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Regional hemodynamics of the eye in optic neuritis

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Background: *Optic nerve disease accounts for up to 28% of all cases of visual disability. Although recent studies have demonstrated abnormal hemodynamics in optic neuritis (ON), results of different studies as well as data on the pathophysiology of vascular abnormalities are contradictory.*

Purpose: *To assess regional hemodynamics on the basis of ophthalmic rheography (ORG) and rheoencephalography (REG) in patients with optic neuritis and those with complications of the disease.*

Material and Methods: *Fifty-seven patients (82 affected eyes; 27 women and 30 men) who were examined for idiopathic ON at the Department of Ocular Inflammatory Disease, Filatov Institute of Eye Disease and Tissue Therapy, were included in the study and divided into four groups. They underwent a clinical ophthalmological examination as well as ORG and REG studies with the computerized rheography apparatus Reocom (Kharkiv).*

Results: *Best-corrected visual acuity (BCVA) values were twofold to threefold lower for the eyes with partial optic atrophy (POA) after ON or those with macular involvement in ON than for the eyes with acute ON or prolonged ON. BCVA showed mild direct correlation with ocular pulse blood filling (OPBF) expressed as RQ ($r = 0.24$; $p < 0.05$), and negative correlation with the presence of complications following ON ($r = -0.35$; $p < 0.05$). RQ values in patients with acute ON were 15.5% higher than in controls ($p < 0.05$) and 35% and 31% higher than in patients with POA following ON and patients developing macular lesion following ON, respectively ($p < 0.05$). RQ values in patients with partial optic atrophy (POA) were 23.6% lower than in controls ($p < 0.05$), which reflected regional ischemic process. The odds ratio (OR) for the presence of a reduced RQ value (a) in the eye with POA following ON compared to the eye with acute ON was 9.2 ($P < 0.05$, 95% confidence interval 2.0–42.4), and (b) in the eye developing macular lesion following ON compared to the eye with acute ON was 4.3 ($P < 0.05$, 95% CI, 1.2–14.7). Pulse blood filling as assessed by rheography index (RI) in the internal carotid artery (ICS) was actually normal in patients with acute ON and 44% increased in patients with prolonged ON or outcome of ON compared to controls ($p < 0.05$). In addition, tonicity of large vessels in the ICS and VBS as assessed by alpha/T (%) was normal in patients with acute ON and at average 15% higher in patients with complications following ON. Moreover, tonicity of small-caliber vessels as assessed by the dicrotic index (DCI) and diastolic index (DSI) values was at average 32.2% and 55%, respectively, higher in patients than in controls.*

Conclusion: *We revealed features of ocular and brain hemodynamics in patients with acute ON, prolonged ON and those with complications of the disease.*

Keywords:

optic neuritis, partial optic atrophy, ocular and brain hemodynamics

Introduction

Optic nerve disease accounts for up to 28% of all cases of visual disability.[1]

Optic neuritis (ON), or inflammation of the optic nerves, is a frequent cause of acute optic nerve injury in children and adults, and manifests as papillitis, neuroretinitis or retrobulbar neuritis.

Studies of recent decades have reported the incidence of undifferentiated optic neuritis cases per 100,000 population/year to be 0.7 to 5.1 in the US, 1.4 to 4.46 in the UK, 5.36 in Spain, 1.55 to 3.28 in Sweden, Norway and Denmark, 0.56 in Israel, 1.62 in Japan, 3.29 in South Korea, and 33 in Taiwan.[2]

Multiple causes of optic nerve inflammation exist: autoimmunity, infection, granulomatous disease, paraneoplastic disorders, and demyelination. In addition, it

can occur independently from these causes. Isolated optic neuritis not associated with any specific neurological or systemic disease is labeled as idiopathic optic neuritis.

Rapid determination of the etiology of optic neuritis is important for implementing timely and appropriate treatment. In addition, understanding the cause of optic neuritis informs on visual prognosis, illuminates future health risks, and directs additional evaluations and treatments. Advances in technology and immunology have enhanced our understanding of the pathologies driving inflammatory optic nerve injury. Clinicians are now able to interrogate optic nerve structure and function during inflammatory injury, rapidly identify disease-relevant autoimmune targets, and deliver timely therapeutics to improve visual outcomes.[3]

Our understanding of the process of optic nerve inflammation has substantially improved in recent years. It was believed that typical ON is associated with multiple sclerosis (MS), whereas atypical ON is not associated with MS. International consensus diagnostic criteria for neuromyelitis optica (NMO) spectrum disorders have been recently published. It defined NMO as an inflammatory central nervous system (CNS) syndrome distinct from MS that is associated with serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG), and highlighted the role of serum myelin oligodendrocyte glycoprotein (MOG) antibodies in demyelinating CNS disease.

