УДК 616.379-008.64:577.169.

Abduvakhopova Nozimakhon Rahmon kizi
Department of Hospital Therapy and Endocrinology
Andijan State Medical Institute

THE FREQUENCY OF ANEMIA IN PATIENTS WITH DIABETES MELLITUS

Resume: According to WHO recommendations, the criterion for the diagnosis of anemia is a decrease in hemoglobin levels < 120 g/l in women and < 130 g/l in men. Similar criteria are used in the European Recommendations for the treatment of anemia in patients with CKD (hemoglobin < 115 g/l in women and < 135 g/l in men aged less than 70 years and < 120 g/l in men over 70 years). If we use these criteria, then about one in four patients with type 1 or type 2 diabetes suffers from anemia (about 23%) [9-11]. A more pronounced decrease in hemoglobin levels (< 110 g/l) is observed in approximately 7-8% of patients.

Key words: anemia, diabetes mellitus, endocrine pathology.

Абдувахопова Нозимахон Рахмон қизи
Кафедра госпитальной терапии и эндокринологии
Андижанский государственный медицинский институт

ЧАСТОТА АНЕМИИ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ

Резюме: В соответствии с рекомендациями ВОЗ, критерием диагноза анемии является снижение уровня гемоглобина < 120 г/л у женщин и < 130 г/л у мужчин. Сходные критерии использованы в Европейских рекомендациях по лечению анемии у больных ХБП (гемоглобин < 115 г/л у женщин и < 135 г/л у мужчин в возрасте менее 70 лет и < 120 г/л у мужчин в возрасте старше 70 лет). Если использовать эти критерии, то анемией страдает примерно каждый четвертый больной СД 1 или 2 типа (около 23%) [9–11]. Более выраженное снижение уровня гемоглобина (< 110 г/л) наблюдается примерно у 7–8% пациентов.

Ключевые слова: анемия, сахарный диабет, эндокринная патология.

Relevance. As a result of studying the mechanisms of the development of anemic syndrome in diabetes mellitus, an idea of the multifactorial nature of this process was formed. Endogenous EPO deficiency, inefficiency and its effects, iron deficiency, vitamin B12 and folic acid, inflammatory processes, autoimmune disorders, side effects of certain medications used in the treatment of diabetes mellitus contribute to this process [3,5]. In the event of chronic renal failure, along with a progressive increase in EPO deficiency, such factors as uremic intoxication, hemolysis, bleeding as a result of hemostasis disorders, systematic blood loss during hemodialysis sessions, parathyroid gland dysfunction and aluminum intoxication may play a significant role [4].

EPO, a glycoprotein hormone with a molecular weight of about 34 kDa, is one of the key regulators of erythropoiesis in humans. The main source of EPO is considered to be peritubular kidney cells, which produce it in response to hypoxia and vasoconstriction. With the development of hypoxia, cells of various tissues produce a universal transcription factor of genes expressed in conditions of oxygen deficiency - HIF (hypoxia-induced factor) [2,5]. As a result of the action of FOMS in the human body, the concentration of both EPO and other biologically active substances increases, in particular vascular endothelial growth factor (Vref) and non-synthase (nos). HIF is a heterodimer consisting of subunits a (HIF-1a) and p (HIF-1p). The destruction of the HIF-1a subunit in the absence of a hypoxic stimulus and under the influence of certain substances is the most sensitive and subtle mechanism for regulating these processes [3].

In patients with diabetes mellitus, under the influence of hyperglycemia, increased capillary pressure and proinflammatory cytokines, cells of both glomeruli and renal tubules are damaged. Destruction of tubules, the formation of interstitial fibrosis, a decrease in the number of peritubular capillaries, an increase in the number of extracellular matrix lead to disruption of EPO

production by peritubular cells [4]. At the initial stages of the development of diabetic nephropathy, the absolute level of EPO is comparable to that of healthy people without anemia (10-30 mMU/ml, which corresponds to 1-7 pmol/L), however, there is a violation of the negative correlation observed in the norm between the concentrations of hemoglobin and EPO in the blood [1]. Thus, the development of anemia in patients with diabetes mellitus does not lead to a significant increase in the level of EPO in the blood, as is observed in iron deficiency anemia, aplastic anemia and other hematological diseases. This phenomenon is called functional (relative) EPO deficiency. As diabetic nephropathy progresses, absolute EPO deficiency may also occur, which is usually associated with the development of severe anemia [3].

