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VITAMIN B_{12} DEFICIENCY IN ELDERLY AND OLD SUBJECTS

Changes in the concentration of vitamin B_{12} in blood serum with age and in its content in the diet were investigated in 30 elderly and old subjects (aged 60–89) without acute diseases or exacerbation of chronic diseases. Despite the fact that consumption of vitamin B_{12} by the majority of subjects under investigation was above the minimum recommended level (3.8 mcg/day) in 76.7 % of them the concentration of vitamin B_{12} in blood serum decreased. Such decrease became more significant after 75 years of age. At the same time, if the consumption of cobalamin exceeded 10–15 mcg/day there was an increase in its blood serum concentration. Thus, the high occurrence of vitamin B_{12} deficiency may be caused, primarily by deterioration of its absorption due to age-related changes of the digestive system. To prevent vitamin B_{12} deficiency, the use of at least 10–15 mcg/day is recommended.

Key words: aging, vitamin B_{12}, food intake, age-dependent pathology.

The dietary intake can change significantly in aging that impacts health condition of the elderly people. Among the factors provoking nutritional changes are reduced energy needs due to lower physical activity and lesser muscle mass. However reduced calorie consumption (and correspondingly food products) leads to lower intake of microelements and vitamins and their deficit may be reaching 30 % at age 80. Moreover, various diseases, drugs, smoking and alcohol consumption also influence absorption and metabolism of the vitamins. Literature provides data showing that blood plasma levels of fat-soluble vitamins and carotinoids, as a rule, rise with age (exception is vitamin D) whereas the levels of water-soluble vitamins fall (especially vitamins B_6 and B_{12}). Thus in SENECA study has been shown that among the elderly Europeans obvious deficiency of vitamin D is registered in 47 %, B_6 in 23.3 %, vitamin B_{12} in 2.7 % and vitamin E in 1.1 % of the population [9].

According to other published data the prevalence of vitamin B_{12} deficiency among general population can reach 40 % and among elderly 60 % [3]. Analysis of blood serum concentrations of cobalamin and its metabolites

in 548 participants of the primary cohort of the Framingham study showed that cobalamin concentration of less than 258 pmol/ml was in 40.5 % of elderly individuals compared to 17.9 % ($P < 0.001$) among young control [15]. Recent American investigations not only demonstrated the high prevalence of vitamin B_{12} deficiency among elderly individuals but they also designated it as a risk factor for cardiovascular diseases, Alzheimer's disease and even accelerated aging [29]. Notably, the majority authors have common opinion that isolated vitamin B_{12} deficiency occurs predominantly among elderly people (with the onset of primary clinical signs within age range of 60-70 years) and rarely under the age of 30 years [19].

Vitamin B_{12} belongs to the cobalamins and does not present a concrete chemical compond. It contains a number of forms: cyano-, methyl-, desoxyadenosyl- and hydroxycobalamin. Only micro organisms are capable to synthesize cobalamin, while animals, humans included, can only transform it by replacing cobalamin-bound radical. Human organism needs two forms of cobalamin: methyl- and 5- desoxyadenosyl-cobalamin which are used as the cofactors for methionine syntase and L-methylmalonyl-CoA-mutase [23].

Vitamin B_{12} has unique properties making it different from other vitamins. Firstly, it has the most complicated chemical structure among vitamins and is a chelate (complex) compound. Secondly, having within its composition a structure that resembles porfirin, the two of its pyrrole cycles are linked not by methylen bridge (like that which is seen in the porphyrin) but directly with each other. Thirdly, cobalt located within the centre of the core structure (while joining the radical (ciano-, hydroxy-, methyl- or desoxiadenosyl-) forms the covalent bond between metal and carbon (the only known in live nature). Fourthly, vitamin B_{12} is the only water soluble vitamin capable to be accumulated in human organism, mainly in the liver [2].

With vitamin B_{12} involvement such reactions take place (SeeUkra) in human organism as methionine synthesis and methylmalonyl-CoA utilization. The former provides for homocystein transformation into methionine and the latter ensures methylmalonyl-CoA convertion to succinyl-CoA [23]. Besides, vitamin B_{12} takes part in the synthesis and methylation of DNA regulating thereby genes activity [25]. That is, vitamin B_{12} is involved not only in all kinds of metabolism but it also regulates them.

The sole natural source of vitamin B_{12} are the animal origin products (meat, fish, eggs, milk and seafoods (including mollusks and crustacea). Sufficient amounts of B_{12} are available in some of the plant products (eg, mushrooms and nori (eatable red seaweeds). It is noteworthy that certain food products (spirulina, some moluscs) contain pseudo vitamin B_{12} (corrinoid) which is inactive in human organism and does not carry on any biological functions [28].

