

IMPROVING OF TREATMENT OF NON-EXUDATIVE AGE-RELATED MACULAR DEGENERATION

Goal of research: Study of influence of the medotilin on clinical and functional conditions of eye in patients with non-exudative age-related macular degeneration (AMD).

Materials: Results of treatment of 68 patients (122 eyes) with non-exudative age-related macular degeneration (AMD). 2 groups were formed: Group 1 (control) - 34 patients (60 eyes) who received standard treatment; and the Group 2 (basic) - 34 patients (62 eyes) who received standard treatment in addition to medotilin.

Methods: Visometry, tonometry, computer perimetry, electroretinography (ERG) and color Doppler imaging (CDI). All studies were carried out before and after 1, 3 and 6 months after treatment.

Results: After treatment in the main group, in the first 3 months 95% of patients (59 eyes) showed a significant improvement of main functions of the eye. By the 6th month, 84% of patients (52 eyes) reported decline down to the original level, and 16% of cases (10 eyes) were stable and exceeded the data before the treatment. When registering macular ERG 1 month after treatment, the study group showed a significant improvement of figures, which remained consistently high also by the 3rd month of observation. By the 6th month of observation, figures declined slightly and came close to the original level. According to CDI, all patients of the main group recorded after treatment an increase in flows in vessels of the eye. Maximum peak increase of hemodynamic parameters were recorded by the 3rd month of observation. By the 6th month, the majority of patients in this group revealed regress of hemodynamic parameters, but at these, exceeded themselves in their capacity as such before treatment.

Conclusion: Medotilin is effective in treatment of non-exudative AMD and improves visual functions, confirmed by electroretinography and hemodynamics.

*E.N. BILALOV,
A.F. YUSUPOV,
SH.A. MUKHANOV*

*Tashkent Medical Academy,
JV "SIHATKO'Z" LLC,
Tashkent, Uzbekistan*

Keywords: Non-exudative age-related macular degeneration, medotilin, choline alfoscerate, electroretinography, color Doppler imaging, central artery of the retina, short posterior ciliary artery

Email: shavkat355[at]yandex(dot).com

Corresponding address: Tashkent Medical Academy 100109, Tashkent, Uzbekistan Farabi street 2

Citation (NLM): Bilalov EN, Yusupov AF, Mukhanov ShA. Improving of treatment of non-exudative age-related macular degeneration. Medical and Health Science Journal. 2017;18(1):14-20.
DOI: <http://dx.doi.org/10.15208/mhsj.2017.02>

Introduction

Age-related macular degeneration (AMD) is one of the most common eye diseases that threaten with significant reduction in vision, blindness and disability. The disease occurs in 25-40% of cases at the age of 40 years and older; in 58-100% of cases for patients older than 60 years [1-4,7]. AMD takes the third place among the all causes of blindness in the

second half of life after glaucoma and diabetic retinopathy; it is a leading cause of blindness and disability in developed countries [1,3-5,8]. Socio-medical significance of this pathology is caused by rapid loss of central vision loss and total disability. Actually, there are no effective ways of treatment and prevention of the disease. For the recent years, the AMD problem remains to be the most urgent one due to increase of lifespan and steady growth of atherosclerosis and associated pathology.

It's a well-known fact that general and local peripheral vascular diseases play primary importance in the development of AMD; they lead to deterioration of blood supply and trophic processes in the eye. In this connection, a series of studies [1,2,6,8] explore the effectiveness of various drugs in correction of eye blood flow in patients with non-exudative AMD. Hemodynamic study of eye plays significant role in determining the complex therapy including use of vasoactive drugs; these drugs have recently enjoyed a well-deserved attention of ophthalmologists.

Medotilin - nootropic and cholinomimetic with central action which contains active compound - Cholini alfosceras. Choline involved in biosynthesis of acetylcholine (one of the main mediators of neural stimulation) is released from the active compound of drug. Alfosceras component performs biological transformation into glycerophosphate, which is a precursor of phospholipids. Acetylcholine improves the transmission of nerve impulses, and glycerophosphate participates in the synthesis of phosphatidylcholine (phospholipid membrane) to improve the elasticity of membrane and function of receptors. In addition, the drug improves blood flow and increases metabolic processes in the central nervous system, activates reticular formation; it increases blood flow velocity of brain and contributes to normalization of spatiotemporal characteristics of spontaneous bioelectric activity of the brain.

Thus, the drug improves brain function, affecting the pathogenetic factors of involutive psychoorganic syndrome, affects synaptic - cholinergic neural impulse (neurotransmission) and plasticity of neuronal membrane improving the function of the receptors.

Feasibility of using of medotilin in ophthalmic practice is not pointed out in indications of the drug. In consideration of the foregoing, the National Ethics Committee of the Ministry of Health (MoH) of Uzbekistan (Order No.6 dated as of 25.08.2012) approved realization of clinical research of medotilin on a limited number of patients with degenerative and dystrophic diseases of eye.

