



The Importance of Vitamin D on the Health of People with Liver Diseases of Viral Etiology

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Abstract: Over the past few years, interest in studying the synthesis, metabolism and action of vitamin D has increased due to the global trend towards a decrease in its intake and the emergence of new knowledge about the mechanisms of action of its active metabolites in the human body. According to some studies, vitamin D deficiency is associated with an increased risk of developing infectious diseases. As a result of this study, it was found that patients with liver cirrhosis with vitamin D insufficiency/deficiency are more often diagnosed with bacterial infections, which requires determination of vitamin D status and, if necessary, its correction in patients with cirrhosis.

Key words: vitamin D, immune system, bacterial infections, liver cirrhosis.

Purpose of the study

To study the relationship between vitamin D concentrations and the severity of liver damage, as well as the incidence of bacterial infections in patients with liver cirrhosis.

Currently, the concept of vitamin D has been formed as a steroid prehormone, which is converted in the body into an active metabolite - D-hormone, which, along with a powerful regulatory effect on calcium metabolism, has a number of other important biological functions. The term "vitamin D" combines a group of two forms of vitamin similar in chemical structure: D2 and D3 [1].

Vitamin D2 (ergocalciferol) enters the body with food and is found mainly in products of plant origin (cereals, fish oil, butter, milk, egg yolk), it is one of the fat-soluble vitamins and is metabolized in the body to form derivatives that have similar properties. vitamin D3 action.

The content of vitamin D3 (cholecalciferol) depends little on external intake; it is formed from a precursor located in the skin (provitamin D3) under the influence of ultraviolet rays and depends on skin pigmentation, latitude of the region, day length, time of year, weather conditions and skin area, not covered by clothes. Another important source of vitamin D is food. Fatty fish such as herring, mackerel, and salmon are especially rich in it, while dairy products and eggs contain small amounts of this vitamin [1].

It has been proven that in order to exhibit biological activity, vitamin D3 undergoes two stages of transformation with the formation of its active metabolites. Different enzymes are involved in the metabolism of the two forms of vitamin D.

The first stage of vitamin D metabolism is carried out mainly in the liver, which absorbs up to 70% of vitamin D₃ from the bloodstream, it is distributed to liver cells - reticulocytes and hepatocytes. In relation to the vitamin, reticulocytes act as a depot, from where it is gradually transported to hepatocytes. In hepatocytes, with the help of cytochrome P450 (both mitochondrial and microsomal), the active metabolite of vitamin D, 25-hydroxyvitamin D (25OHD), is formed. Most studies are devoted to studying the role of CYP27A1, which is localized primarily in the liver and has a high affinity for vitamin D [1, 2].

The first active form of 25OHD formed in the liver is transferred with the help of transport proteins to the kidneys, where it undergoes further transformation with the formation of hormonally active compounds, among which two metabolites have the most important physiological significance - 1,25-dihydroxycholecalciferol (1,25(OH)₂D) and 24,25-dihydroxycholecalciferol (24,25(OH)₂D). The concentration of serum 1,25(OH)₂D is about 0.1% of the level of 25OHD [3]. It is necessary to take into account that various biologically active forms of the vitamin take part in the regulation of the same processes, but at different levels. Therefore, for the regulation of physiological processes in the body, a very important factor is the presence of a certain ratio of the main metabolites of vitamin D₃.

Vitamin D, which is consumed in food or synthesized in the skin, is biologically inactive; activation occurs through enzymatic conversion in the liver and kidneys. In patients with liver diseases of various etiologies, in particular chronic hepatitis of viral etiology, the activation of vitamin D is difficult, which leads to vitamin D deficiency.

Based on scientific knowledge, we can conclude that vitamin D₃ takes part in the regulation of:

- 1) proliferation and differentiation of cells of all organs and tissues;
- 2) protein, lipid, mineral metabolism in the body, synthesis of receptor proteins, enzymes, hormones;
- 3) functional activity of many organs and systems, including the gastrointestinal tract;
- 4) innate and adaptive immunity. Thus, new features of the metabolism and mechanisms of action of vitamin D have recently been established, which influence the pathogenesis of certain human diseases. Research into the molecular mechanisms underlying the development of responses to inflammation and infection has led to a more detailed understanding of the cellular response to vitamin D through the VDR. But at present, the question of the molecular mechanisms of VDR dysfunction in human diseases remains insufficiently studied, which does not allow prescribing vitamin D as a medicine.

