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## **THE SPECIFICITY OF THE MECHANISMS OF ANEMIA DEVELOPMENT IN PATIENTS WITH DIABETES MELLITUS**

**Summary.** Anemia has an undesirable effect on the quality of life of patients, causes a decrease in working capacity and exercise tolerance, deterioration in sexual and cognitive functions and is accompanied by various symptoms (shortness of breath, dizziness, poor appetite, etc.). Moreover, anemia in diabetic patients predicts an increased risk of adverse outcomes (regardless of the severity of nephropathy) and, apparently, in itself contributes to the progression of micro- and macroangiopathy. However, physicians usually do not attach much importance to anemia in such patients.

**Key words:** Diabetes mellitus, anemia, physical activity, nephropathy, chronic kidney disease.

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## **СПЕЦИФИКА МЕХАНИЗМОВ РАЗВИТИЯ АНЕМИИ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ**

**Резюме.** Анемия оказывает нежелательное влияние на качество жизни больных, вызывает снижение работоспособности и толерантности к физической нагрузке, ухудшение сексуальной и когнитивной функций и сопровождается различными симптомами (одышка, головокружение, плохой аппетит и т. д.). Более того, анемия у больных СД позволяет предсказать повышенный риск неблагоприятных исходов (независимо от тяжести нефропатии) и, по-видимому, сама по себе способствует прогрессированию микро- и макроангиопатии. Тем не менее, врачи обычно не придают особого значения анемии у таких пациентов.

**Ключевые слова:** Сахарный диабет, анемия, физической нагрузке, нефропатия, хронической болезни почек.

**Relevance.** Approximately half of patients with CKD are anemic. Accordingly, DM is one of the main causes of renal anemia. In diabetic nephropathy, anemia develops earlier and more often and is more severe than in patients with kidney diseases of a different nature. For example, according to the NHANES III epidemiological study (National Health and Nutrition Examination Survey), conducted in the United States, the incidence of anemia in patients with stage III-IV CKD and DM was 2 times higher than in patients with comparable renal dysfunction who did not suffer from DM.

Diabetes mellitus (DM) is a common disease affecting about 5% of the European population. The prevalence of this disease is increasing every year. It is expected that in the next few years the number of such patients in Europe will exceed 32 million people. A characteristic complication of both type 1 and type 2 diabetes is nephropathy. In industrialized countries, diabetic nephropathy has now become the leading cause of end-stage chronic kidney disease (CKD). As the number of diabetic patients grows, we can expect a proportional increase in the role of diabetic nephropathy in the structure of patients with terminal renal failure.

The leading role in the pathogenesis of renal anemia is played by a deficiency of erythropoietin produced by the kidneys. In this regard, it has been suggested that

its earlier use in patients with diabetic nephropathy may lead to an improvement in the prognosis in this condition.

**Purpose of the study.** To determine the prevalence of anemia in people with type 2 diabetes.

**Materials and research methods.** 80 patients with type 2 diabetes aged over 40 were included. Among the examined were 43 men, 37 women. The mean age of women and men was  $58 \pm 14$  and  $62 \pm 12$  years, respectively. The average duration of diabetes was  $11.42 \pm 2.2$  years. The control group consisted of 38 patients (mean age  $58.6 \pm 2.3$  years) without a history of DM.

