Modern Aspects of Treatment diabetic retinopathy and diabetic macular edema

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Current aspects of diabetic retinopathy and diabetic macular edema

Treatment methods

Abstract: Diabetic retinopathy (DR) and diabetic macular edema (DMO) are the main causes of visual impairment in patients with diabetes. An international multicenter study showed that retinal laser coagulation in the case of DMO reduced the risk of vision loss by 50%, but only 16% of patients could improve vision. The use of Ranibizumab, an inhibitor of vascular endothelial growth factor, opened a new era in the treatment of DMA. Its effectiveness and safety have been proven in a number of international studies.

This article contains our own data on the use of Lucentis in patients with DMO. Intravitreal Luzentis injections and subsequent macular retinal laser coagulation were performed in 43 eyes; observation period - 6 months. Additional injections were required in 19 cases, with an average injection amount of 1.4. Mean corrected visual acuity was 0.37+0.06 before treatment, after 7 days, 1, 3 and 6 months. - 0.41+0.06, 0.49+0.06, 0.51+0.07, and 0.52+0.07, respectively ($r<0.05$). The mean retinal thickness in the central zone was 428+25 μm before treatment, 391+24 μm 7 days after the last injection, 349+23, 313+21, and 308+20 μm after 1, 3, and 6 months ($r<0.05$) formed. In addition, the use of Luzentis in the preoperative period in patients with uncomplicated proliferative DR made it possible to reduce the risk of hemorrhagic complications. Thus, intravitreal injections

of Luzentis improve the functional results of treatment of patients with DMO, increase the efficiency and safety of surgical interventions in patients with complex forms of DR.

Key words: diabetic retinopathy, diabetic macular edema, ranibizumab, treatment.

From 5 to 10 years of age, diabetic retinopathy of varying severity was diagnosed in 30% of patients with type 1 diabetes and in 27% of patients with type 2 diabetes. Thus, in the country as a whole, every fifth patient with diabetes, even with a short course of diabetes (less than 10 years), has DR.

Visual impairment in proliferative diabetic retinopathy may be associated with complications such as recurrent vitreous hemorrhage, secondary neovascular glaucoma, traction retinal detachment, and the development of DME. The only effective treatment for proliferative DR today is timely and adequate panretinal laser photocoagulation (LA). Large-scale, multicenter, randomized controlled trials have shown that panretinal LC reduces the risk of blindness in patients with proliferative DR by 50% and leads to regression of neovascularization in 70–90% of cases [5, 6].

However, the most common cause of vision loss in patients with diabetes is the development of DME, which can accompany any stage of diabetic retinopathy and occurs in 10–25% of patients [7]. In Russia, according to the State Registry, 780,000 patients 62 have DME.

Risk factors for the development of diabetic macular edema include: inadequate glycemic control (high level of glycated hemoglobin), duration of diabetes, arterial hypertension, dyslipidemia, proteinuria.The incidence of DME correlates with the age of diabetes, and after 20 years of the course of the disease, diabetic macular edema occurs in 28% of cases. In 50% of patients, DMO leads to a decrease in visual acuity by 2 or more lines during two years of follow-up [1, 2, 8]. In addition, the results of a large retrospective study are important, which revealed a statistically significant increase in fatal heart attacks in patients with DME, which imposes increased requirements for the safety of macular edema treatment for the cardiovascular system [9].

For many years, the "gold standard" for the treatment of DME was laser photocoagulation (focal or lattice), the effectiveness of which was proven in the multicenter, large-scale, randomized, controlled clinical trial ETDRS. The study found that laser photocoagulation reduced the risk of severe vision loss in about 50% of cases when performed immediately compared to controls (12 vs. 24%) over 3 years Observation. However, only 16% of patients treated with laser treatment were able to achieve an improvement in visual acuity compared to 11% in the control group, which is associated with the known damaging effect of LC on photoreceptors and pigment epithelium [10]. Further long-term clinical experience confirmed the findings.

The search for new treatment options for diabetic macular edema, especially refractory macular edema refractory to laser coagulation, has led to the use of steroids. The effect on DME resorption of these drugs is likely due to the stabilization of the hematoretinal barrier due to their anti-inflammatory effect. The use of triamcinolone acetonide has been the subject of many works both abroad and in our country. All the researchers were unanimous in the opinion that that, despite the decrease in DME, the use of the drug is associated with the risk of increased intraocular pressure and the development of cataracts, and this risk increases with each subsequent injection [11, 12]. The drug has never been registered for intraocular use.