By some authors, the relative and absolute deficiency of EPO is considered as a result of a violation of the "sensory" and later "secretory" mechanisms of EPO production [2,4]. The loss of the "sensory" component may be associated with autonomic neuropathy. This is consistent with the descriptions of cases of normochromic anemia associated with severe diabetic neuropathy, in the absence of significant violations of renal filtration function and manifestations of macroangiopathy [1]. The main methods of quantitative assessment of autonomic neuropathy in clinical practice are the determination of heart rate variability and the conduct of vegetative tests. According to Saito T. et al., patients with type 1 diabetes mellitus with a serum creatinine level of less than 120 mmol/l have a pronounced correlation of the hemoglobin index and the coefficient of variation of the electrocardiographic interval R-R [6]. According to the results of another study, it was found that in patients with type 2 diabetes mellitus and GFR of more than 40 ml/min, the presence of signs of autonomic neuropathy (a decrease in heart rate variability during a deep breathing test, Valsalva test, or-tostatic test) is associated not only with the development of anemia, but also with EPO deficiency [3]. Regarding the mechanisms that cause the interaction of anemia and autonomic neuropathy, there are two almost

opposite hypotheses. On the one hand, the loss of vasomotor control as a result of damage to the nervous system can disrupt the process of vasoconstriction, which is one of the stimuli for the production of EPO. However, contrary to this hypothesis, after kidney transplantation, the donor organ continues to secrete EPO in physiological quantities, despite complete denervation [1,4]. On the other hand, the course of autonomic neuropathy may worsen in the event of a deficiency of EPO, which has proven neuroprotective properties, and this concept is consistent with data on a decrease in manifestations of autonomic neuropathy (in particular, orthostatic hypotension) under the influence of therapy with recombinant human erythropoietin (rfEPO) [5].

There were other hypotheses explaining the development of EPO deficiency in diabetic nephropathy. There have been suggestions about the loss of EPO in the urine and a violation of its biological activity due to the possible glycosylation of the EPO molecule in hyperglycemia. However, at present, these ideas are recognized by most researchers as untenable.

And yet, the absence of an absolute deficiency of EPO in the early stages of diabetic nephropathy does not allow us to consider the question of the causes of the primary decrease in hemoglobin completely resolved. Therefore, other possible mechanisms of anemia in type 1 and type 2 diabetes mellitus are also of great interest.

In patients with type 1 diabetes mellitus, autoimmune processes can make a significant contribution to the development of anemia. So, 15-20% of them are diagnosed with the presence of antibodies to the parietal cells of the stomach, 10% - antibodies to transglutaminase, which can lead to atrophic gastritis, celiac disease and, as a consequence, to impaired absorption of iron, folic acid and vitamin B12. In some cases, small absorption is also facilitated by external secretory insufficiency of the pancreas, which may accompany a violation of the intracretory function (however, to a greater extent this complicates the absorption of fat-soluble vitamins A, D, E and K, which do not play a significant

role in the processes of hematopoiesis). In addition, some patients with type 1 diabetes mellitus suffer from autoimmune thyroiditis with the development of hypothyroidism, which is also often associated with anemia.

The purpose of the study. To study the features of anemic syndrome in patients with type 1 diabetes mellitus to optimize treatment.

Material and methods of research. Screening for the presence of a reduced hemoglobin level was carried out in 567 patients with type 1 diabetes in the clinic of AGMI in Andijan. In Andijan, a single-stage hemoglobin study of a sample of patients with type 1 diabetes who came to an outpatient appointment and were sent to the laboratory for blood sugar testing was conducted. For 1 month, 252 patients with type 1 diabetes were examined.

Results of the study Out of 252 patients with type 1 diabetes in Kazan who applied for outpatient care in a month, a reduced hemoglobin level was detected in 69 patients, i.e. in 27% of the examined, which exceeds the average frequency among patients with diabetes in the Andijan region obtained in another study - 20% Os2 = 9.0; p =0.003). Anemia was statistically significantly more common among women in our study sample than among men: in women, the hemoglobin level is reduced in 35% of cases, in men - in 14% (x2 = 12.8; p = 0.0003).

Thus, a total of 567 patients with type 1 diabetes were examined in RT by continuous screening, and 19% (109/567) of them showed a reduced hemoglobin level, which does not differ from the expected frequency among patients with diabetes - 20% (x2 = 0.39; p>0.05). However, comparing with the frequency of anemia in the general population of the same age category according to various studies from 5% to 10%, a statistically significant difference was obtained (x2 = 52.74; p <0.0001).

When studying the nature of anemia, it turned out that anemia in patients with type 1 diabetes was mild in 86% (p<0.0001), moderate in 11%, severe in 3%. In 63% anemia was normochromic (p<0.0001), in 33% hypochromic, in 1%

hyperchromic. Anemia is normocytic in 56% (p<0.001), microcytic in 13%, macrocytic in 2%. 86% have normoregenerative character (p<0.001), 35% have hyporegenerative character, 1% have hyperregenerative character.

The structure of the anemia syndrome in type 1 diabetes according to the results of our study is presented in Table 2. 36.6% of patients had a combination of causes of the anemia syndrome. IDA is most common in patients with type 1 diabetes: 54.8% (51/93) of the examined patients, which is slightly less than the frequency of IDA among other types of anemia in the general population (70 - 80%) (^2=0,71; p=0.39). Comparing with the frequency of IDA in the population of patients with rheumatoid arthritis (35%), in patients with type 1 diabetes, the frequency of IDA is slightly higher (%2=8.7; p=0.003). It should be noted that 12% (6/51) of IDA patients had no decrease in serum iron levels, but at the same time its amount was reduced in the depot.

