain in weight and length than the so called reference fetus. It is therefore at least questionable if preterm human milk can be used to define the nutritional needs of the preterm infant. To define the optimal composition and amounts of nutrients for the preterm infant a factorial approach can be used. The estimated requirements are calculated from the calculated requirements for maintenance and growth. Though some studies have shown that the protein content of milk from mothers who delivered preterm can be higher in the first few weeks after birth compared to milk of term delivering mothers, soon after there is a rapid decline in protein content after which period the content is not different from the term delivered mother. Providing exclusively mothers own milk leads to suboptimal growth and insufficient accretion of minerals. The needs of the preterm infant in energy, protein, lipids, carbohydrates, minerals, pro- and prebiotics to provide optimal nutrition in the first days after birth are discussed in the paper. It is concluded that nowadays early, aggressive nutrition directly after premature birth with the immediate introduction of amino acids and rapid introduction of lipids is advised. Enteral feeding should be started very soon after birth, preferably on the first day of life and increased in the days thereafter. The first choise for enteral feeding is mothers own milk, supplemented from the second week with a fortifier. Special preterm formula might serve as a good alternative in case when breast milk is not available.

Key words: preterm infants; nutritional needs; feeding; breast milk; preterm formula.

ВСКАРМЛИВАНИЕ НЕДОНОШЕННОГО РЕБЕНКА

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Резюме. Питание очень важно для недоношенного ребенка. Оно обеспечивает не только выживание, но и характерную для последнего триместра интенсивную динамику внутриутробного развития многих органов вне утробы матери. Для дальнейшей жизни важно, чтобы все — в том числе и питание — факторы, потенциально могущие оказать влияние на развитие, были, по возможности, оптимально сбалансированы. Однако, для некоторых пищевых ингредиентов, используемых в неонатальном периоде жизни, могут быть и верхние границы потребления. Скорость роста недоношенного ребенка в пять раз выше по сравнению с доношенным, а грудная железа матери, родившей ребенка недоношенным может быть еще недостаточно зрелой для продукции молока оптимального состава. Известно, что недоношенный ребенок, получающий только материнское молоко, хуже растет и набирает вес, чем так называемый референтный плод. Таким образом, использование материнского молока для удовлетворения потребностей недоношенного ребенка, по меньшей мере, дискутабельно. Для определения оптимального состава и количества нутриентов для недоношенного ребенка может быть использован подход «по факту», при котором фактические потребности приводятся в соответствие с рассчетными, основанными на оптимальном обеспечении его жизнеспособности и роста. Хотя результаты некоторых исследований показали, что в течение первых нескольких недель после родов содержание белка в молоке матерей, родивших детей недоношенными, может быть выше, чем в молоке матерей, родивших доношенных детей, вскоре количество белка у первых быстро уменьшается и впоследствие не отличается от молока матерей, родивших доношенных детей.

Вскармливание исключительно материнским молоком приводит к субоптимальному росту и недостаточному обеспечению минеральными веществами. В статье обсуждены потребности недоношенного ребенка в энергии, белках, жирах, углеводах, минеральных веществах, про- и пребиотиках, учет которых необходим для обеспечения оптимального питания в течение первых дней после рождения. В заключении подчеркнуто, что в настоящее время сразу после рождения недоношенного ребенка рекомендовано раннее агрессивное питание с немедленной фортификацией аминокислотами и быстрым введением в питание жиров. Энтеральное питание должно быть начато вскоре после рождения, предпочтительно — в первый же день, и в дальнейшем постепенно увеличиваться в объеме. Вскармливанием выбора является кормление материнским молоком сразу после родов с его фортификацией, начиная со второй недели жизни ребенка. Специальные смеси, предназначенные для вскармливния недоношенных детей, могут быть хорошей альтернативой в случае отсутствия грудного молока.

Ключевые слова: недоношенные дети; потребности в пищевых ингрединентах; вскармливание; грудное молоко; молочные смеси для вскармливания недоношенных новорожденных.

