Comparative Analysis of Hemodynamic and Electrophysiological Parameters against the Background of Complex Treatment of Glaucomatous Optic Neuropathy with Endonasal Electrophoresis in Combination with Electrical Stimulation

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Abstract

This article discusses a comparative analysis of hemodynamic and electrophysiological parameters in the context of complex treatment of glaucomatous optic neuropathy with electrical stimulation with endonasal electrophoresis. All this justifies the need for new approaches in the treatment of glaucoma and the great clinical significance of neuroprotective therapy (Russ Herman, 2010; Shepard Allan R. et al., 2010).

Key Words: Comparative Analysis, Hemodynamic Parameters, Electrophysiological Parameters, Context, Complex Treatment, Glaucomatous, Optic Neuropathy, Electrical Stimulation, Endonasal Electrophoresis.

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Relevance

Glaucoma is "a chronic progressive optic neuropathy that combines a group of diseases with characteristic morphological changes in the optic nerve head (excavation) and retinal nerve fiber layer in the absence of other ophthalmic pathology" (European Glaucoma Society Terminology and Guidelines for Glaucoma 2017).

It is worth noting that significant progress has been made in the treatment of glaucoma over the past decade in the field of neuro-ophthalmology, however, glaucoma lesion with steady growth still occupies the second place among the causes of blindness and low vision, second only to cataracts [1]. 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 [2,11]. According to domestic authors in Uzbekistan, the increase in the incidence of primary glaucoma among the population over 40 years old reaches 1.5-2.5%.

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Open-angle glaucoma occurs in 20.1% of cases, angle-closure glaucoma (CLG) in 29.9% of cases. In our Republic, according to D.M. Tuychibayeva (2004), the proportion of disability due to primary glaucoma is 14.8%, causing the second place in the structure of all primary visual disability. The number of patients with primary glaucoma who became blind in both eyes reached 4.5 million people, which was the reason for including this pathology in the WHO list of priority eye diseases (Global Initiative for the Elimination of Avoidable Blindness: action plan 2006-2011, WHO 2006).

To date, the theory of multifactoriality of primary open-angle glaucoma (POAG) is recognized as a leader in the study of its pathogenesis (Volkov V.V., 2011; Nesterov A.P., 2010). In this regard, intraocular pressure is 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 [6,10]. 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. According to Melnikov V.A. et al. (1999), the decay of visual functions continues in 55% of patients under conditions of intraocular pressure compensation. All this justifies the need for new approaches in the treatment of glaucoma and the great clinical significance of neuroprotective therapy (Russ Herman, 2010; Shepard Allan R. et al., 2010).

Neuroprotection in glaucoma is understood as the protection of retinal neurons and nerve fibers of the optic nerve (in other words, GCS and their axons) from the damaging effects of various factors, as well as the normalization of neuronal-glial effects and stimulation of macroglial cells to protect neurons (GCS) from the toxic effects of glutamate and others. pathological agents [3,12,]. In this regard, in order to prevent or slow down the processes of apoptosis and the development of glaucomatous optic neuropathy, there is a need for a targeted effect on ganglion cells, as well as the need for the use of antioxidant, nootropic and other drugs with neuroprotective properties [15].

Given the above, it can be assumed that one of the important points of neuroprotection is a decrease in the level of cytotoxicity in the intercellular space surrounding neurons, neutralization of toxic substances or a decrease in sensitivity to them. These requirements are met by peptide bioregulators (Stavitskaya T.V. et al., 2004; Khavinson V.Kh. et al., 2005) [4,5]. Since the violation of ocular microcirculation is one of the fundamental in the pathogenesis of glaucomatous optic neuropathy, the correction of hemodynamic shifts is most effectively achieved by preparations based on ginkgo bilabo extract [7,13,14]. Taking into account the delayed cumulative effect, which is achieved with long-term use of these drugs, targeted methods such as subtenon administration and endonasal electrophoresis solve this problem. It should be noted that after the accumulation of these drugs in the posterior segment of the eye, it is rational to use transcutaneous electrical stimulation in the complex treatment of glaucoma with severe optic neuropathy to increase their effectiveness and improve neuronal effects not only between cells, but also at various levels of the visual system. As a result of electrical stimulation, the functionally inhibited elements of the plexiform layer of the retina are activated, the conductivity of nerve fibers improves due to conformational changes in the molecular structures of the membrane and changes in its viscosity, an increase in the number of neuroglial elements and their conductivity. And most importantly, BSEC contributes to the reorganization of the work of the visual system, resulting in an increase in the efficiency of interaction between neurons of different levels due to an increase in the degree of freedom of work of individual parts of the visual analyzer [8,9].

