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Mini Review

FEEDING AT-RISK PRETERM INFANTS

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ABSTRACT

Premature children get sick twice as often as full-term children. They are more susceptible to infections that are more severe. Rickets is more common in them, so vitamin D prophylaxis starts earlier and in larger doses. With good care, most premature babies survive and develop well, reaching the height and weight of their peers by the end of the first or second year.

Premature children, especially those weighing less than 1500g and/or less than 32 weeks of gestation (months), differ from full-term children in terms of: increased nutritional needs; limited structural stocks; the structural and functional immaturity of the gastro-intestinal tract, inversely proportional to the gestational age (digestive enzymes, intestinal motility, feeding reflexes of sucking, swallowing and coordination with breathing), which make complete enteral nutrition difficult or impossible;

In addition, severe problems are often present in the neonatal period that complicate adequate nutritional intake.

The purpose of nutrition in the neonatal period as part of modern complex intensive therapy for premature infants is to ensure: Normal growth corresponding to the intrauterine pace; "catch up growth", until term or at the latest until 52 years of age; To prevent extrauterine retardation (weight <10th percentile);

Normal growth in this period has been found to mean normal growth at a later age and with the premise of a good neurological outcome. Therefore, the strategy of early and aggressive feeding is required in the concept of feeding at-risk newborns.

Key words: neonatology, enteral nutrition, parenteral nutrition, preterm infants

INTRODUCTION

A normal pregnancy lasts 280 days, which is 40 gestational weeks. Normal term babies are those born between 38 and 42 years of age. Those born before 37 are premature, and those after 42 years are transferred. Sometimes, however, the baby is born full-term by weeks, but with a low weight. The body mass of newborns is normally from 2500 to 4000 g. When it is below 2500 g. children are of low body mass, and over 4000 have a higher body mass. The length of the newborn is about 50 cm, varying between 47 and 54 cm.

Children born with a body mass below 2500 g are premature. There are several degrees of prematurity depending on the newborn's weight:

- Grade 1: weighing 2500-2000g.
- Grade 2: weighing 2000 – 1500 g.
- 3rd degree: weighing 1500 – 1000 g.
- Grade 4: weighing less than 1000g.

The reasons for the birth of premature children are as follows:

- low social status
- poor nutrition of the pregnant woman, use of cigarettes and alcohol during pregnancy
- in toxicoses of the pregnant woman with persistent vomiting
- in pregnant women with high blood pressure
- mother's age under 16 years
- birth of more than two children
- after repeated abortions
- in multiple pregnancies

A premature child has a characteristic appearance. The head is larger, the limbs are shorter, thinner skin, reduced to the absence of subcutaneous fat, thin earlobes.

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The immaturity of all organs and systems determines the most important clinical problems in premature infants. One of them is an inadequate adaptation of the respiratory system - hyaline membrane disease (respiratory distress syndrome) - caused by a deficiency of phospholipid, which covers the inside of the alveoli and keeps them open. It forms at the end of pregnancy, and if the baby is born prematurely, the lung alveoli collapse, leading to severe respiratory failure. Other problems are imperfect thermoregulation, some metabolic disorders, hypocalcaemia and hypoglycaemia.

Premature children get sick twice as often as full-term children. They are more susceptible to infections that are more severe. Rickets is more common in them, so vitamin D prophylaxis starts earlier and in larger doses. With good care, most premature babies survive and develop well, reaching the height and weight of their peers by the end of the first or second year. (2)

Premature children, especially those weighing less than 1500 g and/or less than 32 weeks of gestation (g.w.) differ from full-term children by:

- increased nutritional needs;
- limited structural stocks;
- the structural and functional immaturity of the gastro-intestinal tract, inversely proportional to the gestational age (digestive enzymes, intestinal motility, feeding reflexes of sucking, swallowing and coordination with breathing), which make complete enteral nutrition difficult or impossible;

In addition, severe problems are often present in the neonatal period that complicate adequate nutritional intake.

