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Efficiency of vitamin D deficiency correction depending on the provision of rats with B vitamins

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Summary

If the population of Russia has a combined deficiency of vitamins D and group B, it is often recommended to take cholecalciferol without correcting the supply of vitamins of group B, which are involved in ensuring the biological functions of vitamin D.

The aim of the study is to compare the effectiveness of correcting vitamin D deficiency by replenishing its content in the diet to an adequate level without eliminating the deficiency of B vitamins and by restoring the level of vitamin D in combination with B vitamins against the background of a combined deficiency of vitamins D and B group.

Material and methods . The experiment was performed on male rats Wistar (*n* = 33) with initial body weight of 69.5 ± 0.8 A combined deficiency of vitamins D and Group B (*n* = 24) elicited a factor of 5 reduction in the content of vitamins in a vitamin mixture semisynthetic diet for 23 days Over the next 7 days, to correct vitamin deficiency, 12 rats (group "-B + D") received a diet supplemented to 100% for vitamin D against the background of continuing deficiency of vitamins of group B, and 12 rats (group "+ B + D") - a diet replenished for all the missing vitamins. Control animals (*n* = 9) received a full-fledged semi-synthetic diet throughout the experiment. The concentration of vitamins A and E in the blood plasma and freeze-dried liver and whole brain of rats was determined by high performance liquid chromatography, vitamins B_1 and B_2 in the liver, brain and urine, riboflavin in plasma and 4-pyridoxylic acid in urine - by fluorometric methods, concentration of 25 (OH) D in blood

plasma - by enzyme immunoassay, content of calcium, magnesium, iron, manganese, zinc and copper in freeze-dried liver and brain - by atomic absorption method, biochemical parameters of blood and urine - on a biochemical analyzer.

Results . The addition of vitamin D to the feed against the background of the continuing deficiency of B vitamins did not allow the concentration of 25 (OH) D and osteocalcin to be restored to the level in animals provided with all vitamins. In animals of the "-B + D" group, the blood plasma level of 25 (OH) D was reduced by 17.3% (*p* <0.10), osteocalcin - by 11.7% (*p* <0.05), aspartate aminotransferase activity was 1.5 times less, alanine aminotransferase - 2.3 times (*p* <0.05), lactate dehydrogenase - by 14.9% (*p* <0.10), iron concentration exceeded 2.7 times, glucose - by 15.0%, calcium - by 8.0%, creatinine - by 8.7% (*p* <0.05), urea - by 32.1%, direct bilirubin - by 24.2% (*p*<0.10) the corresponding indicator in rats of the control group; the level of cholesterol and high-density lipoprotein cholesterol was 14.7 and 15.9% higher (*p* <0.10) than that in animals of the "+ B + D" group.

Conclusion . Deficiency of B vitamins inhibits the restoration of adequate supply of vitamin D. In the presence of a lack of B vitamins in rats, vitamin D deficiency and its consequences cannot be completely eliminated. Adequate supply of vitamins D and group B is a synergistic factor in maintaining the level of glucose, plasma cholesterol and other diagnostically significant parameters.

Key words: **vitamin D, vitamins of group B, combined deficiency of vitamins D and group B, correction of vitamin-mineral status, blood plasma, liver, brain, rats**

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HAlong with the main physiological function of vitamin D as a regulator of phosphorus-calcium metabolism and maintaining the normal state of the musculoskeletal system, it has a large number of extra-skeletal (non-calcemic) functions and is necessary for the functioning of almost all organs. Health, duration and quality of life significantly depend on the availability of this vitamin. Lack of this vitamin is, to varying degrees, the most common in the population compared with the frequency of finding other vitamin deficiencies. According to the results of the conducted in 105 cities of Russia in 2014-2018. examinations of 40 878 persons 21-45 years old, vitamin D deficiency was found in 35% of them [concentration of 25-hydroxyvitamin D (25 (OH) D) in the blood <20 ng / ml], deficiency (<30 ng / ml) - in 30.9%. Among people over 45, 37.3% had a deficit, and the disadvantage is 30.2% [1]. Among the residents of Omsk, vitamin D deficiency was detected in 70.9% of those examined [2]. The generalization of the results of assessing the supply of this vitamin showed that deficiency and insufficient supply are detected in 60-92% of the surveyed adults [3].