Purpose of the Study

To evaluate the effectiveness of endonasal electrophoresis in combination with electrical stimulation in the complex therapy of GON based on hemodynamic and electrophysiological parameters.

Materials and Research Methods

80 (116 eyes) patients with GON aged 40 to 78 years were under clinical observation, 44 (55%) of them were women, 36 (45%) were men, diagnosed with stage II or III POAG and PACG under compensation IOP (21.3±3.2). IOP compensation was achieved by medical, laser and surgical methods. It should be noted that patients were included in the study groups after a 6-month

follow-up period with the most stable target pressure achieved in accordance with the recommendations of the European Glaucoma Society. It should also be emphasized that in the absence of stabilization, i.e. when the IOP rose above the tolerant level, appropriate antihypertensive tactics were undertaken until the process stabilized, followed by their inclusion in the appropriate study group. Depending on the treatment, the following representative groups were identified: control, I main and II main. The control, which included 20 patients, of which the number of men 12 (15%), and women 8 (10%). Patients in this group received traditional therapy, which includes the following drugs: Sol. Mildronati 10%-5.0 IV or Sol Mexidoli -5 ml, Tab. Nootropili 800 mg x 3 times Sol. Pyridoxini hydrochloridi 5%-2.0 w / m, Sol. Emoxypini 1%-0.5 parabulbarno, and Sol Retinalamini -2 ml which, depending on the stage and social status of the patient, received intramuscularly №10. I main, which includes 30 patients. The number of men was 16 (20%), the number of women was also 14 (17.5%). The patients of this group, in addition to traditional therapy and Sol Retinalamini -2 ml No. 10, received Sol. Tanacani - 1 ml by 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 using the ECOM apparatus, a rectangular negative pulse with a duration of 1-10 ms, with a frequency of 5-30 Hz and an amplitude of 10-1000 μA for 10 days. For each eyeball, 4-6 series of 15-45 s were performed with an interval between series of 30-60 s. All patients before and after treatment, as well as a month, 3 and 6 months after the course of therapy, underwent clinical studies: visometry, ophthalmoscopy, ophthalmic biomicroscopy, Maklakov tonometry, tonography, gonioscopy, peripheral visual field studies. The study of intraocular blood flow by ultrasonic color Doppler mapping was performed on a multifunctional ultrasound system Sonoscape C 50, while the spectral velocity parameters of hemodynamics were evaluated: maximum systolic velocity (Vmax), end diastolic velocity (Vmin) and peripheral resistance index (RI). Visual evoked potentials were determined on the Neurosoft device, the amplitude and latency of the VEP were assessed.

Results and Discussions

The initial value of visual acuity and the total boundary of the peripheral visual field (TLPVF) 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 TBPF varied within 345.89 ± 8.34 at stage II and 247.84 ± 8.68 at stage III. After the treatment, there was a significant positive trend a month after the treatment in the main group I, which amounted to 0.39±0.07 and was 2.1 times higher than the initial values in stage II and 2.6 times higher with an indicator of 0, 27± 0.07 at stage III ($p \leq 0.05$), then all indicators slightly decreased by the 3rd month of observation and stabilized by the 6th month, however, they had a low significance index, the TLPVF increased significantly by 39.28^0 from 346.25±7.02 to 385.53±12.27 ($p \leq 0.05$) in patients with stage II and by 30^0 from 248.33±9.94 to 278.33±8.33 ($p \leq 0.05$) in patients with stage III from baseline. Further analysis of the TLPVF indicator showed that on the 3rd month after our treatment, TLPVF continued to increase and reached its maximum values, which amounted to 393.39±12.09 ($p \leq 0.05$) in stage II and 290.67±6, 51 ($p \leq 0.05$), and then by the 6th month, these indicators tended to moderately decrease, but nevertheless were higher than the initial values. The analysis of VA indicators in the II main group already on the 10th day after the course of treatment reached 0.37 ± 0.07 at stage II and 0.23 ± 0.07 at stage III, which was almost 2 times more than the initial values and continued significantly improve until the end of the 1st month of observation in patients with stage II and III GON, which was 0.41±0.06 and 0.28±0.07, respectively ($p \leq 0.05$). It should be noted that during the 3-month follow-up, these indicators tended to be strictly stable and did not differ in any way from the indicators of the 1st month. However, by the 6th month, the VA of these patients had a low significance index with a moderate decrease, which amounted to 0.35±0.09 and 0.21±0.06 in groups II and III, respectively. It should be noted that by the end of the 1st month of follow-up, TLPVF increased significantly by 46.980 from 347.67±7.75 to 394.65±8.8 ($p \leq 0.01$) in patients with stage II and by 46.80 s 246.1±8.2 to 292.9±7.5 ($p \leq 0.01$) in

