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HYPOXIA-INDUCIBLE FACTOR-A AS A MARKER IN THE PROGRESSION OF DIABETIC RETINOPATHY IN TYPE 2 DIABETES

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Introduction. Diabetes mellitus (DM) and its numerous complications constitute a serious global health problem associated with a deterioration in the quality of life and premature mortality [1, p. 1331]. Diabetic retinopathy (DR) is one of the most serious complications of DM, the main cause of disabling visual impairment in both working-age adults and patients aged 50 years and older [2, p. 1077669]. Numerous data indicate that hypoxia plays an important role in the development and progression of DR [3, p. 1933]. Retinal hypoxia can occur long before the development of clinically apparent microvascular damage. In the absence of adequate therapy, significantly lower values of superficial and deep perfusion were found in the eyes of diabetic patients with moderate or severe NPDR compared to healthy eyes. The role of hypoxia-inducible factor-α (HIF-1α) in pathological angiogenesis and retinal neurodegeneration in DR has been proven [4, p. 2574; 5, p. 183].

The **aim** of the study was to determine the content of the hypoxia marker – hypoxia-inducible factor-α in the intraocular fluid and the relationship with the progression of diabetic retinopathy.

Materials and methods. 110 patients with type 2 diabetes mellitus were examined, who were divided into groups according to the stage of DR according to the International Classification (2003): 1st – without retinopathy (DR0; 15 eyes), 2nd – with initial non-proliferative DR (NPDR; 40 eyes), 3rd – with moderate NPDR (25 eyes), 4th – with severe NPDR (12 eyes) and 5th –

with proliferative DR (PDR; 18 eyes). The control group included 25 people of the appropriate age and sex who did not have diabetes and DR. The content of HIF-1α (pg/ml) was determined in the in the intraocular fluid (IOF) obtained during cataract phacoemulsification surgery by enzyme-linked immunosorbent assay. For statistical analysis of the results, the EZR v.1.54 package (Austria) was used.

Results. Analysis of the obtained data showed that the studied cohort of patients did not differ significantly when divided into groups by age ($p=0.108$), blood glucose content ($p=0.176$) and glycated hemoglobin ($p=0.101$). The duration of diabetes was associated with the severity of DR – it increased from 5 years in DR0 to 15.5 years in PD ($p<0.001$). The content of HIF-1α in the IOF also progressively increased according to the stages of DR – from 65.3 pg/ml in DR0 to 461.2 pg/ml in PD ($p<0.001$). At the same time, for the duration of diabetes, the threshold for any DR versus DR0 was greater than 11.5 years (OR=11.7; $p<0.001$), for HIF-1α – greater than 118 pg/ml (OR=45.0; $p<0.001$); AUC=1.0 for both cases. It was also possible to predict PD when compared with any NPDR: the thresholds were greater than 14.0 years for the duration of diabetes (OR=5.0; $p<0.001$) and greater than 460.0 pg/ml for HIF-1α (OR=21.0; $p<0.001$); AUC=1.0 for both cases. Thus, the occurrence of DR can be considered highly probable with a diabetes history of more than 11.5 years, and PD with a history of more than 14 years. The corresponding thresholds for the content of HIF-1α in the IOF were 118 pg/ml and 460 pg/ml.

To analyze the level of HIF-1α in the IOF at different stages of DR and to assess the further relationship with the progression of DR by stages, the optimal thresholds were selected using the One-vs-All classification method. The predictive thresholds for the content of HIF-1α in the IOF by stages of DR were calculated: less than 113.8 pg/ml in diabetes without DR, 113.8-247.8 pg/ml in mild NPDR, 247.9-408.4 pg/ml in moderate NPDR, 408.5-509.3 in severe NPDR and more than 509.3 pg/ml in PDR.

Thus, our study showed a direct relationship between the increase in HIF-1α content in the IOF, which confirmed its significance for the development and progression of DR. Determination of the level of HIF-1α can be used as an additional biomarker for stratifying the risk of DR progression. The proposed threshold values allow identifying patients with a high risk of progression and may be the basis for prescribing more intensive ophthalmological monitoring. The inclusion of this indicator in the complex of DR biomarkers can increase the personalization of therapy and improve treatment outcomes.

Conclusions. A direct relationship between the increase in HIF-1α content in the IOF and the progression of DR has been established and the principle possibility of its use as a DR biomarker has been confirmed.

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ЦИФРОВА ТРАНСФОРМАЦІЯ. МЕДИЦИНА 2.0: ШТУЧНИЙ ІНТЕЛЕКТ, ВІРТУАЛЬНА (VR) ТА ДОПОВНЕНА (AR) РЕАЛЬНІСТЬ

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Вступ. Сучасна медицина проходить період кардинальних змін, де ключовим драйвером є **цифрова трансформація**. На цьому шляху особливе місце займають **штучний інтелект (ШІ)**, а також **віртуальна (VR) та доповнена (AR) реальність**.

1. Цифрова трансформація в медицині та потенціал штучного інтелекту

1.1. Штучний інтелект у клінічній медицині та розробці ліків

Штучний інтелект – це каталізатор змін, що проникає в найважливіші медичні спеціальності.