Clinico-functional assessment of patients with pachychoroid neovasculopathy after intravitreal administration of angiogenesis inhibitors with photodynamic therapy

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Клініко-функціональна оцінка пацієнтів з пахіхоріоїдною неоваскулопатією після інтравітреального введення інгібіторів ангіогенезу з фотодинамічною терапією

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Abstract

Objective. *To compare clinical and structural outcomes of combination therapy (anti-VEGF + PDT) versus anti-VEGF monotherapy in patients with pachychoroid neovasculopathy (PNV) during 12-month follow-up.*

Materials and Methods: *The study included 64 patients (74 eyes) with PNV. Examinations were performed prior to treatment and at designated intervals: 1, 3, 6, and 12 months from the beginning of therapy. Patients were divided into two groups: the main group (40 eyes) and the control group (34 eyes). The main group included 34 patients (40 eyes), with baseline central retinal thickness (CRT) of 410.26 ± 113.48 µm and central choroidal thickness (CCT) of 485.89 ± 102.65 µm. The control group included 30 patients (34 eyes), with CRT of 405.89 ± 102.65 µm and CCT of 483.46 ± 102.54 µm. Patients in the main group received the following combined regimen: one intravitreal injection of 6 mg brolucizumab followed by one session of PDT with chlorin e6–based photosensitizer. Thus, during the entire observation period, patients in this group received one Anti-VEGF injection and one PDT session. PDT and brolucizumab injections were performed according to standard protocols. Subsequent treatment cycles were performed in following regimen: the interval between PDT procedures was at least 3 months, while the average interval between brolucizumab injections was approximately 1.5 months. Patients in the control group received three loading injections of 6 mg brolucizumab at 4-week intervals.*

Results. *In the main group, BCVA increased moderately from 0.28 ± 0.14 at baseline to 0.38 ± 0.23 at the 12-month follow-up, whereas in the control group it remained relatively stable, measuring 0.31 ± 0.26 at month 1 and 0.35 ± 0.24 at month 12. Improvement in functional outcomes was accompanied by anatomical improvements: a reduction in central retinal thickness (CRT) from 410.26±113.48 µm to 262.46±146.40 µm at the 12-month follow-up, confirmed by the resorption of subretinal fluid (SRF) and a decrease in retinal pigment epithelium (RPE) detachments. A significant reduction in central choroidal thickness (CCT) was noted—from 485.89±102.65 µm to 413,21±96,23 µm after 1 month, 413,91±92,25 µm after 3 months, 414,21± 106,23 µm after 6 months, 415,30±108,64 µm by the end of the monitoring period. In the control group, improvement in BCVA was less pronounced (0.31±0.26 before treatment and 0.35±0.24 at 12 months). Changes in morphological parameters occurred early: CRT was reduced by the first month of observation (from 405.89±102.65 µm before therapy to 267,35± 43,65 µm after 1 month, 266,45± 93,65 µm after 3 months, 266,45± 93,65 µm after 6 months, followed by a slight raise up to 268,4±43,5µm by the 12-month mark. Therefore, CCT remained stable throughout the treatment period, maintaining a value comparable to baseline (483.46 ± 102.54 µm). A significant reduction in central retinal thickness and central choroidal thickness, as well as improvement in BCVA, was observed in the combination therapy group over the 6- and 12-month follow-up periods compared to the brolucizumab monotherapy group. These effects were associated with the*

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resorption of subretinal fluid as a result of neovascular membrane occlusion.

Conclusion. *The inclusion of photodynamic therapy (PDT) with a chlorin e6-based photosensitizer in the treatment regimen for pachychoroid neovasculopathy (PNV) leads to the restoration of anatomical and functional parameters and reduces the recurrence of the disease in patients with PNV.*

Keywords: *pachychoroid neovasculopathy, age-related macular degeneration, photodynamic therapy, central retinal thickness, central choroidal thickness.*