patients with stage III from baseline. Further analysis of the TLPVF indicator showed that on the 3rd month after our treatment, TLPVF continued to moderately increase and reached maximum values, which amounted to 397.15±9.2 (p≤0.01) at stage II and slightly decreased to 281, 15±7.4 (p≤0.05). By the 6th month of follow-up, TLPVF tended to moderately decrease with low statistical significance from baseline values. There was also a positive trend in the control group by the 3rd month of follow-up with a statistically significant increase in TLPVF both in stages II and III, however, the VA indicators did not increase significantly (Table 1).

Table 1. Dynamics of Visual Function Indicators in Patients I and II of the Main Group in Different Observation Periods

Groups / Terms of observation		I main group		II main group	
		VA	TLPVF	VA	TLPVF
		II stage (n = 28)		II stage (n = 28)	
Before treatment		0,19± 0,07	346,25±7,02	0,19± 0,07	347,67±7,75
After treatment	10 days	0,31± 0,08	367,85±9,75	0,37± 0,07	377,3±12,65
	1 month	0,39±0,07*	385,53±12,2*	0,41±0,06*	394,65±8,8^
	3 months	0,30±0,09	393,39±12,1*	0,41±0,09*	397,15±9,2^
	6 months	0,28±0,09	379,46±11,16	0,35±0,09	382,15±9,37
		III stage (n =15)		III stage (n =13)	
Before treatment		0,10± 0,03	248,33±9,94	0,11± 0,03	246,1±8,2
After treatment	10 days	0,21± 0,08	266,33±9,90	0,23± 0,07	279,2±10,6
	1 month	0,27± 0,07	278,33±8,33*	0,28± 0,07*	292,9±7,5^
	3 months	0,26± 0,08*	290,67±6,51*	0,28± 0,07*	281,15±7,4*
	6 months	0,18± 0,07	273,67±11,72	0,21± 0,06	271,15±7,4

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. Hemodynamic parameters of patients in different periods of observation

Terms of observation		OCAC			CACA		
		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).

A decrease in the initial values of hemodynamic parameters occurred in all examined patients, which was confirmed by ultrasound Doppler mapping of the OCAC and CACA. Thus, the initial values of Vmax and Vmin OCAC 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, however, by the 6th month of observation, all indicators almost did not differ from the initial ones. The initial indicators of CACA in the control group did not differ much from those of the OCAC, 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 OCAC and CACA, 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 OCAC ($p \leq 0.01$). and 18.90 cm/s in CACA ($p \leq 0.05$), 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 CACA than in OCAC 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 OCAC was observed more significantly than in the I main group (Table 2).

Table 3. Dynamics of VEP indicators during treatment

Terms of observation		Control group		I Control group		II Control 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*
	1 month	7,2±0,92	98,3±4,21	7,1±0,99	95,5±5,01	9,4±1,07*	89,6±2,63*
	3 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 ($p \leq 0.05$).

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 indicators and had low statistical significance, while significant differences were 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 was reduced by 88.9 ms ($p \leq 0.05$) and which was associated with a positive effect after receiving transcutaneous electrical stimulation (Table 3).

Conclusion

The use of endonasal electrophoresis with the drug "Tanakan" in combination with transcutaneous electrical stimulation in the complex treatment of GON prevents the development of optic nerve atrophy and, along with improving visual functions, prolongs the positive effect of the main treatment, which was confirmed in a significant improvement in hemodynamic parameters in the main groups already on the 10th day of observation ($p \leq 0.01$) according to Doppler ultrasound, and the shortening of latency and an increase in the amplitude of visual evoked potentials confirms the significant positive effect of transcutaneous electrical stimulation ($p \leq 0.05$). The method of complex treatment proposed in the work will increase the effectiveness of the treatment of patients with compensated open-angle glaucoma, improve the prognosis for vision and the quality of rehabilitation measures.

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