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PECULIARITIES OF PHYSICAL GROWTH AND BODY COMPOSITION OF PRETERM INFANTS, RECEIVED DIFFERENT TYPES OF FEEDING, AT THE DISCHARGE FROM HOSPITAL [2nd developmental care stage]

Background: *This article is devoted to a research and practice problem — optimization of feeding preterm infants.* ***Patients and methods:*** *80 preterm infants of different GA with perinatal pathology were included in the study group. Anthropometric figures of weight and length z-scores and also BMI of preterm infants, received different types of feedings, at the discharge are presented. All patients' body composition (Fat free mass and Fat mass) was estimated by air plethysmography.* ***Results:*** *Less mass and length at the discharge in preterm infants, received breast feeding (including fortified milk), in comparison with the infants, received mixed and formula feeding, were found out. At the same time, preterm infants received breast feeding had more optimal body composition (less fat mass), than the infants received formula feeding.* ***Conclusion:*** *Personalised approach to human milk fortifiers prescription is explained. Important practical value of methodology for estimating body composition by air plethysmography is established.*
Keywords: *preterm infants, body composition, growth, air plethysmography, feeding.*

Introduction

Perinatal survivability of extremely premature patients with very low (VLBW) or extremely low (ELBW) birth weight has improved in the recent decades through the successful primary resuscitation and controlled intensive therapy of low-weight premature infants. This brings to the forefront the issues of long-term development and delayed morbidity of the survived premature infants and study of the correlation of perinatal factors and the future persistent health disorders [1]. Previous studies confirm that inadequate early feeding negatively affects further development of premature infants [2]. It has been demonstrated that insufficient nutrition in the critical period of brain development results in the reduction in the number of brain cells, behavioral disorders, memory disorders and difficulty studying [3]. Inadequate feeding of premature infants negatively affects not only development and establishment of nervous system functions, but also the general health status [4]. More and more data indicating that insufficient physical development of premature infants and further excessive catch-up growth at the inpatient hospital treatment stage may cause development of such metabolic disorders as obesity, hypertonia, cardiovascular diseases and type 2 pancreatic diabetes in the future [5, 6]. That is why it is very important to assess physical development and plastic processes in premature infants by the time of discharge from the inpatient hospital in order to establish prognosis of the further development thereof.

The study was aimed at analyzing physical development and composition of tissues of the body of premature infants, who had undergone different types of feeding (at discharge from the inpatient hospital [2nd developmental care stage]).

Patients and methods

STUDY SUBJECTS

The study involved 80 premature neonates of varying gestational age hospitalized to the premature neonatal unit of the Scientific Center of Children’s Health (Moscow) in the period from November 2009 to October 2012. The children were admitted to the inpatient hospital at the age 2-10 days; they were being examined and treated for 14-48 days depending on the degree of prematurity and the severity of the condition at birth. Premature infants were discharged from the hospital at 36-37 weeks of post-conceptional age (PCA) provided no inflammatory foci were present. Children would usually have weight of at least 2,000 g and physiological maturity sufficient for adequate thermoregulation, spontaneous respiration and sustained sucking reflex by that age.

Gestational age-adequate birth weight and length constituted the primary criteria of study entry. Term infants and premature neonates with intrauterine development retardation, congenital malformations, organic affection of the central nervous system, grade II-III intraventricular hemorrhages, non-communicating hydrocephalus, severe infectious diseases (sepsis, necrotizing enterocolitis), hemolytic neonatal disease, endocrine pathology or genetic pathology were not involved in the study.

The subjects were divided into 3 groups depending on the type of feeding. Each group was further divided into 2 subgroups on the basis of the gestational age at birth: subgroups A involved premature infants born before the 34th gestational week, subgroups B – children born after the 34th gestational week.

Group 1 included 34 premature infants (14 boys, 20 girls) born at the gestational age of 34.0 [29.0-36.0] weeks with body weight of 2,170.0 [1,380.0-2,730.0] g. Due to absence of maternal breast milk, these patients received a specialized feeding formula for premature infants containing 2.2 g of protein / 77 kcal per 100 ml. On the basis of the gestational age, 14 children were classified to subgroup 1A, 20 children – to subgroup 1B.

Group 2 included 22 premature infants (14 boys, 8 girls) born at the gestational age of 34.5 [32.0-36.0] weeks with body weight of 2,160.0 [1,660.0-2,520.0] g. Due to insufficient maternal breast milk, these children underwent mixed feeding. The same specialized milk formula containing 2.2 g of protein / 77 kcal per 100 ml was used for supplemental feeding. 12 of these children were born before the 34th of gestation and constituted subgroup 2A; 10 of these children were born after the 34th of gestation and constituted subgroup 2B.

