O.A. Senkevich, Z.A. Plotonenko, M.A. Chebargina, T.V. Babukh, M.V. Gorokhovsky

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ESCALATION OF VITAMIN D DEFICIENCY FROM BIRTH TO EARLY AGE

The vitamin D supply of healthy newborns and young children living in the Khabarovsk Territory was analyzed. Using a random sampling method, the study included children of two age groups: at birth and the mothers of these children (n=67) and at the age of 1-3 years (n=58), undergoing examination in medical organizations of the Ministry of Health of the Khabarovsk Territory, Khabarovsk. Low vitamin D status was detected in every third child aged 0 to 3 years (29.4%): vitamin D deficiency and insufficiency were diagnosed in 14.4% and 15.0% of children respectively, severe deficiency was defined in 4.0 % of cases. A decrease in the concentration of 25(OH)D in the blood serum was found with increasing age of the child. It was determined that the median concentration of 25(OH)D in the blood serum of children in the first three years of life was 2.5 times higher compared to the control group. The data obtained as a result of the study demonstrate the high prevalence of low vitamin D status among the child population of Khabarovsk, while there is an increase in the deficiency state as they grow older and, as a consequence, the most vulnerable group is adolescents.

Keywords: vitamin D, newborns, young children, teenagers.

Introduction. Recently, there has been an accumulation and rethinking of scientific research on the level of vitamin D in different age categories around the world, since the supply of vitamin D has become a key factor determining the health of both adults and children. Vitamin D deficiency is an internationally recognized health problem of particular importance in certain geographic regions and in certain social and demographic segments of the population. Currently, there is evidence that vitamin D deficiency affects from 24 to 49% of people, insufficiency ranges from 5 to 18%, depending on the region of the world [8]. Numerous studies indicate the diversity of the biological significance of vitamin D and have long been not limited to the "classical" and go far beyond simply "prevention of rickets" and "bone metabolism", its modern undeniable role in the development and functioning of the central nervous system in children, its influence on development chronic somatic pathology and implementation of reproductive function.

The modern scientific idea of research in this area is to summarize the available data and formulate a unified concept for the prevention and treatment of vitamin D deficiency in the pediatric population, taking into account age periodization. On the territory of the Khabarovsk Territory, since 2019, systematic work has been carried out to form a base of vitamin D supply depending on the age of the child from 0 to 18 years [5, 6], since studies of the vitamin D supply of children of different age groups in the Khabarovsk Territory, in accordance with modern diagnostic criteria, have not previously been carried out, which served as the basis for conducting this study. Maintaining adequate vitamin D levels is important throughout childhood because vitamin D deficiency negatively affects children's health.

The largest study of vitamin D levels in children included 1230 studies in 7 regions of the Russian Federation [2]. According to the results of the study, low levels of vitamin D were detected in children from 0 to 3 years of age in the cities of the Far Eastern Federal District - Khabarovsk, Vladivostok and Blagoveshchensk (73.3%, 87.9% and 62.8%, respectively) [2]. Also, low levels of vitamin D in preschool and adolescent children were detected in the Amur region (80.0% and 88.3%, respectively) [1].

The analysis of vitamin D supply in the children's population of various countries revealed some age-related features. European adolescents aged 15-18 years demonstrate a higher prevalence of vitamin D deficiency (12-40%) compared to children aged 1-14 years (4-7%) [9]. The prevalence of vitamin D deficiency and insufficiency among children in mainland China was 7% and 16%, respectively, while the lowest levels of provision were found in newborns (deficiency – 55%, insufficiency – 33%), adolescents had low vitamin D status in 18% and 35% of cases, respectively [11].

The disparity of the results of previous studies regarding the prevalence of vitamin D deficiency depending on the age of the child requires further study with an emphasis on children of the younger age group, since it is in this period of life that the child's health and development program is laid in subsequent years.

The aim of the study: to determine the features of vitamin D supply in healthy newborns and young children living in the Khabarovsk Territory.

Materials and methods of research. An observational, analytical, cross–sectional study was conducted, in which children aged 0 to 3 years (n=125) were included by random sampling, undergoing examination in medical organizations of the Ministry of Health of the Khabarovsk Territory, Khabarovsk - the consultative and diagnostic department of the Children's City Clinical Hospital named after V.M. Istomin and the KGBUZ Perinatal Center named after Professor G.S. Postol. According to the age periodization, the children were divided into study groups: newborns (n=67) and young children (1-3 years old, n=58). The control group consisted of adolescent children

