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The problem of anemia in elderly patients

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Abstract

Introduction and purpose:

As healthcare develops, life expectancy increases. This makes anemia of the elderly an increasingly common problem. The appearance of this disease is influenced by many factors related to the aging process of the organism. The purpose of this study is to review information

about the different mechanisms of anemia development in the elderly and to present the associated difficulties in medical practice.

Description of the state of knowledge:

Many different factors can affect the process of anemia. The causes of this disorder include chronic inflammatory diseases, cancer and nutritional deficiencies. Endocrine status is also important. The chronic inflammatory process may induce haemolysis and lead to the increased synthesis of hepcidin, which by blocking the activity of ferroportin leads to a decrease in the level of iron ions in the blood. Deficiency anemia often results from reduced appetite, inadequate quality of meals, chronic inflammation or taking medications without consulting a doctor. The consequence is a reduced level of iron and vitamin B12 and folic acid, which play a role in erythropoiesis. The hormones that play a significant role in the process of making red blood cells include erythropoietin, testosterone and thyroid hormones.

Summary:

Anemia is a common problem among geriatric patients and one of the factors contributing to the increase in mortality in this age group. In medical care it is difficult to distinguish which symptoms are pathological and which are related to the natural aging process, overlapping symptoms of many diseases and related diagnostic problems. Diagnostics is a particular challenge due to the multi-morbidity, which is associated with taking many drugs with different mechanisms of action and side effects.

Keywords: anemia; aging; comorbidity; nutrient-deficiency anemia; inflammation

Introduction and purpose

In recent years, transformation has become visible in Poland's demographic, so the total number of elderly people increases dramatically and shows a further trend of rapid growth. According to the current demographic data life expectancy in Poland is 72.7 years for men and 80.9 years for women [1]. Compared to the years in the previous decades it is several years longer and still shows an increasing tendency. It is therefore reflected in the general health of the population, which is largely influenced by geriatric patients. It is no wonder that the problem of anemia in the elderly is becoming more and more common. One of the most common ailments of the elderly, next to the so-called of great geriatric problems, is anemia. The WHO defines anemia as lowering hemoglobin levels below 12 g/dL in women and below 13 g/dL in men. However, the diagnostic cut-off values for determining anemia vary with age, gender and possibly race [2].

The overall prevalence of anemia in the elderly is about 17% (47% of people in nursing homes, 40% of hospitalized patients and 13% of seniors in the general population). The NHANES III study shows that the overall incidence of anemia in adults below 65 years old was 11.0% in males and 10.2% in females [3].

The symptoms of anemia are usually similar to those that occur in younger patients, however, they can often be confused with the physiological aging process. Multiple morbidity and polypharmacy have an important impact on the health of patients and contribute to increasing the difficulty of determining what is the norm and what is pathology among the elderly people [2].

Anemia may be asymptomatic and is detected incidentally by laboratory tests. Patients sometimes report symptoms related to associated conditions such as blood loss or associated with decreased oxygen carrying capacity, such as weakness or shortness of breath. There are many different causes of anemia in the elderly. These include, but are not limited to, nutrient deficiency, chronic kidney disease, chronic inflammation, and occult blood loss from gastrointestinal cancer, although the etiology is unknown in many patients [3].

Assessment includes a detailed medical history and physical examination, assessment of risk factors for underlying disease, and assessment of blood parameters, including mean blood cell volume [4]. In most diagnostic algorithms mean cell volume (MCV) plays the greatest role in case of anemia.

Low hemoglobin levels, irrespective of other health conditions, expose the elderly to numerous adverse health effects related to poor tissue oxygen delivery, such as exhaustion, fatigue, muscle weakness and cognitive decline. The increased risk of mortality in older adults with anemia is well documented [5]. The risk is not explained by the underlying disease, which suggests that anemia itself comprise a risk factor for death in the elderly [6].