Резюме

Мета. *Порівняти клінічні та структурні результати комбінованої терапії (анти-VEGF + PDT) з монотерапією анти-VEGF у пацієнтів з пахіхоріоїдною неоваскулопатією (ПНВ) протягом 12-місячного спостереження.* ***Матеріали та методи:*** *У дослідженні взяли участь 64 пацієнти (74 ока) з ПНВ. Обстеження проводилися до лікування та через визначені інтервали: 1, 3, 6 та 12 місяців від початку терапії. Пацієнти були розділені на дві групи. До основної групи увійшли 34 пацієнти (40 очей) з вихідною центральною товщиною сітківки (ЦТС) 410,26 ± 113,48 мкм та центральною товщиною хоріоїдеї (ЦХТ) 485,89 ± 102,65 мкм. Контрольна група включала 30 пацієнтів (34 ока) з CRT 405,89 ± 102,65 мкм та CCT 483,46 ± 102,54 мкм. Пацієнти основної групи отримували комбіноване лікування: одна інтравітреальна ін'єкція 6 мг бролуцизумабу з подальшим одним сеансом фотодіабетної терапії (ФДТ) з фотосенсибілізатором на основі хлорину е6. ФДТ та ін'єкції бролуцизумабу проводилися за стандартними протоколами. Режим наступних циклів лікування: інтервал між процедурами ФДТ щонайменше 3 місяці, середній інтервал між ін'єкціями бролуцизумабу - приблизно 1,5 місяця. Пацієнти контрольної групи отримували три навантажувальні ін'єкції 6 мг бролуцизумабу з інтервалом у 4 тижні.* ***Результати.*** *В основній групі BCVA помірно збільшилася з 0,28 ± 0,14 на початку дослідження до 0,38 ± 0,23 через 12 місяців спостереження, тоді як у контрольній групі вона залишалася відносно стабільною, становлячи 0,31 ± 0,26 через 1 місяць та 0,35 ± 0,24 через 12 місяців. Покращення функціональних результатів супроводжувалося анатомічними покращеннями: зменшенням центральної товщини сітківки (CRT) з 410,26 ± 113,48 мкм до 262,46 ± 146,40 мкм через 12 місяців спостереження, що підтверджено резорбцією субретинальної рідини (SRF) та зменшенням відшарування пігментного епітелію сітківки (RPE). Було відзначено значне зменшення центральної товщини хоріоїдеї (ЦТХ) — з 485,89±102,65 мкм до 413,21±96,23 мкм через 1 місяць, 413,91±92,25 мкм через 3 місяці, 414,21±106,23 мкм через 6 місяців, 415,30±108,64 мкм до кінця періоду спостереження (рис. 3). У контрольній групі покращення BCVA було менш вираженим (0,31±0,26 до лікування та 0,35±0,24 через 12 місяців). Зміни морфологічних параметрів відбулися рано: CRT знизилася до першого місяця спостереження (з 405,89±102,65 мкм до терапії до 267,35±43,65 мкм через 1 місяць, 266,45±93,65 мкм через 3 місяці, 266,45±93,65 мкм через 6 місяців, а потім незначно підвищилася до 268,4±43,5 мкм до 12-місячної позначки). Таким чином, CCT залишалася стабільною протягом усього періоду лікування, зберігаючи значення, порівнянне з вихідним рівнем (483,46±102,54 мкм). Значне зменшення центральної товщини сітківки та центральної товщини хоріоїдеї, а також покращення BCVA спостерігалося в групі комбінованої терапії протягом 6- та 12-місячних періодів спостереження порівняно з групою монотерапії бролуцизумабом. Ці ефекти були пов'язані з резорбцією субретинальної рідини в результаті оклюзії неоваскулярної мембрани.*

Висновок. *Включення фотодинамічної терапії (ФДТ) з фотосенсибілізатором на основі хлорину е6 до схеми лікування пахіхоріоїдної неоваскулопатії (ПНВ) призводить до відновлення анатомічних та функціональних параметрів і зменшує рецидиви захворювання у пацієнтів з ПНВ.*

Ключові слова: *пахіхоріоїдна неоваскулопатія, вікова макулярна дегенерація, фотодинамічна терапія, центральна товщина сітківки, центральна товщина хоріоїдеї.*

Introduction

Pachychoroid neovasculopathy (PNV), first described by Pang and Freund, is a maculopathy characterized by choroidal neovascularization (CNV) occurring in areas of choroidal thickening and dilated choroidal vessels. PNV is considered part of the so-called "pachychoroid" spectrum disorders, which are believed to arise from a pathologically congested choroidal vascular network, and it has been recently proposed that they represent a pathophysiological continuum [1]. This is a rarely encountered subtype of neovascular age-related macular degeneration (nAMD), characterized by dilation of Haller's layer vessels, thinning of the choriocapillaris layer, and type 1 choroidal neovascularization, which can now be differentiated owing to the use of optical coherence tomography (OCT) angiography mode. In the case of neovascular AMD, leakage of dye from pathological new vessels, into retinal structures appears as hyperfluorescence, which increases in intensity and extension throughout the examination duration. This leakage is classified by its location (subfoveal, juxtafoveal, or extrafoveal) and by its features (classic, occult, or mixed) [2]. The prevalence of PNV reaches up to 46% among all AMD cases in Asian populations and up to 13% in Caucasians. The chronic, progressive nature of the disease can have a significant impact on patients' quality of life, imposing substantial time burden, limiting their ability to perform day-to-day tasks and have a significant emotional impact [3]. To assess the morphometric parameters of the retina, an optical coherence tomograph with angiography is used in such patients. Optical coherence tomography includes obtaining a macular map with further ex-

