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Research Article

OCT CHANGES IN MACULAR RETINAL THICKNESS DURING A-VEGF THERAPY

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ABSTRACT

Macular edema is the leading cause of vision loss in the increasingly frequent occurrence of diabetes mellitus, a true epidemic in developed countries. Diabetic macular edema is closely related to lifestyle, obesity, smoking or high blood pressure. Macular oedema is the leading cause of vision loss in people with diabetes in developed countries, and its prevalence is directly related to the duration of diabetes. Its incidence varies from publication to publication, ranging between 7.5% and 15.2%, and is more common in patients with type 2 diabetes receiving insulin.The significance of the incidence of diabetic macular oedema is directly related to the patient's metabolic control and the presence of risk factors, as we will see below.

KEYWORDS

Macular edema, brolicizumab , retina.

INTRODUCTION

The global prevalence of diabetes is increasing, due in part to the obesity epidemic. Prevention and treatment of vision loss caused by diabetic retinopathy, including proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME), is therefore becoming increasingly important. Diabetic macular edema is central macular edema and affects approximately 746,000 adults in the US aged 40 years and older (approximately 4% of people with diabetes develop DME). In some patients, control of blood sugar or blood pressure can prevent or improve the progression or worsening of diabetic retinopathy. For other patients, the standard treatment for DME has been laser photocoagulation, which has been used

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since the mid-1980s. Laser photocoagulation, which is mainly used to treat microangiomas or areas of yellow spot thickening, can reduce the risk of moderate vision loss by 50% and improve vision in 30% of diabetic patients with visual impairment, despite treatment. In 15% of patients, vision was preserved. loss.

In 2001, intravitreal injections of corticosteroids were introduced instead of laser photocoagulation, as diabetic retinopathy was thought to be part of an inflammatory response. Intravitreal steroid injections can reduce macular papilledema and improve vision, but half of patients receiving this therapy experience side effects, including increased intraocular pressure, which can further lead to glaucoma. In addition, almost all DME patients without prior cataract surgery develop cataracts after intravitreal steroids are injected. Further cataract extraction based on DMO is likely to exacerbate macular oedema and lead to further vision loss. In 2006, vascular endothelial growth factor (VEGF) was recognised as playing an important role in retinal neovascularisation and the formation of DME, and researchers began treating with intravitreal anti-VEGF drugs. The first anti-VEGF drug approved by the US FDA for intravitreal injection was pegaptanib, but its efficacy was limited. Bevacizumab was approved for antitumour therapy by intravenous infusion and has since been used to treat neovascular age-related yellow spot degeneration and DMO. The FDA then approved the VEGF inhibitor ranibizumab (ranibizumab) for clinical use. Three anti-VEGF drugs are currently available for the treatment of DMO, including aflibercept (not FDA approved), bevacizumab (not FDA approved) and ranibizumab (FDA approved).

Several clinical trials have evaluated the efficacy of both anti-VEGF therapy and laser photocoagulation, with randomised controlled trials conducted by DRCR.net and industry.ADRCR.net having played a role in the development of DMO treatment regimens. A total of 691 subjects were included, which were divided into groups: vitreous simulation plus laser treatment (control group), intravitreal ranibizumab plus laser treatment, and intravitreal ranibizumab with delayed laser treatment. local treatment) and intravitreal triamcinolone were treated simultaneously with laser photocoagulation. The principle of brolicizumab in the treatment of macular degeneration as formulated by DRCR.net is: visual acuity decreases due to DME and continues to improve after treatment, and it is recommended to continue treatment with ranibizumab; when macular edema is mostly stable, no obvious change after treatment, ranibizumab therapy should be stopped; it is possible to resume ranibizumab therapy if macular edema worsens. Genentech uses a monthly brolicizumab injection for at least 2 years (this indication is FDA approved), Novartis uses a programme similar to DRCR.net, and Regeneron uses aflibercept (aflibercept).

Intravitreal injections of anti-VEGF have now replaced laser therapy as the standard treatment for DME, but laser photocoagulation can still be used if anti-VEGF therapy is completely ineffective. As vision improves, not all patients with DME treated with anti-VEGF or laser photocoagulation have improved their vision. Consequently, other therapeutic approaches, including combination therapy with corticosteroids and anti-VEGF, anti-VEGF conversion factors, increased frequency of injections, use of surgery and other approaches are also being considered.