Of today the question remains still unsolved what daily requirement of vitamin B_{12} should be for humans. E. L. Doets and coauth. calculated that daily B_{12} losses make nearly 1.4-5.1 mcg and 3.8 to 20.7 mcg are to be consumed daily to compensate them [7]. Such high daily needs in B_{12} are caused by very complicated and multi-stage process of its absorption in the

body. For normal B_{12} absorption and delivery, many conitions are to be provided in human organism, in particular: vitamin B_{12} derived from food is bound with protein and there should be a sufficient amount of hydrochloric acid and enzymes in the gastric juice for it decomposition. Then vitamin B_{12} is bound with special protein — Castle's intrinsic factor, which is synthesized by the gastric parietal cells. Further this complex is absorbed in the distal part of intestinum ileum for which a sufficient amount of calcium is needed [23]. Essential is also the normal bile-releasing function for normal B_{12} absorption [26]. In the blood cobalamin is bound with the transporting proteins transcobalamin I and (haptocorrin) та transcobalamin II (holotranscobolamin) to accomplish its further delivery to the cells or depo [23]. Disturbances in any of these links occurring due to pathological process, can essentially worsen vitamin B_{12} absorption and its deficit develops.

Noteworthy is that B_{12} absorption increases proportionally to its dietary income [23]. In parallel there exists an alternative way for cobalamin absorption without transport proteins; the existence of such way has been proved only for the high doses of crystal vitamin.

In aging vitamin B_{12} bioavailability is reduced due to pathological changes in the digestive system. As gastric acidity falls down with an increasing age, the cobalamin absorption is more worsened. But at the physiological aging however the gastric cobalamin absorption does not decrease in elderly people [20, 22]. According to the findings of D. L. Marcus and coath., in the old subjects having normal serum vitamin B_{12} levels or its deficit the serum holotranscobolamin concentration decreased to 4 % against 17 % in the young individuals. These investigators increased the holotranscobolamin level by administering peroral cianocobalamin to their older subjects [18]. Thus in aging it is not only the vitamin B_{12} absorption that undergoes changes but also its transport to the cells is altered serving a preface for the development of its deficiency.

Nowadays vitamin B_{12} deficiency is rarely manifested by the classical symptoms (macrocytic anemia and peripheral neuropathy) and is more frequently masked by various illnesses [8]. In particular, neuro-psychic manifestations like mielopathy, neuropathy, dementia and optic nerve atrophy could precede the hematologic symptoms [5]. Besides vitamin B_{12} deficiency can imitate the so-called senile syndromes, such as weakness, greater risk of falls, cognitive impairments, anorexia and cachexia [5, 24]. With these, the hematologic disturbances may be registered only in one-third patients with vitamin B_{12} deficiency which is frequently linked with folic acid deficiency [4, 6].

Many works revealed the role of vitamin B_{12} in the prevention of atherosclerosis and cardiovascular disease progression. In his early experiments Yu. G. Grigorov (1959) showed that 30 mcg/day of cobalamin supplementation reduced significantly cholesterol levels and increased lecithin levels in the blood of the rabbits with experimental atherosclerosis [1].

Vitamin B_{12} plays an important role in the maintenance of normal rheology of the blood and endothelium functioning [13, 14]. It was demonstrated that serum B_{12} vitamin level was significantly lower in the

patients with acute myocardial infarction than average among the population: (241 ± 185) ng/l vs (608 ± 341) ng/l ($P < 0{,}001$) [12]. High prevalence of vitamin B_{12} deficiency was reported among IHD patients aged over 65 years (86.7 %) vs general population (16.5 %) [17]. Thus the authors demonstrated the important role of vitamin B_{12} in the decrease of the risk of development and progression of cardiovascular diseases.

Our work aimed to assess (a) changes in the blood serum vitamin B_{12} concentration occurring with age as well as (b) its dietary content in the elderly and old people.

Patient population and methods. Thirty elderly and old subjects aged 60–89 years took part in our study. They had no acute pathologies or chronic disease exacerbations like acute infectious or surgical diseases, malignancies, severe 3^{rd}–4^{th} functional class heart failure according to NYHA, renal or liver insufficiency, nervous or endocrine (including diabetes mellitus) diseases. All of them signed the informed concent agreement. The program of our clinical investigation was approved by the Ethics Committee at the D. F. Chebotarev Institute of Gerontology NAMS Ukraine (protocol № 4 dated 19 June 2012).

Blood serum vitamin B_{12} concentration was measured by the immune-enzymatic method on Multiscan Ascent V1.24 device using the DAI kit (USA). An early morning, usually fasting, venous blood sample (5 ml) was taken into sterile tube and sent for immediate centrifugation and storage of blood serum at −80 °C for up to 2 months.

