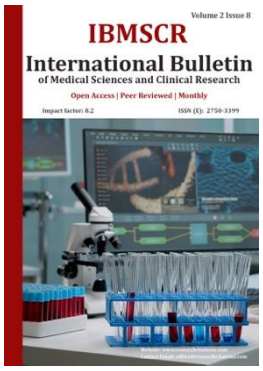

STRUCTURAL AND FUNCTIONAL CHANGES AND THERAPEUTIC EFFICACY IN COMORBID PRIMARY OPEN-ANGLE GLAUCOMA AND DRY AGE-RELATED MACULAR DEGENERATION

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Abstract.

Objective. To conduct a comprehensive assessment of morphological and functional changes in patients with isolated and comorbid forms of primary open-angle glaucoma (POAG) and dry age-related macular degeneration (AMD), as well as to compare the effectiveness of different therapeutic strategies.

Materials and Methods. The study included 184 patients (326 eyes) aged 60 to 84 years. Patients were divided into three groups: isolated POAG, dry AMD, and combined POAG + AMD. In patients with the comorbid form, the effectiveness of three treatment regimens was additionally evaluated: prostaglandins, brimonidine, and brimonidine combined with the antioxidant AREDS 2 formulation. Assessment was performed using optical coherence tomography (OCT), OCT angiography, automated perimetry, and multifocal electroretinography (mfERG), followed by statistical data analysis.

Results. The comorbid form of the disease was associated with more pronounced thinning of the retinal nerve fiber layer, ganglion cell layer, macula, and choroid, as well as deterioration of visual field parameters (MD and VFI). The most favorable outcomes in terms of preservation of morphofunctional parameters and the lowest incidence of adverse effects were observed in the combination therapy group (brimonidine + AREDS 2), where stabilization of visual function was achieved in 87% of eyes.

Conclusions. The coexistence of POAG and dry AMD leads to accelerated progression of neurodegeneration. Combination therapy incorporating neuroprotective and antioxidant components demonstrates an advantage in slowing structural deterioration and preserving visual function in patients with this form of comorbid ophthalmic pathology.

Keywords: glaucoma, age-related macular degeneration, neurodegeneration, combination therapy.

Introduction. The increasing proportion of elderly individuals in the general population is accompanied by a rising prevalence of chronic degenerative eye diseases. Among these, the leading causes of irreversible vision loss in individuals over the age of 60 remain primary open-angle glaucoma (POAG) and the dry form of age-related macular degeneration (AMD) [1,2]. Despite differences in pathogenesis, both conditions share common features: progressive damage to the neurosensory elements of the retina, impaired microcirculation, and gradual decline in visual function [3,4,5].

The coexistence of glaucoma and macular degeneration in a single patient is being diagnosed with increasing frequency. This comorbidity presents diagnostic and therapeutic challenges, as it affects both the central and peripheral parts of the visual system [2,6,7]. It complicates the interpretation of visual field testing and optical coherence tomography (OCT)

findings, increases the risk of underestimating disease progression, and necessitates a more nuanced approach to treatment selection.

Recent studies suggest that isolated approaches to glaucoma treatment may negatively impact choroidal blood flow, potentially worsening the course of macular degeneration. Conversely, the use of neuroprotective agents, such as α2-agonists, along with antioxidant therapy based on the AREDS2 formula, is considered a promising strategy for protecting both ganglion cells and photoreceptors in cases of combined pathology [1,8].

However, the available literature [4,9,10] still lacks comparative clinical studies evaluating the effectiveness of various therapeutic strategies in patients with coexisting POAG and dry AMD. Additionally, the long-term dynamics of structural and functional parameters in this patient group, particularly as assessed by multifocal electroretinography (mfERG) and OCT angiography, remain insufficiently studied.

The aim of this study was to perform a comprehensive assessment of structural and functional changes in isolated and combined forms of POAG and dry AMD, and to compare the effectiveness of three therapeutic approaches with a focus on neuroprotection and macular preservation.

Materials and Methods. This clinical study was conducted as a prospective, comparative-analytical observational investigation with elements of randomization and long-term dynamic follow-up. The total duration of observation was 18 months. The primary objective was to perform a comprehensive assessment of structural and functional changes in both isolated and coexisting forms of POAG and dry AMD, emphasizing the identification of risk factors for disease progression and the evaluation of different therapeutic strategies.

The study included 184 patients (326 eyes) aged between 60 and 84 years (mean age: 70.1±5.9 years). Based on confirmed diagnoses, participants were assigned to one of three groups: Group 1 consisted of patients with isolated POAG (n = 48, 92 eyes), Group 2 included patients with isolated dry AMD (n=46, 80 eyes), and Group 3 included patients with both POAG and dry AMD (n=90, 154 eyes). Group 3 was further subdivided into three therapeutic subgroups: 3a – prostaglandin therapy; 3b – α2-agonist therapy (brimonidine); and 3c – combined therapy with added antioxidant support according to the AREDS2 formula.

Inclusion criteria required participants to be over 60 years of age, have a stable disease course, and have no signs of neovascular AMD or any other ocular diseases affecting the macula or optic nerve. Patients who had undergone ocular surgery within the last 6 months were excluded. Exclusion criteria also encompassed cases of secondary glaucoma, significant systemic or neurological disorders, and any inability to adhere to scheduled follow-up examinations.

All participants underwent a standardized ophthalmological assessment, which included best-corrected visual acuity (BCVA), intraocular pressure (IOP) measurement using Goldmann applanation tonometry, automated perimetry, and OCT to assess retinal nerve fiber layer (RNFL) thickness, ganglion cell complex (GCC), and macular and choroidal structures. OCT angiography (OCTA) was employed to evaluate macular and peripapillary blood flow, and electroretinography (ERG) was used to assess central retinal function. Additional methods included fundus photography and quality of life evaluation using the NEI VFQ-25 questionnaire.