Group 3 included 24 children (14 boys, 10 girls) born at the gestational age of 33 [28.0-36.0] weeks with body weight of 1,875.0 [1,140.0-2,500.0] g. All these children were breast-fed. Subgroup 3A included 12 children born before the end of the 34th gestational week. Due to the relatively low birth weight of patients of this subgroup (1,790 [1,140.0-1,840.0] g) and taking into consideration ESPGHAN recommendations (2010), the breast milk to be consumed by the children was enriched with a breast milk fortifier containing 0.35 g of protein / 6 kcal and intended for fortifying 50 ml of breast milk. Subgroup 3A included 12 children with the gestational age at birth over 34 weeks and body weight of 1,920 [1895.0-2,500.0] g, who consumed unfortified breast milk.

STUDY METHODS

Calculation of the main food nutrients and caloric value of the received diet was conducted on the daily basis. The daily amount of food was calculated with a caloric method, depending on the energy requirements of a premature infant per the actual body weight.

Follow-up measurements of anthropometric parameters, including body weight and length, chest and head circumference were conducted in order to assess nutritional status.

Children were weighed on a daily basis by means of digital scales with approximation of up to 0.1 g and subsequent calculation of the average daily weight gain (g/day). Body length was measured weekly using a height meter with the standard centimeter scale with approximation of up to 0.1 cm (laying children flat on back). Head and chest circumference were measured weekly using the standard centimeter tape measure with approximation of up to 0.1 cm.
Physical development of premature infants was assessed on the basis of the recommendations by G.M. Dementyeva and E.V. Korotkaya (1981).
Z-score was calculated for all children on the basis of somatometric parameters at birth and at discharge from the inpatient hospital; it is the deviation of an individual parameter from the average value for the considered population divided by the standard deviation from the average value. Computer program ANTHRO (WHO, 2009) was used to calculate z-score. Z-score was calculated for birth weight and body weight, length and mass index (BMI) at discharge from the inpatient hospitals in groups of the premature infants, who had undergone different types of feeding.
Use of air plethysmography for determining body tissue composition by means of analyzer PEA POD (LMi, USA) (pic. 1) is a fundamentally new method of assessing nutritional status of premature infants. This test was conducted at the premature neonatal unit of the Scientific Center of Children’s Health (pic. 2, 3). Determination of the absolute lean (LBM, kg) and fat body mass (kg) allowed estimating primary orientation of plastic processes in premature infants of varying gestational age undergoing feeding with breast milk and specialized products. Body tissue composition of the premature infants, who had undergone different types of feeding, was analyzed at discharge from the hospital at the PCA of 36-37 weeks.

Pic. 1. Body tissue composition analyzer PEA POD (LMi, USA).

Pic. 2. Placement of a child into the analyzer chamber.

Pic 3. Body tissue composition determination procedure – test chamber (duration – 2 minutes).

STATISTICAL DATA MANIPULATION

The results were statistically analyzed using software package STATISTICA v 6.0 (StatSoft Inc., USA). The following non-parametric methods were used: Wald-Wolfowitz, Kolmogorov-Smirnov and Mann-Whitney tests. The data are presented as median and interquartile range: Me (min-max, 25^{th}-75^{th} percentiles). In terms of quantitative parameters, several separate groups would be compared non-parametrically using Kruskal-Wallis test and subsequent pairwise comparison using Mann-Whitey test. Analysis of the cause-effect relationships was based on determination of the Spearman's rank correlation coefficient. The differences between the parameters were considered statistically significant at $p < 0.05$.

Results

Table 1. Average concentration of main nutrients and caloric value of the diets at the age of 10 and 20-25 days

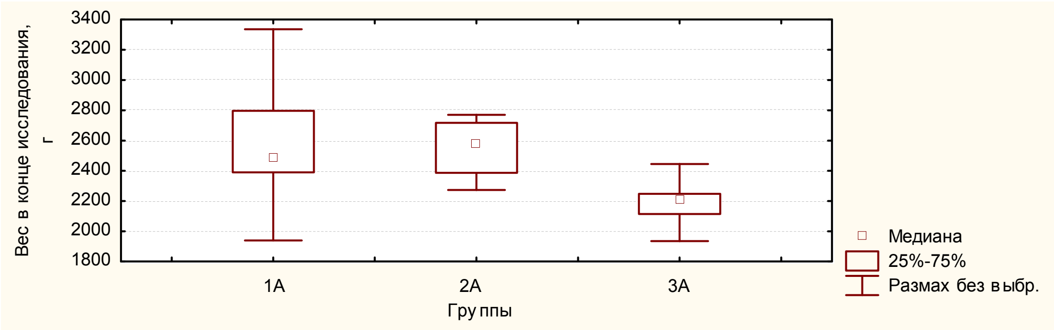
Parameters	Group 1 (*n* = 34)		Group 2 (*n* = 22)		Group 3 (*n* = 24)		Established norms (ESPGHAN [2010])
Children's age	10	20-25	10	20-25	10	20-25	
Protein, g/kg/day	2.9±0.1	3.7±0.2	2.6±0.2	3.5±0.4	2.4±0.3	3.6±0.2	3.2-4.08
Fat, g/kg/day	5.5±0.3	7.5±0.4	5.4±0.3	7.3±0.5	5.6±0.4	7.6±0.4	4.8-6.6
Carbohydrates, g/kg/day	10.3±0.4	13.9±0.4	10.1±0.7	13.4±0.6	10.1±0.5	15.9±0.7	11.6-13.2
Caloric value, kcal/kg/day	102.3±2.8	133.0±4.1	102.1±4.2	128.7±5.2	104.0±3.1	137.4±6.4	110-135

