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Effect of complex therapy by acupuncture, retinalamin and OMK-1 on eye hemodynamics in children with retinitis pigmentosa

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The work concerns the study of retinitis pigmentosa (RP) – a hereditary generalized retinal dystrophy and complex therapy method via acupuncture (AP), endonasal electrophoresis with Retinalmin and OMK-1 instillations. The aim of this work was to assess the effect of complex therapy with the use of AP, endonasal electrophoresis with Retinalmin and OMK-1 instillations on the hemodynamics of the eye in children with retinitis pigmentosa based on the results of colour Doppler imaging (CDI). The study included 25 children (50 eyes) diagnosed with RP at the age of 7-14 years. Of the diagnosed, 10 patients were girls and 15 were boys. All patients underwent routine ophthalmic examination methods, electroretinography (ERG - general, macular, rhythmic, and cone). The state of the eye hemodynamics was determined by using the CDI of the vessels of the eyeball and retrobulbar space. The hemodynamic parameters (Vmax, Vmin, RI) of the ophthalmic artery (OA), central retinal artery (CRA), short posterior ciliary arteries (PSCA) were studied. Complex therapy of patients included AP, endonasal electrophoresis with Retinalamin, and OMK-1 instillations. 10 treatment sessions were carried out at the National Center of Ophthalmology within two weeks (5 sessions per week). Each AP session lasted 25 minutes and included the placement of acupuncture needles in a standard set of points on all patients located on the head, around the eyes, on the hands, feet, arms and legs. Endonasal electrophoresis was performed using Potok-1 apparatus equipped with 2 electrodes. Complex therapy with the use of AP, endonasal electrophoresis with Retinalamin and OMK 1 instillations is a minimally invasive method and has no negative impact. The positive therapeutic effect of our treatment method may pave the way for future research. Thus, complex therapy with the use of AP, endonasal electrophoresis with Retinalamin and OMK-1 instillations is a painless, affordable method, quite feasible in children and has a positive effect on visual functions and hemodynamics of the eye. The complex therapy implemented in our work can be used as a method of treating RP including in children.

Keywords: *Retinitis pigmentosa (RP), colour Doppler imaging (CDI), acupuncture (AP), retinalamin, OMK-1*

INTRODUCTION

Retinitis pigmentosa (RP, retinitis pigmentosa, retinal degeneration) is a hereditary disease of the retina that has a significant impact on the quality of life of patients. RP ranks first among all hereditary retinal pathologies (Ayshegul, 2022).

This pathology refers to heterogeneous hereditary dystrophic changes in the retina, damaging photoreceptors, the frequency of which is 1:4000 (Verbakel, 2018).

One of the clinical signs of this disease is known to be vasoconstriction. However, the role

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of vascular disorders in the development of the dystrophic process has not been practically proven. On the basis of single data on a systemic and local decrease in blood flow parameters, it is assumed that insufficient circulation of the retina can change its chemistry, leading to a violation of metabolism and the structure of cell membranes (Pozdeyeva, 2005). One of the modern and informative methods for studying eye hemodynamics is CDI. This method allows us to explore the orbital vessels of medium and small diameters. It is a non-invasive, painless method. This method is applicable to almost all age groups (Dimitrova, 2010; Steuer, 2005).

Despite the existing number of scientific studies devoted to the study of RP, this problem remains relevant today (Liu, 2022). Plenty of research is devoted to the study of the effectiveness of Retinalamin in dystrophic processes of the retina. Retinalaminis a polypeptide that belongs to the pharmacotherapeutic group - a stimulator of tissue repair. This medication has a stimulating effect on photoreceptors and cellular elements of the retina, improves the functional interaction of the pigment epithelium and the outer segments of photoreceptors, glial cells in dystrophic changes (Khavinson, 2014; Hasanova, 2008). In the literature, there are also works with the use of Omk-1 instillations, that have a neuroprotective effect in various eye pathologies. Citicoline being part of Omk-1 enhances the regeneration of damaged cell surfaces, maintains cellular integrity and prevents apoptotic and necrotic cell death by reducing the content of phospholipases (Matteucci, 2014; Pawel, 2016).

