

INTEGRATED APPROACH TO COMBINED TREATMENT OF DIABETIC MACULAR EDEMA

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Annotation. Relevance. Diabetic retinopathy (DR) is one of the late complications of DM. An important role in the pathogenesis of its appearance is played by endothelial growth factor. **Purpose of the study.** Evaluate the effectiveness of SMPLE and its combination with anti-VEGF therapy in the treatment of diabetic macular edema (DME) against the background of non-proliferative diabetic retinopathy. **Materials and methods.** In total, the study included 42 patients (67 eyes) with DME who were randomized into 2 groups. Group I anti-VEGF therapy in the 1+PRN mode (once + «as needed»). Group II combined treatment was carried out: SMPLE + anti-VEGF therapy (once + «as needed»). **Results and conclusion.** In patients receiving combination therapy, the frequency of additional injections was significantly lower: 67.5% of patients did not need further administration of anti-VEGF drug after the loading phase compared with 11.1% in the monoanti-VEGF therapy group. SMPLE at a wavelength of 577 nm is safe for the structures of the chorioretinal complex, since it does not have a destructive effect on the cells of the retinal pigment epithelium.

Keywords: diabetic macular edema, anti-VEGF therapy, subthreshold micropulse laser exposure, optical coherence tomography.

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КОМПЛЕКСНЫЙ ПОДХОД К КОМБИНИРОВАННОМУ ЛЕЧЕНИЮ ДИАБЕТИЧЕСКОГО МАКУЛЯРНОГО ОТЕКА

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Аннотация. Актуальность. Диабетическая ретинопатия (ДР) является одним из поздних осложнений СД. Важную роль в патогенезе его появления играет эндотелиальный фактор роста. **Цель исследования:** оценить эффективность СМЛВ и его комбинацию с анти-VEGF терапией в лечении диабетического макулярного отека (ДМО) на фоне непролиферативной диабетической ретинопатией. **Материал и методы.** Всего в исследование были включены 42 пациентов (67 глаз) с ДМО на которые были рандомизированы на 2 группы. I группа – анти-VEGF терапия в режиме 1+PRN (однократно + «по необходимости»). II группа – комбинированное лечение: СМЛВ + анти-VEGF терапия в режиме 1+PRN. **Результаты и заключение.** У пациентов, получавших комбинированную терапию, частота дополнительных инъекций была значительно ниже: 67,5% пациентов не нуждались в дальнейшем введении анти-VEGF препарата после фазы загрузки по сравнению с 11,1% в группе моноанти-VEGF терапией. Субпороговое микроимпульсное лазерное воздействие длиной волны 577 нм является безопасным для структур хориоретинального комплекса, так как не оказывает деструктирующего эффекта на клетки пигментного эпителия сетчатки.

Ключевые слова: диабетический макулярный отек, анти-VEGF терапия, субпороговое микроимпульсное лазерное воздействие, оптическая когерентная томография.

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ДИАБЕТИК МАКУЛА ШИШИНИ КОМБИНИРЛАНГАН УСУЛДА ДАВОЛАШГА КОМПЛЕКС ЁНДАШИШ

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Аннотация. Долзарблиги. Диабетик ретинопатия қандли диабетнинг асоратларидан биридир. Унинг пайдо бўлишининг патогенезида эндотелиал ўсиш омили муҳим рол ўйнайди. **Тадқиқот мақсади.** Нопролифератив диабетик ретинопатия фондаги ДМШ даволашда бўсаға ости микропульсли лазер таъсирини (БОМИЛТ) ва унинг анти-VEGF терапияси билан комбинациясининг самарадорлигини баҳолаш. **Материаллар ва усуллар.** Тадқиқотга ДМШ билан касалланган 42 бемор (67 та кўз) киритилди ва улар 2 гуруҳга бўлинди. I гуруҳга анти-VEGF терапиясини 1+PRN режимида олган. II гуруҳда комбинирланган даволаш: БОМИЛТ+анти-VEGF терапияси 1+PRN режимида (бир марта+«керак бўлганда») ўтказилди. **Натижалар ва хулоса.** Моноанти-VEGF терапияси гуруҳидаги 11,1% беморларда такрорий интравитреал инъекцияга талаб кузатилмаган бўлса, комбинирланган терпия гуруҳида эса 67,5% беморларда анти-VEGF препаратини кейинчалик қайта юборишга эҳтиёж кузатилмади. Тўлқин узунлиги 577 нм бўлган бўсаға ости микропульсли лазер таъсири хориоретинал комплекс тузилмалари учун хавфсиздир, чунки у ретинал пигмент эпителийсининг ҳужайраларига ҳалокатли таъсир кўрсатмайди.

Калит сўзлар: диабетик макула шиши, анти-VEGF терапия, бўсаға ости микроимпульсли лазер билан даволаш, оптико когерент томография.

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Relevance. Diabetic retinopathy (DR) is one of the leading causes of blindness in people of working age in economically developed countries. Numerous clinical studies have established that one of the main causes of vision loss in patients with diabetes mellitus is diabetic macular edema (DME) [1,3]. The global incidence of this disease remains high and approximately 130 million people in the world suffer from diabetes. Data from the World Health Organization show that by 2025 the number of patients suffering from diabetes may reach 350 million people [5].