INTRODUCTION

Nutrition is of great importance for the preterm infant. It is not only essential for survival, but also essential because many organs of the preterm infant are in a phase of rapid development. Preterm infants have to face the rapid development that normally takes place in the third trimester, outside the uterus. Early optimal parenteral nutrition has the potential to decrease the incidence of growth failure after birth and the development of BPD, NEC, sepsis and ROP [9]. It is for future life essential that all factors that might influence the development are as optimal as possible, including nutrition. Lucas et al were the first to show that the type of nutrition given in the first weeks after birth influenced the psycho motor development of preterm infants till puberty [13]. They found a better development when the nutrition contained more protein. Ehrenkranz et al showed that the severity of illness as well as the early nutrition practices are both, independently, associated with both survival and neurodevelopmental outcome at discharge and two years of age [10]. Another study showed that not only psychomotor development improved by giving more protein to preterm infants, also was the incidence of infections lower [24]. At the same time however, there might also be an upper limit to the intake of protein and calories in the neonatal period. Rapid catch-up growth after intra-uterine malnutrition is related to an increased risk to develop overweight and obesity in later life [7].

HOW TO DEFINE THE OPTIMAL COMPOSITION AND AMOUNT OF NUTRITION FOR THE PRETERM INFANT?

Human milk is considered the optimal nutrition for infants born at term. The composition of human milk however is rather variable from mother to mother, partly based on the diet of the mother. It is also variable from feeding to feeding and is changing with the period after the delivery. It is reasonable to question if human milk has the optimal composition for the preterm infant. The rate of growth of the preterm infant is at least five times higher compared to term infants. Secondly, the breast of the mother delivering preterm might yet be ready to produce the optimal composition of milk. Preterm infants receiving mother's milk only, show a lower gain in weight and length than the growth of the so called reference fetus [5]. It is therefore at least questionable if preterm human milk can be used to define the nutritional needs of the preterm infant.

A second method to define the optimal composition and amounts of nutrients for the preterm infant is the factorial approach. The estimated requirements are calculated from the calculated requirements for maintenance and growth. Finally, data can be obtained from studies in formula fed infants where the effects of the amounts and addition of nutrients added to the formula can be studied.

COMPOSITION OF HUMAN MILK FROM PRETERM DELIVERING WOMAN

Some, but not all studies have shown that the protein content of milk from mothers who delivered preterm is higher in the first few weeks after birth compared to milk of term delivering mothers. The protein content however is very variable, ranging from 1 to 4 gram/100 ml [28]. Secondly, there is a rather rapid decline in protein content in the first two to four weeks after birth, after which period the content is not different from the term delivered mother. The protein needs of the very- preterm infant at that stage however are still higher compared to the term infant, mainly due to a higher growth rate. During the last trimester of a normal pregnancy there is a rapid increase in body stores of calcium, phosphorus and iron. Human milk does not contain large amounts of these minerals, at least not enough to mimic the intra uterine accretion. Providing exclusively mothers own milk leads to sub-optimal growth and insufficient accretion of minerals [5].

FACTORIAL CALCULATION OF THE NUTRITIONAL NEEDS OF THE PRETERM INFANT

Energy

Different studies have shown that that the resting energy expenditure of the preterm infant is around 60–65 kcal/kg/day [23]. In addition, is energy needed for thermo regulation, activity and growth. The weight gain of a fetus in the last trimester if pregnancy is 15–20 g/kg/day with the highest rate at the lowest gestational age. The average weight gain of a preterm infant in the period 26–36 weeks is around 17 gram/kg/day. The requirements for each gram of growth are estimated as 2–5 kcal/gram growth. The energy needed for growth therefore is 40–50 kcal/kg/day. When we add the energy needed for thermo regulation (5–10 kcal/kg/day), for activity a same amount and 10% of the total intake for unabsorbed losses in feces, can the total energy requirements of a preterm infant be calculated as 110–130 kcal/kg/day. Studies in formula fed preterm infants have shown that increasing the energy intake to 140 kcal/kg/day increase the weight gain, but this is due to an increase in the amount of body fat [15]. The increase in length and head circumference is mainly influenced by the protein intake, the increase in fat by the energy intake. Decreasing the intake to 100 kcal/kg/day resulted in almost no weight gain in small for gestational age infants and a lower fat accretion in these infants compared to results found in the so called reference fetus [25]. These findings support the recommendation to provide 110–130 kcal/kg/day.