traction from it of indicators of central retinal thickness (CRT). In addition, the presence of any type of fluid: fluid under retinal pigment epithelium (RPE) or intraretinal fluid (IRF) is determined by reviewing all structural scans of the macular map [4]. The identification of PNV via OCT has become more precise recently due to advancements in OCT technology, transitioning from time-domain to Fourier-domain systems, including spectral-domain (SD-OCT) and swept-source (SS-OCT) OCT, offering higher resolution and improved depth and eye-tracking capabilities. Subsequently, PNV has been classified into two angiographic subtypes: polypoidal CNV (type 1), located beneath the RPE, and typical PNV (type 2), with the latter more commonly observed in Chinese populations. Both subtypes are characterized by the presence or absence of feeder vessels, which are typically observed in type 1, where vascular networks resemble rakes or umbrellas. For example, the configuration of type 1 may represent a variant of AMD, whereas type 2 is more often a distinct disease entity [5]. According to recent observations, in the Asia-Pacific region, polypoidal CNV is found in 50% of patients with neovascular AMD, a prevalence significantly higher than in Caucasians, where it accounts for approximately 10–20% of nAMD cases [6]. It has also been established that drusen are less frequently detected in eyes with polypoidal CNV compared to eyes with typical nAMD. Some authors have hypothesized that polypoidal CNV may develop against a pachychoroid background, as opposed to a drusen-related one. According to this theory, both polypoidal CNV and typical PNV lie within the pachychoroid spectrum, with PNV possibly being a precursor lesion that evolves into polypoidal CNV [7]. With advances in choroidal imaging, differences in choroidal characteristics have been noted among patients with type 1 neovascularization. Fung described a subgroup of patients with type 1 neovascularization whose clinical and imaging findings aligned more with chronic central serous choroid retinopathy CSC than with AMD. Increased choroidal thickness, absence of drusen, and younger age were key features differentiating this group from nAMD patients. Notably, Fung's study established a clear temporal sequence with CSC preceding the development of type 1 neovascularization (mean interval: 139 months), confirming the pathogenic continuum. The authors also emphasized that this type of neovascularization should be distinguished from that seen in typical nAMD [8]. It is important to note that primary treatments for CSC include photodynamic therapy (PDT), subthreshold micropulse laser, and oral eplerenone or aldosterone, whereas intravitreal administration of anti-vessels endothelial growth factor (anti-VEGF) agents remains the standard for treating nAMD. PDT can prevent leakage and improve visual function in CSC patients compared to anti-VEGF therapy or observation. However, anti-VEGF therapy has proven superior to PDT in preventing leakage and improving visual function in nAMD patients. When patients with nAMD are misdiagnosed as having CSC, micropulse laser treatment may delay nAMD therapy and promote disease progression [9,10]. Subsequently, the origin of type 1 neovascularization was described in patients with other pachychoroid disorders. Pang and Freund described the development of type 1 neovascularization in three eyes with pachychoroid pigment epitheliopathy (PPE)-related changes and introduced the term "PNV" to define this condition [11]. A hallmark of PNV is the presence of type 1 neovascularization, appearing on OCT as a shallow, irregular RPE detachment from Bruch's membrane, forming a "double-layer sign" over pachyvessels [12]. The presence of heterogeneously hyperreflective material beneath the RPE also suggests sub-RPE neovascularization. It is noteworthy that areas of type 1 neovascularization spatially correlate with pachychoroid features [13]. Autofluorescence changes may reveal alterations in the RPE over pachyvessels. Neovascularization is generally confirmed by leakage on fluorescein angiography (FA), manifesting as late leakage of an undetermined source and corresponding late staining resembling a "plaque." Although similar angiographic features may appear in chronic CSC due to diffuse RPE dysfunction and choroidal hyperpermeability, eyes with PNV typically lack classic serous macular detachment or characteristic descending gravitational tracts seen in chronic CSC [4,8]. These differences may help identify the source of subretinal fluid, whether due to PNV or CSC. With the advent of OCT angiography, diagnosing and confirming neovascularization has become easier in suspected cases of pachychoroid neovascularization. Neovascularization may be noninvasively identified on structural OCT as a tangled signal flow network between the RPE and Bruch's membrane, corresponding to a flat, irregular RPE detachment. Eyes with pachychoroid spectrum features and flat, irregular RPE detachment on SD-OCT should be further evaluated using OCTA to detect potential neovascular tissue. AMD is a progressive disease of the macula and the third major cause of blindness worldwide. If not treated appropriately, AMD can progress to involve both eyes. Until recently, the treatment options for AMD have been limited, with photodynamic therapy (PDT) the mainstay of treatment. Although PDT is effective at slowing disease progression, it rarely results in improved vision. Several therapies have been or are now being developed for neovascular AMD, with the goal of inhibiting VEGF. At present, established therapies have met with great success in reducing the vision loss associated with neovascular AMD, whereas those still under investigation offer the potential for further advances. In AMD patients, these therapies slow the rate of vision loss and in some cases increase visual acuity. Although VEGF-inhibitor therapies are a milestone in the treatment of these disease states, several concerns need to be addressed before their impact can be fully realized [14]. Since their initial approval, anti-VEGF treatment regimens have been adapted by physicians to meet patients' needs and healthcare resource availability. It is identified and described that the growing body of evidence supporting the effectiveness of anti-VEGF therapy for the