Diagnostic and therapeutic guidelines are based on the assumed etiology and the pathophysiology of anemia. In patients with microcytic anemia (MCV <80 fl), the levels of ferritin, iron and transferrin are tested to determine the presence of iron deficiency causing the anemia. Vitamin B12 and folic acid are also measured in patients with macrocytic anemia (MCV > 100 fl) in order to exclude vitamin B12 or folic acid deficiency. Normocytic anemias (MCV 80-100 fl) are usually caused by chronic diseases, cancer or bone marrow disorders [1].

This overview of the available database of publications focuses on the most important causes of anemia, including diagnostic methods. Determining the interrelationships between blood test results and clinical symptoms found in the elderly people can help to better understand the mechanisms of aging.

The aim of our article is to review literature on the subject of the various causes and mechanisms, which play a significant role in anemia. Moreover, an important task remains to emphasize the importance of this phenomenon in the context of an aging society and to show the diagnostic and treatment challenges in the group of elderly patients.

Hormonal causes of anemia

The lack of recognition of the cause of low hemoglobin concentration concerns one-third of elderly men with anemia [7]. Testosterone levels decline with age. While total testosterone levels decrease gradually and slowly, free testosterone levels decline sharply after the age of 30 [8].

It is known that androgens stimulate erythropoiesis [7]. Prior to the introduction of current methods of treatment, androgens were used in the treatment of aplastic anemia. The expectation of the treatment was to increase the level of hemoglobin by 0,8-1 g/dL [9]. With age, the level of total and free, bioavailable testosterone as well as the level of hemoglobin decrease, which predisposes to the development of anemia in elderly. Most likely a decrease in androgens levels associated with age contributes to the development of anemia by causing a decrease in erythroid mass. As testosterone levels decline, hemoglobin drops by an average of 1,5 g/dL [8]. Anemia

also affects men suffering from hypogonadism or after hormonal ablation. The hemoglobin level is then usually around 1 g/dL below normal but can be around 2,5 g/dL below normal in patients whose hormonal ablation was complete and in patients after radiotherapy [9,10]. In contrast, testosterone replacement therapy raises hemoglobin levels [8].

The role of testosterone in pathogenesis of anemia in elderly men was investigated in a double - blinded, placebo controlled trial by Roy et al in 2017. The study was conducted on 788 men over or in the age of 65, whose mean testosterone levels were below 275 ng/dL. 126 of the subjects had anemia and 62 of them did not have a diagnosis of its cause. In the survey dose - adjusted testosterone gel or placebo gel were used for 12 months. Among patients with unexplained anemia 54% increased their hemoglobin levels by at least 1 g/dL as a result of testosterone treatment in comparison with placebo (15%). 58,3% of those subjects did not have anemia after 12 months of testosterone treatment (placebo - 22,2%). In case of known cause anemia, patients with an increase in hemoglobin level of at least 1 g/dL after testosterone therapy accounted for 52%, and in case of placebo, 19%. The survey shows that testosterone increases levels of hemoglobin in elderly patients with testosterone deficiency in case of both unexplained anemia and anemia of known cause [7].

In addition to testosterone, thyroid hormones are also important in the etiology of anemia. Thyroid hormone deficiency leads to RBC decrease leading to normocytic anemia. The exact level of hormones deficiency needed to induce anemia is not known, but the more intensified the hypothyroidism, the greater the risk of anemia. Treatment of hypothyroidism usually treats the anemia [8].

Renal causes of anemia

It is known that the function of the kidneys is impaired in the elderly, regardless of the presence of recognized disease. The decline of renal function may be more severe in patients with hypertension and diabetes mellitus [11].

GFR declines with age. Starting with the age of 40 GFR decreases by approximately 1 ml/min/1.73 m²/year. A significant acceleration in the rate of decline takes place after the age of 65 [12]. While under normal conditions, younger people have an average GFR of around 120 mL/min, by the age of 80 this value changes to an average of 50-80 mL/min. At the same time, despite the decline in GFR in the elderly, creatinine levels remain unchanged or slightly increase over time. This is believed to be a result of the reduction in muscle mass associated with aging [13].