In the field of eye dystrophic diseases, works devoted to the use of AP are of interest. AP is one of the methods of reflexology characterized by the impact on certain points on the human body in various ways (acupuncture, cauterization, pressure), differing in strength, nature and duration. In ophthalmology, AP is used in the complex treatment of various eye diseases: glaucoma, dry eye syndrome, keratopathy, refractive error, myopia, optic nerve atrophy, initial cataract, macular degeneration, blepharoptosis and RP. AP has been used in Asian countries since ancient times (Japan, Korea, Egypt, etc.). AP found its application in Europe in the 13th century. The development and practical use of AP by European medicine received a new impetus in the 1950s (Zainullina, 2020; Gavaa, 1992, 2013).

Patients with RP are interested in the use of additional or integrative therapies to slow down the progression of the disease since there is currently no pathogenetic treatment for this pathology (Liu, 2022). Therefore, it seems interesting to study the state of ocular blood flow in order to elucidate the role of the vascular factor in RP.

The aim of this research was to estimate the effect of complex therapy with the use of AP, endonasal electrophoresis with Retinalmin, and OMK-1 instillations on the hemodynamics of the eye in children with retinitis pigmentosa based on the results of CDI.

MATERIALS AND METHODS

The study included 25 children (50 eyes) diagnosed with RP at the age of 7-14 years. Among them 10 patients were girls and 15 were boys. All patients underwent routine ophthalmic examination methods: visometry, tonometry, perimetry, ophthalmoscopy and fundus photography were performed (Fig. 1). To assess the functional activity of the retina, electroretinography (ERG - general, macular, rhythmic, and cone) was performed.

Fig. 1. Fundus photo of the RP patient

The state of the eye hemodynamics was determined using the CDI of the vessels of the eyeball and retrobulbar space. The study was carried out on the Nemio XG SSA-580A

ultrasonic diagnostic system (TOSHIBA) with a linear transducer with a frequency of 8 MHz to visualize blood flow in the ophthalmic artery (OA), central retinal artery (CRA), short posterior ciliary arteries (PSCA). The following hemodynamic velocity parameters were analyzed: maximum systolic blood flow velocity (Vmax), minimum diastolic blood flow velocity (Vmin), and resistance index (RI). The control group consisted of 50 practically healthy children aged 5-14 years. These children underwent CDI of eye vessels to determine the age- normative hemodynamic parameters.

Statistical data processing was carried out using the Excel-2007 program. The results obtained were processed by the method of variation statistics with the calculation of the arithmetic mean values of the sample and the statistical significance index p.

Complex therapy of patients included AP, endonasal electrophoresis with Retinalamin and OMK-1 instillations. 10 treatment sessions were carried out at the National Center of Ophthalmology within two weeks (5 sessions per week). Each AP session lasted 25 minutes and included the placement of acupuncture needles in a standard set of points on all patients located on the head, around the eyes, on the hands, feet, arms and legs (Fig. 2).

Endonasal electrophoresis was performed using Potok-1 apparatus equipped with 2 electrodes. The indifferent electrode was placed at the level of the cervical vertebrae and the active electrode was fixed on a turunda moistened with a Retinalamin solution and placed in the nasal passages. The duration of the procedure was 10-15 minutes. OMK-1 instillations were carried out in the course of 4 months. Hemodynamic parameters were examined before therapy, as well as 3 months after treatment to evaluate the effectiveness.

RESULTS AND DISCUSSION

Based on the results of CDI there was some decrease in OA speed parameters (Vmax and Vmin) in all patients before the therapy but these changes were not statistically significant. The indicator of peripheral resistance RI in this artery was statistically significantly lower (Table 1). Statistically significant changes in the speed indicators and resistance index were observed in CRA and PSCA.