In the Russian Federation, where the natural insolation by sunlight of the UV-B spectrum is insufficient, and the range of foods fortified with vitamin D is small, additional intake of this vitamin in adequate doses is required. However, when recommending taking vitamin D sometimes in extremely high doses, they do not take into account that other vitamins (C, $_{B2}$, etc.) play a significant role in the formation of both transport and hormonal forms of vitamin D [4, 5], necessary for hydroxylation cholecalciferol. Insufficient provision of the body with these micronutrients is accompanied by a decrease in the formation of biologically active forms of vitamin D, which reduces the efficiency of vitamin D performance of its functions. It has been shown that vitamin B $_2$ deficiencyin rats, it led to a decrease in the serum concentration of 25 (OH) D [5]. Meanwhile, the deficiency of B vitamins among the population of our country is the second most common after vitamin D deficiency [6]. The main

biochemical processes regulated by B vitamins, in addition to the hormonal system of vitamin D (B_2, B_3, B_6, B_9), include the metabolism of carbohydrates for energy generation (B_1, B_2, B_3, B_5, B_7, B_{12}), amino acid metabolism and protein synthesis (B_1, B_3, B_5, B_6, B_7, B_9), synthesis of neurotransmitters (B_1, B_3, B_5, B_6), metabolism of fatty acids, lipids and synthesis of cholesterol and steroids (B_1, B_2, B_3, B_5), synthesis of methionine, S -adenosylmethionine and nucleotide bases for the synthesis of DNA and RNA (B_9, B_{12}) [7, 8]. Given that the shortage of vitamin B_2 may be endogenous or Related sequentially developing deficiency of other B vitamins, vitamins of all 8 groups should come from food in optimal amounts simultaneously [8-10].

The aim of the study is to create a model of vitamin D and group B vitamins deficiency in rats, reflecting the real provision of these vitamins in the population of our country, and to compare the effectiveness of vitamin D deficiency correction by replenishing its content in the diet to an adequate level without eliminating the deficiency of B vitamins and by restoring the vitamin level D combined with B vitamins.

To this was estimated security rat body with vitamins A, E, D, B_1 and B_2 and C_2 content in the liver, brain, and blood plasma, urinary excretion of thiamin, riboflavin, and 4-piridoksilovoy acid (vitamin B_6); the supply of minerals by concentration in the blood plasma, liver and brain and excretion in the urine, as well as the biochemical parameters of blood plasma and urine.

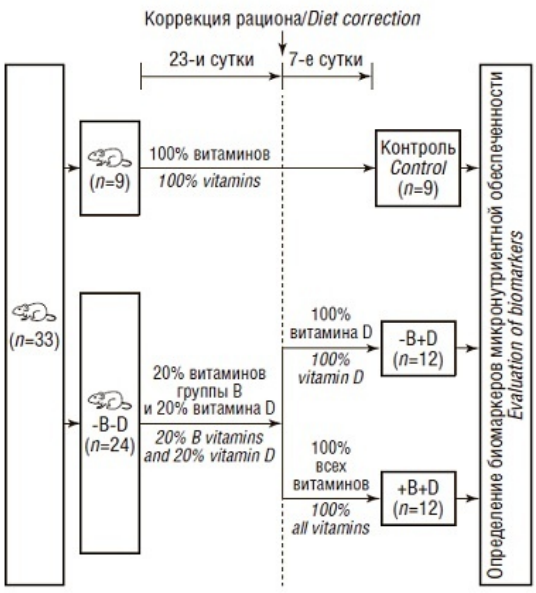
Material and methods

Experimental animals - weaned male rats of the Wistar line - were obtained from the laboratory animals nursery of the Stolbovaya branch of the Federal State Budgetary Institution of Science and Technology of the Federal Medical and Biological Agency of Russia. The studies were carried out in accordance with the order of the Ministry of Health and Social Development of Russia dated 01.04.2016 No. 199n "On approval of the Rules for laboratory practice", the requirements of GOST 330442014 "Principles of good laboratory practice" and GOST 33216-2014 "Guidelines for the maintenance and care of laboratory animals. for laboratory rodents and rabbits ".

The animals were housed in 2 animals in transparent polycarbonate plastic cages under controlled environmental conditions (temperature 20-24 ° C, relative humidity 45-65%, 12/12 h illumination mode) on sawdust bedding. The animals were fed *ad libitum* and had constant access to distilled water.

