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Vitamin B12 - is it worth supplementing?

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Abstract

Introduction

Cobalamin is a vitamin that plays an important role in many processes occurring in our body. It affects, among others, the functioning of the hematopoietic, nervous, and digestive systems and the functioning of the psyche. Its deficiency can be encountered in everyday clinical practice. Many scientific studies have been conducted on it, focusing on the causes and effects of its deficiency.

Purpose

This work aims to identify groups of patients whose risk of vitamin B12 deficiency is higher than in the general population. This will help draw attention to these selected groups of patients, so that in clinical practice, vitamin B12 supplementation may be considered before symptoms of its deficiency occur.

Brief description of the state of knowledge

The most common cause of vitamin B12 deficiency is Addison-Biermer's disease caused by the presence of autoantibodies against Castle's intrinsic factor. However, there are more factors that indirectly affect the level of cobalamin in the body.

Material and methods

In this work, we analyzed the following conditions and diseases that are correlated with vitamin B12 deficiency: medications taken, gastrointestinal diseases, conditions after bariatric surgery, pregnancy, vegan diet, old age, and alcohol.

Discussion:
After analyzing selected issues, we conclude that the risk of vitamin B12 deficiency varies, in some cases, it is correlated with advanced disease, and in others, it is independent of it. Additionally, it should be taken into account that although the pathomechanism leading to vitamin B12 deficiency is known in the above-mentioned conditions, the real risk of its deficiency may be so low that its clinical significance will be low.

Keywords: Vitamin B12, metabolism, deficiency, supplementation

Introduction

Vitamin B12 belongs to the B vitamins, which, like vitamin C, are water-soluble. [1] The history of the discovery of this vitamin dates back to 1835, when a disorder of erythrocyte production called pernicious anemia was first described. Research conducted in 1920 showed that giving liver to bleeding dogs accelerated their recovery. Scientists worked to isolate the liver component that was responsible for these effects. In 1948, a crystalline compound containing cobalt and phosphorus-vitamin B12 was discovered. It was described only 8 years later by D. Hodgkin, who received the Nobel Prize for her research. [2].

Source

Vitamin B12 is not synthesized by eukaryotes, only bacteria have this ability. Therefore, it is necessary to provide this ingredient with food. Products containing cyanocobalamin include, among others: ruminant meat, poultry, fish, eggs, milk, and cheese. [5,6].

Metabolism

After eating foods rich in vitamin B12, it is released with the participation of stomach acid and pepsin. The salivary glands and duodenum secrete R protein, which combines with cyanocobalamin, then in the presence of the alkaline environment of the duodenum it is hydrolyzed and vitamin B12 forms a complex with intrinsic factor (IF) - a product of the parietal cells of the stomach. The terminal section of the ileum contains special receptors that bind the B12-IF complex and, in the presence of calcium ions, enable the complex to be absorbed. The intrinsic factor is degraded, thus releasing cyanocobalamin. Then, transcobalamin II is added and the newly formed complex is actively taken up by the liver, bone marrow, and other tissues of the human body. [17,18]

Role in the body

Cobalamin plays a key role in the formation of erythrocytes in the bone marrow, as well as the synthesis of genetic material in erythroblasts. It also takes part in the metabolism of nutrients, the proper development of the nervous system, and the metabolism of purines and pyrimidines. [7,8] It influences the transformation of folic acid into its active form and together with it stabilizes the human genome. [9]

Effects of the deficit

Vitamin B12 deficiency manifests itself in disorders of many human body systems. The most important symptoms are presented in the table below.[10,11,12]

Table 1.

Neurological	**Psychiatric**	**Hematological**	**Dermal**	**Related to the digestive system**	**Other**
Faint	Chronic fatigue syndrome	Megaloblastic anemia	Discoloration	Jaundice	Increased risk of heart attack
Dizziness	Mood disorders	Thrombocytopenia	Vitiligo	Glossitis	Increased risk of stroke
Hypotonia	Attention deficit	Leukopenia			
Ataxia	Slow thinking				
Convulsions	Cognitive disorders				
Handshaking	Memory disorders				
Tingling and paresthesia	Conduct disorders				

Source: [10,11,12]

The consequences of long-term deficiency can be devastating, which is why supplementation of this vitamin is so necessary, especially in patients at risk of its deficiency.

Below are selected diseases or situations in which patients are at increased risk of vitamin B12 deficiency. Therefore, in clinical practice, such cases should be considered and the need for supplementation should be considered.