These recommended therapies help to prevent vision loss, but many patients with diabetic yellow spot degeneration do not receive these treatments. Health professionals, when managing patients with diabetes, should take care to assess concomitant retinopathy,

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including DME and proliferative retinopathy. People with diabetes need to make regular visits to an ophthalmologist (who can accurately assess the severity of diabetic retinopathy and determine the presence or absence of DME) at the polyclinic. Although good blood pressure and blood sugar control can help prevent the development of diabetic retinopathy, it is not a substitute for an eye examination. Patients without a history of diabetic retinopathy are advised to have an eye examination every 1-2 years; in diabetic retinopathy patients with an appropriate increase in the frequency of examinations and examinations by ophthalmologists experienced in the treatment of diabetic retinopathy.

Purpose of the study: Oct of changes of makular network thickness within a-vegf therapy oct of changes of makular network thickness within a-vegf therapy

Materials and Methods: The work was carried out in the Regional Eye Clinic of Samarkand city. We conducted a retrospective and prospective history analysis of diabetic macular edema patients presenting between 2020 and 2023. In addition, a survey of the elderly in remote areas, early detection of diabetic macular edema. Research methods used were visiometry, fundus biomicroscopy (60D, 75 D lenses). Examination of the eye with ultrasound (A/B scan), ophthalmoscopy, fundus camera, OCT, FAG. A retrospective analysis was made of the results of treatment of patients with wet AMD who received more than 75 IVCs of brolicizumab as anti-angiogenic therapy. The two study groups comprised 18 patients (eyes) aged 52 to 84 years, 15 females and 15 males. The mean age was 65±5 years. All patients in the study groups showed clear positive dynamics during treatment with brolicizumab both in the phase of loading injections and during further treatment. All treated patients had relapses of the wet form of the disease in the form of decreased visual acuity and accumulation of intra- and subretinal fluid. In the last year there was no adherence of neuroepithelium detachment in the macular zone even with monthly injections of brolicizumab, visometry recorded a decrease in visual acuity. Fifteen patients in the first group underwent monthly aflibercept loading IVC [6], while brolicizumab therapy was continued in 11 patients in the second, control, group. To assess the dynamics of the pathological process and effectiveness of the ongoing treatment, all patients were examined using the following ophthalmic diagnostic methods: monthly visometry with correction, ophthalmoscopy, fundus photography, spectral OCT of the macular area of both eyes and perimetry of the central retinal area. SOCT CIRRUS HD (Carl Zeiss) with 5 μm resolution was used for OCT scanning. OCT-angiography of macular zone of patients in the course of A-VEGF therapy enables to evaluate dynamics of neovascular complex area, density and thickness of newly formed vessels, branching and perfusion of subretinal neovascular membrane. These parameters make it possible to differentiate the types of CNV in TMD [18]. When diagnosing different forms of AMD, it is possible not only to register the morphological structural damage of the macula, but also to study the functional state of the central retinal zone using microperimetry. Initial stages of AMD are accompanied by moderate changes in microperimetry data. In case of humid AMD there are considerable disturbances in light sensitivity of the macular zone. Patients of the studied groups had 1 month examination intervals after each TRS and a complex of examinations before the treatment was started. TDF was performed using the standard method in a sterile operating room, in accordance with the instructions for medical use of the drug. In clinical practice, OCT-angiography (OCTA) and microperimetry

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are not decisive for the evaluation of treatment efficacy and further planning of repeated IVI (18-20). In view of this, we did not include OCTA and microperimetry in the set of examination methods for patients with wet AMD receiving A-VEGF therapy switching. Statistical data processing was performed in Excel (descriptive statistics, Student's t-test).

Results of the study: The dynamics of retinal thickness in the macular zone are shown in Table 1. At initial presentation, patients complained of decreased visual acuity and a central "spot" in front of the eye. Distortions in central vision - metamorphopsia, accompanying all observed cases, were of particular discomfort to the patients. In the course of treatment, after each TDF of brolicizumab, patients subjectively noted an improvement in vision, up to full recovery after 3 loading monthly TDFs.