The next step in the treatment of DME — a "breakthrough" in solving this problem — was the use of vascular endothelial growth factor inhibitors. Ranibizumab is specifically designed for ophthalmology and has already proven itself in the treatment of neovascular wet macular degeneration. Ranibizumab blocks endothelial growth factor, which is produced in the early stages of DR, and reduces the permeability of the vascular wall, which leads to a decrease in retinal thickness. Ranibizumab was the first intraocular drug registered for the treatment of DME.

The results of several large-scale multicenter randomized controlled trials made it possible to conclude that the drug is highly effective and safe in the treatment of DME, which was an adequate evidence base for its use in wide clinical practice, including in our country. In the RESTORE study, 345 patients345 eyes were randomized to receive intravitreal injections of rani-bizumab 0.5 mg as monotherapy, combination treatment (ranibizumab + laser coagulation) and laser coagulation, respectively. The results of 12 months of follow-up have now been analysed and published; The study is ongoing and is designed for 2 years. Visual acuityAfter 12 months of treatment in 3 groups, I increased by 6.1; 5.9 and 0.8 letters, respectively. The differences between ranibizumab (Lucentis and Lucentis + LA) and LA were statistically significant ($p<0.001$). Visual acuity data correlated with retinal thickness by optical coherence tomography and indicated a faster and more sustained decrease in retinal thickness in the ranibizumab groups. CheAfter 12 months, the thickness of the central retinal zone decreased by 61.3 μm during LA and 118.7 and 128.3 μm, respectively, during ranibizumab monotherapy and combination of the drug with LA. During the entire follow-up period, ranibizumab, both as monotherapy and in combination with LA, significantly exceeded the efficacy of the existing standard of treatment for DME — laser coagulation. The safety assessment of ranibizumab indicated a favorable systemic and ophthalmic safety profile of this drug [13, 14].

In the «Diabetic Retinopathy Clinical Research Network » (DRCR.net) involved 691 patients (854 study eyes with DME). The study is planned as a 5-year study (it is still ongoing); Currently, the results of 24 months of follow-up have been analyzed. In the

DRCR..NET, the possible benefits of combination therapy (rani-bizumab with immediate or delayed LA) were evaluated compared with laser coagulation with sham injections or with intravitreal administration of triamcinolone acetonide. Patients in the study were randomized into 4 groups, corresponding to 4 types of the listed combination treatment. Immediate was LA 3 to 10 days after the injection of ranibizumab, and delayed was LA after 24 or more weeks after the injection.

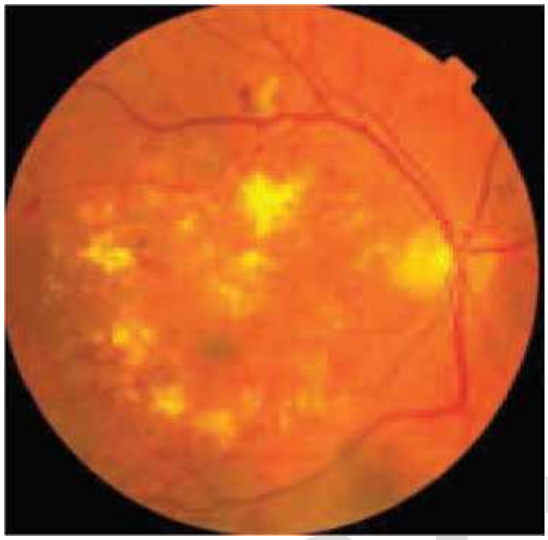


Fig. 1. Color photograph of the fundus. Diffuse DME. Microaneurysms, hemorrhages, lipid exudates in the posterior pole of the fundus. Maximally corrected visual acuity 0.2