Analysis of nutrition of premature infants at the age of 10 days demonstrated that the children undergoing breast feeding received 2.4 g/kg of protein per day and 2.9 g/kg per day (17.2% more) in the event of artificial feeding; caloric value of diets was the same – 100 kcal/day (tb. 1). Protein concentration at mixed feeding – 2.6 g/kg per day – was intermediate. No differences regarding fats and carbohydrates were observed.

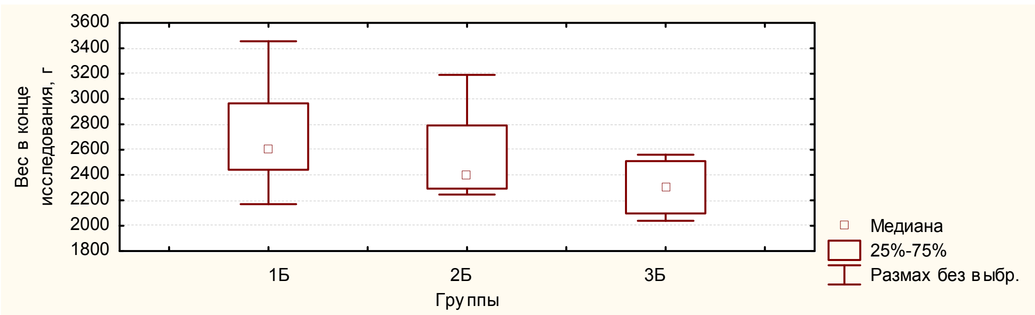
Assessment of nutrition of the observed children, who had undergone different types of feeding, by the 3^{rd} week of life, did not demonstrate any differences regarding concentration of the main nutrients and caloric value of the diets. The obtained results conformed to the recommended standards; this indicates optimal character of the feeding of children of all groups at the unit.

Results of our studies demonstrated that the premature infants, who had been receiving breast milk (fortified and unfortified) in both subgroup 3A and subgroup 3B had significantly lower body weight and length, head and chest circumference ($p < 0.05$) at discharge from the inpatient hospital than the premature infants, who had been receiving the specialized formula (pic. 4).

Pic. 4 (a-d). ***Comparative analysis of anthropometric parameters at discharge from the inpatient hospital in the premature infants, who had undergone different types of feeding*.**



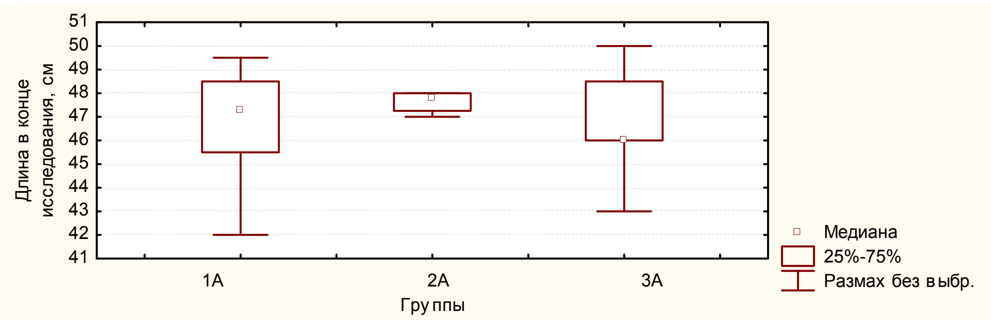
Hereinafter:	
Вес в конце исследования, г	*Weight at the end of the study, g*
Группы	*Groups*
Медиана	*Median*
Размах без выбр.	*Range without outliers*



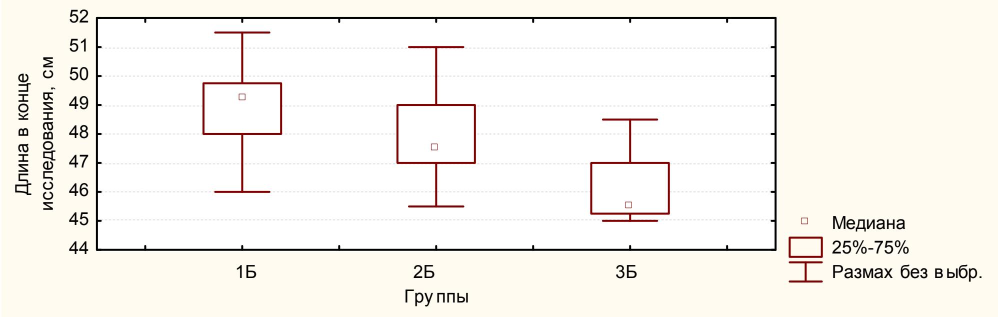
***a)** Comparative analysis of body weight parameters at discharge from the inpatient hospital in the premature infants, who had undergone different types of feeding.*

Similar statistically significant differences (lower body weight and length, head and chest circumference) were registered in the immature premature infants (gestational age under 34 weeks), who had been receiving fortified breast milk, in comparison with the children, who had undergone mixed feeding (see pic. 4).