The most numerous group of patients with the diagnosis of chronic kidney disease are people over 60 years of age [14]. A common complication of chronic kidney disease is normocytic anemia. Anemia in patients over the age of 65 is most commonly caused by chronic kidney disease. The NHANES III study shows that levels of hemoglobin start to decline, usually with GFR under 70 mL/min in men and under 50 mL/min in women. Furthermore the incidence of anemia with hemoglobin levels below 11 g/dL increases in patients with GFR levels below 30 ml/min/1.73 m². A decreased level of erythropoietin (EPO) in the serum plays a principal role in anemia associated with impaired renal function. Other factors common in the elderly, such as malnutrition, chronic inflammation and iron deficiency also contribute to the pathomechanism [13]. In the study on anemic patients over the age of 60, Gowanlock et al

showed that in comparison to iron deficiency anemia levels of erythropoietin were lower in CKD, anemia of chronic disease and UA (unexplained anemia) by 48%, 46% and 27% respectively [15].

Erythropoietin is a glycoprotein cytokine with a molecular mass of 34 kDa. Erythropoietin is an essential hormone for erythropoiesis - it regulates differentiation and hyperplasia of erythroid progenitor cells localized in the bone marrow [16]. Erythropoietin is mostly produced in the kidneys by fibroblasts of interstitial tissue, about 10% in the liver and minimal amounts of erythropoietin are also produced by macrophages [17]. While hypoxic conditions and anemia increase the release of erythropoietin, decreased oxygen demand and adequate oxygen supply to tissues reduce erythropoietin levels. The production of EPO increases with hematocrit level lower than 45% [16].

The Baltimore Longitudinal Study on Aging shows that levels of erythropoietin increase with age [18]. It is probably a compensatory mechanism resulting from tissue hypoxia [19]. On the other hand, in patients with diabetes mellitus or hypertension the rise in EPO levels associated with age was significantly reduced. Likewise, subjects with diagnosed anemia had a smaller increase in EPO levels. This indicates that anemia results from a failure of a compensatory age - related increase in erythropoietin levels [18]. Under normal conditions, hypoxemia leads to a logarithmic rise in levels of erythropoietin depending on anemia status [20]. Anemia in elderly is associated with decreased stem cell reactivity to erythropoietin [18].

Anemia of chronic diseases

It is estimated that one-third of patients over the age of 65 have a chronic disease as the cause of anemia [21]. In another one-third of patients, the reason is defined as unexplained, however, in this group, anemia may be associated not only with physiological changes in the body with age, but also with subclinical chronic inflammation [22].

We can distinguish several pathomechanisms of inflammatory anemia in the elderly, including erythropoietin (EPO) resistance of red blood cell progenitor cells, decreased EPO secretion, shortened red blood cell lifetime and functional iron deficiency [23].

During inflammation, the activation of macrophages secretes tumor necrosis factor- α (TNF- α), interleukin-1 (IL-1), γ -interferon (γ -IFN) and transforming growth factor-B (TGF-B) [24]. TNF- α is its main mediator, affecting many different cells, including inhibition of erythropoiesis [25]. IL-1 reduces the synthesis of EPO receptors on erythrocyte precursor cells. This reduces the erythrocyte precursor cells' response to erythropoietin [26]. These cytokines inhibit erythropoiesis - during which red blood cells are formed - which will result in anemia [24].

In the case of inflammation, renal EPO secretion is reduced [23]. It has been shown that exposure of the organism to IL-1, IL-6 and TNF- α inhibits the expression of EPO genes [27]. In the process of inflammation, we can also deal with oxidative stress that causes eryptosis - that is, hemolysis [23]. Oxidative stress results from an imbalance between antioxidants and reactive oxygen species. Accumulation of reactive oxygen species causes oxidative stress and red blood cells are damaged [28]. This results in the breakdown of red blood cells and thus anemia [23].