During quarantine, for 5 days before the start of the experiment, all animals (*n* = 33) with an initial body weight of 69.4 ± 0.8 g received a full-fledged semi-synthetic diet containing 20% of acid food casein according to GOST 31689-2012, 63% of corn starch according to GOST 32159-2013, 4.5% refined deodorized sunflower oil, 4.5% lard according to GOST 25292-2017, 3.5% standard salt mixture, 2% microcrystalline cellulose, 1% dry vitamin mixture, 0.30% L -cysteine, 0.25% choline bitartrate and 0.95% sucrose [11].

At the end of the quarantine, the rats were randomly divided by body weight into 2 groups: animals of the control group (group K) throughout the experiment (30 days) continued to receive a full diet (*n* = 9), and animals of the 2nd (-B-D) of the experimental group (*n* = 24) for 23 days received food with a 5-fold reduced content of vitamin D and all vitamins of group B in the vitamin mixture relative to the complete diet (see figure).



Scheme of an experiment to study the complete (all missing vitamins) and incomplete (only vitamin D) correction of the combined deficiency of vitamins D and group B

The scheme of the experiment to study the complete (all missing vitamins) and incomplete (only vitamin D) correction of the combined deficiency of vitamins D and B group

The average feed intake in the control and experimental groups during the period of the deficit did not differ (p = 0.529) and averaged 20.9 ± 0.7 g / day.

Then the animals of the experimental group were randomly divided by body weight into 2 subgroups of 12 animals each. Over the next 7 days, to correct vitamin deficiency, these animals received rations replenished to 100% in vitamin D against the background of continuing deficiency of B vitamins (group "-B + D"), or supplemented with vitamin D and B vitamins (group + B + D ").

To collect urine, 18 h before slaughter, rats were placed in metabolic cages, deprived of food and provided with water without restriction. At the end of the experiment, the rats previously anesthetized with ether were removed from the experiment by decapitation.

The concentration of vitamins A (retinol and retinol palmitate) and E (tocopherols) in blood plasma, freeze- dried liver and in the whole brain was determined by high performance liquid chromatography, vitamins B_1 and B_2 in the liver, brain and urine, as well as riboflavin in blood plasma and 4-pyridoxylic acid in urine - fluorometric [11]. The concentration of 25 (OH) D in blood plasma was determined by the enzyme immunoassay using the "25-Hydroxy Vitamin D EIA" kit (Immunodiagnostic Systems Ltd., UK). The content of calcium, magnesium, iron, manganese, zinc and copper in the freeze-dried liver and brain was determined by the atomic absorption method on an atomic absorption spectrophotometer "Z 5300" [Hitachi High-Technologies Corporation (HHC), Japan]. Biochemical parameters of blood plasma and urine were determined using a biochemical analyzer (Konelab, Finland) according to standard methods.

The experimental data were processed using IBM SPSS Statistics 23.0 (IBM, USA). To identify the statistical significance of differences in continuous values, the nonparametric Mann-Whitney *U* test was used . Differences between the analyzed parameters were considered significant at a significance level of p <0.05.

Results and discussion

The general condition of all animals (appearance, coat quality, behavior) was satisfactory on daily examination.

By the end of the stage of creating a deficiency of vitamin D and B vitamins, which lasted 23 days, the body weight of animals of the deficient group (-B-D) was 199 ± 2 g and was statistically significant (p = 0.046) 5.2% less than the control indicator. of the group that reached 210 ± 5 g, which became indirect evidence of the development of micronutrient deficiencies in them, the content of which in the vitamin mixture of the feed was 5 times reduced compared to the diet of the control group that received all vitamins.

By the end of the entire experiment, in the group of animals (-B + D), whose diet was adjusted only for vitamin D against the background of the continuing deficiency of B vitamins, the body weight of the rats was 244 ± 5 g, which is statistically significant (p = 0.015) less by 9 , 6% compared with the indicator of the control group, which was 270 ± 9 g. In the groups of rats whose diet was supplemented with all missing vitamins (+ B + D), the body weight of the animals (252 ± 10 g), although it was 6, 7% less compared to control, but the decrease in the indicator was insignificant (p = 0.193).

There were no statistically significant differences in the absolute mass of organs (liver and brain) in animals from the control and experimental groups.

The content of micronutrients in blood plasma, liver, brain and urine of rats is presented in table. 1-4.