treatment of nAMD in routine clinical practice [15]. Currently, the main treatments for PNV are PDT, intravitreal injections of angiogenesis inhibitors, or their combination [3, 4, 8, 9]. PDT uses photosensitizers (PSs, non-toxic dyes) that are activated by absorption of visible light to initially form the excited singlet state, followed by transition to the long-lived excited triplet state. This triplet state can undergo photochemical reactions in the presence of oxygen to form reactive oxygen species (including singlet oxygen) that can destroy cancer cells, pathogenic microbes and unwanted tissue. The dual-specificity of PDT relies on accumulation of the PS in diseased tissue and also on localized light delivery. Tetrapyrrole structures such as porphyrins, chlorins, bacteriochlorins and phthalocyanines with appropriate functionalization have been widely investigated in PDT, and several compounds have received clinical approval [16]. According to multicenter studies EVEREST and EVEREST II, combination therapy involving PDT with the photosensitizer verteporfin and intravitreal injections of the angiogenesis inhibitor brolucizumab is the most effective for closing neovascular membranes, improving visual acuity, and reducing central retinal thickness (CRT) in PNV patients [10, 11]. In Uzbekistan, verteporfin is not yet approved for clinical use. Domestic researchers have conducted experimental and clinical studies proving the efficacy and safety of chlorin-based photosensitizers in ophthalmology. The only currently available photosensitizer is the trisodium salt of chlorin e6, which has demonstrated high efficacy in treating pachychoroid neovasculopathy [16]. No studies have been found in the literature regarding the use of PDT with chlorin e6-based photosensitizers in combination with angiogenesis inhibitors for PNV.

Objective of the study: To compare clinical and structural outcomes of combination therapy (anti-VEGF + PDT) versus anti-VEGF monotherapy in patients with pachychoroid neovasculopathy during 12-month follow-up.

Material and Methods

In our prospective study, 64 patients (74 eyes) with pachychoroid neovasculopathy (PNV) were enrolled, including 28 men and 36 women, with a mean age of 56.2 ± 6.0 years. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee for Medical Research of the Republic of Uzbekistan. Written informed consent was obtained from all patients prior to inclusion in the study. Inclusion criteria were confirmed diagnosis of pachychoroid neovasculopathy (PNV); absence of previous intravitreal anti-VEGF therapy in the study eye; age > 18 years; ability to comply with study protocol and follow-up schedule. Exclusion criteria were post-thrombotic retinopathy; diabetic retinopathy; inflammatory or degenerative ocular diseases; ocular trauma; autoimmune or syndromic ocular disorders; congenital ocular anomalies; hypersensitivity to brolucizumab or any component of the drug. Follow-up duration was 12 months.

All patients underwent standard ophthalmic examinations, including visometry with the measurement of best-corrected visual acuity (BCVA), tonometry, perimetry, A-scan and B-scan ultrasonography. This was followed by a comprehensive set of specialized ophthalmological procedures.

Morphometric parameters of the retina and choroid were assessed using the DRI OCT Triton plus swept-source OCT system with angiography (Topcon, Japan; Ver. 10.13), equipped with Swept-source 3D macula enhanced-depth imaging. Four SS-OCT protocols were performed for each subject and repeated three times: 3D raster scanning of the optic disc and macula (6 × 6 mm), radial scanning, and linear scanning. Automated measurements were performed using segmentation software. Repeatability was assessed using intraclass correlation coefficients (ICC). A macular thickness map was obtained, and central retinal thickness (CRT) was extracted. The presence of intraretinal fluid (IRF), subretinal fluid (SRF), and sub-RPE fluid was determined by reviewing all B-scans. IRF was defined as hyporeflective round cavities within the neurosensory retina in at least one cross-section. SRF was defined as hyporeflective space between the neurosensory retina and the RPE. Sub-RPE fluid was defined as hyporeflective space between Bruch's membrane and the RPE.

Examinations were performed prior to treatment and at designated intervals: 1, 3, 6, and 12 months from the beginning of therapy.