Functional iron deficiency is related to the action of hepcidin. IL-6, the synthesis of which takes place in the event of inflammation, increases the secretion of hepcidin [29]. It is a protein hormone that is produced in the liver and regulates iron levels in the blood [30]. Hepcidin blocks ferroportin, which is responsible for the transport of iron ions - from enterocytes, hepatocytes and macrophages into the plasma. The increase in hepcidin concentration reduces the concentration of iron ions in the blood [31]. The reduced iron concentration will limit the iron availability needed for erythropoiesis to occur, and eventually iron deficiency anemia will develop [32]. In people with inflammatory anemia, we are faced with a situation where, during oral supplementation with iron-containing preparations, there is no increase in its concentration in plasma, and intravenous supplementation also does not result in the expected increase in iron concentration in the blood [32].

Anemia in chronic inflammation is usually mild, but it can aggravate the course of chronic disorders [33]. This disease is a risk factor for the development of heart failure and other cardiovascular diseases, hypertension, inflammation, and cognitive disorders [22,33]. Research shows that anemia is also an independent risk factor for mortality [22].

Therefore, there is no doubt that patients hospitalized for chronic diseases with lower red cell parameters often require a longer stay in hospital compared to those with normal blood results. This is both predictive of the course of the disease and increases the cost of treatment [33]. It has been estimated that for a population of 1 million, the cost of anemia associated with the most common chronic diseases is approximately \$ 110 million [34].

Many different chronic diseases can lead to anemia in elderly. The most common cause of inflammatory anemia in people over the age of 65 is chronic kidney disease (CKD), which is discussed in detail earlier in this article [35]. Chronic bacterial and viral infections such as pneumonia, infective endocarditis, pyelonephritis, viral hepatitis and tuberculosis lead to anemia mainly by increasing hepcidin levels [36]. Interestingly as shown by the statistics of the World Health Organization (WHO), even 1/3 of the entire human population may suffer from tuberculosis. In patients with tuberculosis, it is very often associated with anemia, it occurs in 32 to 94% of hospitalized tuberculosis patients. The results of the research indicate a discrepancy depending on the population in the types of anemia associated with tuberculosis, however, patients with anemia of chronic disease can be observed much more often than those with iron deficiency anemia [37]. Inflammatory anemia associated with a chronic disease such as tuberculosis is associated with imperfect erythrocytes, shortened erythrocyte lifetime, reduced sensitivity to EPO, or decreased amount of EPO in the body [38].

Another infectious disease associated with anemia is AIDS. The number of people infected with HIV is increasing all the time in the world, and the epidemiology of infections is gradually shifting towards the elderly. The number of people infected with HIV over 50 years of age is constantly growing [39]. One study showed that anemia of varying severity in HIV patients may be as high as 71% [40]. Another study indicated that even 90% of people may have anemia before starting active antiretroviral therapy (HAART) [41]. The most common is normocytic anemia with a reduced number of reticulocytes [40]. The main causes of anemia appear to be gastrointestinal bleeding, opportunistic infections, iron deficiency, hemolysis, or vitamin B12 deficiency, but also medications [42]. In people with a decrease in hemoglobin by 1g/dl, it is recommended to implement an appropriate diet and additional and more frequent screening tests. In the case of a decrease in hemoglobin concentration by 2 g/dl, with mild and moderate

symptomatic anemia, it is suggested to start treatment with recombinant human erythropoietin. However, a decrease in hemoglobin below 8 g/dl in the case of severe symptomatic anemia may already be an indication for blood transfusion [42]. Hemoglobin concentration should be monitored regularly among people living with HIV because anemia is very common in these people and is a factor of increased mortality [43].

Anemia also accompanies malignant tumors. Anemia occurs in about 60% of cancer patients, especially in the advanced stage, and significantly worsens the prognosis [36]. In the case of neoplastic diseases, anemia is not always obvious, because it can be caused by many factors, such as drugs used in the treatment of patients, malnutrition, or various types of bleeding and inflammation [44]. One of the anemia pathomechanisms in neoplastic diseases may be the activation of T cells and macrophages. Their increased activation causes an increase in the secretion of inflammatory cytokines such as TNF- α , INF- α , and IL-1, which will result in e.g. disorders of erythropoiesis, disorders of iron metabolism, or decreased EPO secretion [24, 25, 26, 45]. It should also be remembered that anemia is caused by iron deficiency. Proper determination of the basis of anemia in people with neoplastic diseases and treatment of anemia significantly improves the patient's quality of life, improves prognosis, and reduces mortality [44].