Purpose

Sensitivity analysis of medotilin on clinical and functional performance of patient eyes with non-exudative AMD.

Materials and methods

We studied the results of treatment of 68 patients (122 eyes) (42 women and 26 men) with non-exudative age-related macular degeneration (AMD). Age of patients was from 41 to 82 years (averagely 56.4 ± 5.2). The observation period made 6 months. The following clinical forms of AMD were diagnosed in all patients according to classification of Klein et al. (The Wisconsin Age-Related Maculopathy Grading System) [5]: degeneration of pigment epithelium of retina - 70 eyes, retinal drusen - 46, geographic atrophy of pigment epithelium of retina - 6. Among concomitant diseases, 52 (83.8%) patients registered atherosclerosis, 47 (75.8%) - arterial hypertension, and diabetes found in 4 (5.9%) patients. Two groups were formed by the patients examined. Group 1 (control) made 34 patients (60 eyes) who received standard treatment (antioxidants and lutein-containing drugs). Group 2 (basic) made 34 patients (62 eyes) who received - beyond the standard treatment - medotilin by 1.0 g - 4 ml i.m. within 10 days.

In addition to conventional ophthalmic research methods, including visometry, tonometry, perimetry, all patients underwent optical coherence tomography (OCT), fluorescein angiography (FAG), electrophysiological study of eye - electroretinography (ERG), and color Doppler imaging (CDI). All studies were carried out before and after 1, 3 and 6 months after treatment. According to data of ERG, functional condition of outer layers of retina and pigment epithelium with the help of "Electroretinography" (MBN, Moscow), the electrophysiological diagnostic complex, was quantified. To register biopotential, ERG was recorded locally at red light, from macular area (local conical response).

To assess blood flow in vessels of eyeball and retrobulbar space, the CDI was used via multifunctional ultrasonic diagnostic apparatus VOLUSON 730 Pro of "Kretz" company, using a linear transducer with the frequency from 10 to 16 MHz. Based on CDI data, the functional condition of blood flow in central artery of retina (CAR) and short posterior ciliary arteries (SPCA) were assessed quantitatively and qualitatively. At the end of the study, spectrum of blood flow was recorded and its parameters were defined: maximum systolic velocity (Vs), end-diastolic velocity (Vd) and resistance index or peripheral resistance (RI).

Results and discussion

To evaluate the functional results of treatment with medotilin we examined performance of visual acuity (VA), central visual field (CVF), electroretinography and color Doppler imaging (Tables 1-3; Figures 1-2).

According to results of visometry in main group, improvement of acuity of vision in 85% cases was revealed. Before treatment the acuity of vision in patients of main group made 0.53 ± 0.04 , after 1 month from the treatment start - 0.67 ± 0.03 , after 3 months - 0.72 ± 0.02 ($p < 0.01$). By the 6th month, 84% of patients (52 eyes) revealed declines of acuity of vision down to original level, and 16% of cases (10 eyes) stayed stable and exceeded figures before treatment. With the patients in control group, by the 1st month of observation, improvement of acuity of vision was observed until 0.62 ± 0.06 , 3 months later this figure rose to 0.69 ± 0.03 ($p < 0.05$). Further observation revealed declines below the initial level.

The study results of CVF, patients of main group after 1 month obtained reduction of number of relative scotomata to 5.46 ± 0.35 , or 1.9 times the original one ($p < 0.05$). Positive figures were also registered to the 3rd month of observation with a decrease of relative scotomata to 4.52 ± 0.75 ($p < 0.01$). At a later stage, 16% of patients (10 eyes), registered stable result of treatment, and in 84% of cases figures came close to original data. Thus, the average number of relative scotomata by the 6th month made 9.87 ± 0.32 . In the control group, in early observations, the same results with relatively less positive data compared with main group were registered. However, by the 6th month of observation, an increase in number of relative scotomata is higher than before the treatment. Thus, we found that the use of medotilin positively effects on functional activity of retina in 16% of patients with non-exudative forms of AMD within 6 months, but in 84% - functional indicants of eye came close to original values. That is why, in order to stabilize the achieved result it is necessary to repeat the proposed treatment every six months.

Patients with AMD while registering macular ERG, registered decrease in amplitude of a- and b-waves relative to the norm. Thus, the average value of the amplitude of a- and b-waves before treatment made 1.89 ± 0.06 and 11.6 ± 0.1 mV. 1 month after treatment in the main group, the amplitude of the a-wave increased to 2.28 ± 0.04 , and the amplitude of b-wave up to 15.3 ± 0.2 mkV ($p < 0.05$) and after 3 months - up to 2.94 ± 0.05 and 17.1 ± 0.3 mkV, respectively ($p < 0.01$). By the 6th month of observation, figures declined slightly and came close to original level. In control group, the dynamics was positive by the 1st and 3rd month of observation ($p < 0.05$), and the decline in performance by the 6th month is lower the initial values.