**Research results.** The albumin/creatinine ratio in urine in men was 9.0 (0.8–>1000) mg/g and in women it was 9.9 (1.0–>1000) mg/g, in the general group it was 9.6 (0.8–>1000) mg/g. Creatinine clearance in men -  $112 \pm 42$  ml/min and in women -  $86 \pm 33$  ml/min, in the general group -  $103 \pm 41$  ml/min. Normal serum creatinine ( $<110 \mu\text{mol/l}$ ) was present in 87% of patients (86% men and 84% women). A normal albumin/creatinine ratio ( $<24$  mg/g) was found in 75% of patients (74% of men and 77% of women). The mean Hb level was  $14.2 \pm 1.3$  g/dl in men and  $13.6 \pm 1.5$  g/dl in women. 19 (23.7%) patients were diagnosed with anemia according to WHO criteria, including 11 men and 8 women with a mean Hb level of 12.3 g/dL (from 10.9 to 12.9) and 11.5 g/dL (from 9.2 to 11.9) in men and women, respectively. Mean red blood cell volume (MCV) for 10 anemic men was  $90.1 \pm 5.4$ , with only one patient with  $\text{MCV} < 78$ . The mean MCV for 5 anemic women was  $84.5 \pm 7.8$ , with 3 of 8 patients having an  $\text{MCV} < 78$ . Therefore, the majority (85%) of patients had normocytic anemia. Using the WHO criteria for defining anemia, 74% of anemic patients had serum creatinine  $<110 \mu\text{mol/l}$  and 72% of anemic patients had an estimated creatinine clearance  $>60$  ml/min. Of those with normal serum creatinine ( $<110 \mu\text{mol/L}$ ), 7% of men and 14% of women were anemic, compared with 24% of men and 38% of women with elevated creatinine ( $>110 \mu\text{mol/L}$ ).

During the study, 80 patients with type 2 diabetes were examined, the duration of the disease was more than 5 years, of which 26 (56.5%) were men and

20 (43.5%) were women. Among patients whose disease duration is less than 5 years, 15 (44.1%) men and 19 (55.8%) women. HbA1C in men was 7.1% (4.8–15.0), in women it was 6.6% (4.9–11.1), in the general group its value was 6.9% (4.8–15.0). In 36 (28.8%) patients, DM was combined with anemia. Hb, HbA1C levels and urinary albumin excretion, as well as measurement of the urinary albumin/creatinine ratio, were considered individually for each sex.

The results of this study coincide with the conclusions of foreign authors. However, in this study, associations with age, serum creatinine, and estimated creatinine clearance were stronger in men. The lack of further associations may be due to the relatively small sample size. Another important finding was the association between the duration of diabetes and the prevalence of anemia. Persons with a duration of diabetes of more than 5 years had a 1.7 times higher risk of developing anemia than those with a duration of diabetes of less than 5 years. These observations suggest that detection of anemia should occur during the routine examination of individuals with DM and facilitate timely treatment to minimize the risk of microvascular complications such as nephropathy and retinopathy.

According to the results of this epidemiological study, the prevalence of anemia among people with type 2 diabetes is 23.7%. Although creatinine clearance had the highest correlation in the presence of anemia, approximately 75% of anemic patients had normal serum creatinine ( $<110 \mu\text{mol/l}$ ) and creatinine clearance ( $>60 \text{ ml/min}$ ). Measurements of the prevalence of anemia in the publications of foreign authors vary depending on the studied population and the diagnostic methods used [15]. This study shows that in the age group of about 60 years with preserved kidney function (glomerular filtration rate -  $60 \text{ ml / min per } 1.73 \text{ m}^2$ ), the prevalence of anemia is 23.7%, which coincides with the data of studies by foreign authors [15]. The severity of anemia in individuals with DM has been associated with a number of factors, including glomerular filtration rate, urinary albumin excretion, and HbA1C levels [4]. In addition, the prevalence of

anemia in patients with DM is 2–3 times higher than in patients with comparable renal impairment in the general population [4, 15].

**Conclusion:** Currently, information is accumulating about slowing down the progression of chronic complications of diabetes mellitus (nephropathy, neuropathy, retinopathy) and cardiovascular pathology under the influence of antianemic therapy using rhEPO preparations. At the same time, the question of the relationship between the effects of normalizing the hemoglobin level and the direct cardio-, nephro-, and neuroprotective effects of EPO remains unclear. On the basis of further study of the mechanisms of development of anemia in patients with diabetes mellitus and the pathogenetic role of EPO in these processes, clear indications for the start of therapy with rhEPO drugs, optimal treatment regimens, and target hemoglobin levels for various groups of patients should be determined.

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