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COMPARATIVE ASSESSMENT OF THE STRUCTURAL AND FUNCTIONAL PARAMETERS OF THE OPTIC NERVE IN COMPLEX NEUROPROTECTIVE TREATMENT OF GLAUCOMATOUS OPTIC NEUROPATHY

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Abstract. Relevance. Glaucoma is a chronic progressive optic neuropathy with characteristic morphologic changes in the head of optic nerve and progressive death of retinal ganglion fibers with narrowing of the visual field. Thus, a search of a new direction of the drug therapy is needed because of the fact that hypotensive therapy is not completely effective. The most perspective of them is neuroprotection in combination with percutaneous electrostimulation and endonasal electrophoresis that protect neurons of the retina and nerve fibers of optic nerve from different damage factors. **Purpose of the study.** To assess structural and functional changes in optic nerve after complex neuroprotective treatment in glaucomatous optic neuropathy. **Materials and methods.** Clinical observation includes 80 (116 eyes) patients with GON aged 42 to 79 years. 45 (56,2%) of them were women, 35 (43,7%) were men, diagnosed with stage II or III POAG and PACG under compensation IOP (21.4±3.1). **Results.** Analysis of the following observation demonstrate stability of the given functional parameters, that was not noted in the control group where given parameters had comparatively not reliable changes.

Key words: GON, Retinalamin, neuroprotection, Tanakan, endonasal electrophoresis, electrostimulation, ultrasound doppler, OCT.

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СРАВНИТЕЛЬНАЯ ОЦЕНКА СТРУКТУРНЫХ И ФУНКЦИОНАЛЬНЫХ ПАРАМЕТРОВ ЗРИТЕЛЬНОГО НЕРВА В КОМПЛЕКСНОМ ЛЕЧЕНИИ ГЛАУКОМНОЙ ОПТИЧЕСКОЙ НЕЙРОПАТИИ

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Аннотация. Актуальность. Глаукома является хронической прогрессирующей оптической нейропатией с характерными морфологическими изменениями в головке зрительного нерва и прогрессирующей смертью ганглионарных волокон сетчатки с характерными сужениями полей зрения. Таким образом в виду недостаточной эффективности гипотензивной терапии поиск новых лекарственных средств с целью предотвращения прогрессирования глаукомной оптической нейропатии продолжается. Наиболее перспективным из них является нейропротекторное лечение в сочетании с чрескожной электростимуляцией и эндоназальным электрофорезом, что позволяет максимально зашитить нейроны сетчатки и нервные волокна зрительного нерва от повреждающих факторов. **Цель.** Оценить структурно-функциональные изменения зрительного нерва после комплексного нейропротекторного лечения при глаукоматозной нейропатии зрительного нерва. **Материал и методы.** Клиническое наблюдение включает 80 (116 глаз) больных ГН в возрасте от 42 до 79 лет. Из них 45 (56,2%) женщин, 35 (43,7%) мужчин с диагнозом ПОУГ II или III стадии и ЗКУГ при компенсации ВГД (21,4±3,1). **Результаты.** Анализ следующего наблюдения свидетельствует о стабильности данных функциональных показателей, чего не было отмечено в контрольной группе, где данные параметры имели сравнительно недостоверные изменения.

Ключевые слова: ГОН, Ретиналамин, нейропротекция, Танакан, эндоназальный электрофорез, электростимуляция, ультразвуковое допплеровское картирование, ОКТ

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GLAUKOMATOS OPTIK NEYRAPATIYADA KO`RUV NERVINING STRUKTURAVIY VA FUNKSIONAL KO`RSATGICHLARNI QIYOSIY BAXOLASH

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Annotatsiya. Dolzarbligi. Glaukoma bu surunkali progressive optic neyropatiyada o`ziga xos ko`ruv nervidagi morfologik o`zgarishlar va progressive to`r parda ganglionar tolalarining o`limi xamda ko`ruv maydonining torayishi bilan kechayotgan jarayon xisoblanadi. Shu uchun gipotensiv davo bilan birgalikda yangi dori vositalar ixtirosi glaukomatos jarayonini to`xtatish maqsadida davom etmoqda. Ulardan eng samaralisi neyroproteksiya va teri orqali elektrostimulasiya xamda endonasal elektroforez xisoblanadi. Chunki ushbu usul orqali maksimal ravishda to`r parda ko`ruv nervining xujayralarini zarar yetkazuvchi omillardan asrab qolish mumkin. **Tadqiqot maqsadi.** Glaukomatoz optik neyropatiyani murakkab neyroprotektiv davolashdan so'ng optik asabdagi strukturaviy va funktsional o'zgarishlarni baholash. **Material va usullar.** Klinik kuzatuv 42 yoshdan 79 yoshgacha bo'lgan GN bilan kasallangan 80 (116 ko'z) bemorni o'z ichiga oldi. Ulardan 45 (56,2%) ayollar, 35 (43,7%) erkaklar POAG II yoki III bosqichlari va GİB kompensatsiyasi bilan CCG (21,4±3,1). **Natija.** Quyidagi kuzatuvni tahlil qilish ushbu funktsional ko'rsatkichlarning barqarorligini ko'rsatadi, bu ko'rsatkichlar nisbatan ishonchsiz o'zgarishlarga ega bo'lgan nazorat guruhida qayd etilmagan.