Macular edema occurs in 10–15% of patients with type 2 diabetes DME is the most common cause of visual impairment in patients with diabetes and can occur at any stage of diabetic retinopathy and is observed in the proliferative stage in 70% of cases. The prognosis of the visual functions of the organ of vision is unfavorable, in the absence of timely treatment of intraocular complications of DM [3]. According to the results of Figueira J. and others, in patients with type 2 DM, the detection of DME increases depending on the duration of diabetes from 3% for the first time 5 years from the onset of the disease, to 28% with a history of diabetes for more than 20 years [4]. In patients with type 2 DM, the incidence of DME is higher (27.15%) than with type 1 DM (11.84%) [2].

Antivascular endothelial growth factor (anti-VEGF) therapy is the standard of care for patients with DME in high-resource settings due to its rapid and pronounced effect in improving vision [4].

Subthreshold micropulse laser exposure (SMPLE) is devoid of these shortcomings and is selective with

respect to the retinal pigment epithelium [2]. There are several treatment strategies regarding micropulse laser surgery. Some of them can be combined with anti-VEGF therapy [1].

Thus, the standard continuous laser has been an effective option for decades despite its collateral damage to the retina. Despite the slow spread, the potential of the subthreshold micropulse laser is also gaining recognition.

Purpose of the study. To evaluate the effectiveness of SMPLE and its combination with anti-VEGF therapy in the treatment of DME against the background of non-proliferative diabetic retinopathy.

Materials and methods. The study included patients treated at the eye clinic «SIHAT KO‘Z» and was a 12-month prospective follow-up. The comparison was based on the analysis of morphofunctional parameters of the central retina in 42 patients (67 eyes) with DME against the background of non-proliferative diabetic retinopathy. The age of the patients ranged from 46 to 64 years. There were 24 women, 18 men. Depending on the treatment, all patients were divided into 2 clinical groups:

- Group I (18 patients, 29 eyes) – anti-VEGF therapy in the 1+PRN mode (once + “as needed”);
- Group II (24 patients, 38 eyes) – combined treatment: SMPLE + anti-VEGF therapy in 1+PRN mode.

Before and after treatment, a comprehensive ophthalmological examination was performed, including the thickness of the retina in the central

zone of the fovea, which was determined using optical coherence tomography (OCT). Parameters were assessed before treatment and 12 months after treatment.

SMPLE was performed on an Easyret diode laser device (Quantel medical, France), with a wavelength of 577 nm in a micropulse mode with a power of 200–400 mW.

With intravitreal administration of an anti-VEGF drug, Viz'ku (Novartis, Switzerland) was prescribed. International nonproprietary name: brolucizumab.

With combined treatment, the SMPLE session was performed 3 days after a single loading of the anti-VEGF drug.

Results and discussion. BCVA in group I one after 12 months anti-VEGF therapy was 12 months 0.68 ± 0.03 ($p < 0.05$). In group II, BCVA one after 12 months combination therapy was 0.76 ± 0.03 ($p < 0.01$).

In turn, in group I, the OCT values after 12 months anti-VEGF therapy were $285.5 \pm 17.9 \mu\text{m}$ ($p < 0.05$). In group II, OCT values after 12 months combination therapy were $260.4 \pm 17.7 \mu\text{m}$ ($p < 0.01$).

Re-introduction of intravitreal injections in group I during 12 months of observation was required in the amount of 2 injections in 8 cases (29.6%), 3 injections in 6 (22.3%), 4 injections in 5 (18.5%), 5 injections – in 3 (11.1%), more than 5 injections – in 2 (7.4%), and only in 3 cases (11.1%) a single administration of anti-VEGF drug was sufficient.

In this article, we compared the effectiveness of a SMILV session, anti-VEGF therapy, and their combination over a 12-month follow-up period. All groups achieved significant improvement in vision and reduction in retinal thickness in the foveal region. The final BCVA values in the combination treatment group were higher (0.76 ± 0.03).

In group II, during 12 months of observation, repeated administration of intravitreal injections was required in the amount of 2 injections in 7 cases

(22.5%) and 3 injections in 3 cases (10.0%), and in other cases (67.5%) a single dose of anti-VEGF drug was sufficient.

In patients receiving combination therapy, the frequency of additional injections was significantly lower: 67.5% of patients did not need further administration of anti-VEGF drug after the loading phase compared with 11.1% in the monoanti-VEGF therapy group.

Thus, adding a session of SMPLE after anti-VEGF drug loading appears to significantly reduce the injection load without compromising visual improvement. SMPLE provides a statistically significant improvement in BCVA and a decrease in retinal thickness in the foveal region in DME with a central foveal thickness of up to $400 \mu\text{m}$. SMPLE may be an option for patients who do not respond well to anti-VEGF therapy or are unable to adhere to it due to its high cost, or have problems with adherence due to the frequent visits required for injection and ophthalmic monitoring. Unlike suprathreshold, subthreshold laser mode is a non-damaging procedure. According to the selected duty cycle, the laser remains on only 5% of the time, thus generating less heat with subsequent less damage to the retina than continuous photocoagulation. Our personal experience shows that micropulse laser treatment for DME is more effective in patients whose central retinal thickness with its edema is less than $400 \mu\text{m}$.

Conclusion. Combination treatment combining anti-VEGF therapy and SMPLE for DME with central retinal thickness less than $400 \mu\text{m}$ is effective, and their combination can significantly reduce the number of injections required to improve visual acuity and sustained resolution of foveal edema.

Combined treatment with DME, combining SMPLE with intravitreal administration of Viz'ku, is effective in 67.5% of cases within 12 months.

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