Protein

Protein is one of the most important components of nutrition for the preterm infant. Protein is not only essential for maintenance, but also for psychomotor development, for length growth and for the synthesis of many essential proteins in the body like enzymes and immunoglobulins. Proteins are built from amino acids (AA). A number of AA's can not be synthesized in the human body and need therefore to be taken up with nutrition. The exact requirements of most essential AA's are not yet known for the preterm infant. Studies in intravenously fed preterm infants showed that cysteine also might be an essential AA for them. An other factor that must be taken into account when calculating the protein requirements of a preterm infant is that it is recently found that a number of AA's provided with oral nutrition are metabolized by the gastro-intestinal tract [21]. This might indicate that the AA requirements of the intravenously fed infant might be different from the orally fed infant.

Amino acids are needed to compensate the obligatory losses in urine, feces and through the skin. Secondly, they are needed for growth. The obligatory losses of urea, the end product of protein degradation, in urine is 0.6–0.8 g/kg/day. It is remarkable that these figures are equal for preterm infants and adults. The amino acid requirements for growth are dependent on the gestational age at birth and the postnatal age. The more preterm, the higher the growth and the higher the protein needs. The protein requirements for growth are 0.1–0.2 grams of protein per 1 g of weight gain. This indicates an amount of 2–3.4 gram/kg/day for a very preterm infant with a weight gain comparable to the intra uterine situation [2].

In order to assure a sufficient supply of all essential amino acids, and the fact that no protein might have the optimal composition regarding the essential AA, some extra protein needs to be given. The advised amount of protein for a growing preterm infant, when given orally, ranges therefore from 4–4.5 gram/kg/day for an infant with a body weight of less than 1000 gram and 3.5–4.0 gram for infants above 1 kg.

Formula contains cow's milk protein, a combination of whey and casein. The amount of these proteins is balanced in formula to mimic as possible the AA composition of human milk. Recent studies might indicate that exclusively partly hydrolyzed whey protein might have advantages for the preterm infant, but more studies are clearly needed. There is presently no good evidence that proteins should be given as hydrolysates to preterm infants.

Lipids

Lipids are much more than a simple source of energy for preterm infants. Lipids can be divided according to chain length, level of saturation and essential vs non essential.

Human milk contains as prominent fatty acid palmitic acid, a saturated fatty acid with 16 carbon atoms. Palmitic acid in human milk is mainly bound to the sn-2 position of glycerol. After digestion by lipase's, a mono glyceride with palmitic acid still at the sn-2 position remains. This is more rapidly absorbed than free palmitic acid. Free palmitic acid binds to Ca in the intestine, forming soaps. Thereby both palmitic acid and Ca are less well absorbed. Formula's contain vegetable oil, where palmitic is bound to the outer positions of glycerol. After cleaving vegetable fat, free palmitic acid is produced. This explains the more hard stools found in formula fed infants and causes malabsorption of both fatty acid and Ca. The lipid structure is adapted in modern formula's with palmitic being present in the more favorable sn-2 position.

There are two families of essential fatty acids, derived from linolenic acid (C 18:2 n-6) and linolenic acid (C18:3 n-3). From linoleic acid arachidonic acid (AA) (C20:4 n-6) is formed, from a-linolenic acid, after chain elongation and desaturation steps, Eicosapentanoic acid