Table 1

OCT dynamics of macular retinal thickness changes during A- VEGF therapy

Examination period	Retinal thickness in the macular zone (μm)	
	Group 1 M±σ	Group 2 M±σ
Before treatment start	339,8±40,7	316,2±31,7
After 3rd intravenous infusion of brolicizumab	241,5±12,0	249,7±13,0
After 15th Brocizumab TDF	342,9±44,6	309,0±18,7
At the end of treatment	After IVIG loading	After the 20th IVU of brolicizumab

Note: statistical significance of differences: * - p<0.05 (with group 1); ** - p<0.05 (with data before treatment)

Table 2

OCT dynamics of macular retinal thickness changes during A- VEGF therapy

Examination period	ICCO	
	Group 1 M±σ	Group 2 M±σ
Before treatment start	0,45±0,06	0,44±0,1
After 3rd intravenous infusion of brolicizumab	0,75±0,1	0,72±0,1
After 15th Brocizumab TDF	0,44±0,1	0,41±0,09

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At the end of treatment	After the IVF load	After the 20th IVU of brolicizumab

Note: statistical significance of differences: * - p<0.05 (with group 1); ** - p<0.05 (with data before treatment)

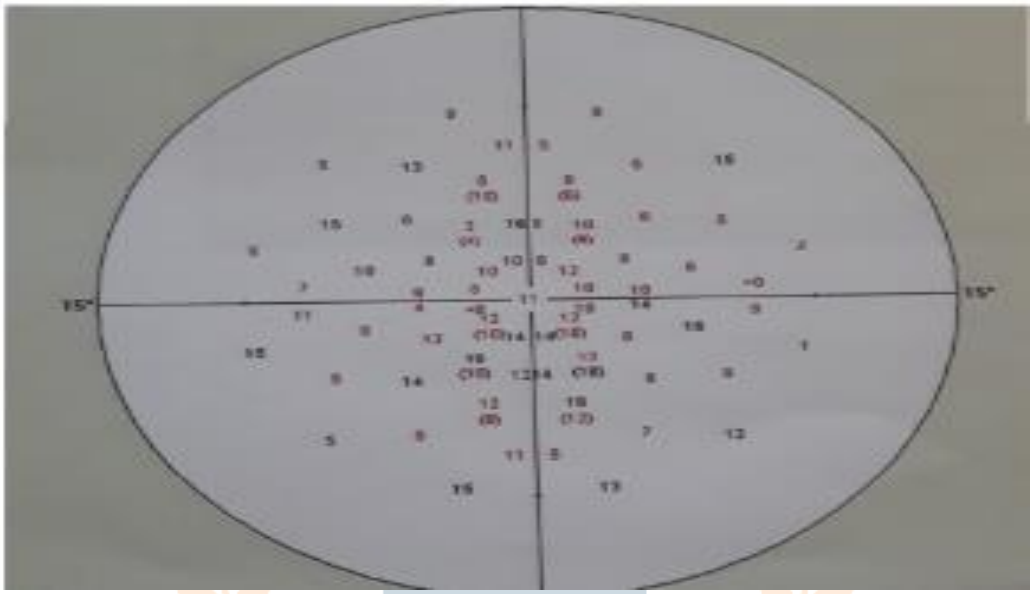

Fig. 1a Central microperimetry data of patient H.

