UDC: 616-78-659801/6.13

CURRENT VIEWS ON THE TREATMENT OF MACULAR OEDEMA IN PATIENTS WITH DIABETES MELLITUS


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ҚАНДЛИ ДИАБЕТ БИЛАН ОҒРИГАН БЕМОРЛАРДА МАКУЛА ШИШИНИ ДАВОЛАШНИНГ ЗАМОНАВИЙ ҚАРАШЛАРИ

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СОВРЕМЕННЫЕ ВЗГЛЯДЫ ЛЕЧЕНИЯ МАКУЛЯРНОГО ОТЕКА У БОЛЬНЫХ С САХАРНЫМ ДИАБЕТОМ

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Резюме. *Дунёнинг кўплаб мамлакатларида, шу жумладан Ўзбекистон Республикасида диабетик макула шишининг (ДМШ) тарқалиши юқори. Жаҳон соғлиқни сақлаш ташкилоти диабетик ретинопатияни диабет билан боғлиқ асосий кўз асоратларидан бири деб билади. ДМШ диабетик ретинопатиянинг ўзига хос кўриниши бўлиб, макула ичидаги қон томирларидан суюқлик оқиши туфайли ретинанинг шиши билан тавсифланади. ДМШ кўришнинг бузилишига ва даволанмаса, кўрликка олиб келиши мумкин, шунингдек, соғлиқ билан боғлиқ маҳсулдорлик ва ҳаёт сифатининг пасайишига олиб келади, бу эса жамият учун катта ижтимоий-иқтисодий юкга олиб келади.*

Калит сўзлар: *диабетик макула шиши, қон томир эндотелиал ўсиш омили, ранибизумаб, бевасизумаб, пегаптаниб, афлибертсепт.*

Abstract. *There is a high prevalence of diabetic macular oedema in many countries of the world, including the Republic of Uzbekistan. The World Health Organisation considers diabetic retinopathy to be one of the major ocular complications associated with diabetes mellitus. Diabetic macular oedema (DMO) is a frequent manifestation of diabetic retinopathy, characterised by swelling of the retina due to fluid leakage from blood vessels within the macula. DME can lead to visual impairment and, if left untreated, blindness, as well as reduced productivity and health-related quality of life, resulting in a significant socioeconomic burden on society.*

Keywords: *diabetic macular oedema, vascular endothelial growth factor, ranibizumab, bevacizumab, pegaptanib, aflibercept.*

Introduction. This study compares the relative effectiveness of first-line drugs with available data. Prior to the advent of vascular endothelial growth factor therapy (anti-VEGF), the treatment standard was laser photocoagulation, which provides vision stabilization in patients with DMOS, but has limited effectiveness in providing clinically significant improvement in vision[12]. Anti-VEGF therapy is the current standard of treatment. Ranibizumab (Lucentis) is part of the anti-VEGF-a monoclonal antibody given as intravitreal (VVT) injections and was the first drug approved to treat VN caused by Dmo. The second measure against VEGF, aflibercept (Eylea), was filed for registration in the European

Union on 7 November 2013. The efficacy and safety of pegylated aptamer against VEGF in pegaptanib (Macugen) has been studied in Phase II and III trials in Dmo-induced VI treatment, but in the UK the application for a licence was cancelled in 2011 and it is assumed that the application for a licence will no longer be considered[11].Bevacizumab (Avastin), a full-size anti-VEGF-A antibody designed to treat cancer, has not been developed or licensed for use in VVT and is therefore excluded from this analysis. This complies with guidelines from the UK's National Institute for health and quality improvement (NICE), in which they "cannot consider comparing ranibizumab to bevacizumab" and " evidence of a balance of harm and benefit in particular was not readily available to people with bevacizumab, a diabetic macular disease. shish". Ivt triamcinolone (ta), a synthetic glucocorticoid, is not licensed for the treatment of DMO[13]. IVT TA NICE is not considered a regular use comparator when evaluating anti-VEGF therapy and is therefore not considered appropriate for this analysis. The implantation of Fluocinolone Acetonide (FA) (Iluvien) ivt has only been approved as a secondary therapy in Europe (for the treatment of chronic Dmo-related VI, which cannot be adequately treated) and is therefore not considered appropriate for this analysis. Several recent reviews have summarized these Dmo treatments and related randomized controlled trials (RCTs)[8]. In addition, several recent systematic reviews (SR) compared RCT results for different treatment comparisons and concluded that anti-VEGF therapy consistently showed higher efficacy than alternative treatments.Three of these studies presented traditional pairwise meta-analyses, but none included network meta-analyses and none compared all potential first-line treatments (ranibizumab, aflibercept and laser photocoagulation)[14]. This analysis compares the reported efficacy of laser photocoagulation, intravenous ranibizumab injection, intravenous ranibizumab injection combined with laser, intravenous aflibercept injection, and false injection plus rescue laser therapy in a network meta-analysis[15]. In addition, this analysis updates the current state of evidence by including data from two large pivotal phase III RCTs (VIVID/VISTA) on aflibercept in DME. Thus, this work is important for treatment and resource allocation decisions, including technology assessments such as those conducted by NICE in the UK. Finally, the method is adjusted for effect modifiers such as baseline best-corrected visual acuity (BCVA) and central retinal thickness (CRT) to account for differences between study populations. Inclusion of appropriate disease modifiers is critical for robust network meta-analyses[7].