SENKEVICH Olga Aleksandrovna – MD, Professor, Head of the Department of Pediatrics, Neonatology and Perinatology with the Emergency Medicine course, Far Eastern State Medical University, e-mail: senkevicholga@ya.ru; **PLOTONENKO Zinaida Anatolyevna** – PhD, Associate Professor of the Department of Pediatrics, Neonatology and Perinatology with the Emergency Medicine course, Far Eastern State Medical University, e-mail: basset_2004@mail.ru; **CHEBARGINA Maria Aleksandrovn** – PhD, Assistant of the Department of Pediatrics, Neonatology and Perinatology with a course of Emergency Medicine, Far Eastern State Medical University, e-mail: marie_work95@mail.ru; **BABUKH Tatyana Viktorovna** – head of the department of clinical diagnostic laboratory, Regional State budgetary healthcare institution G.S. Postol Perinatal Center of the Ministry of Health, Khabarovsk Territory; **GOROKHOVSKY Mikhail Vadimovich** –Assistant of the Department of additional professional education of the Institute of Continuing Professional Education and Accreditation of the Far Eastern State Medical University; e-mail: mixa_gor@mail.ru

(10-18 years old, n=30). In addition, the analysis of vitamin D supply in 67 mothers of newborns included in the study was carried out.

Inclusion criteria: conditionally healthy children aged 0-3 years, born with average physical development from a singleton physiological pregnancy and the mothers of these children, from whom had a sampling done umbilical cord blood (newborns) and venous blood (mothers of the early postpartum period and children 1-15 years old), living in the Khabarovsk and undergoing examination in selected medical organizations at the time of the study, from whose legal representatives a written voluntary informed consent to participate in the study was obtained.

Quantification of the level of 25-hydroxyvitamin D (25(OH)D) in blood serum was performed by solid-phase enzyme immunoassay based on the principle of competitive binding using a set of reagents 25-OH-Vitamin D ELISA (DRG Instruments GmbH, Germany). The range of detectable concentrations is 25(OH) D was (according to the instructions of the test manufacturer) 2.89–130 ng/ml. No results beyond the specified values were found in this study. The study was performed on a Model 680 Microplate Reader photometer (Bio-Rad, USA). The biomaterial set was carried out in the autumn-winter period of 2021-2022. The level of vitamin D supply was determined according to the recommendations set out in the national program [7].

The study was approved by the local Ethics Committee at the Far Eastern State Medical University of the Ministry of Health of the Russian Federation (Protocol No. 10 of 06/10/2020), conducted in accordance with the ethical principles of conducting medical research involving people as subjects (Helsinki, 1964; revised - Scotland, October 2000).

Statistical analysis of the results of the study was carried out using statistical programs Statistica 12.0 (StatSoft Inc., USA) and IBM SPSS Statistics 20. The description of quantitative indicators was performed indicating the average value (M), the error of the arithmetic mean (m), the median (Me), the 25th and 75th percentiles. The normality of the data distribution was checked using the Shapiro-Wilk criterion. The statistical significance of the differences in the study groups was assessed by the Student's t-test for independent samples with a normal distribution of data. The comparison of quantitative indicators in the comparison groups with the distribution of data that do not have a normal distribution was carried out using the Mann-Whitney criterion. The statistical significance of the differences in relative indicators was assessed using Pearson's χ^2 criterion and Fisher's exact criterion. Spearman's rank correlation coefficient was used to determine the degree of correlation between the indicators. To quantify the relationship between a certain outcome and a risk factor, when comparing two groups, the statistical indicator odds ratio (OR) was used with the calculation of a 95% confidence interval (CI). The differences between the groups were considered statistically significant at $p<0.05$.

Results and discussion. According to the study, a low vitamin D status was detected in every third child aged 0 to 3 years (29.6±4.1%). At the same time, vitamin D deficiency and insufficiency were diagnosed equally in 14.4±3.1% and 15.0±3.2% of children, respectively, severe deficiency was determined in 4.0±1.8% of cases, the optimal vitamin D level was in 70.4±4.1% of the examined children.

Concentration analysis of 25(OH)D in the blood serum of children in the comparison groups showed significant differences in vitamin D supply depending on age ($p<0.001$) (Table 1). The highest

Table 1

Concentrations of 25(OH)D in the blood serum of the examined children of the comparison groups

Vitamin D supply. abs. (%)	Age groups: Newborns	Age groups: 1-3 years	*p*
Concentration of 25(OH)D. ng/ml (Me (25%; 75%))	49.1 (39.3; 60.0)	34.5 (22.0; 53.0)	0.001
Supply of vitamin D. abs. (%): Deficiency	4 (6.0)	14 (24.1)	0.005
Severe deficiency	3 (4.5)	2 (3.4)	1.000
Insufficiency	6 (8.9)	13 (22.4)	0.066
Optimal level	57 (85.1)	31 (53.4)	< 0.001

Table 2

Comparative analysis of vitamin D supply in the examined young children with the control group (adolescents)

