V.B. Spirichev

Vitamin D_3 + 12 Vitamins as a Modern Concept of Effective Use of Vitamins in Prevention of Human Diseases

ABSTRACT

Realization of numerous and vital functions of vitamin D in a human body closely depends on supply of an organism with all other vitaminsnecessary for formation of hormonally active form of vitamin D and normal implementation of the vital biochemical and physiological processescontrolled by it.The above mentioned proves expediency of the combined use of vitamin D and a complex of all other 12 vitamins as in the medical, andpreventive purposes (the concept vitamin D + 12 vitamins)

Keywords: vitamins, vitamin D, vitamin D – the action mechanism, 1α, a 25-dioxyivitamin of D, a role of vitamins, vitamins supply.

The tremendous success has been achieved for the last decades in the study of the vitamin D exchange and mechanism has clearly demonstrated the vital role of its **hormone-active** form,**1α,25-dioxyvitamin D,**not only in rickets prevention among children and osteoporosis prevention among the elderly but also in decreasing the risk of the most frequent and gravest modern diseases, such as cardiovascular, oncologic diseases, diabetes and a large variety of others being the main reason of the early disability and death of many million people.

This huge amount of data presented in dozens of thousands of publications by independent authors served as a scientific basis for the practical proposals on the wide use of vitamin D aimed at reducing risk and preventing the abovementioned diseases. Those proposals were considered by European Parliament and USA Senate in spring and summer 2010.

Both European Parliament and the U.S. Senate discussed the proposal on increasing the recommended daily use rate of this vitamin from 200-400 IU (5-10 μg) to 2000 IU (50μg) per day. However, this proposal has never been formally adopted as a general compulsory practice – at least, until the present time.

Such guardedness is rather understandable, for it is widely known that vitamin D has rather narrow therapeutic amplitude and, if used in doses exceeding one's physiological need, may cause hypercalcemia and metastatic calcification of such vital organs as heart and kidneys.

In the 40-50s of the last century one of the outstanding pediatricians used to say that an experienced doctor must be able to lead a baby "between the Scylla of rickets and the Charybdis of D-hypervitaminosis".

Now it is not only pediatricians that are facing the problem to the full extent but also many other specialists, primarily nutritionists dealing with the adult and aged people.

The more so as the duality ofeffect produced by vitamin D depending on the dose has also been discovered by modern studies of the impact this vitamin has on the frequency and outcome of the cardiovascular, oncologic and other diseases.

An obvious example of such duality is the result of a research published by a group of authors in October publication ofAm.J.Clinic Nutrition, 2010 [28]. Within 13 years the authors of the research had watched the state of

health of 1194 men at the age of 71 and older who had a concentration of 25-oxyvitamin 25(OH)D in the blood serum at the beginning of the research, which is the most reliable indicator of sufficiency of vitamin D in the body of the examined.

It was found that the dependence of general mortality within the research period on the original sufficiency of vitamin D in the bodies of the examined had a U-nature, i.e. was definitely higher for the men with both originally low and originally high sufficiency of vitamin D. For instance, approximately 50% higher mortality was recorded both among the men with the original concentration of 25(OH)Din the blood plasma being lower than 46 nmol/l (<115 ng/ml) and among the men having the same indicator higher than 98 nmol/l (<245 ng/ml) [28].

This being the case, considering the inconsistency of the available information on the admissible limits and possible consequences of the decrease of the recommended vitamin D consumption rate, as well as of the absence of relevant positive decisions from the European and American higher governmental bodies, we find it reasonable, at least, at this stage to approach the problem of enhancing the provision of vitamin D to the population masses in a slightly different and, to our opinion, a more efficient and safer way.

To be more specific, we must try to identify and eliminate the problems of nutrition faced by a modern man which are still the biggest obstacle both to the natural transformation of vitamin D in a human body into its hormonal form and to the realization of the abovementioned vital functions by this form.