Table 1. Biochemical parameters of blood plasma of rats after complete and incomplete correction of vitamin D and group B deficiency *(M ± m)*

Table 1. Biochemical parameters of rat blood plasma after complete and incomplete correction of deficiency of vitamins D and B group (M ± m)

Показатель/*Indicator*	Группа животных/*Group of animals*		
	1 (контроль/*control*)	2 (-B+D)	3 (+B+D)
Холестерин липопротеинов высокой плотности, ммоль/л/*HDL cholesterol, mmol/l*	1,45±0,11	1,50±0,07	$1,32±0,07^{2**}$
Холестерин, ммоль/л/*Cholesterol, mmol/l*	1,82±0,15	1,95±0,07	$1,70±0,08^{2**}$
Триглицериды, ммоль/л/*Triglycerides, mmol/l*	0,86±0,15	0,93±0,08	0,82±0,09
Глюкоза, ммоль/л/*Glucose, mmol/l*	8,0±0,4	$9,2±0,3^{1*}$	$8,4±0,3^{2*}$
Аспартатаминотрансфераза (АСТ), МЕ/л/*Aspartate aminotransferase (AST), IU/l*	223±12	$151±6^{1*}$	$197±6^{1**,2*}$
Аланинаминотрансфераза (АЛТ), МЕ/л/*Alanine aminotransferase (ALT), IU/l*	56,9±2,4	$26,3±1,7^{1*}$	$51,8±1,1^{1**,2*}$
АСТ/*АЛТ* / AST/*ALT*	4,0±0,3	$5,6±0,3^{1*}$	$3,8±0,1^{2**}$
Лактатдегидрогеназа, МЕ/л/*Lactate dehydrogenase, IU/l*	1506±108	$1281±94^{1**}$	1486±88
Белок общий, г/л/*Total protein, g/l*	67,6±1,6	68,5±1,0	67,2±1,1
Альбумин, г/л/*Albumin, g/l*	33,3±0,6	34,4±0,5	33,0±0,5
Глобулины, г/л/*Globulins, g/l*	32,7±0,9	34,1±0,9	34,2±0,9
Билирубин общий, мкмоль/л/*Total bilirubin, μmol/l*	4,5±0,6	6,4±1,3	4,9±0,5
Билирубин прямой, мкмоль/л/*Direct bilirubin, μmol/l*	3,3±0,4	$4,1±0,3^{1**}$	3,9±0,5
Остеокальцин, нг/мл/*Osteocalcin, ng/ml*	1066±43	$941±37^{1*}$	$1050±34^{2*}$
Железо, мкмоль/л/*Iron, μmol/l*	21,6±3,9	$58,7±7,8^{1*}$	$33,6±3,7^{2*}$
Кальций, ммоль/л/*Calcium, mmol/l*	3,01±0,09	$3,25±0,03^{1*}$	$2,76±0,13^{2*}$
Магний, ммоль/л/*Magnesium, mmol/l*	1,03±0,02	1,01±0,02	1,01±0,02
Фосфор, ммоль/л/*Phosphorus, mmol/l*	3,19±0,08	3,04±0,07	2,97±0,09
Щелочная фосфатаза, МЕ/л/*Alkaline phosphatase, IU/l*	745±88	735±84	588±57
Креатинин, мкмоль/л/*Creatinine, μmol/l*	47,2±0,4	$51,3±0,9^{1*}$	$48,3±0,7^{2**}$
Мочевая кислота, мкмоль/л/*Uric acid, μmol/l*	47,9±4,9	47,1±2,9	44,0±3,6
Мочевина, ммоль/л/*Urea, mmol/l*	5,3±0,5	$7,0±0,3^{1**}$	6,1±0,3

*Note. Here and in table. 2-4: [1] and [2] - the number of the group with respect to which the differences are indicated; * - statistically significant difference (p <0.05); ** - tendency to difference (p <0.10).*

*N ot e. The superscript in tabl. 2-4 reflects the number of the group relative to which the differences are indicated; * - statistically significant difference (p <0.05); ** - the trend towards difference (p <0.10).*

Table 2. Influence of complete and incomplete correction of the combined deficiency of B and D vitamins in the diet of rats on biomarkers of vitamin supply in blood plasma (*M ± m*)