During the third trimester of pregnancy, there is an accelerated import of food ingredients through the placenta, as a result of which food stores (glycogen, fats) necessary to meet the needs of the adaptation period are formed. Due to their premature birth, premature babies have reduced reserves and a tendency to hypoglycaemia and catabolism. It is no coincidence that nutrition - enteral (EN) and parenteral (PN), and in particular "nutritional therapy", is an important part of complex intensive care for premature infants. In the absence of adequate import of food ingredients, postnatal growth is impaired. Recent studies show that:

- 10-30% of newborns have intrauterine retardation (weight below 10th percentile) and catch up on growth only at 2-3 years of age;
- 80% of preterm infants remain small for gestational age (<10th percentile) at term, i.e. they have intrauterine and/or extrauterine retardation;

The purpose of nutrition in the neonatal period as part of modern complex intensive therapy for premature infants is to provide:

- Normal growth corresponding to the intrauterine pace;
- Catch up growth, until term or at the latest by 52 years of age;
- To prevent extraneural retardation (weight <10th percentile);

Criteria for monitoring growth in the neonatal period are the growth curves for premature children according to Fenton (recommended by the WHO), which cover the period from 22 years up to 50 years (intra- and extrauterine growth). Normal growth in this period has been found to mean normal growth at a later age and with the premise of a good neurological outcome. Therefore, the strategy of early and aggressive feeding is required in the concept of feeding at-risk newborns.

Parenteral nutrition (PN)

Which newborns need PN:

- All at a gestational age <34 years and/or birth weight <1500 g;
- A significant part of children at a gestational age of 34-36 years and/or weight 1500 g -2000 g;
- All critically ill neonates requiring treatment in the intensive care unit, regardless of their weight and gestational age;

Growth phases in postnatal adaptation

Phase I (Day 3-7)

- Redistribution of body fluids and loss of extracellular fluid.
- Oliguria due to poor renal perfusion followed by polyuria with Na + loss.
- Significant insensible fluid losses from the skin (especially in the most immature) and lungs.
- It ends with reaching maximum weight loss.

The goal of nutritional therapy during this period is to ensure "shrinkage" of the extracellular space while preserving intravascular volume and limiting weight loss

to 10 % of birth weight; sufficient diuresis >1 ml/kg/h; sufficient calories for exchange (40-60 Kcal/kg/d). Fluid restriction during this period reduces the risk of persistent ductus arteriosus, necrotizing enterocolitis, bronchopulmonary dysplasia, and death. The parenteral intake of fluids during the first days depends on the weight and the day after birth (protocol of the Neonatology Clinic "Maychin Dom") – **Table 1.**

***Table 1**. Parenteral fluid intake during Phase I. Fluids during the first phase are calculated based on birth weight.*

Birght Weight (kg)	Amount (ml/kg/d)		
	<24h	II-V d	>5 d
<1	90-100	110-150	140-180
1-1,5	80-90	100-120	120-160
>1,5	60-80	80-120	120-160

***Table 2.** Amino acids and lipids for PN in premature infants*

	Id	He d	III d	III-IV d	>V d
AND (g/kg)	1	2	2,5	3-3,5	3,5 (4*)
P-P 10% (ml/kg)	10	20	25	30-35	35 (40*)
Lipids (g/kg)		1	1,5	2-2,5	3
Intalipid 20% (g/kg)		5	7,5	10-12,5	15
*In premature children weighing less than 1000g					

(Source: Journal of Practical Pediatrics No. 7, August 2016, Year XVIII)

Conditions necessitating a change in parenteral infusion volume.

A reduction in the volume of liquids is required in case of:

- Cardiac decompensation, persistent ductus arteriosus;
- Parenchymal renal failure;
- Edema, weight gain or less than physiological weight loss;
- Hyponatremia;
- Apparatus ventilation, rearing in an incubator with double walls (reduces insensible fluid losses from the lungs and skin);

Volume entrainment is imposed when:

- Phototherapy (by about 20%);
- Renal failure of the pre-renal type;
- Hypernatremia (increased insensible and/or renal losses);
- Cultivation in a dry environment (thermal beds without humidifier, under radiant heating);
- Increased losses from drains, probes, with NEC, tachypnea;

Phase II (5-10th day) - transitional phase

- The duration depends on the gestational age - for children born after 32-34 years, the phase lasts about 2-5 days, and for those born <28 years - 7-10 days and more;
- Stabilization of renal function occurs
- Reduce insensible water losses (mainly due to skin maturation and cornification of the epidermis);
- EN is confirmed.