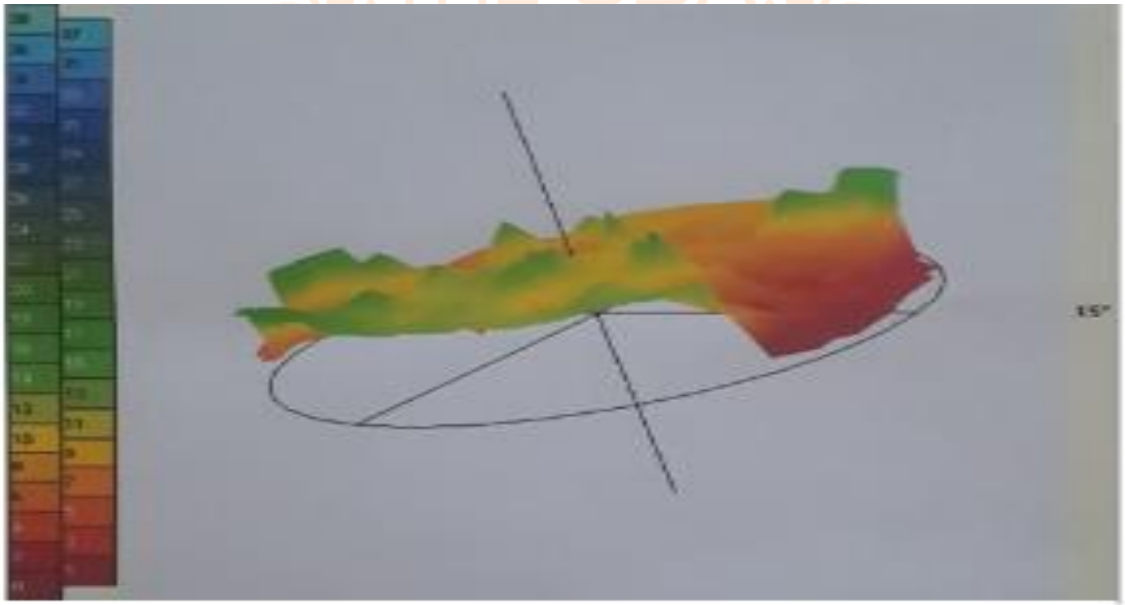

Fig. 1.b 3D graph of central microperimetry of patient H.

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Computer macular microperimetry in all patients recorded a decrease in light sensitivity by an average of 10 dB

Changes in light sensitivity during A-VEGF therapy averaged 2 dB, which was not statistically significant criterion for assessing treatment outcomes and planning further tactics. An analysis of the clinical course of the retrospective study showed an average duration of CNV suppression of 98±10 days. The planning of subsequent IVI of brolicizumab in each patient was carried out individually. IVI was repeated in 3-4 months according to the results of control OCT when CPV appeared. The maintenance regimen in patients of the study groups was 3-5 injections of brolicizumab per year. Over 3 years of A-VEGF therapy with ranibizumab, patients in the study group received an average of 21(±3) TDF. The results of dynamic OCT and visometric observation registered a significant decrease in the anatomical and functional retinal response to brocizumab TDF. Even with monthly injections, there was insignificant resorption of SRW (Table 1), no improvement of visual acuity subjectively and according to visometry data (Table 2) in all patients in the study groups. Aflibercept therapy was instructed to give a TRV1 once every 2 months after three monthly booster injections in the first year of therapy. In the prospective arm of the study, all patients in Study Group 1 received a 2 mg TRV of aflibercept. In 7 and 10 patients a complete resorption of SRW with adherence of neuro- and pigment epithelium was recorded 1 month after the first injection. Two patients in the first group underwent a second IV of aflibercept to achieve complete anatomical stabilisation. One patient underwent three monthly IVUs of aflibercept, after which no SRJ was recorded. Retinal thickness in the macula averaged 238.3±18 µm. Maximum corrected visual acuity in all patients (10 eyes) after loading of aflibercept significantly improved from 0,45±0,06 to 0,71±0,01, p<0,05 according to visometry data (Table 2). Subjectively, all patients noted improvement of quality and contrast of the central vision. Patients in control group 2 continued monthly brolicizumab IVC. In all patients there was no complete resorption of retinal pigment epithelium, neuro- and pigment epithelium detachment persisted. Retinal thickness in the macula averaged 301.3±19µm versus 238.8±18.0 in Group 1, p<0.05, where macular edema had resolved. Corrected visual acuity in all 8 patients in the course of treatment according to visometry data had slightly decreased. Subjectively, patients in the control group had no improvement of central visual acuity and contrast. When assessing the duration of exudative activity suppression in the macula, the terms of oedema and neuroepithelial detachment resumption on monthly OCTs were monitored. The duration of remission with aflibercept averaged 2.1±0.2 months. Therapy with brolicizumab of patients in group 2 was followed by a 4-week period of decreased exudative activity followed by an increase in macular edema. The duration of suppression of "wet" process in the macula for more than 2 months that we found suggests the possibility of increasing the time interval between infusions of aflibercept, comparable with the results of Queguiner F (2020) who showed that "switching from brolicizumab to aflibercept in "non-optimal" patients significantly reduced the number of follow-up visits and IVV, with comparable effectiveness".

CONCLUSIONS

Analysis of the retrospective study results confirms the efficacy of exudative content resorption in the macula when brolicizumab is used initially as a treatment. However, we further found that after multiple (more than 15) IVIs of brolicizumab, patients with wet AMD develop resistance of retinal edema to ranibizumab, up to and including complete resistance to therapy, which

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is consistent with findings of other investigators [13, 14, 17]. When A-VEGF pharmacotherapy is switched to aflibercept in these patients, a pronounced positive dynamics accompanied by a reduction of edema in the macular zone is noted already after loading injections, as confirmed by SOCT and visometry data.

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