(EPA) and Docosahexaenoic acid (DHA) (C22:6 n-3). AA and EPA are precursors of prostaglandines, while DHA is essential for the development of the brain and the eyes. DHA is recently found to have important effects also on gene expression and is a important substrate causing DNA methylation in utero. Studies have shown that the administration of DHA to mothers during pregnancy is related to a better psychomotor development of the offspring. Although some studies indicated a better psycho motor development with supplementation of formula with DHA, there is still debate on this topic and no definite conclusions are possible at the moment [17]. Studies have shown that excess EPA might be harmful for newborn infants, it might have a negative effect on growth. Although it is recommended to supplement formula's with fish oil, one has to be prudent with the amount of EPA in this oil. The amount of EPA should be less than the DHA intake. Although we found that preterm infants are capable to synthesize AA and DHA from they parent compounds soon after birth, levels decrease rapidly after birth when these fatty acids are not supplied with nutrition [6]. Human milk contains both AA and DHA. The estimated requirements for the parent compounds are linoleic acid 400–1500 mg/kg/day and more than 55 mg/kg/day for a-linolenic acid. The estimated requirements for DHA are 12–30 mg/kg/day and 18–42 mg/kg/day for AA. There is a competition between the chain elongation and desaturation of both parent essential fatty acids. The intake of linoleic acid is always higher compared to a-linolenic acid. Due to the competition between the chain elongation and desaturation between both lipid classes, might a high intake of linoleic acid result in a low formation of the essential fatty acid DHA. The ratio of these fatty acids should be around 5 to 1, for AA to DHA a ratio of 1–2 is advised [2].

Carbohydrates

The main carbohydrate in human milk, as well as cow's milk is lactose, the combination of glucose and galactose. Why human and cow's milk contains galactose is unknown. Galactose needs to be converted in the liver to glucose before it can be released as glucose in blood. Glucose is a very important substrate for the preterm infant due to the high consumption of glucose by the brain. Studies have shown a glucose utilization of preterm infants of 6 mg/kg/min [15]. When the supply is less than this amount, endogenous glucose production is needed, from glycogen and amino acids. The glycogen stores of preterm infants are very limited and might be exhausted after a few hours. The risk to develop a hypoglycemia therefore is high in preterm infants and especially in preterm infants born small for gestational age. Studies already done many years ago showed that neurodevelopment was impaired in preterm infants with repetitive periods of hypoglycemia (blood glucose <2.8 mmol/l) [16]. The -semi- continuous administration of carbohydrates, with an amount of around 12 gram/kg/day therefore must be advised. At the same time there also is a limit to the carbohydrate administration. Increasing the intake above 12–15 gram/kg/day is related to the excess formation of body fat, it does not result in an increase in glucose oxidation to provide sufficient amount of calories.

Minerals

The fetus in utero increases in weight from around 1000 gram at 26 weeks to 3500 gram at term. This increase in weight is accompanied by an important increase in minerals, especially sodium, potassium, calcium, phosphorus and iron. The preterm infant has to achieve this gain in minerals after birth.

The accretion of calcium and phosphorus during the last trimester of normal pregnancy is estimated as 60–80 mg/kg/day. It is very difficult to provide the preterm infant with sufficient amounts of calcium. Therefore ostopenia is frequently seen in preterm infants. The resorption of calcium in the gastro intestinal tract of preterm infants is around 60%. Given the low rate of absorption is an intake of 120–140 mg/kg/day advised [2]. This intake however might result in the formation of sedimentation of calcium at the bottom of a bottle and the formation of calcium soaps. Carefully designed formula's therefore are needed. Phosphorus is much better absorbed than calcium, around 90% of the administered P is absorbed. The amount of P needed is related to the amount of Ca absorbed, for bone growth the ratio is almost 1:1. When the estimated Ca absorption is 60–80 mg/kg/day, the phosphorus intake should be 70–90 mg/kg/day.

Iron is essential for brain development, iron deficiency therefore should be prevented. There is a large transfer of iron during the last trimester of pregnancy, the preterm infant lacks these iron stores. An overdose of iron also must be prevented in the preterm infants, as iron is a potent pro-oxydant and might cause the formation of free oxygen radicals. Excessive iron supplementation is also related to an increased rate of infection, poor growth and a disturbed absorption of other minerals. Studies have shown that an iron intake of less than 2 mg/kg/day will likely result in iron deficiency in very low birth weight infants. As a high iron intake might cause adverse effects, an iron intake of 2–3 mg/kg/day is advised [2, 8]. Iron supplementation must be started at 2–4 weeks after birth. Higher iron intake is needed in infants who have undergone frequent blood sampling with higher volumes, while iron supplementation must be restricted in infants receiving multiple blood transfusions.

