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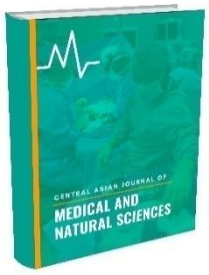

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The Use of The Drug Visque in Age-Related Macular Degeneration of The Retina

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Abstract: The study involved 25 patients (25 eyes) with nAMD (neovascular age-related macular degeneration). Among them were 13 women, 12 men. The inclusion criteria for the study were: the presence of active CNV, the absence of any previous antiangiogenic therapy. Non-inclusion criteria: a history of previous antiangiogenic therapy.The study was conducted at Yusupov A.A. Clinic LLC. In addition to standard examination methods, all patients underwent optical coherence tomography (OCT) using the RS-3000 Advance2 instrument (NIDEK, Japan). In the angiography mode (angio-OCT), the localization and area of the neovascular complex, the density and thickness of the newly formed vessels, the branching and perfusion of the subretinal neovascular membrane were determined, and their dynamics after treatment was assessed. In addition, retinal photosensitivity was assessed using Maia microperimetry (CenterVue, Italy). All patients underwent intraocular injections of Vizque® according to the standard loading scheme - 3 monthly injections. All of them were performed by one surgeon in a sterile operating room in accordance with the instructions for the medical use of the drug (at a dose of 6.0 mg / 0.05 ml).

Key words: age-related macular degeneration, drug Visque, optical coherence tomography, intraocular injections

Introduction

One of the leading causes of central vision loss and visual impairment in the adult population of developed countries is age-related macular degeneration (AMD) [1, 2]. It should be noted that more than 80% of cases of visual loss in AMD are observed as a result of the formation of choroidal neovascularization and its consequences, namely: exudation, retinal hemorrhages and disciform scars [3, 4]. Currently, the leading role of dysregulation of vascular endothelial growth factor (VEGF) in the pathogenesis of neovascular AMD (nAMD) has been proven [5, 6]. Modern advances in the treatment of nAMD are primarily due to the active use of drugs that suppress neoangiogenesis. Ranibizumab was the first drug registered in the Russian Federation in 2008 for anti-VEGF therapy of nAMD [6–8]. This drug is an antigen-binding Fab fragment of a humanized recombinant monoclonal antibody that affects all isoforms of VEGF-A. The low molecular weight of ranibizumab, which is 48 kDa, ensures its good penetration through the retinal layers to interact with the VEGF receptors of newly formed vessels [9]. But with the development of clinical experience, it turned out that a number of patients have resistance or tachyphylaxis to this drug. Moreover, their proportion in the total population of patients with nAMD is quite high: from 10% to 50% [10–13]. Later, another drug for the treatment of nAMD was developed - aflibercept with a molecular weight of 97 kDa. It was registered in the Russian Federation in 2016. Aflibercept is a fully human fusion protein, a decoy receptor, specially designed for antiangiogenic therapy [14–16]. Its molecule consists of the VEGF-binding domains of VEGFR1 and VEGFR2, connected to the Fc fragment of human immunoglobulin G. The advantage of aflibercept compared to ranibizumab is its ability to form a very stable inert ligament with VEGF-A immune complexes, characterized by high affinity, strictly in a ratio of 1 :1 [14, 15]. In addition, aflibercept has the ability to bind placental growth factor (PIGF), which plays an important role in the pathogenesis of neovascularization [17–19]. However, despite all the advantages of aflibercept, individual cases of chorioretinal atrophy have been identified with its use [20–22]. In this regard, the search for the most effective and safe method of treating AMD is still relevant. Brolucizumab (Visquie, Novartis Pharma AG, Switzerland), which has recently appeared in clinical practice, has become a new angiogenesis inhibitor. The structural basis of brolucizumab is a humanized single-chain antibody fragment with a much lower molecular weight (~26 kDa) compared to both ranibizumab and aflibercept. These properties allow it to successfully inhibit VEGF-A binding to the VEGFR1 and VEGFR2 receptors. According to the multicenter studies HAWK and HARRIER, the clinical efficacy of brolucizumab in achieving reduction of intraretinal and subretinal fluid was significantly higher than that of aflibercept (up to 30% or more) [23].

Objective: to analyze the direct clinical efficacy of brolucizumab in the treatment of choroidal neovascularization in patients with age-related macular degeneration (AMD).

Material and methods

The study involved 25 patients (25 eyes) with nAMD. Among them were 13 women, 12 men. The inclusion criteria for the study were: the presence of active CNV, the absence of any previous antiangiogenic therapy. Non-inclusion criteria: a history of previous antiangiogenic therapy.The study was conducted at Yusupov A.A. Clinic LLC. In addition to standard examination methods, all patients underwent optical coherence tomography (OCT) using the RS-3000 Advance2 instrument (NIDEK,

Japan). In the angiography mode (angio-OCT), the localization and area of the neovascular complex, the density and thickness of the newly formed vessels, the branching and perfusion of the subretinal neovascular membrane were determined, and their dynamics after treatment was assessed. In addition, retinal photosensitivity was assessed using Maia microperimetry (CenterVue, Italy).