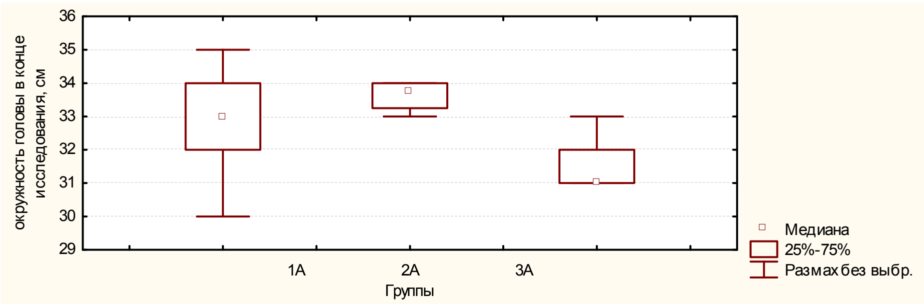
No significant differences between anthropometric parameters at 36-37 weeks of PCA of mature premature infants (gestational age over 34 weeks, subgroups 2B and 3B), who had been undergoing mixed and breast feeding, were observed (see pic. 4).



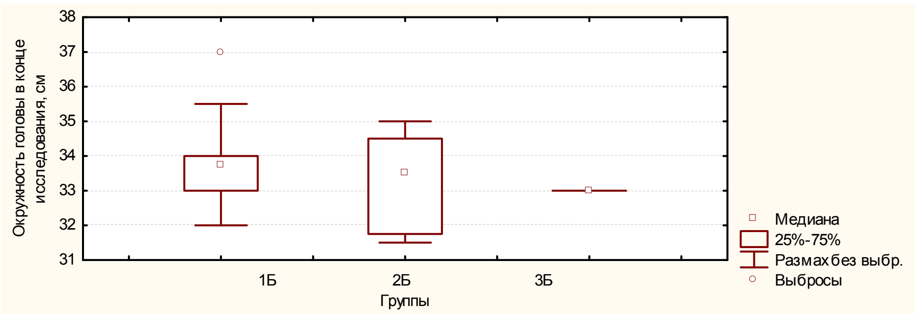
Hereinafter:	
Длина в конце исследования, см	*Length at the end of the study, cm*



***b)** Comparative analysis of body length parameters at discharge from the inpatient hospital in the premature infants, who had undergone different types of feeding.*

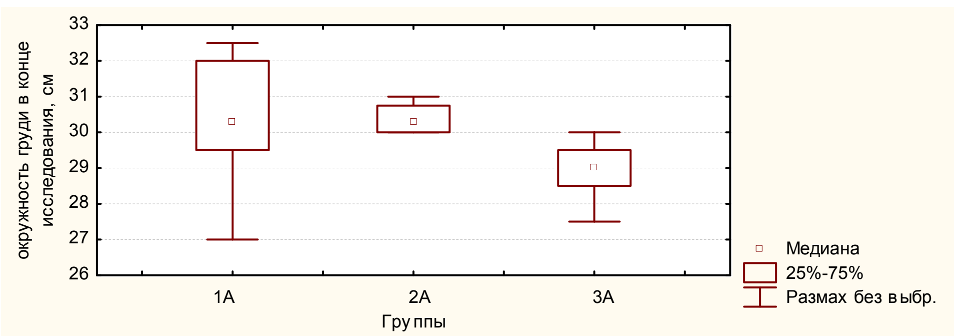


Hereinafter:	
Окружность головы в конце исследования, см	*Head circumference at the end of the study, cm*

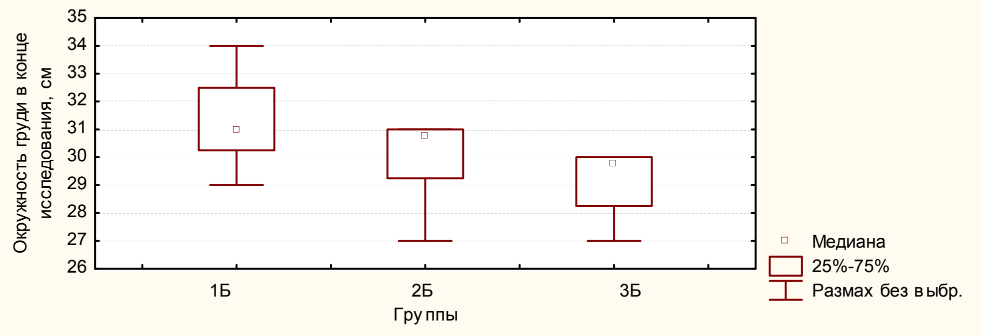


Выбросы	*Outliers*

***c)** Comparative analysis of head circumference parameters at discharge from the inpatient hospital in the premature infants, who had undergone different types of feeding.*