Objective of the study. To evaluate the safety of comparative effect of intravitreal application of brolucizumab and ranibizumab in the treatment of diabetic macular oedema in diabetic patients.

Materials and methods of research. The work was carried out at the departments of ophthalmology and in the regional eye hospital of Samarkand city. 150 patients diagnosed with diabetic macular edema in the period from January 2021 to December 2023 were under observation. A retrospective analysis of treatment results of patients with wet form of AMD who received more than 75 IVB of brolicizumab as anti-angiogenic therapy was performed. The two study groups consisted of 18 patients (eyes) aged 52 to 84 years - 15 women and 15 men [6]. The mean age was 65±5 years. All patients of the studied groups against the background of treatment with brolicizumab showed a pronounced positive dynamic both in the phase of loading injections and during the period of further treatment. In all treated patients relapses of the wet form of the disease were registered in the form of decreased visual acuity and accumulation of intra- and subretinal fluid. In the last year the absence of neuroepithelial detachment adhesion in the macular zone was observed even at monthly injections of brolicizumab, visometry registered a decrease in visual acuity. In 15 patients of the first group monthly loading infusions of aflibercept were performed [7], in 11 patients of the second - control - group therapy with brolicizumab was continued. To assess the dynamics of the pathological process and the effectiveness of the treatment, all patients were examined using the following methods of ophthalmological diagnostics: monthly visometry with correction, ophthalmoscopy, photoregistration of the ocular fundus, spectral OCT of the macular zone of both eyes and perimetry of the central retinal zone. SOCT CIRRUS HD (Carl Zeiss) with a resolution of 5 μm was used for OCT scanning. OCT-angiography of the macular area of patients in the process of A-VEGF therapy allows to evaluate the dynamics of the neovascular complex area, density and thickness of newly formed vessels, branching and perfusion of the subretinal neovascular membrane.

These parameters make it possible to differentiate the types of CNV in TMD [8]. When diagnosing various forms of TMD, not only the registration of morphological structural damage of the macula is possible, but also the study of the functional state of the central zone of the retina using microperimetry. The initial stages of AMD are accompanied by moderate changes in microperimetry data. In the wet form of TMD, significant disturbances in the light sensitivity of the macular zone are noted [10]. The intervals between examinations in the patients of the studied groups were 1 month after each IVC, and a set of examinations was also performed before the start of treatment. IVUS was performed by the standard method in a sterile operating theatre in accordance with the instructions for medical use of the drug.