Material and methods

In this work, we analyzed the following conditions and diseases that are correlated with vitamin B12 deficiency: medications taken, gastrointestinal diseases, condition after bariatric surgery, pregnancy, vegan diet, old age, and alcohol. A review of the literature available in the National Library of Medicine database at https://pubmed.ncbi.nlm was performed. nih.gov and Google Scholar. Articles were searched using keywords such as Vitamin 12, vitamin B12 deficiency, supplementation, and cobalamin.

Medicines

Metformin

Metformin may increase the risk of vitamin B12 deficiency through several mechanisms. Firstly, this substance stimulates the growth of bacteria in the small intestine, leading to bacterial overgrowth, which results in digestion and absorption disorders and, consequently, cobalamin deficiency. Another aspect worth mentioning is reducing the concentration of intrinsic factors, which is necessary for proper absorption. [13]

Additionally, metformin inhibits the calcium-dependent absorption of the cobalamin-intrinsic factor complex, which occurs in the distal ileum. The longer this drug is used, the higher the dose, and the older the age, the risk of deficiency increases. [14,15,16]

IPP and H2 receptor antagonists

The mechanism of action of these groups of drugs is to block H+K+ATPase, which leads to inhibition of the release of H+ ions by parietal cells into the stomach lumen. Thus, chloride ions cannot combine with hydrogen cations and the production of hydrochloric acid is inhibited. [19]

The lack of an acidic environment prevents the activation of pepsinogen into pepsin, thus blocking the pathway of vitamin B12 release from the food consumed, reducing the amount that is absorbed. [20]

Other drugs that negatively affect the absorption of vitamin B12 include sulfasalazine, para-aminosalicylic acid, colchicine, cholestyramine, and potassium in the form of prolonged release. It is also worth mentioning nitrous oxide, often used by anesthesiologists, which inactivates methylcobalamin, thereby limiting the amount of active vitamin B12.[21,22]

Digestive tract diseases

The actual incidence of vitamin B12 deficiency in patients with inflammatory bowel diseases varies and depends on the type of disease, its advancement, and surgical interventions implemented.

In the case of Crohn's disease, the only factor that increases the risk of B12 deficiency is the condition after resection of a fragment of the ileum >30 cm long. There was no correlation between cobalamin deficiency and the location of the disease in the gastrointestinal tract or its removal.

The problem of vitamin B12 deficiency may also affect patients with celiac disease who are not undergoing treatment. Although this disease mainly affects the proximal small intestine, vitamin B12 deficiency is common in untreated celiac disease. [34]
To normalize the level of vitamin B12 in this group of patients, a gluten-free diet is sufficient. However, in patients presenting clinical symptoms of vitamin deficiency, supplementation may be necessary. [34]

Chronic pancreatitis (CP) increases the risk of vitamin B12 deficiency. [4] This has to do with:
- malnutrition of patients suffering from CP and therefore a lower amount of enzymes responsible for the absorption of vitamins,
- lack of degradation of haptocorin, which may prevent the binding of vitamin B12 to intrinsic factor,
- impaired secretion of pancreatic enzymes and changes in the pH of the stomach, bile, and intrinsic factor [4]
However, despite the known factors influencing the occurrence of vitamin B12 deficiency in CP patients, clinical symptoms of its deficiency are rare in this group. There is also no clear data that the degree of pancreatic insufficiency affects this risk.[4]

Bariatric surgery
Intestinal absorption of vitamin B12 is dependent on intrinsic factor (IF). Obesity, which is a lifestyle disease, correlates with the growing number of patients undergoing bariatric surgery. One of the techniques used in bariatric surgery is the creation of a Roux-en-Y gastric bypass. The production of IF is then disturbed and, consequently, the absorption of vitamin B12. [33]

Pregnancy
Many important processes occur during pregnancy. These include DNA synthesis and its methylation during fetal development. The key ingredients for this process are vitamin B12, folic acid, and vitamin B6. They play an important role in the process of folate metabolism, ensuring its proper course. During pregnancy, we may notice a decrease in vitamin B12 levels. This happens as a result of hemodilution, hormonal changes, fluctuations in the concentration of binding proteins, and most importantly, increased transport to the fetus.
The deficit in a pregnant woman increases the risk of preeclampsia and premature birth, while in a child it may cause IUGR, megaloblastic anemia, or neural tube defects. Deficiency during lactation may lead to cognitive disorders in the child's development. [27,28]
In pregnant women, the symptoms of vitamin B12 deficiency are often obscured by folic acid supplementation, thus increasing the risk of vitamin B12 deficiency. That is why it is so important to simultaneously supplement the deficiency of folic acid and cobalamin in pregnant women. [29,30]

Vegan diet

According to research, the biggest problem for vegans is vitamin B12 deficiency. Although plant foods contain analogs of this vitamin, they are not absorbed in the human small intestine. In addition, they have a similar structure to cobalamin, so they additionally block its absorption from the digestive tract. The only organisms that can produce vitamin B12 are bacteria that live in the digestive tract of animals. The final section of the human small intestine is also inhabited by bacteria, but this only covers a small amount of the human body's total needs. Therefore, the basic products that ensure the appropriate level of cobalamin are meat, milk, and eggs. [32].