Hereinafter:	
Окружность груди в конце исследования, см	*Chest circumference at the end of the study, cm*



d) *Comparative analysis of chest circumference parameters at discharge from the inpatient hospital in the premature infants, who had undergone different types of feeding.*

Assessment of physical development of premature infants using program ANTHRO demonstrated that premature infants of group 3 had lower z-scores of body weight (-3.92), length (-3.81) and BMI (-3.12; $p < 0.05$) than patients from groups 1 (-2.87, -2.57, -2.30) and 2 (-3.01, -2.72, -2.15) by the time of discharge from the inpatient hospital; this indicates significant deviation of the main anthropometric parameters of the premature infants, who had been receiving breast milk, from the average population values (tb. 2).

Table 2. ***Physical development parameters and body tissue composition of the studied children by groups at discharge from the inpatient hospitals***

Parameter	Group 1 (n = 34)	Group 2 (n = 22)	Group 3 (n = 24)
Body weight, kg	2.57 [2.41-2.88]§	2.48 [2.29-2.72]	2.27 [2.16-2.56] *
Length, cm	48.5 [47.0-49.5]§	47.5 [47.0-48.0]§	46.5 [45.5-49.0] *#
Body weight, z-score	-2.87 [(-3.53)-(-2.51)]§	-3.01 [(-3.41)-(-2.30)]§	-3.92 [(-4.64)-(-3.33)]*#
Length, z-score	-2.57 [(-3.42)-(-1.79)]§	-2.72 [(-3.22)-(-2.29)]§	-3.81 [(-4.44)-(-2.35)]*#
BMI, z-score	-2.30 [(-3.02)-(-1.77)]§	-2.15 [(-2.94)-(-1.98)]	-3.12 [(-3.73)-(-2.62)]*
Head circumference, cm	33.5§ [33.0-34.0]	33.75§ [32.5-34.25]	32.5*# [31.0-33.0]
Weight gain since birth, g	566.5§ [390.0-820.0]	479.0 [370.0-556.5]	376.5* [185.0-649.0]
Average daily weight gain, g/kg per day	14.0§# [12.7-15.9]	11.9* [11.3-12.65]	12.4* [10.5-15.0]
LBM, kg	2.34§ [2.16-2.5]	2.09 [2.01-2.37]	2.08* [1.95-2.25]
Fat body mass, kg	0.44 [0.34-0.63]	0.36 [0.23-0.44]	0.30 [0.27-0.37]
Body fat, %	16.2§ [13.1-18.3]	12.85 [9.55-16.6]	13.8* [11.4-16.6]

Note. * - differences are statistically significant in respect of group 1 ($p < 0.05$), # - differences are statistically significant in respect of group 2 ($p < 0.05$), § - differences are statistically significant in respect of group 3 ($p < 0.05$); BMI – body mass index.
Hereinafter: LBM – lean body mass.

The highest body weight gain from birth to the time of discharge from the inpatient hospital and the average daily weight gain were registered in the premature infants, who had been receiving the specialized formula (566.5 [390.0-820.0] g and 14.0 g/kg per day); it differs significantly ($p < 0.05$) from the corresponding parameters of premature infants in other groups (479.0 [370.0-556.5] g and 11.9 g/kg per day in group 2; 376.5 [185.0-649.0] g and 12.4 g/kg per day in group 3) (see tb. 2).
Overall, analysis of dynamics of anthropometric data of premature infants of varying gestational age depending on the type of feeding indicates that the premature infants, who had been receiving breast milk, have significantly lower body weight and length, head and chest

circumference by the end of the study than the premature infants, who had been fed with the specialized formula, regardless of the degree of maturity at birth. Immature premature infants (gestational age under 34 weeks), who had been receiving fortified breast milk, in comparison with the children, who had been receiving mixed feeding, featured similar significant differences (lower body weight and length, head and chest circumference) at discharge. However, no differences were observed between mature premature infants, who had been receiving breast or mixed feeding.

Analysis of the body tissue composition demonstrated that by the time of discharge from the inpatient hospital group 3 premature infants had lower ($p < 0.05$) lean body mass (LBM, kg); at the same time, group 1 patients had higher fat body mass (16.2 a 13.8%, respectively; $p < 0.05$) than group 3 premature infants (see tb. 2).

Further study of the correlation between physical development and body tissue composition (lean [LBM] and fat body mass) in premature infants at discharge from the inpatient hospital was conducted separately for each group of children, who had been undergoing different types of feeding.