Considering that vitamin D metabolism occurs with the participation of the liver and its deficiency is associated with an increased risk of developing infectious diseases [3, 4], it is of interest to study the concentration of vitamin D metabolites in patients with chronic viral liver damage and establish an association with the development of infections.

Vitamin D affects the viral load in viral hepatitis of the liver.

Vitamin D affects many body functions, including the immune system. It has been proven that a lack of vitamin D in the body leads to more intensive reproduction of the hepatitis virus.

Viral hepatitis remains one of the most common diseases in the world, despite the availability of a vaccine to prevent infection. According to WHO, more than 2 billion people are infected with this virus. This is also a dangerous disease, since the destructive effect of the hepatitis virus on the liver often leads to cirrhosis - irreversible and incompatible with life liver damage. About 60 million people newly infected with the hepatitis virus are registered in the world every year, and 600,000 die per year from the consequences of cirrhosis.

Antiviral drugs for the treatment of hepatitis do not remove the virus from the body in most cases. It remains lifelong, threatening health and requiring constant monitoring of the activity of the virus and the condition of the liver.

The hepatitis virus is not always dangerous and often does not require treatment with antiviral drugs. The question of treatment tactics is decided by a hepatologist after a full examination, and during control - depending on the activity of the virus and the degree of fibrosis (liver damage by the virus).

The activity of the virus is determined by its amount in the blood, which reflects the intensity of virus reproduction and liver destruction. A recent discovery by German scientists showed that the amount of vitamin D in the body affects the activity of the virus. With a deficiency of this vitamin, the level of viral load is significantly (reliably) higher than in those who have normal values.

Professor Christian Lange (University of Frankfurt) suggests including vitamin D supplements in the treatment of hepatitis.

Material and research methods

We examined 20 patients with cirrhosis of the liver, who underwent clinical, laboratory and instrumental (general and biochemical blood tests, general urinalysis, esophagogastroduodenoscopy, ultrasonography of the abdominal organs and kidneys) studies in accordance with the "Temporary protocols (standards) for the examination and treatment of patients with pathologies of the digestive organs in outpatient and inpatient settings." The concentration of the active metabolite of vitamin D - 25 OHD in blood serum was determined by an immunochemical method. Vitamin D status was determined according to the following criteria for the content of 25 OHD in the blood serum: above 50 nmol/l - normal, 50-25 nmol/l - deficiency, 25-12.5 nmol/l - deficiency, less than 12.5 nmol/l - severe deficiency. The representativeness of the sample was ensured by random selection of patients for the study.

Results and discussion

20 patients with liver cirrhosis aged 46.9 ± 13.6 years were examined, including 9 women and 11 men. As a result of the study, insufficiency and deficiency of vitamin D were detected in 13 (65%) patients with liver cirrhosis, of which vitamin D insufficiency was found in 6 (46.1%), deficiency - in 6 (46.1%), severe deficiency - in 1 (7.8%) patient. In 7 (53.8%) patients with a decrease in 25 OHD levels, a decrease in serum calcium and phosphorus levels was detected. When conducting a correlation analysis, a direct relationship was revealed between the concentration of 25 OHD and phosphorus ($R = 0.48$, $P = 0.04$).

The severity of liver damage was determined according to the Child-Pugh cirrhosis severity class. The examination included 5 (25%) patients with cirrhosis of severity class B and 15 (75%) - class C. According to the literature, with severe liver failure, the synthesis of 25OHD decreases [1]. According to our data, in 4 (80%) patients of class B and 9 (60%) of class C, the level of 25 OHD was reduced. Vitamin D deficiency was diagnosed in 2 (40%) patients of class B and 4 (26.7%) - class C, vitamin D deficiency - in 1 (20%) patient of class B and 5 (33.3%) - class C, severe vitamin D deficiency - in 1 (20%) class B patient. A comparative analysis did not reveal significant differences between the frequency and degree of reduction of 25 OHD in patients with liver cirrhosis of severity classes B and C.