A high iron intake as well as multiple blood transfusions are correlated with an increased risk to develop retinopathy of prematurity.

The need for sodium and potassium is higher for the preterm infant compared with the term infant due to an immaturity of the kidneys, minerals needed for growth and losses through the skin with evaporation. The sodium and potassium requirements for preterm infants are given in table 1.

Table 1

Recommended intakes for macro- and micronutrients expressed per mg [middle dot] kg-1 [middle dot] day-1 and per 100 kcal unless otherwise denoted Agostoni et al., 2010 [2]

Min–max	Per $kg^{-1} \cdot day^{-1}$	Per 100 kcal
Fluid, mL	135–200	
Energy, kcal	110–135	
Protein, g <1 kg body weight	4.0–4.5	3.6–4.1
Protein, g 1–1.8 kg body weight	3.5–4.0	3.2–3.6
Lipids, g (of which MCT <40%)	4.8–6.6	4.4–6.0
Linolenic acid, mg*	385–1540	350–1400
α-linolenic acid, mg	>55 (0.9% of fatty acids)	>50
DHA, mg	12–30	11–27
AA, mg†	18–42	16–39
Carbohydrate, g	11.6–13.2	10.5–12
Sodium, mg	69–115	63–105
Potassium, mg	66–132	60–120
Chloride, mg	105–177	95–161
Calcium salt, mg	120–140	110–130
Phosphate, mg	60–90	55–80
Magnesium, mg	8–15	7.5–13.6
Iron, mg	2–3	1.8–2.7
Zinc, mg‡	1.1–2.0	1.0–1.8
Copper, μg	100–132	90–120
Selenium, μg	5–10	4.5–9
Manganese, μg	≤27.5	6.3–25
Fluoride, μg	1.5–60	1.4–55
Iodine, μg	11–55	10–50
Chromium, ng	30–1230	27–1120
Molybdenum, μg	0.3–5	0.27–4.5
Thiamin, μg	140–300	125–275
Riboflavin, μg	200–400	180–365
Niacin, μg	380–5500	345–5000
Pantothenic acid, mg	0.33–2.1	0.3–1.9
Pyridoxine, μg	45–300	41–273
Cobalamin, μg	0.1–0.77	0.08–0.7
Folic acid, μg	35–100	32–90
L-ascorbic acid, mg	11–46	10–42
Biotin, μg	1.7–16.5	1.5–15
Vitamin A, μg RE, 1 μg ~ 3.33 IU	400–1000	360–740
Vitamin D, IU/day	800–1000	
Vitamin E, mg (α-tocopherol equivalents)	2.2–11	2–10
Vitamin K_1, μg	4.4–28	4–25
Nucleotides, mg		≤5
Choline, mg	8–55	7–50
Inositol, mg	4.4–53	4–48

AA = arachidonic acid; DHA = docosahexaenoic acid; IU = international unit; MCT = medium-chain triacylglycerols.

Calculation of the range of nutrients expressed per 100 kcal is based on a minimum energy intake of 110 kcal/kg.

* The linoleic acid to α-linolenic acid ratio is in the range of 5 to 15:1 (wt/wt).

† The ratio of AA to DHA should be in the range of 1.0–2.0 to 1 (wt/wt), and eicosapentaenoic acid (20:5n-3) supply should not exceed 30% of DHA supply.

‡ The zinc to copper molar ratio in infant formulae should not exceed 20.