3 months after complex therapy improvement of all arteries' hemodynamics was revealed as evidenced by the data of the CDI. Hemodynamic parameters were statistically significantly increased in CRA and PSCA. A statistically significant increase of RI in OA was observed (Table 1).

As for changes in visual acuity, there were subjective symptoms of improvement in all types of visual function in most cases (Table 2). As can be seen from Table 2, a minor improvement in all types of vision was observed in over 50% of patients.

From the available literature sources, there are works whose results are consistent with the results of our studies. Thus, the violation of blood flow in retinitis pigmentosa is confirmed by the authors G. Dimitrova and E. Steuer (Dimitrova, 2010; Steuer, 2005).

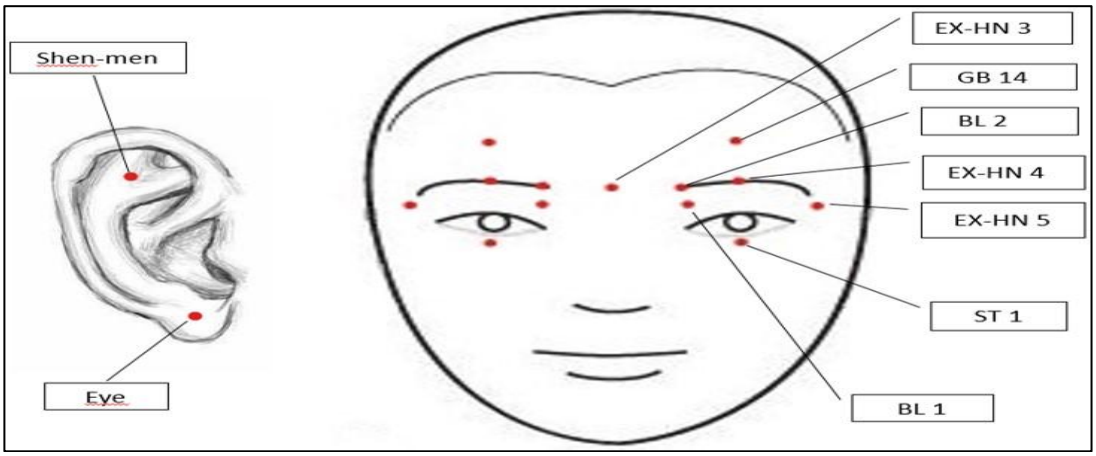

Fig. 2. Acupuncture points used on the patient (Ayshegul, 2022).

Table 1. CDI results

Arteries	Parameters	Before therapy	3 months after	Norm
OA	Vmax (cm/sec)	36.8±2.01	38.3±1.1	38.8±0.3
	Vmin (cm/sec)	8.91±0.8	9.07±0.06	9.19±0.14
	RI	0.75±0.01*	0.76±0.001#	0.76±0.003
CRA	Vmax (cm/sec)	9.8±0.13**	11.6±0.5###	12.8±0.1
	Vmin (cm/sec)	3.44±0.2*	3.57±0.06#	3.63±0.04
	RI	0.61±0.003***	0.67±0.02 ##	0.7±0.002
PSCA	Vmax (cm/sec)	7.2±0.5**	8.7±0.08 ###	9.1±0.1
	Vmin (cm/sec)	3.2±0.1*	3.4±0.1 ###	3.61±0.04
	RI	0.55±0.1**	0.59±0.02 ###	0.60±0.002

* - p < 0.05; ** - p < 0.01; ***- p < 0.001 –statistically significant difference in relation to the norm
# - p< 0.05; ## - p< 0.01; ###- p< 0.001 – statistically significant difference in relation to the initial data