Average daily dietary consumption of vitamin B_{12} was assessed by frequency method. Assessed was also the frequency and amount of intakes of the food staffs containing vitamin B_{12} during the last year. Based on the average contents of cobalamin, the average daily B_{12} intake was estimated.

Data were analyzed using the regression analysis.

Results and discussion. Our data confirm high prevalence of vitamin B_{12} deficiency among elderly and old people. Thus cobalamin lack (<200 ng/l) was found in 5 (16.7 %) subjects and its deficiency (<150 ng/l) in 18 (60 %) individuals. That is only 7 (23.3 %) of study subjects had normal blood serum vitamin B_{12} level. In 23 subjects (76.7 %) we registered either the deficiency or lack of cobalamin.

The regression analysis revealed a regular deacrease in the serum vitamin B_{12} concentration with age (fig. 1). Notably after 75 years there exists a high probability of cobalamin deficiency (<150 ng/l) and of its further lowering with aging.

It is possible to assume that serum vitamin B_{12} concentration decreases because people eat less as they grow older. The main source of cobalamin is meat, fish and sea products. Because they are costly and the chewing apparatus deterioration in old age, the elderly receive less cobalamin with the food. On the other hand the valuable source of vitamin B_{12} are milk products and eggs which are quite accessible and do not require long chewing. So, lower dietary consumption of vitamin B_{12} cannot fully explain its decrease in the blood serum. In this sense, our conclusion is in the accord with

J. M. Howard and coauth., who have found that only 1.7 % of people beyond 60 years consume less than 2 mcg of cobalamin daily while 39.9 % consume less than 6 mcg/day that does not however lead to a regular decrease of vitamin B_{12} concentration in the blood [10].

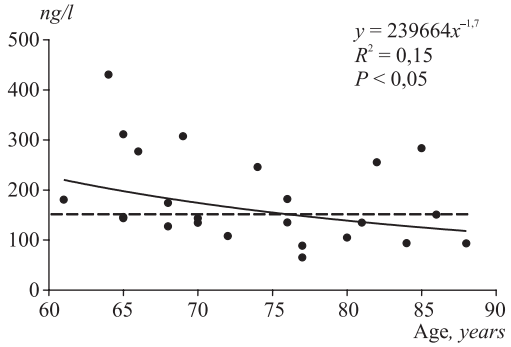

Fig. 1. Changes of vitamin B_{12} concentration in blood serum with aging. Here and on the fig. 3 dashed line is a border level of deficiency vitamin B_{12} (150 ng/l).

Dietary consumption of vitamin B_{12} in the majority of our study participants was much higher than recommended minimum (3.8 mcg/day). Only after the age of 80 years we observed a tendency towards decrease its consumption making it lower than the recommended level after the age of 85 years (fig. 2).

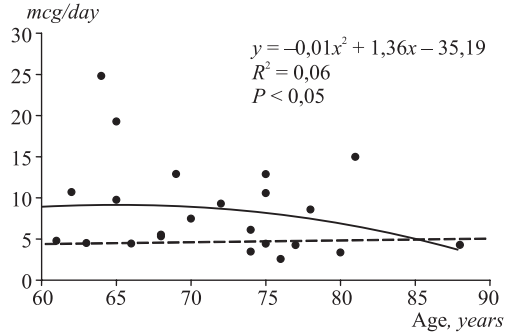

Fig. 2. Changes with aging vitamin B_{12} consumption with nourishment products. Dashed line is a minimal level of vitamin B_{12} consumption per day (3.8 mcg).

So, an increasing prevalence of vitamin B_{12} deficiency with age cannot be explained by its reduced dietary intake as decrease of cobalamin concentration in the serum is observed earlier than the decrease of its consumption with food products (see figs 1 and 2).

According to literature data, approximately 2 % of cases of vitamin B_{12} deficiency appear because of its insufficient amount in the diet, but more frequent reason of the deficit is the disturbance of its absorption due to age-

related changes in the digestive system [11]. R. D. Montgomery and coauth., investigating the reasons of disturbances of vitamin B_{12} absorption in the patients over 65 years, showed that the majority of them had more than one reason for malabsorption, among them: secretory deficiency of the pancreatic gland, gastroectomy, small intestine diverticulosis, celiac disease and an increased bacterial growth in the intestine [21]. At the same time M. G. van Oijen and coauth. found that atrophic gastritis was the reason of vitamin B_{12} deficiency in more than 20 % of their patients [27].

Following from this, it is impossible to single out the concrete risk group relative vitamin B_{12} deficiency among people 60 years and over. To clarify this issue, Loikas S., Koskinen P., Irjala K. et al recommend a population-based screening for the blood levels of cobalamin and it metabolites in the above population group [16]. Other authors mentioned that B_{12} absorption rose proportionally to its serum concentration [23]. Having all this in mind, we have analyzed the dependence of serum cobalamin concentration from its dietary consumption (fig. 3).

