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Vascular Endothelial Growth Factor in Tear Fluid as a Marker of Treatment Effectiveness in Patients with Diabetic Retinopathy and Hypertensive Disease

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Annotation: Diabetic retinopathy is a severe microvascular complication of diabetes mellitus and a leading cause of blindness. Intensive glycemic and blood pressure control slows its progression [1,2]. Elevated cholesterol and triglyceride levels increase the risk of vision loss. Studies (FIELD, ACCORD-Eye) have demonstrated the effectiveness of fenofibrate in systemic therapy for retinopathy, reducing the need for laser treatment and vitrectomy. The mechanisms of action include both lipid and non-lipid effects: apoptosis reduction, decreased oxidative stress and inflammation, strengthening of the blood-retinal barrier, and neuroprotection [3,4,5].

Keywords: diabetic retinopathy, diabetes mellitus, fenofibrate, lipids, inflammation, glycemia, blood pressure, ETDRS, FIELD, ACCORD-Eye.

Introduction: Vascular endothelial growth factor (VEGF) plays a key role in the pathogenesis of diabetic retinopathy, especially when combined with hypertension [6 , 7] . The study evaluates the level of VEGF in the lacrimal fluid as a potential marker of the effectiveness of patient treatment. Analysis of the dynamics of VEGF indicators before and after therapy allows us to determine the correlation with clinical improvement and stabilization of the pathological process. The results confirm the importance of monitoring VEGF in the lacrimal fluid for

individualizing patient management tactics and optimizing the therapeutic approach [8,9,10].

The aim of the study was to study the level of vascular endothelial growth factor (VEGF) in the lacrimal fluid of patients with diabetic retinopathy associated with hypertension and to evaluate its role as a marker of the effectiveness of the treatment.

Materials and methods. The total number of patients (40 people) was divided into two groups. The first group (20 patients, 13 women and 7 men, 40 eyes) with proliferative diabetic retinopathy (DR IIIa according to the classification of Bochkareva A.A. and Ivanishko Yu.A.) aged 57-63 years (mean age 59.8±0.8 years) received panretinal laser coagulation of the retina (LRC). The second group (20 patients, 16 women and 4 men, 40 eyes) with a similar stage of retinopathy aged 54-66 years (mean age 59.2±2.1 years) received panretinal LRC in combination with intravitreal ranibizumab (IVVR). All patients had a diagnosis of type 2 diabetes mellitus and were under the supervision of an endocrinologist and a therapist. The control group consisted of 20 healthy individuals (40 eyes) aged 49–73 years (mean age 60.9±7.4 years). No complications were observed during treatment. In the long term, 4 patients in the first group (4 eyes) developed partial hemophthalmos , requiring posterior vitrectomy in one case and resolving spontaneously in three cases. Transpupillary Panretinal LCS was performed in four sessions with an interval of 2 weeks using the Nd:YAG laser "VISULAS TRION" (561 nm) according to the standard technique (power 180-420 mW, coagulate diameter 500 μm, exposure 0.1 ms, total number of coagulates - 2500-3000). In some cases, focal laser coagulation of the central zone of the retina was additionally performed for diabetic macular edema with the Nd:YAG laser "VISULAS" (532 nm) with the following parameters: power 60-120 mW, coagulate diameter 50 μm, exposure 0.05-0.1 ms. Intravitreal administration of ranibizumab in the main group was performed on the 7th day after the first session of LCS. The content of vascular endothelial growth factor (VEGF) in the lacrimal fluid was determined by enzyme immunoassay using test systems (Human VEGF ELISA Kit , BioSource International Inc. , USA; « ChemiKine ™ Pigment Epithelium-Derived Factor Sandwich ELISA Kit », Chemicon International Inc., USA). Samples of tear fluid were taken before the start of treatment, on the 14th day after laser intervention and 1 month after therapy. A comprehensive ophthalmological examination included visometry (with and without correction, a projector of signs « Carl Zeiss SZP-350), autorefractokeratometry (Reichert RK-600), biomicroscopy (slit lamp Carl Zeiss SL-120), ophthalmoscopy (direct and indirect with Meinster lens), gonioscopy (Goldman lens), fluorescein angiography (fundus camera Carl Zeiss FF 450 plus ") and optical coherence angiography ("Carl Zeiss OCT Cirrus HD").

Results. The study evaluation criteria included the fundus condition, VEGF level, visual acuity and retinal thickness according to OCT of the macular zone. After the first session of LKS in the first group, regression of retinal Neovascularization was observed in 35% of eyes, in the second group (LKS + IVVR) - in 100% of cases. In the first group, a decrease in retinal thickness was noted from 342.5 ± 38.6 to 322.8 ± 24.1 μm ($p < 0.05$), in the second - from 326.4 ± 52.2 to 228.1 ± 16.8 μm ($p < 0.05$). IVVR not only reduces macular edema and neovascularization , but also makes LKS more effective and safe. Laser coagulation increases the level of VEGF in the tear fluid due to the damaging effect, while intravitreal administration of ranibizumab reduces its concentration, improving vision indicators and retinal thickness . The main criteria for the effectiveness of PRLC: disappearance of neovascularization , downgrading according to ETDRS, minimal non-proliferative changes. If there is no effect, additional laser treatment is required. In some cases (hemorrhages, macular traction , tractional retinal detachment) , vitrectomy is necessary . Given the increase in diabetes, diabetic retinopathy remains a serious medical and economic problem. However, timely compensation of diabetes and ophthalmological treatment can prevent blindness in more than 90% of cases.

Conclusion Analysis of cases of proliferative diabetic retinopathy, accompanied by the need for vitrectomy due to vitreous hemorrhage, indicates the advisability of full-scale panretinal laser coagulation (PRLC) already at early stages of the disease. Our results showed that early PRLC

promotes increased synthesis of angiogenic factors. Insufficient laser coagulation in this group of patients leads to progression of neovascularization , which negatively affects the state of the visual organ and increases the risk of further loss of visual functions. Intravitreal administration of VEGF inhibitors (IVVR) not only helps reduce macular edema and regress neovascularization , but also provides the possibility of safer PRLC and promotes significant stabilization of the course of diabetic retinopathy.

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