Bacterial infections were more often diagnosed in patients with liver cirrhosis with vitamin D insufficiency/deficiency - in 11 (84.6%) compared to patients with normal vitamin D levels - in 4 (57.1%). Among the laboratory parameters reflecting the degree of the inflammatory process, the levels of C-reactive protein (CRP), rheumatoid factor (RF), and antistreptolysin-O (ASL-O) were studied. In 9 (69.2%) patients with liver cirrhosis with vitamin D insufficiency/deficiency, the level of CRP was increased (> 5 mg/l), in 2 (15.4%) the level of RF and ASL-O was increased. According to a comparative analysis, no significant differences were found between the level of these laboratory parameters in groups of patients with liver cirrhosis with normal/reduced vitamin D levels. When

conducting a correlation analysis, an inverse relationship was established between the level of 25 OHD and ASL-O ($R = -0.45$, $P = 0.05$).

Conclusion

According to the study, the majority of patients with liver cirrhosis (65%) showed a decrease in the serum level of the active metabolite of vitamin D. The identified changes in its status in patients with liver cirrhosis may be associated with several reasons: a decrease in insolation in winter (the patients were examined in December 2010 – February 2011) and intake of vitamin D from food, malabsorption, impaired hydroxylation of vitamin D in the liver, decreased synthesis of vitamin D binding protein as a result of liver dysfunction. However, our study did not reveal significant differences between the frequency and degree of reduction of 25 OHD in patients with cirrhosis of severity classes B and C. This may be due to the fact that the study did not include patients of severity class A and the number of patients examined was small. The concentration of vitamin D has not been studied depending on the etiological factor. According to the literature, in 85% of patients with liver cirrhosis of alcoholic etiology and in 47% of patients with primary biliary cirrhosis, a decrease in 25 OHD was found.

According to the study, patients with liver cirrhosis with vitamin D insufficiency/deficiency tend to develop bacterial infections more often (84.6%) compared to patients with normal vitamin D levels (57.1%). This may be due to the fact that vitamin D has a suppressive effect on the adaptive immune system, inhibiting cell proliferation, immunoglobulin synthesis and slowing down the differentiation of B cell precursors into plasma cells; provides an integrating and regulatory role in the activation and implementation of the innate immune response to microbial pathogens; regulates the level of pro- and anti-inflammatory cytokines. It has been proven that the administration of vitamin D at an average dose of 547 IU/day for 2–5 years leads to a decrease in the level of CRP by 23%, and in patients of the ITAR department, the administration of high doses of vitamin D (500 IU) reduces the level of CRP and IL-6 by compared with the administration of low doses (200 IU) ($P < 0.05$) [2, 3, 4]. According to our data, there were no significant differences in the level of CRP in groups of patients with liver cirrhosis with normal/reduced levels of vitamin D. However, an inverse relationship was established between the level of 25 OHD and ASL-O.

The established relationship between 25OHD and phosphorus concentrations will allow phosphorus to be used as a screening test for determining vitamin D metabolism.

Thus, the study of vitamin D status in patients with liver cirrhosis is relevant and when 25 OHD decreases, its correction should be carried out in order to reduce the risk of complications associated with vitamin D deficiency.

Further study of vitamin D and VDR will help explain the pathogenesis of various human diseases and find new approaches for their prevention and treatment.

Literature

1. AKBAROV, A., & TOLIPOVA, M. (2022). COMPARATIVE CHARACTERISTICS OF CERAMIC AND COMPOSITE VENEERS. Журнал "Медицина и инновации", (2), 191-204.
2. Alieva, N. M., & Tolipova, M. A. (2022). INFLUENCE OF VIRAL LIVER DISEASES ON THE STATE OF THE ORAL CAVITY. Innovative Development in Educational Activities, 1 (5), 264–270.
3. Алиева, Н. М., Очилова, М. У., & Толипова, М. А. (2022). ШИНИРУЮЩИЕ СИСТЕМЫ В ЛЕЧЕНИИ ПАРОДОНТИТА СРЕДНЕЙ СТЕПЕНИ ТЯЖЕСТИ. RESEARCH AND EDUCATION, 1(9), 74-78.

