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CHRONIC DISEASE ANEMIA IN DIABETES

Abstract: A total of 135 patients were examined: 51 people with type 1 diabetes and 84 with type 2 diabetes. After establishing the type of anemia, the patients were stratified into groups: 1) patients with ACD; 2) patients with IDA; 3) patients with latent iron deficiency; 4) patients without ferrokinetic disorders. As a result of ROC analysis in the general sample of patients with diabetes mellitus, the following parameters showed high information content in the diagnosis of ACD: ESR — sensitivity 92%, specificity 85% with a diagnostic threshold of 26.5 mm/h (area under the curve 0.943; p<0.0001), leukocyte count — sensitivity 69%, specificity 64% with a diagnostic threshold of 7.50×109/l (area under the curve 0.727; p=0.007), MAU — sensitivity 71%, specificity 72% with a diagnostic threshold of 29.5 mg/l (area under the curve 0.744; p=0.003).

Keywords: diabetes mellitus, iron deficiency anemia, anemia of chronic disease, soluble transferrin receptor.

INTRODUCTION

Among the potential mechanisms for the development of anemia in patients with diabetes mellitus, one can single out impaired iron absorption due to autoimmune processes. It has been shown that in 15–20% of cases of type 1 diabetes, the presence of antibodies to gastric parietal cells is detected, and in 10%, antibodies to transglutaminase, which can lead to the development of atrophic gastritis and, accordingly, impaired iron absorption [1]. The destruction of erythrocytes in the microcirculation is considered as a factor in the formation of anemia in individuals with diabetes mellitus: chronic hyperglycemia increases the concentration of sorbitol and reduces the activity of Na+/K+-ATPase in erythrocytes, thereby changing the properties of their membrane and disrupting osmotic resistance [2]. Diabetes mellitus is one of the pathological conditions in which an increase in eryptosis is observed - programmed death of erythrocytes before the onset of their physiological aging [3]. The mechanisms that trigger eryptosis under conditions of chronic hyperglycemia are well studied. These include oxidative stress and energy depletion of cells. The eryptotic phenotype in type 2 diabetes is caused, among other things, by increased activity of peroxide dismutase and the formation of reactive oxygen species, factors that promote the transformation of the phospholipid of the erythrocyte cell membrane.

MATERIALS AND METHODS

Chronic kidney disease (CKD) occupies a special place among the etiological causes of anemia in diabetes mellitus. The mechanism of development of nephrogenic anemia is traditionally associated with a violation of the endogenous production of the main erythropoiesis-stimulating hormone erythropoietin (EPO) [4] - due to hyperglycemia-induced synthesis of fibrogenic growth factors: tumor necrosis factor α (TNF-α), vascular endothelial growth factor and transforming growth factor-β (TGF-β), as well as due to the suppression of antifibrogenic growth factors, such as hepatocyte growth factor [1]. Dysregulation of the synthesis of fibrogenic and antifibrogenic growth factors under conditions of prolonged hyperglycemia

leads to the formation of nephrosclerosis. In addition, a direct inhibitory effect of proinflammatory cytokines, TNF-α and interleukin-1 (IL-1), on EPO synthesis has been proven [2] and the role of these cytokines in upregulating HAMP gene expression via the SMAD/STAT3 signaling pathway with increased secretion of hepcidin (a negative regulator of iron metabolism) [3]. There is evidence of downregulation of EPO in relation to hepcidin production by hepatocytes. A decrease in EPO production in the context of progressive nephropathy indirectly leads to an increase in hepcidin levels and, accordingly, to impaired iron mobilization from cells [3]. As CKD develops and worsens in patients with diabetes, the clearance of hepcidin itself may also be impaired, resulting in an increase in its level in the blood plasma. The developing hyperhepsidinemia limits the bioavailability of iron and aggravates the course of ACD [4].

RESULTS AND DISCUSSION

A total of 135 patients with diabetes were examined and divided into groups: 51 people (37.8%) with type 1 diabetes and 84 people (62.2%) with type 2 diabetes. All patients included in the study signed voluntary informed consent.

Inclusion criteria. Established diagnosis of type 1 diabetes or type 2 diabetes, age from 18 to 70 years, disease duration from 1 year to 30 years, glycated hemoglobin level from 6.5 to 10.0% and CKD stage C1–C4 (estimated glomerular filtration rate (eGFR) according to the CKD-EPI formula more than 15 ml/min).

Exclusion criteria: acute infectious diseases, specific infectious diseases (HIV/AIDS, viral hepatitis, liver cirrhosis, tuberculosis), cancer, chronic obstructive pulmonary disease, bronchial asthma, blood transfusions at the time of inclusion and in the period of 1 month before inclusion in the study, treatment with oral and parenteral iron preparations, preoperative and postoperative period, acute renal, hepatic and heart failure, CKD stage C5, nephropathy stage proteinuria, decompensation of diabetes (ketoacidosis and/or osmotic dehydration), patient refusal to participate in the study.

Among the 135 patients included in the study, 51 people (37.8%) suffered from type 1 diabetes (group 1), 84 people (62.2%) — from type 2 diabetes (group 2). Among the patients with diabetes, there were 45 (33.3%) men and 90 (66.7%) women. Patients in group 2 were significantly older than patients in group 1 ($p < 0.0001$): the median ages were 60.00 [56.0; 65.0] and 34.00 [26.0; 52.0] years, respectively. The groups of patients with type 1 and type 2 diabetes were comparable in terms of disease duration ($p = 0.430$). Table 1 presents the clinical characteristics of the study patients [4]. Patients with type 2 diabetes had a significantly higher BMI than patients with type 1 diabetes ($p < 0.0001$). Groups 1 and 2 were comparable in terms of glycated hemoglobin levels ($p=0.231$). These groups of patients were also comparable in terms of MAU levels ($p=0.112$), but eGFR in the group of people with type 2 diabetes was lower than in patients with type 1 diabetes ($p=0.006$). Patients with type 1 and type 2 diabetes were comparable in terms of aspartate aminotransferase levels, while alanine aminotransferase concentration was significantly higher in type 2 diabetes ($p=0.011$).

CONCLUSION

Thus, in the differential diagnosis of IDA and ACD in diabetes mellitus, ESR, leukocyte count, MAU level, as well as sTGF and sTGF/logFerritin index are highly informative. This fact allows using these markers as additional ones for the differential diagnosis of anemia in patients with carbohydrate metabolism pathology.

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