Positive correlation of body weight, z-score of BMI and chest circumference by the time of discharge from the inpatient hospital and LBM, fat body mass and body fat parameters was observed in the premature infants, who had been undergoing artificial feeding. Head circumference and body length correlated positively both with LBM and fat body mass (tb. 3).

Table 3. ***Interconnection of body tissue composition parameters and nutritional status at discharge in premature infants, who had been receiving the specialized formula***

Parameter	LBM, kg	Fat mass, kg	Body fat, %
Body weight, kg	**0.875***	**0.788***	**0.703***
Length, cm	**0.796***	**0.821***	-0.039
BMI, z-score	**0.693***	**0.705***	**0.612***
Length, z-score	**0.633***	-0.006	-0.107
Head circumference, cm	**0.732***	**0.587***	0.478
Chest circumference, cm	**0.759***	**0.635***	**0.520***
Weight gain, kg	0.278	**0.830***	**0.840***
Length gain, cm	0.236	-0.023	-0.039
Average daily weight gain, g/kg per day	-0.014	0.389	0.432
Average length gain, cm/week	0.167	0.139	0.146

Note (hereinafter): * - $p < 0.05$.

Thus, analysis of the correlation of body composition and physical development of group 1 children demonstrated that feeding with a specialized formula in the early neonatal period results in the increase in absolute and relative (%) amount of fat tissue along with the increase in lean body mass; the revealed positive correlation of weight gains with relative (body fat, %) and absolute (fat body mass, kg) amount of fat tissue indicates intensive fat mass accumulation in the body tissue composition in the process of children's growth.

Positive correlation of the main nutritional status parameter – body weight – and amount of lean (LBM) and fat body mass was observed in the premature infants, who had been receiving mixed feeding; however, only in respect of LBM and z-scores of BMI, body length, head and chest circumference by the time of discharge from the inpatient hospital (tb. 4). Body weight and length gains and average daily weight gain were accompanied by increase in absolute and relative amount of fat tissue in body composition in patients of this group, as well as in the children, who had been receiving artificial feeding.

Table 4. ***Interconnection of body tissue composition parameters and nutritional status at discharge in premature infants, who had been undergoing mixed feeding***

Parameter	LBM, kg	Fat mass, kg	Body fat, %
Body weight, kg	**0.802***	**0.824***	-0.619
Length, cm	0.602	0.305	0.432
BMI, z-score	**0.538***	0.305	0.122
Length, z-score	**0.692***	0.500	0.500
Head circumference, cm	**0.651***	0.566	0.566
Chest circumference, cm	**0.439***	0.422	0.224
Weight gain, kg	0.107	**0.786***	**0.630***
Length gain, cm	0.602	**0.822***	**0.822***
Average daily weight gain, g/kg per day	-0.143	**0.833***	**0.833***
Average length gain, cm/week	0.109	-0.218	-0.218

Table 5. ***Interconnection of body tissue composition parameters and nutritional status at discharge in premature infants, who had been receiving breast milk***

Parameter	LBM, kg	Fat mass, kg	Body fat, %
Body weight. kg	**0.848***	**0.576***	0.376
Length. cm	**0.689***	0.288	0.096
BMI. z-score	**0.787***	0.444	0.261
Length. z-score	**0.662***	0.037	-0.161
Head circumference. cm	**0.548***	0.252	0.070
Chest circumference. cm	**0.780***	**0.558***	0.361
Weight gain. kg	0.012	0.480	0.413
Length gain. cm	-0.621	-0.323	-0.213
Average daily weight gain. g/kg per day	-0.418	0.291	0.446
Average length gain. cm/week	-0.402	0.199	0.199

Physical development parameters (z-scores of BMI, body length; body length and head circumference) of the premature infants, who had been receiving breast milk, correlated positively only with LBM (tb. 5). No correlation of body weight gain, including average daily weight gain, with the increase in absolute and relative amount of fat tissue in body composition was observed in these children (unlike in the children, who had been receiving the formula).

In general, assessment of body tissue composition in the premature infants, who had been undergoing different types of feeding, demonstrated that BMI positively correlated only with LBM at discharge of the children, who had been undergoing breast and mixed feeding. The obtained data indicate that body weight and length of these children in the early postnatal period increases by means of predominant accumulation of lean mass in tissues. At the same time, BMI z-score positively correlates with the increase in specific weight of both lean body mass and absolute and relative increase in the amount of fat tissue (fat body mass and body fat) in the premature infants, who had been receiving the specialized formula; that means, early physical development thereof is accompanied by significant accumulation of fat tissue.

Thus, assessment of body composition demonstrated that physical development of the premature neonates receiving breast milk (including fortified breast milk) for feeding correlates with the increase in specific weight of lean body mass in body composition. The premature infants receiving breast milk have more optimal body composition (less fat body mass and body fat) in comparison with the infants fed with the specialized formula.