Pro- end Prebiotics

The gastro intestinal tract of an adult contains more bacteria than the total number of cells of the body. It is estimated that the gastro intestinal tract contains bacteria. Many of these bacteria are not yet characterized. A number of these bacteria are considered "healthy" bacteria, an other part as potential pathogens. Examples of "healthy" bacteria are Bifido Sps and lactobacillae, while gram negative bacteria as E. coli, Pseudomonas and others are considered as potential pathogens. The gastro intestinal tract of the preterm infant becomes colonized with bacteria during the passage trough the vaginal tract during delivery. Some bacteria might pass the fetal membranes and cause a first colonization before birth. Further colonization takes place after birth, partly from the environment, but also from the mother through breast milk. Human milk contains bacteria. Studies have shown that the gastro intestinal flora of an infant born by cesarean section is different from the vaginally born infant, most likely due to a lack of bacteria transmitted during the passage through the birth canal [4]. The variability of bacteria is higher in infants receiving breast milk compared to formula fed infants [3]. Bacteria in the gastro intestinal tract play an important ant role in the development of the immune system, what is related to the presence of many lymph nodes around the g. e. tract.

The gastro intestinal flora of formula fed infants generally contains less of the "healthy" bacteria Bifido sps and lactobacillae. Many studies have evaluated if the supplementation of formula with live bacteria (probiotics) has positive effects for the preterm infant. A recent meta analysis of all studies done in preterm infants receiving pro-biotics concluded that the incidence of NEC was reduced in infants receiving pro-biotics [1]. It is not clear at this moment which pro-biotic bacteria should be given at what dose. More studies are needed to delineate what the advantages of pro-biotics might be, which bacteria should be given and at what dose.

Another way to influence the g. e. flora is the administration of prebiotics. This are soluble long chain sugars that are not absorbed in the g. e. tract. These sugars stimulate the growth of the so called "healthy" bacteria. Studies have shown higher levels of these bacteria after the supplementation of formula with these sugars [3]. Studies in term infants with a family history of allergic symptoms have shown a reduction of infections and allergic symptoms. In a large European study in infants without a family history of allergy, we hardly found a difference in the incidence of infections in relation with the supplementation with pre-biotics [11, 26]. Studies in preterm infants found a lower incidence of infections in infants receiving a combination of pre-biotics [19]. More studies are needed to define to potential role of pre-biotics in a preterm formula.

NUTRITION IN THE FIRST DAYS AFTER BIRTH

Optimal nutrition of the preterm infant in the first few days after birth is very important. A weight loss up to 10% is frequently seen in these infants. This is not only due to a loss of water, but also of tissue, including lean body mass. Regaining these losses is difficult, therefore is it important to prevent these losses.

The fetus receives before birth up to 3 g/kg/day amino acids. Interruption of this supply will result in a negative nitrogen balance. Many studies in preterm infants have shown that protein balance can be achieved already at the first day of life when at least 1 gram amino acids is provided intravenously [12]. This is also true at a relatively low caloric intake of 40 kcal/kg/day. Many recent studies have evaluated the administration of up to 3.5 gram amino acids from the first day of life. Although a positive protein balance can be achieved with this intake, in a number of infants an increase in blood urea was found. If this might be harmful for these infants is presently unknown. It might be advisable to start with 1–1.5 grams of amino acids as soon as possible after birth and to increase this dose to 2.5 grams on day two and 3–3.5 gram on day three. Which amino acid solution is the most optimal is still a matter of debate. This is partly due to the fact that the exact needs of all essential amino acids is yet unknown. Secondly, not all amino acids are very well soluble in the i. v. Amino acid solutions. like cysteine. An amino acid solution with 10% AA has advantages as less fluid is needed to provide sufficient AA.

The amount of glucose that can be give on the first days of life is limited due to the risk of hyperglycemia. As indicated before, is an minimum intake of 6 mg/. kg/min advised. In order to provide sufficient calories is the administration of i. v. lipids is advised. Most reviews advise to start with 1 g/kg/day on day one or two and increase this dose in three days to 2.5–3 gram/kg/day. It is yet unclear which i. v. Lipid emulsion is most optimal for preterm infants. Emulsions with 20% lipids are better tolerated compared to 10% emulsions. Most emulsions contain high amounts of linoleic acid, and very limited amounts of a-linolenic acid. This might lead to a deficiency of DHA. Some recently developed i. v. lipid emulsions contain DHA and less linoleic acid [20]. More studies regarding the i.v, lipid emulsions are needed.