Vitamin D supply, abs. (%)	Age groups: 1-3 years	Age groups: Adolescents	*p*
Concentration of 25(OH)D, ng/ml (Me (25%; 75%))	46.0 (27.0; 59.0)	18.2 (12.0; 28.0)	< 0.001
Supply of vitamin D, abs. (%): Deficiency	18 (14.4)	17 (56.7)	< 0.001
Severe deficiency	5 (4.0)	7 (23.3)	0.002
Insufficiency	19 (15.0)	7 (23.3)	0.425
Optimal level	88 (70.4)	6 (20.0)	< 0.001

Table 3

Comparative analysis of vitamin D supply in children of the studied age groups living in Khabarovsk and Moscow

Vitamin D supply, abs. (%)	Age groups					
	0-3 years	**0-3 years**	p	Adolescents	**Adolescents**	p
Deficiency	18 (14.4)	**45 (17.5)**	0.014	17 (56.7)	**496 (65.0)**	0.041
Severe deficiency	5 (4.0)	**4 (1.6)**		7 (23.3)	**75 (9.8)**	
Insufficiency	19 (15.0)	**69 (27.0)**		7 (23.3)	**211 (27.7)**	
Optimal level	88 (70.4)	**142 (55.5)**		6 (20.0)	**56 (7.3)**	

Note: the data published by Kondratieva E.I. et al. are highlighted in bold [4] levels of vitamin D in the child's body, corresponding to a sufficient level of supply, were found in the group of newborns. The median concentration is 25(OH)D was 49.1 ng/ml and was higher than calcidiol concentrations in young children (34.5 ng/ml, p = 0.001).

As a result of the study, it was found that vitamin D deficiency and insufficiency occurred in young children in 46.4±6.6% of cases, much less often in newborns – 14.9±4.4% (p<0.001). There were no statistically significant differences in the prevalence of vitamin D insufficiency in children of the comparison groups (p = 0.066) (Table 1).

When determining the relationship between the level of vitamin D supply and the age group of children, a statistically significant negative relationship was established as a result of correlation relations (r = -0.349, p < 0.001). Thus, a decrease in the concentration of 25(OH) was determined in the blood serum with an increase in the age of the child.

It is interesting to note that a multicenter, prospective, cohort pharmacoepidemiological study conducted about 10 years ago to assess the supply of vitamin D in the younger age group of children in the Russian Federation "Rodnichok" revealed a high prevalence of vitamin D deficiency (42.9±6.6%) and vitamin D insufficiency in children in Khabarovsk (30,4±6,1%) [2]. Vitamin D deficiency in young children according to the results of this study amounted to 24.1±5.6%, which is almost 2 times less than in the Rodnichok study (p = 0.035). The number of children with a sufficient level of security was increced from 26.8±5.9% to 53.4±6.6% (p = 0.004). The improvement in the level of vitamin D supply is probably due to the implementation by pediatricians of the recommendations on cholecalciferol subsidies set out in the National Program for the Elimination of Vitamin D Deficiency, greater awareness and commitment of parents to alimentary correction of deficiency using vitamin and mineral complexes containing cholecalciferol.

In a pairwise comparison of concentrations of 25(OH)D in blood serum, as well as relative indicators of varying degrees of vitamin D supply in children aged 0-3 years (main group) and adolescents (control group), statistically significant differences were revealed (p < 0.001). The median concentration is 25(OH)D in the blood serum of children of the first three years of life was 2.5 times higher compared with the control group (46.0 and 18.2 ng/ml, respectively, p<0.001), the prevalence of low vitamin D status was 3 times less (29.6±4.1% and 80.0±7.3%, respectively, p = 0.049) (table 2).

When calculating the odds ratio, it was found that the prevalence of vitamin D deficiency in adolescent children was almost 8 times higher (OR = 7,774; 95% CI 3,231-18,703) compared with children from 0 to 3 years old. It was found that adolescents were 4 and 20.5 times more likely to be deficient in vitamin D than young children and newborns (respectively, OR = 4.110; 95% CI 1,606-10.519 and OR = 20.596; 95% CI 5,948-71.323). The obtained comparative analysis data indicate, probably, a greater commitment to cholecalciferol subsidies in children of the first three years of life and its absence in older age groups.

The data obtained in the course of our study are consistent with the results of Kondratieva E.I. et al. in a continuous study of groups (from children less than 3 years old to adults 76 years old and older). A study by Kondratieva E.I. et al., conducted in 2021 in Moscow, showed that the content of 25(OH)D is at a sufficient level only at a younger age, immediately after the child reaches the age of 3 years, there is a biochemical manifestation of a deficiency of 25(OH) D, and then insufficiency and deficiency of 25(OH)D persist throughout the rest of life. The lowest concentration of 25(OH)D was noted precisely during the period of active growth of the body (from 11 to 21-22 years old) and in old age [4] (Table 3).

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