Patients were divided into two groups: the main group (40 eyes) and the control group (34 eyes). The main group included 34 patients (40 eyes), with baseline central retinal thickness (CRT) of 410.26 ± 113.48 μm and central choroidal thickness (CCT) of 485.89 ± 102.65 μm. The control group included 30 patients (34 eyes), with CRT of 405.89 ± 102.65 μm and CCT of 483.46 ± 102.54 μm (Fig. 1).

Patients in the main group received the following combined regimen: one intravitreal injection of 6 mg brolucizumab at baseline, followed by one session of photodynamic therapy (PDT) with a chlorin e6-based photosensitizer 48 hours later. During follow-up, additional brolucizumab injections were administered on a pro re nata (PRN) basis if OCT/OCT-A signs of disease activity (intraretinal/subretinal fluid, increase in CRT, or CNV reactivation) were detected. Repeat PDT was not included in the study protocol. Patients in the control group received three loading intravitreal injections of 6 mg brolucizumab at 4-week intervals, followed by PRN injections using the same retreatment criteria.

Photodynamic therapy was performed using (chlorin e6–based photosensitizer) at a standard dose of 6 mg/m² of body surface area, administered intravenously over 10 minutes. PDT was performed 48 hours after intravitreal brolucizumab injection to reduce neovascular activity and minimize exudative complications. Laser irradiation was delivered at 662 nm, energy density 50 J/cm², with a spot

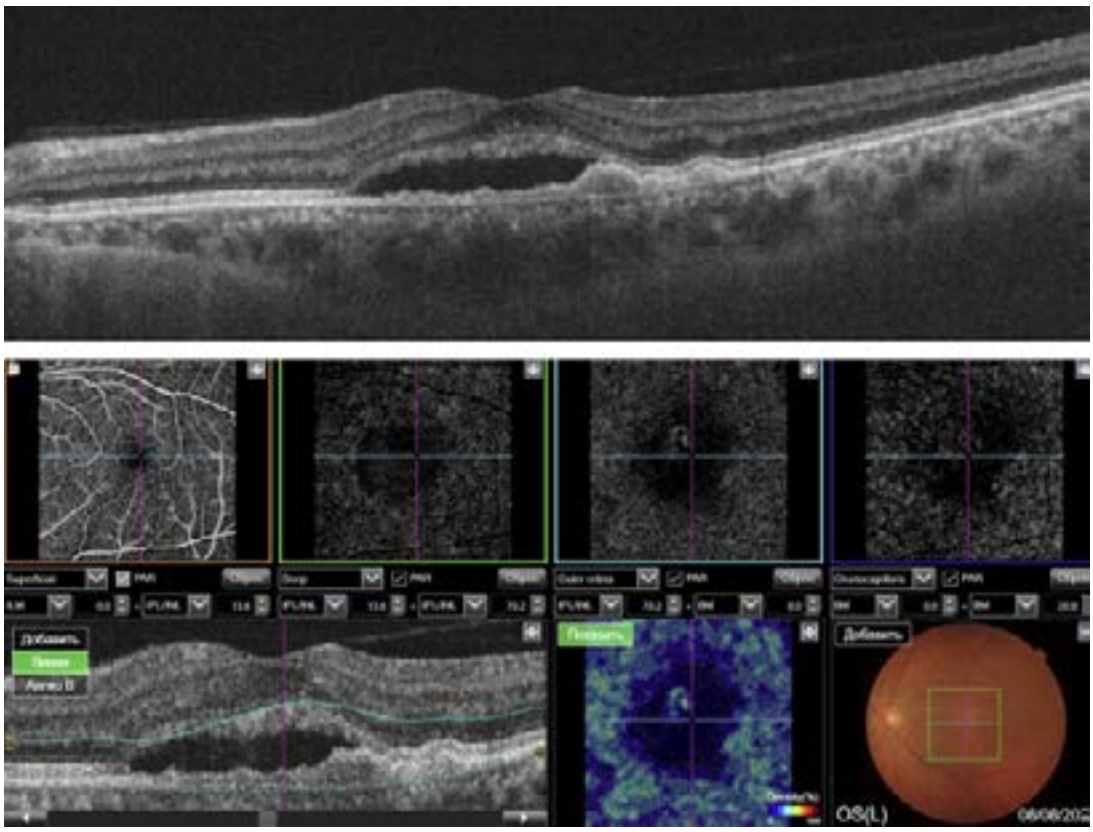

Fig.1. Results of OCT angiography before the use of anti-VEGF therapy (En-Face and transverse scan). The patient's best corrected visual acuity is OD 0.2.