FIGURE 1. INDICANTS OF VISUAL ACUITY DURING TREATMENT

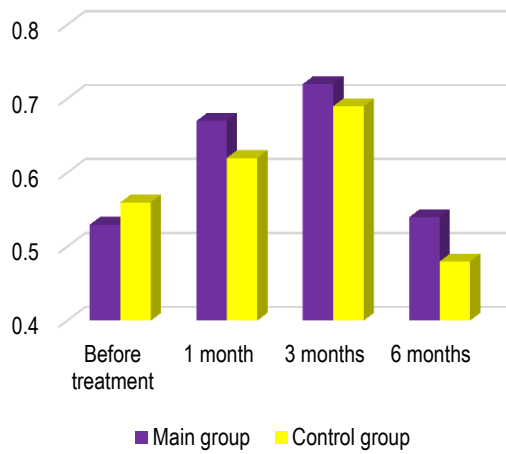


FIGURE 2. INDICANTS OF CENTRAL VISUAL FIELD DURING TREATMENT

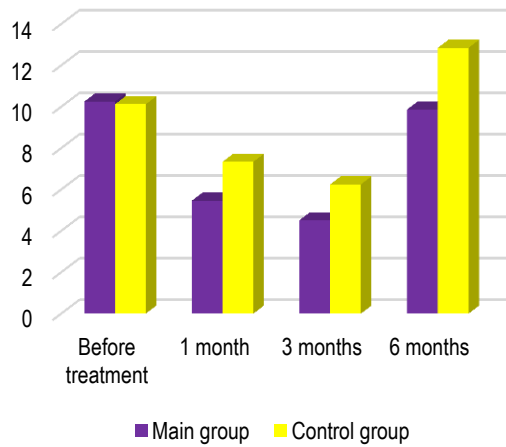


TABLE 1. CLINICAL-FUNCTIONAL INDICANTS OF EYE DURING TREATMENT

Follow-up period		Groups	Indicants of macular ERG	
			Amplitude of a-wave (mkV)	Amplitude of b-wave (mkV)
Before treatment		Main	1.89±0.06	11.6±0.1
		Control	1.90±0.05	11.2±0.2
After treatment	1 month	Main	2.28±0.04*	15.3±0.2*
		Control	2.18±0.03*	14.5±0.4*
	3 months	Main	2.94±0.05**	17.1±0.3**
		Control	2.35±0.05*	16.3±0.4*
	6 months	Main	1.94±0.08	11.9±0.4
		Control	1.78±0.07*	9.8±0.3*

Note: * - Differences were significant compared with the period before treatment (p<0.05). ** - Differences were significant compared with the period before treatment (p<0.01).

Thus, the results of treatment demonstrate a positive effect of medotilin on functional condition of pigment epithelium and outer layers of retina, in particular cone photoreceptors of its central zone, which can be evidenced by more accurate increase of figures of macular ERG on red color.

Decline of hemodynamic parameters before treatment took place in all patients with non-exudative AMD, which was evidence of deficiency of blood flow in ophthalmic artery system, central artery of retina and posterior ciliary arteries. This affirms important role of hemodynamic factor in pathogenesis of this disease. As a result of Doppler sonography, an intense reduction of peak systolic, end-diastolic blood flow velocity and increase of resistance index in CAR and SPCS in comparison with standard were revealed.

After treatment regimen, all patients were recorded increased flows in CAR and PSCA. With the patients of main group, maximum peak of increase of hemodynamic parameters were recorded by the 3rd month of observations: At that, maximum systolic velocity of blood flow increased 1.5 times in CAR (p<0.01) and 1.4 times in SPCA (p<0.01). Index of peripheral resistance was decreased from 0.91±0.02 to 0.71±0.03 (p<0.01) in the CAR and from 0.85±0.04 to 0.71±0.01 (p<0.01) in SPCA. By the 6th month, most patients in this group were revealed a regress of hemodynamic parameters, but thus the data exceeded in their capacity as such before the treatment.

TABLE 2. DYNAMICS OF BLOOD FLOW IN CAR IN PATIENTS WITH NON-EXUDATIVE AMD

Follow-up period		Groups	Indicants		
			Vs (cm/s)	Vd (cm/s)	RI
Before treatment		Main	9.6 ±1.6	1.3±0.06	0.91±0.12
		Control	9.4±1.5	1.4±0.05	0.9±0.11
After treatment	1 month	Main	12.7±1.2**	2.1±0.02**	0.77±0.15**
		Control	10.4±1.3*	1.8±0.04*	0.81±0.13*
	3 months	Main	14.3±1.9**	2.8±0.09**	0.71±0.14**
		Control	11.3±1.4*	2.1±0.05*	0.75±0.16*
	6 months	Main	10.5±1.6*	1.9±0.06*	0.8±0.16*
		Control	8.5±1.7*	1.3±0.05	0.95±0.17

Note: * - Differences were significant compared with the period before treatment (p<0.05). ** - Differences were significant compared with the period before treatment (p<0.01).