In this context, we find it reasonable to turn to the results of the research carried out in 1980-90s at the **Laboratory of Vitamins and Mineral Substances at Institute of Nutrition RAMS**by the then Senior Fellow of the laboratory and current professor at South Dakota University **Igor Sergeev**together with his young associates: a postgraduate from the Republic of Cuba **Raul Fernandez Regladoand** a postgraduate from North Korea **Kim Ren Ha**.

In his research that served as a basis for his doctoral thesis, I.N.Sergeev has clearly demonstrated the role of a large variety of **vitamins** both **in the biosynthesis of the hormone-active form of vitamin D: 1,25(OH)$_2$D** and in the realization of its multiple vital functions [7, 31], basing on vast experimental material.

Let us consider these data in more detail.

Table 1contains information on the specific role of **vitamins C, B$_2$, B$_6$, PP, folic acid,α-tocopherol and vitaminK**in the biosynthesis process and the mechanisms of realization of the specific functions of the hormone-active form of this vitamin, i.e. 1,25(OH)$_2$D$_3$ [6, 7].

For instance, **ascorbic acid** ensures normal realization of the **steroidogenesis** processes, including the synthesis of the primary predecessor of vitamin D, cholesterol [8, 27].

Coferment forms of **vitaminB$_2$** (riboflavin) comprise the active center of the flavoproteinmonooxigenases responsible for the hydroxylation of vitamin D in the process of its transformation into a hormone-active form 1,25(OH)$_2$ D [7, 9].

Nicotinomidecoferments (derivatives of nicotinamide – **vitamin PP**) are necessary as a source of regenerative equivalents in the abovementioned processes of hydroxylation of vitamin D with the production of1,25(OH)$_2$of vitamin D [7].

Folic acidis responsible for maintaining the proliferative capacity of cells, including those of the bone tissue in the process of its growth and renewal[7].

VitaminE as an antioxidant acts as a protector of the microsomal and mitochondrial hydroxylases, including those taking part in the synthesis of the hormone-active form of vitamin D [7, 10].

Vitamin Kparticipates in the post-translation modification of the calcium binding proteins, including the one, which synthesis on the genetic level is induced by the hormone-active form of vitamin D [11-13, 30, 32].

Table2shows the results of the experimental research by I.N.Sergeev and his associates demonstrating the certain character and depth of the specific disorder of synthesis and mechanism of $1,25(OH)_2D$ in the conditions of deficiency of each of the mentioned vitamins in the organism [7].

There are good reasons to compare the information on a certain role of the above listed vitamins in the creation and realization of the vital functions of the hormone-active form of vitamin D with the data on the real provision of the abovementioned vitamins to the population of the developed countries, specifically, with the results of the **mass studies of provision of vitamins to large groups of child and adult population in Russia** pursued by Institute of Nutrition RAMS both in the 90s of the last century and in the last 5-7 years [16, 19, 20] using most reliable up-to-date methods and criteria based on the direct analytic definition of the concentration of vitamins and activity of the corresponding vitamin-dependent ferments in the biological fluids of the organism (blood, urine) [23].

The results of these surveys expressly speak for the **insufficient consumption of vitamins as the most popular deviation of nutrition from the rational physiologicnorms**.

Most serious problems concern the consumption of vitamins C, B_1B_2, B_6, folic acid and beta-carotene, which deficiency is typical for the significant share of the child and adult population of the Russian Federation.

For instance, the 1983-92 examination of the adult working population of Moscow, Yekaterinburg, Kuzbas, Norilsk, Bashkiria, Mari El and other cities and regions of Western and Eastern Siberia and the farm workers of Kuban revealed the deficiency of vitamin C among 88% (70% suffering strong deficiency), B vitamins (B_1, B_2, B_6) among 60-80% (30-47% suffering strong deficiency), folic acid among 80-85% (25-30% suffering strong deficiency) of all the examined [1-5, 17-23, 26].