Table 2. *Influence of complete and incomplete correction of combined deficiency of B group and D vitamins in the rats' diet on biomarkers of vitamin supply in blood plasma (M ± m)*

Показатель/*Indicator*	Группа животных/*Group of animals*		
	1 (контроль/*control*)	2 (-B+D)	3 (+B+D)
25(OH)D, нг/мл/*25(OH)D, ng/ml*	9,8±0,5	$8,1±0,6^{1**}$	8,8±0,4
Рибофлавин, нг/мл/*Riboflavin, ng/ml*	38,2±1,9	$19,3±2,3^{1*}$	$41,4±4,4^{2*}$
Ретинол, мкг/дл/*Retinol, μg/dl*	35,4±2,0	32,4±2,3	34,6±2,1
α-Токоферол, мг/дл/*α-Tocopherol, mg/dl*	1,15±0,14	1,24±0,07	$1,00±0,08^{2**}$
α-Токоферол/ТГ, мкМ/мМ/*α-Tocopherol/TG, μM/mM*	34,0±4,1	32,6±2,4	30,0±3,5
α-Токоферол/ХС, мкМ/мМ/*α-Tocopherol/Chol, μM/mM*	15,3±2,1	14,8±0,8	13,7±1,0
α-Токоферол/(*ТГ + ХС*), мкМ/мМ/*α-Tocopherol/(TG + Chol), μM/mM*	10,1±1,1	10,0±0,4	9,3±0,8

N ote. TG - triglycerides; Cholesterol - cholesterol. N ot e. TG - triglycerides; Chol - cholesterol.

Table 3 . Effect of complete and incomplete correction of the combined deficiency in the diet of rats of B vitamins and vitamin D on the content of vitamins and minerals in the liver and brain of rats (μg per 1 g of raw tissue) *(M ± m)*

Table 3. *Influence of complete and incomplete correction of the combined deficiency of B-vitamins and vitamin D in the diet on the content of vitamins and mineral substances in rat liver and brain (pg per 1 g of raw tissue) (M ± m)*

Показатель/*Indicator*	Группа животных/*Group of animals*		
	1 (контроль/*control*)	2 (-B+D)	3 (+B+D)
Печень/*Liver*			
Ретинола пальмитат, мкг РЭ/*Retinol palmitate, μg RE*	10,5±0,6	10,3±0,5	9,0±0,6
α-Токоферол/*α-Tocopherol*	194±26	200±25	$137\pm19^{1**,2**}$
Витамин B_1/*Vitamin B_1*	10,0±0,8	$2,3\pm0,1^{1*}$	$9,9\pm0,6^{2*}$
Витамин B_2/*Vitamin B_2*	27,6±1,1	$22,6\pm0,6^{1*}$	$28,6\pm0,5^{2*}$
Кальций/*Calcium*	1200±50	1350±60	1330±50
Магний/*Magnesium*	187±8	185±7	200±3
Железо/*Iron*	48,4±4,4	$69,7\pm7,8^{1**}$	55,6±3,7
Марганец/*Manganese*	1,56±0,10	1,67±0,08	1,67±0,06
Цинк/*Zinc*	34,9±1,0	33,6±0,8	34,7±1,4
Меды/*Copper*	3,27±0,17	3,32±0,14	3,11±0,14
Головной мозг/*Brain*			
α-Токоферол/*α-Tocopherol*	17,9±0,8	19,4±1,0	18,9±0,6
Витамин B_1/*Vitamin B_1*	4,59±0,24	$3,38\pm0,10^{1*}$	$4,88\pm0,29^{2*}$
Витамин B_2/*Vitamin B_2*	2,68±0,09	$2,34\pm0,05^{1*}$	$2,44\pm0,08^{1*}$
Кальций/*Calcium*	753±50	$862\pm47^{1**}$	750±34
Магний/*Magnesium*	142±7	143±2	136±4
Железо/*Iron*	22,5±1,9	22,5±1,2	19,6±1,2
Марганец/*Manganese*	1,00±0,20	$1,50\pm0,14^{1**}$	$1,46\pm0,17^{1**}$
Цинк/*Zinc*	11,6±0,3	11,7±0,3	11,2±0,2
Меды/*Copper*	1,31±0,30	1,42±0,29	1,44±0,19

Table 4. Biomarkers of micronutrient status in the urine of rats fed diets with a combined deficiency of vitamin D and B vitamins, followed by its correction *(M ± m)*