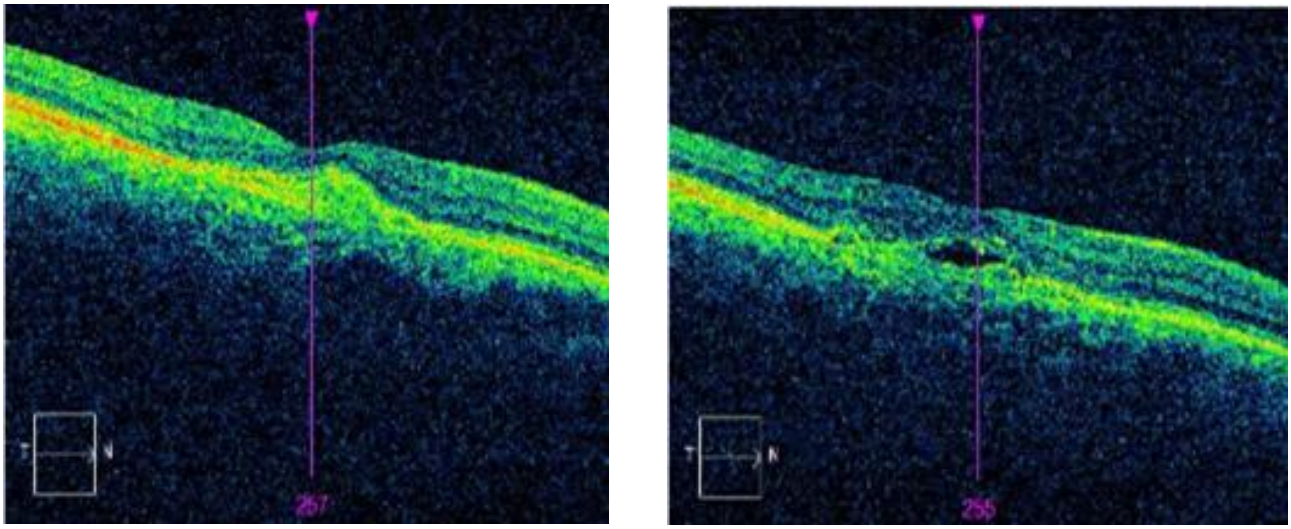

Fig. 1. OCT at initial treatment

In clinical practice, OCT angiography (OCTA) and microperimetry are not decisive for the assessment of treatment efficacy and further planning of repeated IVUS [11]. In view of this, we did not include OCTA and microperimetry in the complex of examination methods for patients with wet AMD receiving switching A-VEGF therapy. Statistical processing of data was performed in Excel programme (descriptive statistics, Student's criterion)[12].

Study results: The studied groups were comparable in terms of sex, age and concomitant pathology. All patients complained of visual impairment at the first visit. The presence of intra- and subretinal fluid, as well as elevation of pigment epithelium according to OCT data were registered (Fig. 1). In accordance with the instructions for the use of the drug ranibizumab, all patients in the study groups underwent loading infusions with an interval of 1 -2 months. After loading 3 monthly brolicizumab infusions, all 26 patients retrospectively registered positive dynamics according to OCT data (Fig. 2) and visual acuity. Diffuse retinal oedema, local defects and elevations of pigment epithelium in the macula were ophthalmoscoped before treatment. SOCT determined intraretinal oedema, neuroepithelial detachment, elevation and disaggregation of pigment epithelium. After 3 IVB of brolicizumab, complete adherence of the pigment epithelium and absence of subretinal fluid (SRF) were visualised ophthalmoscopically. OCT scans showed restoration of the foveal profile of the macular zone, resorption of intraretinal and subretinal fluid.

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OCT scans recorded restoration of the foveal profile of the macular zone, resorption of intraretinal and subretinal fluid.

Conclusions: Diabetic macular oedema is one of the most frequent and serious complications of diabetes mellitus (Sain et al., 2015). It is due to the unstable condition of prolonged high blood glucose levels, which causes damage to the retinal vascular network, resulting in increased permeability of retinal vessels and fluid accumulation in the macular area, causing diabetic macular oedema (Shin et al. , 2014). Once diabetic macular oedema occurs, it can significantly reduce vision. Data show that about one-third of people with diabetes will develop retinopathy, and about 2.6% of blind syndromes worldwide may be related to diabetes (Leasher et al. , 2016). With the development of a large number of randomised clinical trials, intravitreal injection has gradually displaced the photocoagulation method with retinal laser and has significantly improved the efficacy of macular oedema treatment.

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СОВРЕМЕННЫЕ ВЗГЛЯДЫ ЛЕЧЕНИЯ МАКУЛЯРНОГО ОТЕКА У БОЛЬНЫХ С САХАРНЫМ ДИАБЕТОМ

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Резюме. *Во многих странах мира, в том числе в Республике Узбекистан, отмечается высокая распространенность диабетического макулярного отека. Всемирная организации здравоохранения рассматривает диабетическую ретинопатию одним из основных глазных осложнений, связанных с сахарным диабетом. Диабетический макулярный отек (ДМО) является частым проявлением диабетической ретинопатии, характеризующимся отеком сетчатки из-за утечки жидкости из кровеносных сосудов внутри макулы. ДМО может привести к нарушению зрения и, если его не лечить, к слепоте, а также к снижению продуктивности и качества жизни, связанного со здоровьем, что приводит к существенному социально-экономическому бремени для общества.*

Ключевые слова: *диабетический макулярный отек, фактор роста сосудистого эндотелия, ранибизумаб, бевацизумаб, пегаптаниб, афлиберцепт.*