All patients underwent intraocular injections of Vizque® according to the standard loading scheme - 3 monthly injections. All of them were performed by one surgeon in a sterile operating room in accordance with the instructions for the medical use of the drug (at a dose of 6.0 mg / 0.05 ml).

The criterion for the effectiveness of treatment was the positive dynamics of the following indicators: BCVA, CTS in microns, macular volume (OM) in mm3. Diagnostic examinations were performed at baseline and after each of the 3 injections of brolucizumab. The observation period was 4 months.

Research results

The mean age of the patients was 68±5 years (from 58 to 74 years). Ophthalmoscopy in 15 eyes initially parafoveolarly revealed typical ophthalmoscopic signs of neovascular AMD: subretinal gray-green CNV focus, multiple "hard" drusen, retinal single multiple hemorrhages. The presence of a voluminous hyperreflective spindle-shaped area above the level of the pigment epithelium was determined on OCT images (Fig. 1). According to angio-OCT data, in all 15 eyes there was a loop-shaped vascular network of varying intensity in the zone corresponding to the fusiform area in the image. In addition, in 5 eyes in the macular zone, an exudative detachment of the neuroepithelium was determined with an area of 1.5 to 2 diameters of the optic nerve head with heterogeneous hyperreflective content. According to angio-OCT data, a loop-like vascular network with numerous branches was observed in these 5 eyes. In another 5 patients, ophthalmoscopy revealed subretinal hemorrhage in the macular region, drusen, and atrophy of the pigment epithelium. According to OCT data, they showed detachment of the pigment epithelium with hyperreflective content. Angio-OCT revealed the presence of a loop-like vascular network in the zone, which corresponds to the fusiform area on the OCT image

After each injection, a decrease in CTS and OM and an increase in BCVA were recorded. After the 3rd injection of the study drug, there was a statistically significant decrease in CTS and OM and an increase in BCVA compared to baseline.

Only in 1 patient, 72 years old, with nARMD, after the 1st injection, there was a decrease in BCVA from 0.1 to 0.05. At the same time, a moderate increase in the CTS index from 294 to 300 microns was noted. After the 2nd injection, these values of the CTS index remained at the same level and amounted to 300 μm. Only after the 3rd injection of brolucizumab did the CTS decrease to 270 μm. At the same time, an increase in BCVA from 0.05 to 0.2 was noted.

Computer microperimetry of the macular zone in all patients before the course of treatment recorded a decrease in light sensitivity by an average of 10 dB. Against the background of anti-VEGF therapy, changes in light sensitivity were insignificant and fluctuated by an average of 2.5 dB, which was not statistically significant for assessing the results of treatment and planning further tactics.

Already after 1 month. after the 1st injection, in 22 of 25 patients, adherence of the neuro- and pigment epithelium with complete resorption of the subretinal fluid was recorded. In 3 patients, a complete reduction in the detachment of the neuro- or pigment epithelium occurred only after 3 monthly

intravitreal injections of the study drug, while subretinal fluid was not recorded in them. Subjectively, all patients noted an improvement in the quality and contrast of central vision in the operated eyes.

Discussion

The problem of effective treatment of neovascular AMD is one of the most urgent in clinical ophthalmology. This is due to the high degree of decrease in visual functions and the prevalence of this pathology. In clinical practice, drugs belonging to the pharmacological group of VEGF inhibitors, such as ranibizumab, aflibercept, are widely used. The new drug Visque® is an innovative molecule with a unique structure, specially designed for better control of nAMD [23]. This drug is superior to aflibercept and ranibizumab in achieving stable control of nAMD activity for 2 years [23, 25]. According to the data of multicenter studies, the use of this drug allows stable control of the disease with longer intervals between injections, which potentially increases patient compliance [26].

In this study, on a small clinical material, we traced the dynamics of changes in the main indicators characterizing nAMD - CTS, OM, BCVA with standard loading administration of brolucizumab (3 consecutive injections). In almost all cases, after each injection, there was a gradual statistically significant improvement in the studied parameters. At the same time, BCVA values showed a clear upward trend. Our data are in full agreement with similar data of foreign authors [25, 27].

In our study, no inflammatory reactions of the eyes were noted. According to studies, their frequency in real clinical practice can be about 2.4% [28]. The limitations of our study are the small number of cases included and the short follow-up period, however, all patients were examined using multimodal diagnostic methods, and we can expect that not a single case of intraocular inflammation, even the mildest, was missed.

Conclusions

The clinical results of 3 standard loading injections of the new drug Vizque® in the treatment of nAMD showed that after each injection there was a progressive statistically significant reduction in the main morphometric parameters of the macular area - CTS and OM. This was combined with an increase in the average values of visual acuity by the 4th month of observation.

For deeper conclusions about the degree of effectiveness of this drug, long-term observations on a large clinical material are required. However, already now preliminary data allow us to talk about the good efficacy of this drug.

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