Table 4 *. Urinary biomarkers of micronutrient status in rats fed diets with a combined deficiency of vitamin D and B-vitamins, followed by its correction (M ± m)*

Показатель/*Indicator*	Группа животных/*Group of animals*		
	1 (контроль/*control*)	2 (-B+D)	3 (+B+D)
Тиамин, мкг/*Thiamine, μg*	4,8±0,9	$2,3\pm0,6^{1*}$	$6,6\pm1,4^{2*}$
Рибофлавин, мкг/*Riboflavin, μg*	38,8±3,6	$2,8\pm2,3^{1*}$	$37,3\pm3,1^{2*}$
4-пиридоксиловая кислота, мкг/*4-pyridoxic acid, μg*	47,2±1,6	$21,8\pm4,9^{1*}$	$39,9\pm3,3^{2*}$
Глюкоза, мкмоль/*Glucose, μmol*	3,6±0,7	2,5±0,5	3,2±0,6
Кальций, мг/*Calcium, mg*	0,93±0,21	$0,42\pm0,08^{1*}$	0,68±0,13
Креатинин, мг/*Creatinine, mg*	4,4±0,3	4,2±0,2	4,2±0,2
Кальций/креатинин, мг/г / *Calcium/creatinine, mg/g*	0,20±0,04	$0,10\pm0,02^{1*}$	$0,16\pm0,03^{2**}$
Магний, мкмоль/*Magnesium, μmol*	67,4±11,1	48,5±3,9	45,9±5,4
Мочевая кислота, мкмоль/*Uric acid, μmol*	11,0±0,7	10,5±0,7	10,0±0,6
Мочевина, мкмоль/*Urea, μmol*	3,2±0,3	2,7±0,1	2,8±0,2
Фосфор, мкмоль/*Phosphorus, μmol*	0,36±0,04	0,44±0,03	0,41±0,05
Реабсорбция фосфата, %/*Phosphate reabsorption, %*	84,5±2,6	$79,7\pm1,5^{1*}$	82,2±1,7

We have previously shown that a deep deficiency of all vitamins, including all 8 vitamins of the B group and vitamin D, in rats leads to a decrease in the activity of B_6 in the blood plasma.-dependent alanine (ALT) and aspartate aminotransferase (AST) 1.4 times with a simultaneous increase in the concentration of glucose by 32%, iron by 31%, urea by 58% [12]. As follows from the table. 2, in comparison with the control, in animals of the (-B + D) group with a preserved deficiency of B vitamins, the activity of AST was reduced by 1.5 times, ALT - by 2.3 times, and the activity of lactate dehydrogenase (LDH), the coenzyme of which is nicotinamide adenine dinucleotide, - by 15% (at the tendency level), which indicated the development of a deficiency of B vitamins in animals. The concentration of iron in blood plasma was 2.7 times higher than the level in rats of the control group, calcium - by 8%, glucose - by 15 % ($p<0.05$), urea - by 32% (at the trend level). The data obtained show that in polyhypovitaminosis, a significant contribution to the violation of the listed parameters is made by the deficiency of B vitamins.

The increased plasma level of creatinine by 8.7% ($p<0.05$) and direct bilirubin by 24.2% ($p<0.10$) in rats of the (-B + D) group, apparently may be due to hyperglycemia. At the same time, the absence of a simultaneous increase in the excretion of glucose, creatinine and urea in the urine (see Table 4) may indicate a deterioration in the functioning of the kidneys.

Noteworthy is the 11.7% decrease in the concentration in the blood plasma of the vitamin D-dependent protein osteocalcin, which is used in the diagnosis of osteoporosis. Thus, the addition of vitamin D to the feed of animals with polyhypovitaminosis without eliminating the deficiency of B vitamins did not allow the concentration of osteocalcin to be restored to the level in animals provided with all vitamins.

The addition of all deficient vitamins (+ B + D) to the diet of animals deficient in vitamins D and group B normalized most of the impaired parameters to the level of the control group. The concentration of glucose, cholesterol, calcium, iron, urea, osteocalcin was restored to the values in the animals of the control group. Only the activity of AST and ALT took an intermediate position between the indicators of two groups: control and deficient in vitamins of group B.