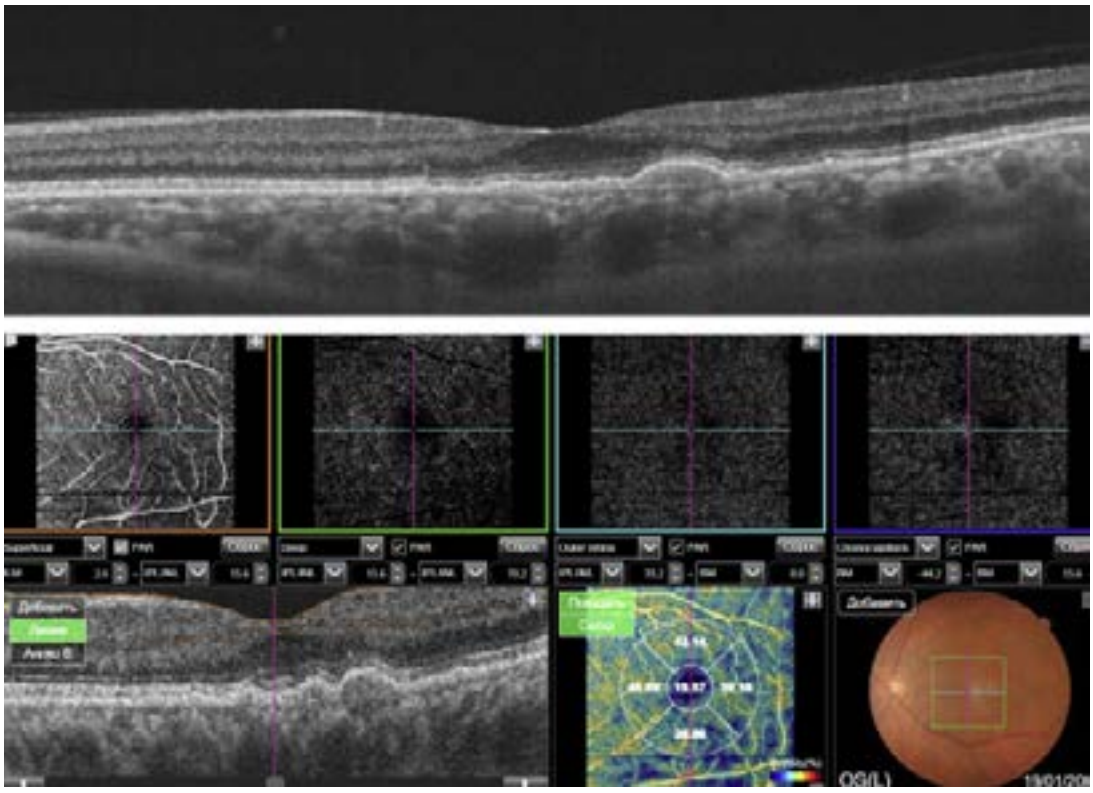

Fig. 2. Results of OCT angiography after 12 months of the use of anti-VEGF therapy (En-Face and transverse scan). The patient's best corrected visual acuity is OD 0.4.

size corresponding to the neovascular membrane plus a 500-μm safety margin.

Repeat PDT was not included in the study protocol. In cases of recurrence, patients were withdrawn from the study and treated individually outside the protocol, and relapse frequency was recorded.

Primary outcomes of the treatment were: change in best-corrected visual acuity (BCVA); change in central retinal thickness (CRT). Secondary outcomes were: change in central choroidal thickness (CCT); presence or resolution of intraretinal fluid, subretinal fluid, and sub-RPE fluid on OCT; rate of disease recurrence; number of injections/PDT procedures during follow-up; safety outcomes, including ocular and systemic adverse events (Fig. 2).

For statistical data processing, MedCalc 18.4.1 (MedCalc Software, Belgium) was used. Data are presented as mean ± standard deviation. One-way repeated-measures ANOVA was applied to evaluate the significance of changes in visual acuity before treatment and after three injections. Differences were considered statistically significant at $p < 0.05$.

Results

In the main group, BCVA increased moderately from 0.28 ± 0.14 at baseline to 0.38 ± 0.23 at the 12-month follow-up, whereas in the control group it remained relatively stable, measuring 0.31 ± 0.26 at month 1 and 0.35 ± 0.24 at month 12 (Table 1, Fig 3).

Baseline characteristics (age, BCVA, CRT, and CCT) did not differ significantly between the groups (Table 1).