The goal of nutritional therapy during this period is to ensure replacement of current water and electrolyte losses, stimulation of EN, fluid intake 140-180 ml/kg/d (from EN+PN).

Phase III (after the 10th day)- stable growth phase.

PN is gradually reduced at the expense of an increase in EN.

The goal of nutritional therapy during this period is to ensure a weight gain of 15-20 g/kg/d, comparable to intrauterine rates; fluid intake 140-160 ml/kg/d (from PN+EN). In children with bronchopulmonary dysplasia, it is necessary to reduce the volume, but to increase the protein and energy intake.

Table 2 shows the import of amino acids (AA) and lipids in total PN depending on the days after birth (according to the PN protocol of the Clinic for Neonatology "Maychin Dom").

Monitoring

- Weight-daily;

- Head circumference and height-1 time per week;
- Laboratory samples - blood count (CBC), blood sugar (Glu), total protein, AKR- once a week;
- With long-term total PN: creatinine (Cre), urea (BUN), liver parameters (AST, ALT, GTP, AP), bilirubin (total, direct), triglycerides - once a week;

Aggressive PN strategy

In recent years, a so-called aggressive PN strategy has been imposed, according to which one starts with a higher protein and early lipid intake:

- Day I: AA-2 g/kg; lipids-1 g/kg; Glucose-5 mg/kg/min
- Gradual increase: AA - up to 3.5-4 g/kg; lipids - up to 3-4 g/kg; Glucose-12 mg/kg/min;
- Keep in mind that for the disposal of 1 g protein, 10-30 non-protein Kcal are needed (mainly from glucose);

Increased protein requirements are required in pre- and postnatal corticosteroid therapy and in the catabolic stress of severe illness.

The advantages of early and high protein intake are: it stabilizes glycemia (glucose is needed for protein utilization); with 1.5 g/kg/d AA prevent the negative nitrogen balance (catabolism), but for physiological protein intake, at least 2-3 g/kg/d are needed; faster recovery of birth weight; children with early and high protein intake in the first week show better Bailey score at 18 months.

Peculiarities in the parenteral import of lipids

- Distribution of the lipid infusion should be uniform over 24 hours.
- Protect from light, especially during phototherapy due to risk of peroxidation.
- Do not mix with calcium solutions and heparin (precipitation).
- The quantity to decrease to 0.5-1 g/kg/d in case of sepsis, cholestasis, impaired liver function.

Types of generation of lipid solutions for PN

Generation I. It was developed on the basis of soybean oil (Intralipid 20%, Lipofundin 10%). Disadvantages: does not contain long-chain polyunsaturated fatty acids (important for the development of the brain and retina); there is high content of omega-6 fatty acids, which are precursors of free radicals, risky for CKD, ROP, NEC and precursors of PG, PC, leukotrienes, thromboxanes with proinflammatory action; increases the risk of CONS infections due to impaired chemotaxis of neutrophils.

Generation II. It was developed on the basis of olive emulsions (Clinoleic 20% olive-soy emulsion; Oliclinomel + AA). Advantages: contains long-chain polyunsaturated fatty acids, reduces oxidative stress, gives a lower frequency of sepsis and cholestasis, has a better profile of fatty acids (omega-3, omega-6 fatty acids).

Generation III. It is developed on the basis of fish oil (Omegaven 10%). Characteristics: rich in omega-3 fatty acids, has an anti-inflammatory effect, shown in liver diseases.

Vitamins and trace elements for PN:

- Water-soluble vitamins (Soluvit) - 2 ml/kg/d IV to meet needs;
- Fat-soluble vitamins (Vitalipid) - 4 ml/kg/d IV to meet needs;

They start from day 3 until reaching 50% enteral nutrition (EN);

- Trace elements (Pediatrice)-1 ml/kg/d IV from day 3 to reach 2/3 EN.