The combined deficiency of vitamins D and group B in the diet of animals did not have a statistically significant effect on the level of retinol in the blood plasma of rats from all groups (see Table 2). Filling in the diet of rats (+ B + D) all deficient vitamins allowed almost completely restore the concentration of 25 (OH) D in the blood plasma (unlike control group is absent), as well as virtually all indicators vitamins security group B (with the exception of vitamin B_2 in the brain, which remained reduced by 9%). The persisting deficiency of B vitamins in rats from the (-B + D) group was confirmed by a 4.3 times lower content of vitamin B_1 in the liver compared to animals provided with all vitamins (control) , in the brain - by 26.4%, vitamin B_2in the liver - by 22%, in the brain - by 12.7% (see Table 3), and riboflavin in blood plasma by 2.1 times (see Table 2). The addition of vitamin D to the feed against the background of a persisting deficiency of B vitamins (-B + D) was accompanied by a noticeable tendency for the recovery of 25 (OH) D concentration to lag behind to the level in control animals. Thus, the deficiency of B vitamins inhibits the restoration of an adequate supply of vitamin D.

The combined deficiency of vitamins D and group B in the diet of rats with subsequent replenishment of the vitamin value of the feed to the norm (+ B + D) did not have a statistically significant effect on the level of α-tocopherol in the brain and blood plasma. At the same time, the content of this vitamin in the liver of rats of the (+ B + D) group (see Table 3) was lower (p <0.10) in comparison with the indicators of animals provided with all vitamins during the entire experiment (control), and deficient in vitamins of group B (-B + D), which, apparently, reflected a lower content of cholesterol in tissues. This is confirmed by the fact that when correlating the concentration of vitamin E in blood plasma with cholesterol, the differences disappeared (see Table 2).

As can be seen from the data in the table. 3, the content of all elements, with the exception of manganese, in the liver and brain of animals after complete replenishment of the lack of vitamins in the diet (+ B + D) did not differ from those of the control group. However, after correction of the diet only for vitamin D with the preservation of the deficiency of vitamins of group B in the liver of rats (-B + D), the level of iron was 44.0% higher (p <0.10) relative to that in the control. In the brain, the content of manganese was 1.5 times increased and calcium was increased by 14.5% (p <0.10). Although the differences have not reached the level of statistical significance, they indicate a tendency for the redistribution of mineral elements in organs, which can negatively affect the physiological processes in the brain.

As follows from the data table. 4, after replenishing the vitamin D deficiency, but with the remaining deficiency of B vitamins, the excretion of metabolites of vitamins B_1 , B_6 , as well as calcium, both in absolute terms and in terms of creatinine, was statistically significantly reduced by about 2 times, the excretion of riboflavin was 13.9 times. Phosphate reabsorption was also less than that of the control group (p <0.05). The addition of B vitamins D deficient in the diet for 7 days to an adequate level restored these indicators almost completely.

Conclusion

Thus, in growing rats on an experimental model of combined deficiency of vitamins D and group B, reflecting the real provision of these vitamins in the population of our country, a comparison was made of the effectiveness of correcting vitamin D deficiency by replenishing its content in the diet to an adequate level without eliminating the deficiency of B vitamins. diet and in combination with vitamins of group B. It has been shown that with an alimentary deficiency of vitamins of group B in rats, it is not possible to completely eliminate the deficiency of vitamin D, as evidenced by the reduced level in the blood plasma of the hydroxylated form of vitamin D and the marker of osteoporosis - osteocalcin, while, accordingly , metabolic disorders associated with a deficiency of these vitamins (increased plasma levels of glucose, cholesterol, urea, iron, etc.) persist.

This study shows that an adequate supply of vitamins D and group B is a synergistic factor in maintaining the level of glucose, plasma cholesterol and other diagnostically significant parameters. Thus, the deficiency of several B vitamins in mice (B_1 , B_2 , B_6), as well as vitamin D (in clinical studies), led to an increase in the blood plasma concentration of proinflammatory cytokines (tumor necrosis factor a, interleukins-1β, -6) and various metabolic disorders [13-16]. At the same time, the results obtained indicate the insufficient effectiveness of the prescription of cholecalciferol practiced by doctors in order to correct vitamin D, even in higher doses, if the adult and child population lacks not only vitamin D, but multiple deficiencies of other micronutrients (vitamins and / or minerals). Thus, the advantages of the combined use of vitamins D and group B have been proven.

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