4. Алиева, Н. М., Толипова, М. А., & Очилова, М. У. (2022). ОПРЕДЕЛЕНИЕ СТАБИЛЬНОСТИ ИМПЛАНТАТОВ ПРИ РАЗЛИЧНЫХ МЕТОДАХ ПРОТЕЗИРОВАНИЯ НА ДЕНТАЛЬНЫХ ИМПЛАНТАТАХ. *RESEARCH AND EDUCATION*, 1(9), 222-230.
5. Очилова, М. У., Толипова, М. А., & Алиева, Н. М. (2022). Молекулярные основы развития хронических колитов как предрака толстой кишки. *MedUnion*, (1), 112-115.
6. Очилова, М. У., Толипова, М. А., & Алиева, Н. М. (2022). Молекулярные основы развития хронических колитов как предрака толстой кишки. *MedUnion*, (1), 112-115.
7. САЛИМОВ, О. Р., АЛИЕВА, Н. М., АХМЕДОВ, М. Р., & ОЧИЛОВА, М. У. (2022). ОРТОПЕДИЧЕСКИЕ МЕТОДЫ ЛЕЧЕНИЯ ЗАБОЛЕВАНИЙ ВИСОЧНО-НИЖНЕЧЕЛЮСТНОГО СУСТАВА (литературный обзор). *Journal of new century innovations*, 18(3), 3-29.
8. АЛИЕВА, Н. М., ОЧИЛОВА, М. У., ТОЛИПОВА, М. А., & КАСИМОВА, Э. В. (2022). ОРТОПЕДИЧЕСКИЕ МЕТОДЫ ЛЕЧЕНИЯ ПАРОДОНТИТА СРЕДНЕЙ СТЕПЕНИ ТЯЖЕСТИ ШИНИРУЮЩИМИ СИСТЕМАМИ ТАШКЕНТСКИЙ ГОСУДАРСТВЕННЫЙ СТОМАТОЛОГИЧЕСКИЙ ИНСТИТУТ. *Journal of new century innovations*, 18(3), 119-143.
9. Салимов, О. Р., Очилова, М. У., Толипова, М. А., & Касимова, Э. В. (2022). МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ УЗБЕКИСТАН ТАШКЕНТСКИЙ ГОСУДАРСТВЕННЫЙ СТОМАТОЛОГИЧЕСКИЙ ИНСТИТУТ. *MODELS AND METHODS FOR INCREASING THE EFFICIENCY OF INNOVATIVE RESEARCH*, 2(18), 217-232.
10. Касимова, Э. В., Салимов, О. Р., Очилова, М. У., & Толипова, М. А. (2022). ВЗАИМОСВЯЗЬ МЕЖДУ ДЕФИЦИТОМ ЭСТРОГЕНОВ И ЗАБОЛЕВАНИЯМИ ПАРОДОНТА У ЖЕНЩИН В ПЕРИОДЕ ПОСТМЕНОПАУЗЫ. *Journal of new century innovations*, 18(3), 49-71.
11. Алиева, Н. М., Шоахмедова, К. Н., & Толипова, М. А. (2022). ИСПОЛЬЗОВАНИЕ ДИОКСИДА ЦИРКОНИЯ В СТОМАТОЛОГИИ. *RESEARCH AND EDUCATION*, 1(9), 68-73.
12. Alieva, N. M., Tolipova, M. A., & Ochilova, M. U. (2022). ASPECTS OF DENTAL DISEASES IN PATIENTS WITH CHRONIC HEPATITIS B.(LITERATURE REVIEW). *RESEARCH AND EDUCATION*, 1(9), 215-221.
13. Махмудов, М. Б., Меликузиев, Т. Ш., Рахимов, Б. Г., & ТОЛИПОВА, М. А. (2022). ЗАЯВЛЕНИЕ О КЛИНИЧЕСКИХ И ФУНКЦИОНАЛЬНЫХ ИЗМЕНЕНИЯХ СЛИЗИСТОЙ ОБОЛОЧКИ ПРОТЕЗНОГО ЛОЖА ДО И ПОСЛЕ ПРОТЕЗИРОВАНИЯ У ПАЦИЕНТОВ С ДИАБЕТОМ. *Journal of new century innovations*, 18(2), 240-255.
14. Алиева, Н. М., Малика Улмасовна, О., & Толипова, М. А. (2022). ДЕПРОГРАММАТОР КОЙСА-КАК ИННОВАЦИОННАЯ ТЕХНОЛОГИЯ В ОРТОПЕДИЧЕСКОЙ СТОМАТОЛОГИИ (ЛИТЕРАТУРНЫЙ ОБЗОР). *RESEARCH AND EDUCATION*, 1(9), 60-67.