Oral nutrition in the first days after birth

There are basically no contraindications to start with oral feeding within hours after birth in the preterm infant. One exception could be the infant born with severe asphyxia. Early introduction of enteral feeding might enhance the maturation of the gastro intestinal tract [22]. The gastrointestinal tract might — partly-be dependent on nutrition delivered in the tract itself. The most published advise is to start on the first day of life with 20 ml/kg/day and increase this with the same amount daily. There are no randomized controlled trials to show with which intake to start and how to increase the intake daily. Neither are there good studies about the gastric residuals as indicator to stop or continue feeding. Residuals just before a next feeding of 3 ml in ELBW infants and 5 ml in VLBW infants probably is physiologic.

The question is with which feeding to start. Human milk of the own mother has the clear preference. The mother will be able, in most situations, to provide this rather small amount of milk during the first few days after birth. It is questionable if, in the absence of mothers own milk, donor human milk or formula must be given. Given the composition of donor human milk and formula seems a preterm formula more appropriate. There are no convincing studies to show that -partially- hydrolyzed formula has advantages.

Oral nutrition after the first few days of life

Mothers own milk is considered to be the most optimal feeding for the preterm infant. As indicated before, the composition of mothers own milk is quite variable and in most cases insufficient regarding the content of protein, minerals, especially Ca and P and vit D and vit K. When mothers own milk is given, it is advisable to add fortifiers, including these compounds that might be too low in this milk. How much fortifier to add is not simple. Ideally, the composition of human milk should be measured before supplementing it. This might not always be possible. A too low intake of protein will result in a low gain in length and weight, a too high intake in an increased urea in blood. Whether sufficient Ca and P is provided can be estimated from the excretion of Ca and P in urine, there should be small, but almost equal loss of both in urine. A higher Ca than P loss indicates a low P intake, a lower Ca than P loss a low Ca intake.

When mothers own milk is not available, is it advised by some authors to provide donor milk. One must realize however that the protein content, as well as the content of other vital products in donor milk, might be rather low and insufficient for the preterm infant, as is donor milk obtained from mothers who delivered at term. When donor milk is used, one should measure the content of protein, calcium, phosphorus and calories in that milk and add supplements as needed.

Industry has designed a number of special preterm formulas. There are some differences between these formulas, it is not likely that these differences are clinically important. Recently the use of hydrolyzed whey protein was advised, but more studies are needed to show if this has advantages fore the preterm infant.

All preterm formula's are supplemented with essential fatty acids, both the parent compounds and DHA and AA. Some formula's are supplemented with probiotics, others with prebiotics. Formulas are also supplemented with nucleotides, if this has advantages for the preterm infant needs more studies.

A number of studies, but certainly not all, have shown a lower incidence of necrotizing enterocolitis in preterm infants receiving human milk. It is, in these studies, difficult to differentiate between the effect of the composition of human milk and other factors that might be related to the development of this disease. It might for instance well be that the mother of a very sick infant might have problems to produce milk, while the illness of the child might be a risk factor for the development of NEC.

Another component that might be advantageous or preterm infants is glutamine. Glutamine might improve gut integrity and thereby reduce bacterial translocation. In a meta-analysis no evidence for a lower incidence of invasive infections was found in infants receiving a glutamine enriched nutrition [18]. Some, but not all studies, showed a higher gain in weight, length and head circumference in infants receiving supplemental glutamine [27]. More studies are needed to firmly determine the role of glutamine in neonatal nutrition.

The European Society for Pediatric Gastroenterology and Nutrition published in 2010 recommendations for the intake of nutrients for the preterm infant. These data are shown in table 1.

CONCLUSION

In conclusion, optimal nutrition is of vital importance for the preterm infant. It not only promotes growth, it stimulates the neurodevelopment and reduces the risk for complications like infections, retinopathy of prematurity, BPD and NEC. Early, aggressive nutrition directly after birth with the immediate introduction of amino acids and rapid introduction of lipids is advised. Enteral feeding should be started very soon after birth, preferably on the first day of life and increased in the days thereafter. The first choise for enteral feeding in mothers own milk, supplemented from the second week with a fortifier. Special preterm formula serves as a good alternative in cases breast milk is not available.

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