TABLE 3. DYNAMICS OF BLOOD FLOW IN SPCS IN PATIENTS WITH NON-EXUDATIVE AMD

Follow-up period	Groups	Indicants			
		Vs (cm/s)	Vd (cm/s)	RI	
Before treatment	Main	11.2±2.1	1.7±0.06	0.85±0.16	
	Control	11.5±1.2	1.8±0.08	0.86±0.12	
After treatment	1 month	Main	13.5±1.6*	3.6±0.09**	0.75±0.11*
		Control	12.5±1.9*	2.3±0.04*	0.81±0.13*
	3 months	Main	15.2±1.8**	4.1±0.05**	0.71±0.15**
		Control	13.2±1.5*	3.1±0.06**	0.79±0.16*
	6 months	Main	11.9±1.4*	2.3±0.06*	0.81±0.12
		Control	10.2±1.6	1.7±0.07	0.89±0.14

Note: * - Differences were significant compared with the period before treatment (p<0.05). ** - Differences were significant compared with the period before treatment (p<0.01).

Patients in control group also reported improvement of hemodynamic parameters until the 3rd month of observation; however data were slightly different with its intensity as compared with main group. Further observation of hemodynamics in this group showed declines of parameters below the original level.

Thus, after treatment regimen with medotilin, the improvement of hemodynamics in eye vessels was observed in all patients with non-exudative forms of AMD. The increase of maximum systolic and end-diastolic velocity of blood flow in CAR, SPCA and decrease of vaso-resistancy can be interpreted as an improvement in blood supply of choroid and eye retina.

It should be noted that the improvement in visual acuity, and positive results of indicants of computer perimetry after treatment with medotilin correlated with improvements in electroretinography and hemodynamics.

Conclusion

Medotilin is effective in treatment of non-exudative forms of age-related macular degeneration and improves visual function, confirmed by hemodynamic parameters and electroretinography.

Increase of speed of blood flow in arteries of eye after treatment regimen with medotilin indicates an improvement in blood supply to choroid and eye retina, which is a hopeful sign for prognosis of disease.

The inclusion of medotilin in the complex treatment of non-exudative age-related macular degeneration enhances the effectiveness of pharmaceutical treatment up to 6 months. In connection with this, the proposed course of treatment should be repeated every six months.

References

1. Bikbov MM, Fayzrakhmanov RR, Yarmukhametova YL. Age-related macular degeneration [Vozrastnaya Makulyarnaya Degeneratsuya]. Moscow: Ufa. 2013. 196p. Russian.
2. Gregori G, Wang F, Rosenfeld PJ, Yehoshua Z, Gregori NZ, Lujan BJ, Puliafito CA, Feuer WJ.

- Spectral domain optical coherence tomography imaging of drusen in nonexudative age-related macular degeneration. *Ophthalmology*. 2011;118(7):1373-1379.
3. Hartmann KI, Bartsch DU, Cheng L, Kim JS, Gomez ML, Klein H, Freeman WR. Scanning laser ophthalmoscope imaging stabilized microperimetry in dry age-related macular degeneration. *Retina*. 2011;31(7):1323-1331.
 4. Kiseleva TN, Lagutina YM, Kravchuk EA. Role of vasoactive drugs in the therapy of non-exudative age-related macular degeneration. *Refraction Surgery and Ophthalmology*. Moscow. 2006;6(2):41-45. Russian.
 5. Klein R, Moss SE, Surawicz TS. The Wisconsin age-related maculopathy grading system. *Ophthalmology*. 1991;98(7):1128-1133.
 6. Leuschen JN, Schuman SG, Winter KP, McCall MN, Wong WT, Chew EY, Hwang T, Srivastava S, Sarin N, Clemons T, Harrington M, Toth CA. Spectral-domain optical coherence tomography characteristics of intermediate age-related macular degeneration. *Ophthalmology*. 2013; 120(1):140-150.
 7. Monés J, Biarnés M, Trindade F, Arias L, Alonso, J. Optical coherence tomography assessment of apparent foveal swelling in patients with foveal sparing secondary to geographic atrophy. *Ophthalmology*. 2013;120(4):829-836.
 8. Yehoshua Z, Wang F, Rosenfeld PJ, Penha FM, Feuer WJ, Gregori G. Natural history of drusen morphology in age-related macular degeneration using spectral domain optical coherence tomography. *Ophthalmology*. 2011;118(2):2434-2441.