Discussion

Modern perinatal technologies helped to considerably improve survivability of premature infants, including the infants born with VLBW and ELBW, in the past decade [1]. However, the problem coming to the forefront after the issue of survivability improvement in premature infants is prevention of the diseases associated with premature birth, including growth disorders in neonates and infants.

Early postnatal period is extremely important for further development of children. Latal-Hajnal et al. studied effect of birth weight and postnatal growth on nervous system development in VLBW premature infants. The results demonstrated that the children with gestational age-low birth weight (below the 10th percentile) had a lower psychomotor development index (PDI) than the children with catch-up growth and birth weight over the 10th percentile at the age of 2 years. The premature infants with gestational age-adequate birth weight featuring no catch-up growth (weight below the 10th percentile at the age of 2 years) had lower average mental (MDI) and psychomotor (PDI) development indices than the children with weight over the 10th percentile at the age of 2 years [7]. Therefore, insufficient postnatal growth may be an independent factor of unfavorable consequences in VLBW premature infants. Ehrenkranz et al. dedicated their study to the issue whether the growth rate in the inpatient treatment period is a predictor of the further physical and neuropsychic development of ELBW children and demonstrated that the growth rate in this period largely contributes to the further development, even despite correction of demographic and clinical data [4]. The authors observed 500 ELBW neonates assessed at the corrected age of 18 and 22 months. It has been proved that increase in the body weight gain rate from 12.0 in the 1st week of life to 21.2 g/kg per day in the 4th week of life correlated with the reduced frequency of cerebral palsy, neuropsychic development disorders with MDI and PDI < 70 and the need in another hospitalization. Thus, the authors demonstrated that growth rate of ELBW premature infants in the period of hospitalization to the resuscitation and intensive care unit produce a significant and, possible, independent effect on the further growth and neuropsychic development. According to data of the latest studies, the calories and the protein consumed in the 1st week of life independently correlate with MDI [8]. Thus, every 42 kJ (10 kcal/kg per day) correlated with 4.6 points, every 1 g/kg of protein per day – with 8.2 points of increase in MDI in the 1st week of life. According to the authors, optimal development of nervous system functions requires emphasis on providing more adequate protein and energy consumption in the 1st week of life.

Still, almost 100% of VLBW patients have weight under the 10th percentile for the PCA thereof by the time of discharge from the inpatient hospital [9]. Such insignificant body weight gain may preserve from childhood until adulthood and be associated with physical and neuropsychic development retardation.

Committee on Nutrition of the American Academy of Pediatrics and the European Committee on Nutrition recommend the following: premature infants must be provided with nutrients in the amount required to maintain growth rate and body composition of a fetus of the same gestational age capable of preserving normal concentrations of nutrients in blood and tissues. However, provision of the recommended consumption, especially in the case of the premature infants born with severe diseases of ELBW may take a rather long time [10]. Enteral feeding increment is usually gradual in order to minimize the risk of feeding complications, primarily associated with necrotizing enterocolitis. As soon as the recommended nutrient consumption level is attained, it may in certain cases not be maintained due to food intolerance, clinical complications, metabolic instability and suspension of feeding for manipulations and procedures. As a result, nutrient deficiencies may aggravate, since the recommended demand is based on the amount of nutrients required to maintain growth with almost no reserve for catch-up growth.

Embleton et al. [11] quantitatively assessed the accumulated nutrient deficiency of premature infants with birth weight of up to 1,750 g with the diet based on the "aggressive" standard protocol tactics. Cumulative energy deficiency by the end of the 1st and the 5th weeks was 406±92 and 813±542 kcal/kg, respectively, in the children with gestational age of up to 30 weeks. Protein deficiency at that age was 14±3 and 23±12 g/kg, respectively. The neonates with gestational age over 31 weeks also featured deficiencies, although less considerable. Ernst et al. [12] also reported that the currently used feeding techniques result in significant energy and protein deficiencies in children with VLBW.

Accumulated nutritional deficiency may cause moderate and severe physical development disorders in the hospitalized premature infants [9, 10-12]. VLBW premature infants are often discharged from the inpatient hospital only by the 35th week of PCA with body weight of ca. 2,000 g (under the 10th percentile of birth weight of the term age-peers thereof) [10]. Lemons et al. [9] reported that insufficient growth rate at the inpatient hospital was the most frequent cause of morbidity of 4,438 VLBW children. Growth disorders, i.e. weight under the 10th percentile at 36 weeks of PCA, were observed in 97% of all the children with birth weight under 1,500 g and in 99% of the children with birth weight under 1,000 g. Clark et al. [13] studied frequency of insufficient postnatal physical development of almost 24,000 children under 35 weeks of gestational age at discharge from the inpatient hospital. They defined physical development disorder as a weight equal or under the 10th percentile of the estimated intrauterine growth considering the PCA. Rates of detection of the lower weight, length and head circumference in the whole group of studied children were 28, 34 and 16%, respectively. The factors independently associated with restricted postnatal growth included male sex, need in performing artificial pulmonary ventilation and effect of postnatal steroids. Severity of the postnatal growth restriction is the worst in children with the lowest birth weight. Steward and Pridham [14] reported that 89% of ELBW children had weight under the 10th percentile at discharge from the inpatient hospital, while Ehrenkranz et al. [10] also demonstrated that most children born before the 29th gestational week did not attain the average weight of born fetuses of the same PCA. Clinical factors affect the degree of physical development retardation, since the children who develop diseases in the neonatal period recover birth weight at a later age and gain weight slower [10]. The researchers surmised that the main principles of therapeutic diets for premature infants must take into consideration the need in catch-up growth along with the requirements for normal growth [12].