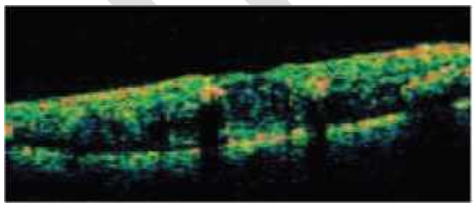
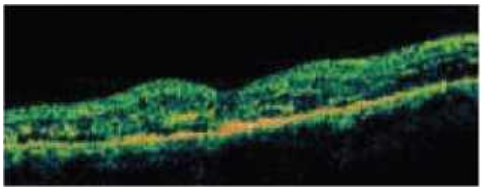
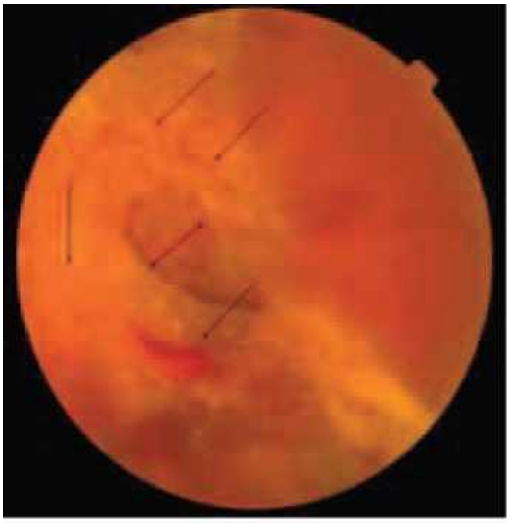
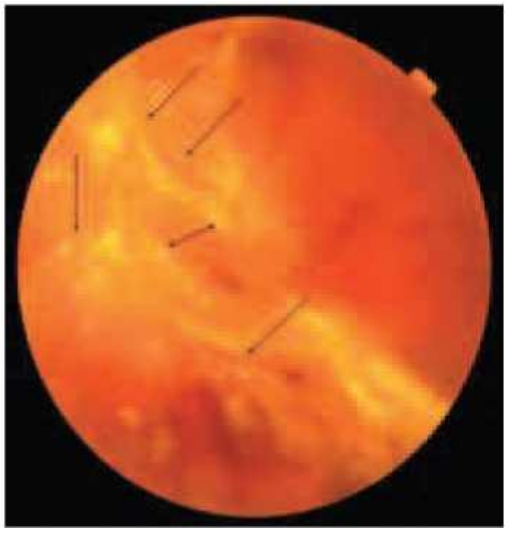


Fig. 2. OCT, horizontal slice. The retina is thickened. Intraretinal accumulation of fluid in cysts. Hyperreflexivity of lipid (solid) exudate deposits in the retina







Rice. 5. Color photograph of the fundus before administration of ranibizumab. The arrows indicate the newly formed vessels

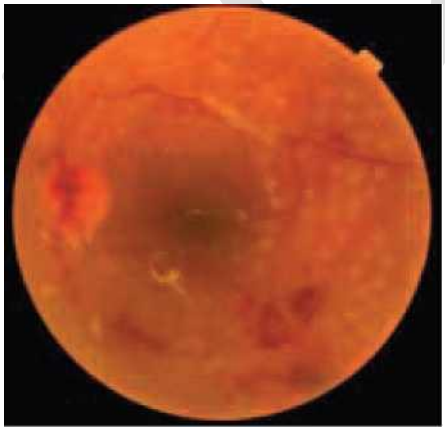


Fig. 6. Color photograph of the fundus after administration of rani-bizumab. Arrows indicate areas with reduced newly formed vessels, contraction of proliferative tissue

As an indication for a second injection of the drug. During 6 months of follow-up, 19 cases (44%) received repeated injections of ranibizumab. The average number of injections over six months of follow-up was 1.4.

In all cases, the drug was well tolerated by patients, and in 5-7% of adverse events, eye pain, conjunctival hyperemia, and subconjunctival hemorrhage were observed. Among the systemic complications, one case was found to be a fatal myocardial infarction (2.3%). In all likelihood, this can be explained by the existence of proven evidence increased risk of fatal cardiovascular disease in patients with DME and requires close and long-term attention of specialists.

There were no cases of cataract progression or elevation of intraocular pressure.

Thanks to the use of intravitreal injections of ranibizumab, it was possible to significantly improve the functional outcome of the treatment of patients with diabetic retinopathy. This also applies to patients with diabetic macular edema, in whom the use of ranibizumab improves visual acuity by 1-2 lines compared to standard LA, and patients with rubeosis of the iris and neovascular glaucoma, in whom the use of the drug allows achieving temporary regression of newly formed vessels and being able to carry out the necessary interventions (panretinal laser coagulation, anti-glaucoma surgery) to stop it in an adequate volume proliferative process on the fundus of the eye in DR and stabilization of visual functions.

Finally, the use of ranibizumab as a preparatory step for surgical intervention in severe proliferative diabetic retinopathy complicated by traction retinal detachment and recurrent vitreous hemorrhages can significantly reduce the risk of hemorrhagic complications during surgery and the postoperative period (Figures 5-7). This opens up new opportunities for vitreoretinal surgeons, who, through the use of ranibizumab, have begun to achieve both anatomical and functional success in situations that previously seemed hopeless.

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