The examination of preschool and school-aged children of Moscow, Yekaterinburg, Orenburg and other cities conducted in the same years revealed the deficiency of vitamin C in 27 - 63%, folic acid in 23 - 30%, B_1in 40 - 58%, B_6in 24 - 70% cases, accordingly. 23-32% of the examined children suffered strong deficiency of vitaminsB_1, B_2, B_6 and ascorbic acid [4, 14, 15, 25].

According to the March-April 2001 examination of Moscow schoolchildren, 38% of children had the vitamin C deficiency (according to its level in blood), 79% - vitamin B_2 deficiency,64% - vitamin B_6deficiency, 22% - vitamin E deficiency and84% of children had beta-carotene deficiency.

A similar examination among the schoolchildren of the first four grades in St. Petersburg in February 2006 showed the vitamin C andB_1deficiency among 50%and vitamin B_2 deficiency among 30% of the examined. Only 10% of children had a more or less sufficient level of all three vitamins. Half of the examined population suffered from combined deficiency of two or, rather, three vitamins at once.

In October 2007, specialists of the Laboratory of Vitamins and Mineral Substances at Institute of Nutrition RAMS in cooperation with OGK-2 employees conducted an objective survey of the vitamins C, A, E, B_2, B_6 and beta-carotene sufficiency among the staff of various departments of OGK-2 branch of Pokrovskaya GRES power plant – in all, 174 men and women [2].

Despite the autumn season, which is abundant in fruit and vegetables, the **vitamin C** deficiency was discovered among **34.8%** of the total number of the examined staff, 6 people having strong vitamin C deficiency and 2 being close to scorbutic.

The situation turned to be even worse with **B vitamins** that are found not in vegetables but in high-quality meat products. For instance, **vitaminB_2**insufficiency was discovered among**47.4%** of the examined (**82** people from **174**) and**vitaminB_6**deficiency among 72.6% (**126**people). **108**people (62%) hadlow**beta-carotene**levelintheirblood**.**

Only 5 women (!)from152 men and womenhad a sufficient level of all 6 vitamins, and no such men were found at all. 64% of women and 84 % of men had **combined deficiency of two, three or four vitamins** at once [2].

The September 2010 survey conducted among the children of 11-17 that were going in for swimming under control of the Nutrition Department for Healthy and Sick Children at the Scientific Children's Health Center RAMS showed that the level of Vitamin E in their blood was below the line among 30.8% of children, vitaminB_2among 53.8% andbeta-carotene among 79.5% of children. Combined deficiency of 2-4 vitamins was found among 73.9% of boys and 56.2% of girls. Only one girl from 39 examined children had the necessary level of all the above mentioned vitamins [21].

Thus, summarizing the numerous data based on the results of the clinical and biochemical examination of the representative child and adult groups in various regions of the country, we can characterize the general vitamin situation among the child and adult population of the Russian Federation in the following way:

1. The revealed deficiency implies not one single vitamin but has the form of combined vitamin C, B vitamins and carotene deficiency, which is **polyhypoavitaminosis**.

2. The vitamin deficiency may be found not only in spring but also in the summer and autumn period, which seems to be most favorable time of the year, and thus is characterized as a **permanent negative factor**.

Insufficient consumption of vitamins and a number of mineral elements with food is not some specific trait of the food status of the Russian population but is a common problem in all the developed countries. It emerged as an unavoidable consequence of a strong socio-economic and scientific-and-technical progress, which led to the sweeping reduction in energy expenditure and the relevant decrease of the general amount of food being the source of energy and consumed by modern man.

Physiologic need of vitamins and mineral substances of a human organism have been formed in the course of the human evolution as a species and the human metabolism has gradually adjusted to the amount of the micronutrients than he received with the large volumes of plain natural food that matched the large energy expenditure of our ancestors.

Within the last decades, the technical revolution and large-scale social changes resulted in the 2-2.5-time and greater decrease in human energy expenditure. Food consumption has, or must have, decreased accordingly – otherwise, it would lead to overnutrition, overweight, which means diabetes, hypertensive disease, atherosclerosis and other "civilized" diseases.