Kalit so`zlar: GON, Retinalamin, neyroproteksiya, Tanakan, endonasal elektrofores, elektrostimulasiya, doppler, OKT

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Relevance. Glaucoma unites a group of diseases with different ethology, but they includes a set of general features in pathogenesis, clinics and methods of treatment. Distinctive symptoms of glaucoma are elevated intraocular pressure over the level of tolerance for head of optic nerve, development of glaucomatous optic neuropathy and appearance of the typical visual fields defects [A. P. Nesterov, 2005]. A considerable increase of the morbidity rate of glaucoma all over the world and leading role in forming irreversible blindness is made up medico-social importance in the given pathology [H. A. Quigley at al., 2006; J.Goldberg, 2000].

According to a statement by the World Health Organization, in 2017 the number of patients with glaucoma lesions of the optic nerve ranged from 60.5 to 105 million people. According to statistics, the number of patients with glaucoma lesions is most likely to double by 2030 [9,14,16]. According to local authors in Uzbekistan, the increase in the incidence of primary glaucoma reaches 39,8±0,4 to 100 000 among the population over 19 years old. According to findings of D. M. Tuychibayeva, open-angle glaucoma (POAG) occurs in 53,1±0,1% of cases among primary determined patients, whereas angle-closure glaucoma (ACG) made up 46,9±0,1% of cases. In other words, POAG is predominated, although given proportion is widened in some regions [5,6,7].

The theory of multifactoriality of primary open-angle glaucoma (POAG) recognized as a leader in the study of its pathogenesis (Volkov V. V., 2011; Nesterov A. P., 2010). In this regard, intraocular pressure assigned the role of only one of the risk factors in the development of GON. Targeted impact on reducing IOP to a safe level using therapeutic, laser, surgical methods may not always guarantee the stabilization of the glaucoma process [2,8]. According to a number of large multicenter studies (Advanced Glaucoma Intervention Study, Collaborative Normal Tension Glaucoma Study, Collaborative Initial Glaucoma Treatment Study, Early Manifest Glaucoma Trail), progression of the glaucoma process was noted in 20–25% of cases, even despite stable normalization of ophthalmotonus.

Neuroprotective therapy directed to correction of metabolic disorder that occurs in the head of optic nerve during the glaucoma process and to improvement of local microcirculation and tissue trophic, normalization of rheological properties of blood and improvement of main and collateral blood circulation [12, 13].

These requirements are met by peptide bioregulators (Stavitskaya T. V. et al., 2004; Khavinson V. Kh. et al., 2005) [1, 3]. One of the perspective direction in clinical medicine is the usage of new groups of drugs — biogenic peptides such as cortexin, retinylamine, as well as extract of Gingko Bilabo 761 (tanakan) that possesses especially antioxidant, antiexititoxic, blocking calcium channel and neurotropic influence. These days, considering delayed, cumulative effect of extract of Gingko Bilabo Egb 761 that achieved during prolonged systematic usage, it is advisable to increase effectiveness because of targeted delivery with a help of endonasal electrophoresis [4, 11].

The works of the last years demonstrate positive prolonged effect of electrostimulation in treatment of glaucomatous optic neuropathy. Electrostimulation restores conductivity of the nerve fibers, improves

blood supply of affected nerves and has an antiparabiotic effect on the nerve fibers that contributes to the normalization of the electro excitability of the damaged nerve [10, 15]. Consequently, the method based on combined effect of galvanic current and pharmaceutical substance on the one hand and electrostimulation on the other hand presence a great interest in neurodegenerative process of the posterior segment of the eye and is considered indispensable chain to work out reasonable complex and more effective neuroprotection.

Purpose of the study. To assess structural and functional changes in optic nerve after complex neuroprotective treatment in glaucomatous optic neuropathy.