Surprisingly, contrary recommendations are provided in order to accelerate physical development and decrease severity of the future metabolic and cardiovascular complications [5, 6].

Introduction of new methodological approaches to the evaluation of nutritional status in neonates and infants (double X-ray absorptiometry, DXA, air plethysmography) based on the study of body tissue composition and of the modern approaches to the interpretation of anthropometric data including calculation of the deviations (z-scores) of individual parameters from the average age-adequate population values in practice helped, on the one hand, to obtain a more complete insight into the plastic processes in premature infants in the postnatal growth period and, on the other hand, led to a new discussion of the optimal provision of premature infants with the main nutrients (protein and energy).

Cooke and Griffin studied anthropometric parameters (z-score) and body tissue composition (DXA) of 149 premature infants at discharge from the inpatient hospital (PCA - 37±1.2 weeks) [15]. They revealed lower body weight and length, lower amount of lean body mass and increase in specific concentration of fat in body tissues at discharge in comparison with the reference fetus. The authors concluded that reduction in linear growth and lean mass in body tissues result

from insufficient protein delivery; increase in fat body mass raises anxiety due to the possibility of insulin resistance and metabolic syndrome development in the high-risk neonates.
Further studies of body tissue composition of premature infants are given in the meta-analysis published in 2012 [12]. Analysis of the 8 reviewed studies (733 children) demonstrated that premature infants had lower body weight and length, high specific weight of fat tissue and lower lean muscular mass at the time of attainment of the term delivery age than the term infants.
These data correspond completely with the results obtained in our study.
The authors assume that the mechanisms determining peculiarities of body composition in premature infants may be multifactorial (transfer from parenteral to enteral feeding, immaturity of enzyme systems of the digestive tract, neonatal diseases, use of postnatal glucocorticoids, insufficient delivery of protein and energy etc.).
It is assumed that insulin-like growth factor (IGF) 1 may be a promoter of excessive catch-up growth and fat mass accumulation in the body composition of premature infants. However, programming and long-term consequences of the early high level of IGF-1 require further research.
According to the authors of the meta-analysis, additional attention must be given to quality of the diet-delivered protein and adequacy thereof in terms of the essential amino acids. Given complexity of nutritional demands and interaction thereof, it appears probable that neither nutrient restricts accumulation of lean mass in premature infants; it is rather a combination of associated factors, including specific biological availability of nutrients, especially of protein.
This assumption correlates with the results obtained in our study in respect of varying concentration of fat tissue in body composition of premature infants undergoing different types of feeding and detected peculiarities of correlation of physical development parameters (body weight, BMI) with accumulation of primarily lean mass in the premature infants, who had been undergoing feeding with breast milk, at discharge. It ought to be mentioned that such data were obtained and analyzed for the first time both for Russia and foreign countries. We did not find similar studies of tissue composition in the premature infants, who had undergone different types of feeding, in the accessible literature.
Taking into consideration data of the literature analysis and the obtained results, we believe that individualization of dietary regimen (energy and protein) for premature and low-weight neonates is the primary task for neonatologists at the moment, as it will contribute to attainment of the optimal neurocognitive development and prevention of late metabolic disorders.

Conclusion

Study results demonstrated that physical development of the premature infants receiving breast milk, including fortified breast milk, is significantly worse at discharge from the inpatient hospital than in the children undergoing mixed or artificial feeding. Nutritional status of the premature infants receiving breast milk is associated with increase in the specific weight of lean body mass in body composition; however, intensity of accumulation thereof at this type of feeding does not attain he intrauterine growth rate. At the same time, the premature infants, who had been receiving breast milk, had a more optimal body composition – less fat mass (%) and body fat (%) – than the children fed with the specialized formula.
Optimal protein provision of the premature infants receiving breast milk is possible by means of modern breast milk fortifiers and personified approach implying determination of breast milk composition before fortification and use of the target and/or adjustable fortification technique.
Early physical development of the premature infants undergoing artificial feeding is characterized by close-to-intrauterine growth rate; however, it is accompanied by higher accumulation of fat tissue in body composition.
Thus, this complex study of nutritional status of premature infants of varying gestational age including determination of body tissue composition and determination of orientation of the main

plastic processes significantly complements criteria of evaluation of feeding adequacy in premature infants and helps to predict further development thereof.

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