Anemia associated with chronic inflammation also occurs in: autoimmune diseases such as rheumatoid arthritis or systemic lupus, inflammatory bowel disease, hematological neoplasms (such as Hodgkin's lymphoma and some types of non-Hodgkin's lymphoma) and is also possible in people with chronic heart failure, chronic obstructive pulmonary disease or cystic fibrosis [46]. Another causes of inflammatory anemia in the elderly are diabetes mellitus, obesity and metabolic syndrome, which may result from impaired renal function, chronic inflammation and oxidative stress, or hormonal changes [36].

However, it should be remembered that older people commonly suffer from more than one disease and the use of many medications that may lead to anemia [21,33].

Treatment of anemia of chronic diseases is primarily causal treatment aimed at reducing inflammation. Although in the elderly it is not easy due to the coexistence of many diseases, many studies have documented that such treatment gives the best results [21, 46]. Examples include patients with Castleman's disease and rheumatoid arthritis treated with immunoglobulins, giant cell arteritis after treatment with glucocorticosteroids, or treatment of tuberculosis with appropriate antibiotics. Improvement in red cell parameters was observed a few weeks after the treatment. If a specific treatment is not possible, erythropoietin derivatives can be used with iron supplementation, which is used especially in patients with CKD [46]. Both dialysis and non-dialysis patients benefit from such therapy in the form of an increase in red cell parameters, but studies on the improvement of their quality of life are not consistent. According to the latest recommendations, patients with CKD should have hemoglobin levels monitored annually and maintained above 11.0 g/dl but below 13.0 g/dl. It has been proven that maintaining the hemoglobin concentration above 13.0 g/dl did not improve the clinical condition and was even associated with more frequent hospitalization and death due to congestive heart failure and the occurrence of thromboembolism [35]. It should be remembered that erythropoietin therapy does not limit the progression of renal failure and its use is limited in cancer patients due to the possible increase in the proliferative properties of neoplastic cells

[35,46]. The elderly patients also have a worse response to erythropoietin therapy than younger patients [47].

Erythropoiesis stimulants are also registered in the European Union in patients with myelodysplasia [21,22]. As for the use of this therapy in the course of other chronic diseases, there are still insufficient data to assess the effectiveness and safety [46].

If a patient coexists with absolute iron deficiency, supplementation is necessary. The safest route is the oral route, however, due to the low bioavailability in these patients, it may be necessary to consider intravenous iron administration [36]. Another effective form of treatment is blood transfusion. The timing of such treatment in the elderly, the number of transfusions, and the target hemoglobin level must take into account the individual clinical condition of the patient [21]. It is usually indicated in patients with severe symptoms of anemia, as transfusions may be associated with complications such as acute transfusion lung injury, infections, and cardiovascular overload [22].

Thanks to the development of knowledge on the pathogenesis of inflammatory anemia, the search for new forms of therapy began. Some of them are aimed at reducing the level of hepcidin by inactivating it or inhibiting its synthesis [46]. There are also studies on the effects of antioxidant substances, fursultiamine, and hypoxia inducible factor (HIF)–prolyl hydroxylase inhibitors [21,36]. In addition, it appears that vitamin D deficiency in the elderly is associated with anemia associated with CKD and other chronic diseases. However, this dependence requires further detailed research [22].

Nutrient-deficiency anemia

The NHANES III study showed that nutrient deficiency accounts for one third of all anemia cases diagnosed in people over the age of 65. It is most often caused by iron deficiency, less often folate or vitamin B12 deficiency [48]. Nutritional deficiencies in the elderly result primarily from unfavourable socioeconomic conditions, decreased appetite, improper lifestyle, dementia, disability and lack of patient care. The risk of deficiency anemia is particularly high in the case of elderly people living in nursing homes, because meals in these institutions often do not provide sufficient amount of energy, protein and micronutrients [49,50].