Improvement in functional outcomes was accompanied by anatomical improvements: a reduction in central retinal thickness (CRT) from 410.26±113.48 μm to 262.46±146.40 μm at the 12-month follow-up, confirmed by the resorption of subretinal fluid (SRF) and a decrease in retinal pigment epithelium (RPE) detachments. Similar increases in choroidal thickness, dilated Haller's layer vessels, and thinning of the choriocapillaris were observed at the sites of type 1 choroidal neovascularization. A significant reduction in central choroidal thickness (CCT) was noted—from 485.89±102.65 μm to 413,21±96,23 μm after 1 month, 413,91±92,25 μm after 3 months, 414,21± 106,23 μm after 6 months, 415,30±108,64 μm by the end of the monitoring period (Fig 3.). In the control group, improvement in BCVA was less pronounced (0.31±0.26 before treatment and 0.35±0.24 at 12 months). Changes in morphological parameters occurred early: CRT was reduced by the first month of observation (from 405.89±102.65 μm before therapy to 267,35± 43,65 μm after 1 month, 266,45± 93,65 μm after 3 months, 266,45± 93,65 μm after 6 months, followed by a slight raise up to 268,4±43,5μm by the 12-month mark. Therefore, CCT remained stable throughout the treatment period, maintaining a value comparable to baseline (483.46 ± 102.54 μm). This suggests that the positive anatomical and functional response was achieved during the "loading dose" phase—three intravitreal injections of brolucizumab at 4-week intervals—followed by regression over time. It should be emphasized that in some cases in both the main and control groups, relapses were observed by the third month, with reaccumulation of CRT and CCT, subretinal hemorrhages, and the need for additional treatment.

When comparing the main and control groups, CRT and CCT values at months 6 and 12 were lower in the main group than in the control group. Thus, adding PDT with chlorin e6 to the PNV treatment regimen led to improved anatomical and functional outcomes by month 6, with sustained effects through month 12. The reduction in CCT, corresponding with improved BCVA and decreased CRT in the combination therapy group, indicates the pathogenetic validity of PDT in PNV treatment. PDT, acting on abnormal choroidal vessels involved in the disease process, reduces their activity. Meanwhile, anti-angiogenic therapy promotes SRF resorption. Therefore, combination therapy provides superior anatomical and functional outcomes compared to brolucizumab monotherapy in PNV patients at the 6- and 12-month follow-ups.

During the 12-month follow-up period, patients in the main group received one intravitreal brolucizumab injection and one PDT session. Patients in the control group received three loading injections of brolucizumab. At 12 months, CRT and CCT values in the main group remained lower than those in the control group. Thus, inclusion of PDT with chlorin e6 resulted in significant anatomical and

Table 1. Baseline values of the parameters studied in patients before treatment

Parameter	Main group (combined therapy)	Control group (brolucizumab monotherapy)	p-value
Number of patients, n	34	30	-
Number of eyes, n	40	34	-
Age, years (M ± SD)	56.2 ± 4.0	58.4 ± 6.0	0.074
Best-corrected visual acuity (BCVA)	0,28 ± 0,14	0,31 ± 0,26	0.55
Central retinal thickness (CRT), μm (M ± SD)	410.26 ± 113.48	485.89 ± 102.65	0.004
Central choroidal thickness (CCT), μm (M ± SD)	405.89 ± 102.65	483.46 ± 102.54	0.002

Notes: BCVA – best-corrected visual acuity; CRT – central retinal thickness; CCT – central choroidal thickness; SD – standard deviation.