Materials and Methods. Clinical observation includes 80 (116 eyes) patients with GON aged 42 to 79 years. 45 (56,2%) of them were women, 35 (43,7%) were men, diagnosed with stage II or III POAG and PACG under compensation IOP (21.4±3.1). Depending on the treatment, the following representative groups were identified: control, I main and II main. The control that included 20 patients. Distribution by gender were male 12 (15%), and female 8 (10%). In given group patients took traditional therapy and Sol Retinalamini –2 ml № 10. I main group, which includes 30 patients. The number of men was 16 (20%), the number of women was also 14 (17.5%). Patients of this group, along with traditional therapy and Sol Retinalamini –2 ml, received Sol. Tanacani — 1 ml via endonasal electrophoresis on a galvanization apparatus Flow 1. II main, which includes 30 patients. The number of men was 16 (20%), the number of women was also 14 (17.5%). Patients in addition to traditional therapy and Sol Retinalamini –2 ml No. 10, endonasal electrophoresis using Sol. Tanacani — 1 ml 1 time per day, for 10 days, received transcutaneous neuroelectric stimulation of the optic nerve. All patients before and after treatment, as well as a month, 3 and 6 months after the course of therapy, underwent common ophthalmologic clinical studies. The study of intraocular blood flow by ultrasonic color Doppler mapping was performed on a multifunctional ultrasound system Sonoscape C 50, Visual evoked potentials were determined on the Neurosoft device, the amplitude and latency of the VEP were assessed. Structural analysis of the optic nerve was carried out with optical coherence tomography «Cirrus HD-OCT 4000».

Results and Discussions. The initial value of visual acuity and the total boundary of the peripheral visual field (TBPVF) in all three groups in patients with GON varied within 0.07–0.3 with correction, depending on the stage of the disease, the average value of VA differed: Stage II 0.19 ± 0.07 and Stage III 0.10 ± 0.03, while TBPVF varied within 345.89 ± 8.34 at stage II and 247.84 ± 8.68 at stage III. By contrast to the control group, there were a positive increase in the both main group that were 2,1 times in II stages and 2,6 times higher in the III one according to visual acuity findings after proposed therapy, TBPVF had also changed reliably and were 400 higher than initial indications (p≤0,05). Analysis of the following observation demonstrate stability of the given functional parameters, that was not noted in the control group where given parameters had comparatively not reliable changes.

A decrease in the initial values of hemodynamic

Table 1
Hemodynamic parameters of patients in different periods of observation

Date of observation		CRA			ShPCA		
		Vmax	Vmin	RI	Vmax	Vmin	RI
Control group (n=32 eyes)							
Before treatment		11,28±1,36	4,17±0,73	0,63	11,79±1,07	4,13±0,80	0,65
After treatment	10 days	14,73±1,47	5,54±0,29	0,62	15,01±1,42*	5,21±0,53	0,65
	3 months	14,45±1,56	5,14±0,52	0,64	13,51±1,32	4,91±0,55	0,64
	6 months	12,19±1,04	4,50±0,69	0,63	12,10±0,84	4,38±0,59	0,64
I main group (n=43 eyes)							
Before treatment	11,7±1,53	4,31±0,41	0,63	12,07±1,15	4,12±0,51	0,66	
After treatment	10 days	19,58±2,03^	7,51±0,30^	0,61	18,90±1,86*	7,02±0,81^	0,63
	3 months	18,44±1,82*	7,22±0,37^	0,61	17,81±1,72^	7,21±0,63^	0,60
	6 months	14,09±1,31	5,53±0,75	0,61	13,49±1,36	5,78±0,81	0,57
II main group (n=41 eyes)							
Before treatment	11,55±1,39	3,97±0,52	0,66	12,02±1,01	4,19±0,43	0,65	
After treatment	10 days	19,68±1,95^	6,90±0,85*	0,64	17,90±1,83*	6,54±0,85*	0,64
	3 months	18,18±1,57^	6,94±0,76^	0,62	17,35±1,23^	6,94±0,75^	0,60
	6 months	14,41±1,17	5,65±0,69	0,61	13,06±1,23	5,41±0,54	0,59

Note: * - significant in relation to the initial values in this group (p≤0.05).
^ - significant in relation to the initial values in this group (p≤0.01).

Table 2
Dynamics of VEP indicators during treatment

Date of observation		Control group		I main group		II main group	
		Amplitude (μV)	Latency (ms)	Amplitude (μV)	Latency (ms)	Amplitude (μV)	Latency (ms)
Before treatment		6,8±1,03	102,4±7,96	6,7±1,34	101,5±6,58	6,3±1,25	103,6±6,46
After treatment	10 days	7,2±1,01	97,9±5,06	7,9±1,19	95,2±4,39	10,1±1,28*	88,9±2,60*
	3 months	7,2±0,92	98,3±4,21	7,1±0,99	95,5±5,01	9,4±1,07*	89,6±2,63*
	6 months	6,9±0,74	101±4,57	6,8±0,78	100,2±5,47	8,5±0,85	99,1±4,60

Note: * - significant in relation to the initial values in this group (p≤0.05).