Iron deficiency anemia (IDA) accounts for nearly 60% of nutrient deficiency anemia cases [48]. In the elderly, IDA may be caused by chronic blood loss, most often from the gastrointestinal tract, poor diet, reduced iron absorption, comorbidities, and also be a side effect of medications [51,52]. A diet rich in oxalates, phosphates, phytates and tea, as well as a low-protein diet reduce iron absorption from the gastrointestinal tract. IDA diagnosis in elderly patients can be problematic due to difficulties in interpreting laboratory tests. According to the latest guidelines, serum ferritin concentration <30 ng / ml indicates iron deficiency. However, this value is unreliable in the elderly, as the concentration of ferritin increases with age [49]. Furthermore, ferritin is an acute phase protein, which means that its concentration increases during infection as well as inflammation associated with chronic diseases, which is a common phenomenon in the geriatric population. IDA is usually microcytic anemia, but in the elderly it may be normocytic due to the frequent occurrence of other hematological disorders that increase the volume of blood cells [53]. In the treatment of IDA, oral iron preparations at a dose of 100-200 mg of elemental iron per day are used. However, studies with the elderly

indicate that lower doses may be equally effective, and at the same time may reduce the risk of side effects [54]. Alternatively, iron preparations can be administered parenterally, which may be particularly beneficial to elderly patients. In the elderly, oral therapy is often ineffective due to reduced iron absorption from the gastrointestinal tract and increased hepcidin levels. Moreover, iron administered intravenously in a single dose is convenient for the patient as it allows to avoid frequent visits to the hospital and daily use of the drug [53]. When diagnosing IDA in older patients, in addition to iron deficiency supplementation, it is recommended to exclude neoplastic disease, especially if treatment with iron preparations is unsuccessful.

In the case of malnutrition, hepcidin plays an important role in iron metabolism disorders. It is a hormone that inhibits the absorption of iron from the lumen of absorptive enterocytes and inhibits the release of iron from the reticuloendothelial system. Hepcidin binds to ferroportin (Fpn), a transmembrane protein receptor, resulting in inhibition of iron release from cells such as absorptive enterocytes, hepatocytes and macrophages. In people with protein-energy deficiencies, an increase in serum pro-inflammatory cytokines, including interleukin 6, may be observed. IL-6 induces hepcidin expression and thus lowers serum iron concentration and limits its use in the process of erythropoiesis, contributing to the development of IDA [55]. Moreover, a high - fat diet can also increase hepcidin levels, which means that anemia caused by nutritional deficiencies can occur in people with reduced body weight as well as in obese patients [49].

The median incidence of vitamin B12 deficiency anemia is approximately 70-80 years [56]. The main cause of vitamin B12 deficiency in elderly patients is food cobalamin malabsorption (FCM), less frequently Addison-Biermer disease or insufficient amount of vitamin B12 in food. FCM is caused primarily by type B atrophic gastritis, the incidence of which is increasing in older patients. Atrophic gastritis leads to achlorhydria, which impairs the release of vitamin B12 from protein complexes, and also promotes bacterial proliferation in the intestine by limiting the availability of vitamin B12. Insufficient supply of cobalamin in the diet may be caused by meat restriction or low socioeconomic status. A consequence of vitamin B12 deficiency is hyperhomocysteinemia, which increases the risk of dementia, depression, osteoporosis, thrombosis, dose atherosclerosis, ischemic heart disease, and strokes, which is very significant in the geriatric population [57]. Vitamin B12 deficiency can be difficult to diagnose in the elderly because neurological symptoms may develop before hemoglobin levels drop below normal. Furthermore, anemia caused by vitamin B12 deficiency is usually macrocytic, but in older patients, in the case of iron deficiency anemia or anemia of chronic diseases, blood cells may be microcytic or normocytic [58]. Vitamin B12 is most often administered intramuscularly at a dose of 1000 µg once a day for a week, and then once a week until the anemia resolves. For maintenance treatment, 1000 µg of vitamin B12 is administered once a month [57]. An alternative is the oral administration of high doses of vitamin B12 (1000-2000 µg/d), which may be equally effective, also in the elderly [51].