Table 2. Subjective feelings of patients with PR after complex therapy

Types of visual function	No improvement	Minor improvement	Moderate improvement	Significant improvement
Scotopic (night)	23.2%	62.7%	14.1%	–
Photopic (daytime)	9.1%	68.8%	22.1%	–
Central visual acuity	22.4%	61.8%	15.8%	–
Peripheral visual acuity	8.9%	53.2%	32.6%	5.3%

In a study by E. Steuer et al. (2005) the average value of Vmax in the CAS was reduced to 7.07±1.6 cm/sec, in the PCA - to 8.56±3.4 cm/sec. The authors also mention a decrease in vascular resistance in both vessels. G. Dimitrova et al. (Dimitrova, 2010) studied hemodynamic parameters in the CRA using CDI. The authors note a significant decrease in blood flow velocity, Vmax, and Vmin in this artery. Changes in the hemodynamic parameters in these studies are similar to the results of our work. But there are some differences in the level of indicators in different arteries, which may be due to the age of the studied patients. In the available literature, only a few publications are devoted to the study of the state of eye hemodynamics in retinitis pigmentosa, and in pediatric patients, these studies are practically absent.

In a number of works with the use of AP in patients with RP, positive results are noted. Ayshegul Elbir et al. revealed signs of restoration of the function of optic nerve cells and an increase in the regenerative capacity of the CNS (Ayshegul, 2022). H. Xu et al. (2016) used the AP in 26

patients with retinitis pigmentosa and published data after 3 months of treatment in a 20-year study. At the end of the sessions, 2/3 of the patients noted an improvement in visual acuity and quality of life. H.Huang et al. created a protocol for a randomized controlled trial on this issue in 2021 (Huang, 2021). The authors concluded that this method improves local microcirculation of the eye and limits the pathological reaction associated with RP. F. Fereydouni et al. conducted a study involving 23 patients with RP and found a significant improvement in visual acuity after AP sessions (Fereydouni, 2017).

Also, in the literature of recent years, there are a number of works devoted to the study of the effect of Retinalamin and OMK-1 in various pathologies of the eye (Khavinson, 2014; Hasanova, 2008; Matteucci, 2014; Pawel, 2016; Trofimova, 2003). So, according to Hasanova and Belyaeva (Hasanova, 2008), the use of Retinalamin in experimental animals leads to a significant increase in the ERG b-wave compared to the control. So, with a moderate degree of retinal damage, the therapeutic effect of Retinalamin is detected already on the 15th day of observation, reaching its maximum by 35 days. The positive effect of Retinalamin is also observed in the case of severe damage of the retina in dystrophic processes of various origins (Khavinson, 2014; Trofimova, 2003). All these data prove the positive effect of Retinalamin on the retina. In the works of various authors with the study of the effect of OMK-1 eye drops, positive results were obtained (Matteucci, 2014; Pawel, 2016). So, A. Matteucci et al. prove the neuroprotective effect of OMK-1 on the basis of improved ERG, perimetry and optical coherence tomography in various degenerative retinal pathologies (Matteucci, 2014). In the work of G.Pawel et al., patients with primary open-angle glaucoma were studied. Positive perimetry and VEP results were obtained after the use of OMK-1 drop in these patients (Pawel, 2016).

CONCLUSION

In a disease such as retinitis pigmentosa, possessing extremely limited treatment options it is important to explore the potential of integrative therapy to improve visual function. Complex therapy with the use of AP, endonasal electrophoresis with Retinalamin and OMK-1 instillations is a minimally invasive method and has no negative impact. The positive therapeutic effect of our treatment method may pave the way for future research. Further research will explore the potential of the integrated treatment modality to improve ocular hemodynamics and visual function, thereby improving the quality of RP patients' life. While other promising therapies such as stem cells, gene therapy and pharmacological agents are still under development.

Thus, complex therapy with the use of AP, endonasal electrophoresis with Retinalamin and OMK-1 instillations is a painless, affordable method, quite feasible in children and has got a positive effect on visual functions and hemodynamics of an eye. The complex therapy used in our work can be recommended as a method of treating RP including in children.

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