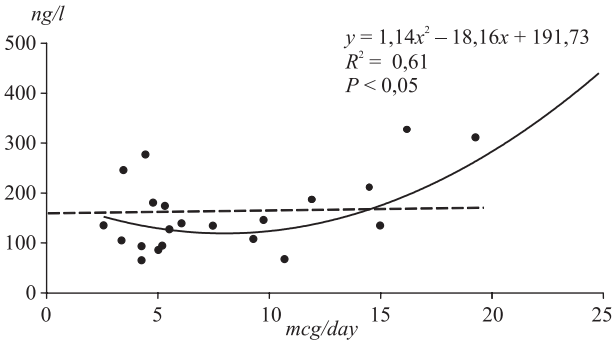

Fig. 3. Changes of vitamin B_{12} concentration in blood serum depending on its average daily consumption by elderly people.

Figure 3 shows that vitamin B_{12} consumption of less than 10 mcg/day does not essentially impact its serum levels and the majority patients with cobalamin deficiency consume as much of B_{12} as 10 mcg/day. Simultaneously we observed the rise of its serum concentration while at B_{12} consumption of more than 15 mcg/day we did not observe cobalamim deficit in the blood. So, the consumption of vitamin B_{12} by the elderly in the amount of more than 10–15 mcg/day allows prevent the development of its deficit. This evidence indicates that people over 60 years are recommended to consume more than 15 mcg/day of B_{12}. However, when nutritional correction is impossible (excess of calorie content or animal proteins, fat), food supplements or B_{12} preparations can be recommended.

In this sense, of special attention are the fortified foods with a definite component in order to increase their biological value. In our opinion, the fortifying of foods by vitamin B_{12} will allow to fulfil the prophylaxis and even treatment of its deficit and insufficiency.

Conclusions

1. The individuals beyond 60 years of age have marked prevalence of vitamin B_{12} deficiency that increases with an increasing age.
2. The fall of serum vitamin B_{12} concentration with age occurs earlier than reduction of its dietary consumption. This evidences for the essential role of the disturbance of cobalamin absorption in the development of its deficit due to age-related changes in the digestive system.
3. The recommended amount of dietary vitamin B_{12} is nearly 10–15 mcg/day. This increases its bioavailability and prevents its deficit onset.

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ДЕФИЦИТ ВИТАМИНА B_{12} У ЛЮДЕЙ ПОЖИЛОГО И СТАРЧЕСКОГО ВОЗРАСТА

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Определяли изменения концентрации витамина B_{12} в сыворотке крови с возрастом и его содержания в рационе питания 30 человек пожилого и старческого возраста (60–89 лет) без острых или обострения хронических заболеваний. Несмотря на то, что потребление витамина B_{12} у большинства обследованных было выше минимально рекомендуемого уровня (3,8 мкг/сутки), у 76,7 % из них отмечено снижение концентрации витамина B_{12} в сыворотке крови, которое становится более выраженным после 75 лет. Вместе с тем, выявлено, что при потреблении кобаламина более 10–15 мкг/сутки наблюдается возрастание его концентрации в сыворотке крови. Таким образом, высокая распространенность дефицита витамина B_{12} может быть вызвана в первую очередь ухудшением его усвоения вследствие возрастных изменений пищеварительного тракта. Для предупреждения дефицита витамина B_{12} следует рекомендовать его потребление не менее 10–15 мкг/сутки.

ДЕФІЦИТ ВІТАМІНУ B_{12} У ЛЮДЕЙ ЛІТНЬОГО ТА СТАРЕЧОГО ВІКУ

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Визначали зміни концентрації вітаміну B_{12} у сироватці крові з віком та його вмісту в раціоні харчування 30 людей літнього та старечого віку (60–89 років) без гострих чи загострень хронічних захворювань. Незважаючи на те, що споживання вітаміну B_{12} у більшості обстежених було вище мінімального рекомендованого рівня (3,8 мкг/добу), у 76,7 % із них відзначено зниження концентрації вітаміну B_{12} у сироватці крові, яке стає більш вираженим після 75 років. Поряд із цим, виявлено, що при споживанні кобаламіну більше 10–15 мкг/добу спостерігається зростання його концентрації у сироватці крові. Отже, значна поширеність дефіциту вітаміну B_{12} може бути спричинена в першу чергу погіршенням його засвоєння внаслідок вікових змін травного тракту, тому для попередження дефіциту вітаміну B_{12} слід рекомендувати його споживання не менше 10–15 мкг/добу.

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