The incidence of folate deficiency anemia also increases with age. It is estimated that it occurs in about 5% of people aged 65 to 75 years and in 10% of people over 75 years of age [56]. Unlike vitamin B12 deficiency, folate deficiency is most often caused by a poor diet lacking in fresh, green vegetables. In addition, total parenteral nutrition without folate supplementation also increases the risk of anemia. The body's reserves of folate last for about 4 months, therefore the symptoms of anemia appear faster than in the case of vitamin B12 deficiency [56, 58]. The most serious health effects in the case of the elderly are caused by high levels of homocysteine,

which increases the risk of cognitive impairment, cancer and cardiovascular diseases [59]. Treatment of deficiency consists in oral folate supplementation at a dose of 1 mg/d [49]. In elderly patients, chronic folate supplementation is recommended due to the frequent malabsorption and the coexistence of inflammatory and neoplastic diseases that increase the need for folate [60].

Anemia in the elderly may also result from deficiency of other vitamins or elements. However, this occurs much less often than anemia caused by deficiency of iron, vitamin B12 or folate. Vitamin E is an antioxidant that reduces the concentration of free radicals in the serum. The deficiency of this vitamin may cause haemolytic anemia as a result of oxidative damage to erythrocytes [61]. Vitamin C increases the absorption of iron from the gastrointestinal tract, therefore its supplementation is important in the treatment of IDA. Moreover, vitamin C directly inhibits the expression of hepcidin [49]. A study by Sim et al. showed a relationship between vitamin D deficiency and an increased risk of anemia. It was found that vitamin D can decrease the production of cytokines, and thus reduce inflammation and prevent anemia of chronic diseases [62]. Copper is an element that takes part in the process of transporting and absorbing iron from the gastrointestinal tract, therefore its deficiency may cause IDA.

A common phenomenon in elderly patients is polypharmacy, i.e. the use of several drugs at the same time, which in turn increases the risk of anemia. Proton pump inhibitors and H₂-receptor antagonists inhibit the secretion of gastric acid, and thus reduce iron absorption, which leads to the development of IDA. Iron deficiency can also be caused by taking non-steroidal anti-inflammatory drugs and anticoagulants, which can cause bleeding, especially from the gastrointestinal tract. Long-term use of proton pump inhibitors, H₂-receptor antagonists, and biguanides (metformin) increases the risk of atrophic gastritis and thereby may lead to vitamin B12 deficiency anemia. When using antiepileptic drugs, co-trimoxazole, sulfasalazine, and folate antagonists (methotrexate, trimethoprim), the risk of folic acid deficiency anemia increases [51].

Summary

The aim of our article is to present the clinical problem of anemia in relation to the population of geriatric patients. The importance of this issue seems to be more and more important in the face of the aging of the population and the increase in the percentage of elderly patients.

It is worth paying attention to the economic aspect, because the coexistence of chronic diseases with a reduced number of red blood cells extends the hospitalization time, which leads to an increase in treatment costs. Moreover, the presence of anemia may aggravate the course of chronic diseases and increase mortality. An accurate diagnosis is difficult due to the fact that the clinical manifestation of anemia may resemble symptoms associated with the physiological aging process of the organism. In addition, it is precisely the changes that occur with age - such as the gradual deterioration of kidney function or the decrease in testosterone levels in men - that can lead to disorders in the red blood cell system. Another factor that hinders the diagnosis of anemia is multi-morbidity, common among geriatric patients, which may result in taking large amounts of drugs with various mechanisms of action and side effects.

Currently, scientific activity is focused on studying the so far unproven correlations and searching for new methods of anemia therapy. Due to a better understanding of the mechanisms that play an important role in the pathogenesis of inflammation - induced anemia, research is underway on drugs that inhibit the synthesis or inactivate hepcidin.

Summarizing our article, the problem of anemia among geriatric patients is a challenge for medical staff and requires a holistic approach and taking into account common phenomena occurring in this age group, i.e. multiple diseases and polypharmacy.

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