The second most common in the general adult population is AHZ. According to our study, AHZ occurs in 23.6% (22/93) of cases. This frequency does not differ from the frequency of anemia in elderly patients (30%) (x = 1.84; p= 0.17). However, when compared with the population of patients with various chronic diseases, for example rheumatoid arthritis, the frequency of AHZ is 47% (/2=20.8; p<0.0001), and oncological diseases reaches 90%, the frequency of AHZ in patients with type 1 diabetes is slightly lower (x2=20.7; p<0.0001). 4.3% (4/93) of patients had a combination of IDA and AHZ. In total, according to the results of our study, AHZ and IDA account for 81.6% of all cases of anemia.

When further studying the structure of the anemia syndrome in patients with type 1 diabetes, it can be noted that 37.7% (35/93) had folic acid deficiency: in one third (11/35) of patients, folic acid deficiency was the only cause of the anemia syndrome, and in the rest (24/35) folic acid deficiency was combined with AHZ or with IDA. The frequency of DFC in patients with type 1 diabetes is higher than the frequency of DFC in the general population

(according to various authors from 1% to 25%) (x2=8.31; p=0.004). 4.3% (4/93) were found to have vitamin Vp deficiency (DVitV12), in one case combined with AHZ and in one with IDA.

When analyzing the causes of anemic syndrome in groups differing in the degree of kidney damage, it turned out that IDA prevailed in the group of patients with DM without clinical manifestations of DN: IDA was found in 62% of cases, and AHZ in 21% (p=0.01). In the group of patients with CKD of 1.2 art., IDA also prevails in 53% of patients, AHZ - in 21% (p<0.001). In the group with CKD 3.4 art. AHZ was the cause of decreased hemoglobin in 30%, IDA - in 50%, but this difference is not statistically significant (p>0.05). The frequency of folic acid and vitamin B12 deficiency in groups with different stages of CKD is the same in all fgroups (p>0.05).

In the group of DM patients with anemia, a statistically significant decrease in GFR can be noted with an increase in the duration of DM (p=0.005) and a statistically significantly low level of GFR compared to the control group for any duration of DM (control 121 [102.0; 149.0]; duration of DM less than 5 years 88.0[81.0; 101.0] p=0.002; from 5 to 15 years 82.0[60.0;95.0] p<0.0001; more than 15 years 66.0[44.5;81.8] p<0.0001) . Also, it can be noted that with a duration of DM from 5 to 15 years, the GFR level in patients with DM with anemia is lower than in patients without anemia (p=0.04). Thus, it can be noted that in patients with type 1 diabetes with anemia, as the hemoglobin level decreases, a more significant and rapid decrease in GFR occurs compared to patients with diabetes without anemia with an increase in the duration of diabetes.

Analysis of the level of daily excretion of amine nitrogen in urine, reflecting the reabsorption function of the proximal tubular apparatus of the kidney, showed that patients with DM without anemic syndrome have an increase in the level of daily excretion of amine nitrogen in urine compared with the control group for any duration of DM (up to 5 years 627.9 [419.3; 1082.2]

p=0.02; from 5 to 15 years 1406.9[1217.5;2250.6] p=0.0006; more than 15 years 336.4 [178.3;575.7] p=0.03). At the same time, they have a direct moderate correlation between the level of daily excretion of amine nitrogen and GFR (g=0.71; p=0.004), i.e. an increased level of excretion of amine nitrogen in the urine showing an increase in the rate of reabsorption is probably associated with an increase in the filtration rate in these patients.

Conclusion. The necessity of differential diagnosis of anemic syndrome in patients with type 1 diabetes is shown. Prerequisites have been found for the use of the detected anemia of chronic diseases in patients with type 1 diabetes mellitus without clinical signs of diabetic nephropathy, as a sign of the patient's belonging to the risk group for the early development and progression of diabetic nephropathy.

A frequent combination of the causes of anemic syndrome, independent of the duration of DM and kidney function, has been demonstrated.

REFERENCES:

1.Shestakova M. V., Dedov I. I. Diabetes mellitus and chronic kidney disease. Moscow: LLC "Medical Information Agency", 2009.

2.Zoppini G., Targer G., Chonchol M. et al. Anemia, independent of chronic kidney disease, predicts mortality from all causes and cardiovascular diseases in patients with type 2 diabetes mellitus // Atherosclerosis. In the Press. 2009.

3. Joss N., Patel R., Paterson K. et al. Anemia is a common phenomenon and predicts mortality in diabetic nephropathy // QJM. 2007. Vol.100. pp. 641-647.

4. Bosman D. R., Winkler A. S., Marsden J. T. et al. Anemia associated with erythropoietin deficiency occurs in the early stages of diabetic nephropathy. Wedge. Practicality. 2000. Volume 50. Addition. 1. p. 265.

5. Magri K. J., Fava S. The role of damage to the tubules in diabetic nephropathy // European Journal of Internal Medicine. 2009. Volume 20. pp. 551-555.

6. Najafyan B., Mauer M. Progression of diabetic nephropathy in patients with type 1 diabetes mellitus. Wedge. Practicality. 2009. Volume 83. pp. 1-8.