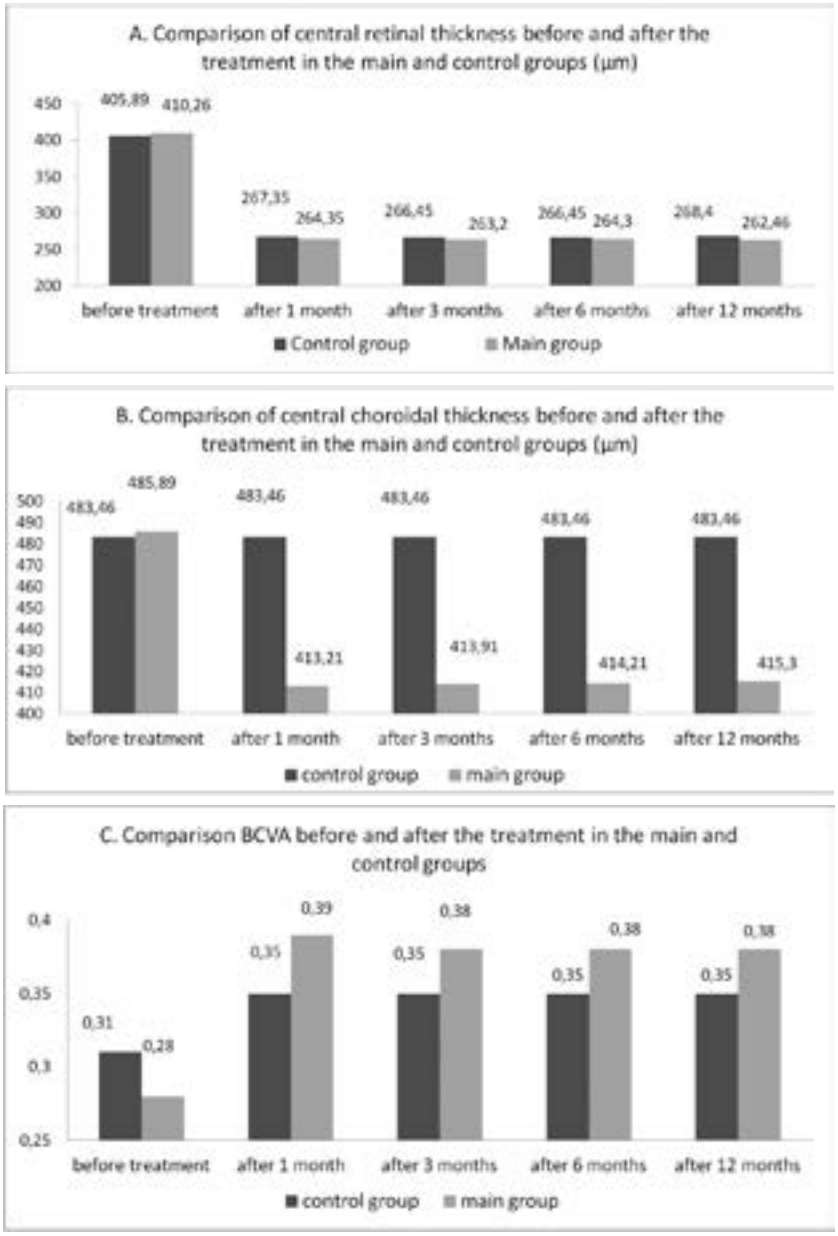

Fig. 3. Comparison of the central retinal thickness (A), central choroidal thickness (B), Best corrected visual acuity (C) before and after the treatment in the main and control groups (μm).

functional improvement by month 6 and stability of outcomes up to 12 months.

No severe ocular or systemic complications related to therapy were detected.Some patients in both groups developed recurrence by month 3 with CRT/CCT increase and occasional subretinal hemorrhage, requiring additional treatment. These events reflected disease activity rather than treatment-related complications.

Discussion

A significant reduction in central retinal thickness and central choroidal thickness, as well as improvement in BCVA, was observed in the combination therapy group over the 6- and 12-month follow-up periods compared to the brolucizumab monotherapy group. These effects were associated with the resorption of subretinal fluid as a result of neovascular membrane occlusion. The inclusion of photodynamic therapy (PDT) with a chlorin e6-based photosensitizer in the treatment regimen for pachychoroid neovasculopathy (PNV) leads to the restoration of anatomical and functional parameters and reduces the recurrence of the disease in patients with PNV.

The findings of the present study are consistent with current concepts of pachychoroid-driven neovascular activity and its responsiveness to adjunctive vascular-targeted therapies described in recent reviews of the pachychoroid spectrum [11, 12]. The observed post-PDT reduction in choroidal thickness parallels prior reports linking therapeutic vascular remodeling with decreased choroidal hyperperfusion and suppression of type 1 neovascularization

[9, 11]. These findings complement existing evidence that optimized anti-VEGF strategies alone may not fully address the pachychoroid component of disease, thereby supporting the rationale for combination approaches [2, 8, 15]. From a mechanistic perspective, the use of chlorin e6–based photosensitizers is consistent with established photodynamic principles demonstrating selective vascular occlusion and sustained inhibition of pathological neovascular complexes [16]. Thus, incorporation of PDT into combined therapy for PNV not only improves anatomical and functional outcomes by month 6 but also ensures sustained treatment efficacy for up to 12 months.

Author Contributions

Yu.A.F.: Conceptualization, Analysis, Project Administration, K.M.Kh.: Conceptualization, Writing – review & editing; R.D.A.: Data collection and analysis, Writing – original draft; Kh.U.Sh.: Writing – original draft; Writing – review & editing, Formal Analysis. Kh.Z.A.: Data collection and analysis, Formal Analysis. All authors read and approved the final manuscript.

Disclaimers

The views expressed in this article are solely those of the authors and do not necessarily represent the official position of their affiliated institution or any funding source.

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Conflict of Interest

The authors declare that they have no conflicts of interest related to this work.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request. Due to institutional policy and patient confidentiality, raw data are not publicly available.

Abbreviations

PNV – pachychoroid neovasculopathy, PDT – photodynamic therapy, SRF – subretinal fluid, RPE – retinal pigment epithelium, CNV – choroidal neovascularization, nAMD – neovascular age-related macular degeneration, OCT – optical coherence tomography, SD-OCT – spectral-domain OCT, SS-OCT – swept-source OCT, CSC – central serous chorioretinopathy, anti-VEGF – anti-Vascular Endothelial Growth Factor.

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