Statistical analysis was performed using SPSS v.27.0 and GraphPad Prism v.10.0. Analytical methods included descriptive statistics, Student's t-test, ANOVA, as well as

correlation and regression analyses. A p-value of less than 0,05 was considered statistically significant.

Results and Discussion. Analysis of demographic characteristics revealed that age and sex distribution were statistically comparable between groups (p=0.432 and p=0.509, respectively), thus excluding these factors as potential confounders. In contrast, mean intraocular pressure (IOP) was significantly higher in the groups with glaucoma (Groups 1 and 3) compared to the isolated AMD group, consistent with expected pathophysiological differences. The lowest best-corrected visual acuity (BCVA) was observed in the combined pathology group, indicating a more pronounced functional deficit in this patient cohort (tab. 1).

Table 1.

Demographic and clinical characteristics of patients.

Parameter	Group 1 (POAG) (n=48)	Group 2 (AMD) (n=46)	Group 3 (POAG + AMD) (n=90)	*p*
Mean age (years)	69,6±5,8	70,4±5,6	70,2±6,1	*0,432*
Female, n (%)	26 (54,2%)	30 (65,2%)	53 (58,9%)	*0,509*
Male, n (%)	22 (45,8%)	16 (34,8%)	37 (41,1%)	–
Mean IOP (mmHg)	22,4±2,2	15,7±1,7	22,3±2,3	*<0,05*
BCVA (best-corrected visual acuity)	0,73±0,11	0,59±0,11	0,48±0,13	*<0,05*

OCT and functional test results revealed that patients with combined POAG and dry AMD exhibited significantly greater thinning of both the RNFL and the GCC compared to those with isolated forms of either disease (p<0,05). Additionally, a reduction in macular and choroidal thickness was observed, indicating multifactorial degeneration affecting both central and peripheral regions of the retina. From a functional perspective, the comorbid group demonstrated a notable decline in visual field index (VFI: 77,9±9,1%) and a more pronounced mean deviation (MD: −5,7±2,2 dB), underscoring an accelerated progression of visual impairment when both pathologies coexist (tab. 2).

Table 2.

OCT parameters and functional measures across the three groups.

Parameter	POAG (92 eyes)	AMD (80 eyes)	POAG + AMD (154 eyes)	*p*
RNFL thickness (μm)	84,6±9,5	96,4±7,1	78,8±10,2	*<0,05*
GCC thickness (μm)	76,1±7,2	82,3±6,3	69,4±8,0	*<0,05*
Macular retinal thickness (μm)	263,2±14,8	249,6±13,7	236,2±16,9	*<0,05*
Central choroidal thickness (μm)	202,1±23,7	186,1±21,2	169,3±22,7	*<0,05*
Mean Deviation (MD, dB)	−3,0±1,7	−2,1±1,5	−5,7±2,2	*<0,05*
Visual Field Index (VFI, %)	89,2±6,5	91,8±5,3	77,9±9,1	*<0,05*

In the group of patients with comorbid ophthalmic pathology, a comparative assessment of the effectiveness of three therapeutic approaches was conducted. The most pronounced reduction in IOP was observed in the subgroups receiving brimonidine, either as monotherapy or in combination with AREDS2-based antioxidant support. Notably, the combined therapy

demonstrated the least decline in GCC and macular thickness over the 18-month follow-up period ($p<0,05$), along with better preservation of functional parameters. The proportion of eyes with stable VFI (<5% change) was 87% in subgroup 3c, compared to 60% in the prostaglandin-only group (3a), supporting the potential neuroprotective and vasculoprotective benefits of the combined treatment approach (tab. 3).

Table 3.

Treatment effectiveness in the POAG + AMD group (Group 3).

Parameter	3a: Prostaglandins (n=30)	3b: Brimonidine (n=30)	3c: Brimonidine + AREDS2 (n=30)	*p*
IOP reduction (mmHg)	−3,2 ± 1,3	−4,1 ± 1,1	−4,3 ± 1,0	*0,0014*
Change in GCC thickness (μm) over 18 months	−5,9 ± 1,8	−3,5 ± 1,4	−2,6 ± 1,5	*<0,05*
Change in macular retinal thickness (μm)	−13,0 ± 3,5	−8,1 ± 3,0	−5,3 ± 2,9	*<0,05*
Progression of MD over 18 months (dB)	−1,8 ± 0,8	−1,0 ± 0,6	−0,7 ± 0,5	*<0,05*
Eyes with stable VFI (<5% change), %	60%	77%	87%	*0,0078*

Thus, the obtained data demonstrate that patients with comorbid POAG and dry AMD represent a clinically vulnerable group, characterized by synergistic progression of structural and functional deterioration. The use of combined therapy involving an α2-agonist and AREDS2-based antioxidant support enables greater stabilization of visual function and structural parameters, while offering a more favorable safety profile.

Conclusion. The results of this study demonstrated that the combination of POAG and dry AMD is associated with more pronounced morphofunctional impairments than either condition alone. Patients with comorbid ophthalmic pathology exhibited significant thinning of the RNFL, GCC, macular region, and choroid, as well as worsened visual field parameters, indicating a synergistic pattern of neurodegeneration in the presence of dual pathology. The most favorable outcomes in terms of preserving structural integrity and visual function were achieved with combined therapy that included an α2-agonist and AREDS2-based antioxidant supplementation. This regimen showed superior VFI stabilization and a lower incidence of adverse effects compared to prostaglandin monotherapy or α2-agonist monotherapy.

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