Elderly

The main cause of vitamin B12 deficiency in older people is consuming fewer products rich in this vitamin. Elderly people eat less meat. The reasons for this are various: vegetarianism, religious beliefs, or low economic status.

The diet of elderly people is also less diverse. Combining this with deteriorated absorption in the small intestine gives a picture of deep deficits of this macronutrient. The second very important cause is atrophic gastritis with achlorhydria, which results in blocking the separation of the B12-protein complex. Increased pH also promotes the multiplication of bacteria in the intestine, limiting the absorption of cobalamin [24].

Alcohol

Alcohol consumption causes deficiencies in many vitamins and other nutrients necessary for the proper functioning of the human body. Taking into account the deficits of B vitamins, cobalamin takes the lead. The reason for this state of affairs is the negative effect of alcohol on the secretion of Castle factor, B12 transport, and its active absorption in the ileum. [3.36].

Vitamin B12 supplementation

The daily dose of vitamin B12 is approximately 2.4 μg for adults, and 2.6-2.8 μg for pregnant women. [23] Its exact guideline values vary by region. [2] Taking into account that in the above-mentioned groups the supply of vitamin is insufficient or its absorption process is disturbed, supplementation should be considered both by supplementing the diet with appropriate products and by using vitamin preparations. [24]

There are two types of replacement therapy - oral and parenteral. Considering the parenteral route, an intramuscular form is available in Poland. In the beginning, the treatment is quite intensive, we start with a dose of 1 mg every day for a week, then gradually reduce the frequency to 1 mg twice a week for 2 weeks, then 1 mg once a week for 4 weeks. However, the therapy regimen for chronic treatment is 1 mg once a month or once every 3 months, depending on the causes of the deficit and the effects of therapy.

These schemes, of course, vary from country to country, as each country has its own guidelines. [24,25]
The second supplementation option is oral administration, which is quite rarely used in Poland. Recommended doses also depend on the causes of the deficiency.
People whose deficit is related to the diet, but absorption is normal, should use a dose of 0.05 mg/day, patients with impaired absorption of food - 0.5 mg/day, and those suffering from Addison Biermer's anemia - 1 mg/day.
According to research on pernicious anemia, a sufficient dose is 1000 μg of vitamin B12 administered orally. However, patients usually have deep deficits and serious clinical symptoms, so supplementation of deficiencies begins parenterally. In case of absorption disorders, supplementation should be used for life.
An important element of therapy should be the implementation of dietary recommendations that include foods rich in animal protein, the flagship product is liver, which contains the largest amounts of vitamin B12. [24]

Table 2.
Food products of animal origin containing the highest amount of cobalamin:

Product	μg/100 g
liver of slaughtered animals	25 – 110
fish	1 – 24,0
milk and dairy products	0,3 – 2,6
eggs	1,6
meat	0,7 – 1,3

Source: [35]

Summary

The main causes of cobalamin deficiency include its inadequate supply in the diet, medications that affect its absorption in the gastrointestinal tract, and disorders of enzymes involved in its metabolism. Vitamin B12 deficiency disturbs, among other things, the functioning of the nervous and circulatory systems, and also affects mental processes.
As the examples we have cited show, the risk of vitamin B12 deficiency varies; in some cases, it is correlated with advanced disease, and in others, it is independent of it. When encountering the above-mentioned groups of patients in clinical practice, it should be borne in mind that they are more susceptible to cobalamin deficiency. However, each case should be approached individually, because even in groups exposed to cobalamin deficiency, the risk of its deficiency may be minimal.

DISCLOSURE

Author's contribution

Conceptualization, Katarzyna Polańska, and Marta Wojaczek; methodology, Weronika Szafrańska; software, Marta Wojaczek; check, Dominika Poborowska and Weronika Kahan; formal analysis, Emilia Bąk and Oliwia Najjar; investigation, Jacek Fordymacki and Oliwia Najjar; resources, Tomasz Gańko; data curation, Weronika Szafrańska; writing - rough preparation, Weronika Kahan; writing - review and editing, Katarzyna Polańska; visualization, Dominika Poborowska; supervision, Katarzyna Polańska and Jacek Fordymacki; project administration, Emilia Bąk, and Tomasz Gańko; receiving funding - no specific funding.

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The authors deny any conflict of interest

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