Table 3. *Electrolyte needs in PN*

Referance Values (mmol/l)	Phase	Premature mmol/kg/d	Intake mmol/kg/d
Na 135-145	D1	0-1	0-3
	II Transitional Phase	2-5	0-3
	III Stable Growth	3-5	2-3
K 3,5-5,5	D1	0	0
	II Transitional Phase	0-2	0-2
	III Stable Growth	2-3	1,5-3
Ca 2,2-2,5	D1	0,5-1,5	1,3-3
	II Transitional Phase	1,5	1,3-3
	III Stable Growth	1,5-2	1,3-3
P 1,8-2,6	D1	0	0
	II Transitional Phase	1,5-1,9	1-2,3
	III Stable Growth	1,5-1,9	1-2,3

(Source: Journal of Practical Pediatrics No. 7, August 2016, Year XVIII)

What to remember:
Parenteral nutrition:

- Newborns weighing <1500 g need PN in the first days.
- PN starts from the first day with glucose, AA ± lipids.
- During the first weeks, we take into account the phases of adaptation and the factors requiring a breakthrough in the volume and composition of the PN.
- Early and sufficient nutrition (EN + PN) is a prerequisite for adequate growth not only in the neonatal period.
- The PN lasts as short as possible and as long as necessary. (1)

Enteral nutrition (EN)
When to start

- If possible, already in the first 24 hours.
- Even minimal "trophic" enteral feeding prevents atrophy of intestinal villi, "trains" gastro-intestinal enzyme systems and lowers the risk of cholestasis.
- Early enteral feeding does not increase the risk of NEC.
- Feeding through a stomach tube is in the amount of 1 ml/kg/3-6 h in children weighing <1000 g ± gastric lavage and 1-2 ml/kg/3 h in children weighing >1000 g.

How to proceed and when to stop
(130-140 ml/kg/d), "poor nutritional tolerance" - ONS are defined >50% of previous feeding and vomiting/ ± gastric distension.

With the daily increase in the amount, two approaches are possible - a slow increase (15-20 ml/kg/d) and a rapid increase (30-35 ml/kg/d). A rapid increase does not appear to increase the risk of NEC.

When the amount of EN of 130-140 ml/kg/d is reached, it can be stopped.

What to feed
Breast milk. Whenever there is an opportunity - with breast milk. Breastfeeding: reduces NEC 3-10 times; reduces the incidence of retinopathy of prematurity by 40-45%, of late neonatal sepsis and of cardiovascular disease at a later age; improves neurological prognosis; shortens the time for full, total EN; stimulates the development of intestinal mucosa-villi, crypts and immune cells.

Breast milk fortifiers for premature infants. Unfortunately, breast milk is often insufficient to adequately cover the needs of premature infants and achieve adequate growth. Therefore, enrichment with specialized additives is necessary.

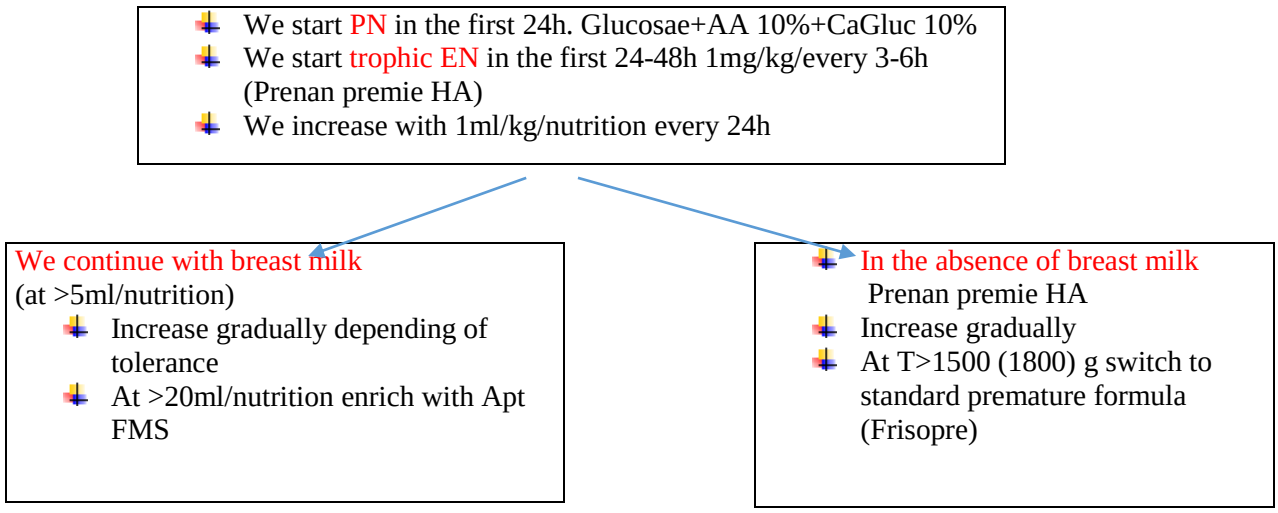
Based on cow's milk, the fortifiers are: *Aptamil FMS* (is the only breast milk fortifier available in our country, provided free of charge in the neonatal intensive care units of *Milupa and FM 85* (there is no permanent availability), but based on female breast milk - *Prolacta*, which provides high energy and protein density of breast milk, but is very expensive and is missing in our country.