However, food is not only a source of energy, but also a source of vitamins, macro- and microelements. By reducing the general amount of the food consumed we inevitably doom ourselves to vitamin hunger, as well as to the deficiency of a number of vital mineral substances.

The calculations show that even the best diet involving the consumption of 2500 kcal per day (which equals average energy expenditure of a modern Russian) lacks, at least, 20% of most vitamins.

Without going into details of the reasons and consequences of this mass polyhypovitaminosis state among the population of the developed countries and the efficient methods of its correction and prevention, which is the subject of our other publications [17], we would like to underline here that the necessary condition of successful realization of all the vital functions of vitamin D discussed above is the **comprehensive provision of all vitamins responsible for the creation of the hormone-active form of vitamin D and successful realization of the multiple processes controlled by this form**.

Taking into account the wide spread of the polyhypovitaminosis state, especially among the older and elderly, we may suggest that perhaps the reason of some inconsistency or insufficient persuasiveness of a number of studies evaluating the efficiency of vitamin D in prevention of cardiovascular, oncologic and other diseases lies not

with the absence of such effect or insufficiency of doze of vitamin D but rather with **the lack of other vitamins necessary for the normal creation of the hormone-active form of this vitamin and (or) realization of its function in the organism**.

In this respect, it becomes clear that both the effective use of vitamin D in rickets prevention and the decrease of risk of the above mentioned grave diseases require the application of this vitamin **in combination with the complete variety of vitamins necessary for the realization of its useful features in the dozes meeting the physiologic needs of a human organism**.

These requirements are to a great extent met by multivitamin and vitamin-mineral complexes, as well as the vitamin-enriched protective diet products containing **vitamin D and the entire variety of the rest of twelve vitamins** in quantities providing **from50 to 100%**of the recommended daily rate (**The D+12 vitamins approach**).

Table1.

Role of vitamins in the processes of biosynthesis and realization of the specific functions of the hormone form of vitamin D (according to I.N.Sergeev, 1991) [7]

Vitamin C	Necessary for normal realization of the steroidogenesis processes
Vitamin B_2	In the forms of FMN and FAD, comprises the active centers of flavoproteinmonooxigenases responsible for the hydroxylation of vitamin D with the formation of its active oxyforms: 25(OH)D; $1,25(OH)_2D$
VitaminB_6	In the form of PALF, takes part in modification of some proteins, incl. receptors of steroid hormones
VitaminPP	In the form of NAD(F)N, is the source of regenerative equivalents in the process of synthesis of the vitamin D oxy derivatives: 25(OH)D; $1,25(OH)_2D$ and others.
Folacin (folic acid)	Plays an important role in the biosynthesis of proteins, including the fast-renewed protein receptors of the active forms of vitamin D
VitaminE (α-tocopherols)	As an antioxidant, acts as a protector of microsomal and mitochondrial hydroxylases taking part in the formation of active oxyforms of vitamin D: 25(OH)D; $1,25(OH)_2D$ and others.
VitaminK	Takes part in the post-translation modification of the calcium binding proteins

Table2.

Deregulations in the biosynthesis of functions of the hormone-active form of vitamin D in the conditions of insufficient level of other vitamins in the organism (According to I.N.Sergeev, 1991) [7]

Vitamin deficiency	25(OH)D concentration in blood	1(OH) activity of hydroxylase 25(OH)D in liver	$1,25(OH)_2D$ concentration in blood	Concentration of $1,25(OH)_2D$ used receptors in kidneys
C	↓	↓↓	↓	↓↓
B_2	↓	-	-	-
Folic acid	-	↓	-	↓↓
E	-	↓↓	↓	-
B_6	-	↓↓	↓	↑↑
K	-	-	-	↑

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Authors:

1. V.B.Spirichev, honoured worker of science, Doctor of Biological Sciences, professor, ValetekProdimpex JSC,Moscow, Russia