parameters occurred in all examined patients, which was confirmed by ultrasound Doppler mapping of the CRA and ShPCA. Thus, the initial values of Vmax and Vmin CRA in all the studied groups were within 11.5 and 4.5 cm/s, and the resistance index varied from 0.63 to 0.66. On the 10th day after the treatment in all groups, positive dynamics were noted in varying degrees of severity, for example, in the control group, Vmax increased to 14.73, and Vmin to 5.54, which was almost 1.3 times higher than the initial values, and the index resistance decreased from 0.63 to 0.62. The initial indicators of ShPCA in the control group did not differ much from those of the CRA, and in dynamics there was a tendency to decrease in RI by 0.01 and amounted to 0.64. In the main group I, there was a significant improvement in the hemodynamic parameters of both the CRA and ShPCA, especially the maximum systolic blood flow velocity, which was maximum already on the 10th day of the examination of 19.58 cm/s in the CRA (p≤ 0.01). and 18.90 cm/s in ShPCA (p≤ 0.05), which undoubtedly confirms the improvement in blood supply due to the drug "Tanakan", however, starting from the 3rd month, these indicators tended to slightly decrease, and by the 6th month these indicators almost did not differ from the initial ones. It should be noted that a marked decrease in the resistance index was observed more in ShPCA than in CRA from 0.66 to 0.57. In the II main group, almost identical significant dynamics was observed, followed by a decrease by the 6th month, however, a decrease in the resistance index in the CRA was observed more significantly than in the I main group (Table 1).

The VEP indicators during treatment in all three groups differed in amplitude and latency, so in the control and main group I, these indicators in dynamics did not differ much from the baseline

Table 3
Dynamics of structural parameters according to OCT findings in a variety period of observation

Stages	Groups	Date of observation			
		Before treatment	After treatment		
			1 month	3 months	6 months
Thickness of RNFL in all segments at patients with GON during observation (μm)					
II Stage	Control	80,52 ±3,3	86,08±2,9	84,59±2,7	82,2±2,7
	I main	81,1±1,1	87,6±1,9*	86,5±2,1*	82,9±1,6
	II main	80,5±1,6	88,8±1,8*	85,8±2,4*	82,3±2,1
III Stage	Control	59,8 ±1,9	63,3±1,6	62,8±1,2	60,6±1,9
	I main	60,3±2,4	64,9±2,1	63,8±2,3	61,7±2,9
	II main	59,1±4,1	66,1±2,7	64,8±2,8	61,6±1,8
Square of the neuroretinal rim (NRP) at patients with GON during observation					
II Stage	Control	0,879±0,003	0,892±0,004	0,884±0,003	0,881±0,003
	I main	0,882± 0,006	0,897±0,004*	0,901±0,006*	0,888±0,009
	II main	0,878± 0,006	0,898± 0,007*	0,905± 0,006*	0,888±0,009
III Stage	Control	0,729±0,002	0,738±0,003	0,733±0,003	0,728±0,003
	I main	0,731±0,003	0,746±0,006*	0,736±0,006	0,731±0,003
	II main	0,729±0,003	0,749±0,005*	0,744±0,006*	0,734±0,004

Note: * - significant in relation to the initial values in this group (p≤0.05).

indicators and had low statistical significance. While significant differences observed already on the 10th day of observation during second main group, which amounted to 10.1 μV and the duration of the nerve impulse reduced by 88.9 ms (p≤0.05) and which was associated with a positive effect after receiving transcutaneous electrical stimulation (Table 2).

A major parameter of the optic nerve was evaluated and thickness of the RNFL as well as NRP findings were analyzed. Initial findings of the RNFL in the II stage and III stage were about 81,1±1,1 and 60,3±2,4 in average respectively than after 1 month a steady reliable increase were fixed in both main groups with II stage that were 1,1 times higher than initial indications. In control group also was registered a positive improvement, however it had not comprise a reliable importance. In all patients with III stages of GON given parameters had changed positively but none of the group had reliable changes that supported fact about usage of complex neuroprotection in the early stages. Alteration in the square of the NRP correspond with changes in RNFL findings, but unlike RNFL where changes had a tendency to a little decrease by th 3-d month, whereas a square of NRP continues to increase from 1 to 3-d period of after treatment in the II stages of GON. In both main groups, square of NRP had reached a maximum value 0,901±0,006 and 0,905± 0,006 that were 1,021 times more than initial indicators. It should be said that reliable changes were fixed in the main groups after a month observation in patients with III stages, however given indication had a steady decrease and almost returned to initial values by 6-th month of observation (Table 3).

Conclusion

According to our results, inclusion of endonasal electrophoresis with tanakan following with electrostimulation in complex treatment of glaucomatous optic neuropathy has the effect of protecting from detrimental influence of IOP to retina, promotes prolongation of the main treatment and recovery of visual function of the eye. Given method associate with electrostimulation has sufficient comfort, cost-effectiveness, fast and stable positive effect and can be used in both inpatient and outpatient condition

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