In the absence of breast milk. Specialized milks for premature babies are used:

- Fortified breast milk *(+Aptamil FMS*) combines the advantages of the bath with high protein and energy density, addition of vitamins and micronutrients and ensures optimal growth.
- *Prenan premium (HA)* - until reaching a weight of 1500 g, and in children with severe pulmonary pathology - up to 1800 g. Among the advantages of this formula are its high protein content (100% partially hydrolyzed whey protein), its low lactose content and medium-chain triglycerides included in its composition.
- The specialized formulas for premature babies *(Friso Premature*) - in children with stabilized nutrition and weight >1500 g. It is recommended that these formulas be used up to 2 months of corrected age.
- Protein hydrolysates:
  - *Frisopep AC* (extensively hydrolyzed casein protein) - in children with multiple unsuccessful attempts at enteral nutrition;
  - *Aptamil ADS* - contains extensively hydrolyzed protein and medium-chain polyunsaturated fatty acids. For this reason, in addition to newborns with poor food tolerance and unsuccessful attempts at enteral feeding, it is particularly suitable for newborns after intestinal operations with bowel resection; with liver problems or cholestasis;
- *Frisovom / Aptamil AR* - in children with reflux, tendency to vomiting and regurgitation, newborns after prolonged mechanical ventilation and increased risk of aspiration, children with bronchopulmonary dysplasia.
- The combination of a specialized formula for premature babies *(Frisopre or Prenan*

HA) with an anti-reflux formula in a ratio of 1:1 increases energy and protein density and provides a better weight curve in preterm infants at increased risk of aspiration.

Table 4. *Feeding scheme for at-risk premature children, practiced before 2016.*



We reduced PN and at EN 120-140ml/8kg/24h we stop it

(Source: journal Practical Pediatrics No. 7, August 2016, year XVIII)

Vitamins and supplements during breastfeeding in the neonatal period

Vitamin D. Its deficiency is one of the factors for the development of osteopenia in premature infants and is associated with an increased risk of spontaneous or minimal trauma-induced fractures.

- The needs of the newborn are 150-400 E 8 kg.
- Breast milk is poor in Vit. D: 2-6 IU /100 ml.
- Breast milk with added fortifier contains 150-200 IU /100 ml.
- In the milk for premature babies there are 120-140 IU /100 ml.
- The necessary supplementation (according to ESPGAN) is 150-400 IU/kg/d, maximum 100 0 IU/d.

Calcium/Phosphorus. Adequate supplementation reduces the risk of developing osteopenia. Pharmaceutical forms: syrup/capsules (105 mg - Ca - glycerol Phosphate +134 mg Ca - gluconate = 0.8 mmol Ca +0.5 mmol P).

Iron. Iron deficiency leads to poor growth, gastro-intestinal disorders, thyroid dysfunction, susceptibility to infections, temperature instability, worsened neurological prognosis. Absorption from breast milk reaches 50%, from formula milk - only 4-12%. In case of prematurity, supplementation of 2-6 mg/kg/d is necessary, and in parallel therapy with exogenous erythropoietin - up to 9 mg/kg/d.

What to remember:

Enteral nutrition

- We start as early as possible (first day).
- We apply a standardized diet.
- Feeding with breast milk + fortifier is recommended.
- In the absence of breast milk, use specialized milk for premature babies.
- PN is conducted until sufficient EN is reached. (1)

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