At present, there are no clear guidelines on classification of the pathology. The nomenclature defining the different subtypes of optic neuritis continues to be refined. The different subtypes include isolated optic neuritis (ION), relapsing isolated optic neuritis (RION), chronic relapsing inflammatory optic neuropathy (CRION), multiple sclerosis associated optic neuritis (MS-ON), neuromyelitis optica associated optic neuritis (NMO-ON), and myelin oligodendrocyte antibody associated optic neuritis (MOGON), although most experts in the field would agree that there is currently no consensus as to these definitions. [2, 4]

ON is typically diagnosed on the basis of findings from ophthalmoscopy, tangent screen examination, perimetry, the presence of dyschromatopsia, low contrast sensitivity, abnormal current threshold for eliciting phosphenes and abnormal critical flicker fusion frequency (which is characteristic for an afferent defect of the pupillary light reflex), and visual-evoked potential (VEP) findings. The VEPs are electrical potentials recorded from the scalp derived from electrical currents generated in the visual cortex in response to visual stimulation. The cortical response to visual stimulation is absent or delayed in the presence of demyelination or other visual pathway disorders. Thorough optical coherence tomography-based (OCT) and fluorescein angiography (FA)-based assessment of the optic disc, peripapillary area, and macula area is essential for differentiating ON from other visual disorders. There have also been conflicting reports of impaired hemodynamics in the orbital vessels ocular artery and vein in ON, with the authors hypothesizing about the cause of this phenomenon.[5, 6] The role of ischemia in optic neuritis has been considered.[7] Inflammation of the retinal vascular endothelium can precede demyelination and is sometimes visibly manifest as retinal vein sheathing. [8] Retinal vasculitis (with the characteristic cuffing of the affected vessels) is a sign that can be found in a patient with ON even by routine ophthalmoscopy.[9]

Changes in regional hemodynamics and relationships between hemodynamic and immunological characteristics in different phases of the course of ON have been recently reviewed in isolated papers.[10,11] The prognosis for visual function preservation in patients with ON is important because inflammation-induced death of neural cells and vascular abnormalities, if occur, can result in ischemic and persistent trophic abnormalities and lesions of the internal retina with loss of retinal ganglion cells due to retrograde axonal degeneration, with all these leading to poor resolution of the visual system and visual field defects. The pathophysiology and natural course of idiopathic optic neuritis have not been investigated sufficiently.[12]

The purpose of the study was to assess regional hemodynamics on the basis of ophthalmic rheography (ORG) and rheoencephalography (REG) in patients with optic neuritis and those with complications of the disease.

Material and Methods

Fifty-seven patients (82 affected eyes; 27 women and 30 men) who were examined for idiopathic ON at the Department of Ocular Inflammatory Disease, Filatov Institute of Eye Disease and Tissue Therapy, were included in the study and divided into four groups. Group 1 consisted of 25 patients (36 eyes) with primary acute ON and the median [interquartile range (IQR)] time from initial symptoms to the diagnosis of 12 (7–30) days. These included 14 patients (14 eyes) with unilateral ON and 11 patients (22 eyes) with bilateral ON. Group 2 consisted of 9 patients (14 eyes) with prolonged ON and the median time from initial symptoms to the diagnosis exceeding 90 days. These included 4 patients (4 eyes) with unilateral ON and 5 patients (10 eyes) with bilateral ON. Group 3 consisted of 10 patients (14 eyes) with partial optic atrophy (POA) following ON and the median (IQR) time from initial symptoms to the diagnosis of 1080 (180–1825) days. These included 6 patients (6 eyes) with unilateral ON and 4 patients (8 eyes) with bilateral ON. Group 4 consisted of 13 patients (18 eyes) with ON which resulted in complications (macular edema, macular degeneration, and posterior hyaloid detachment with macular traction) and the median (IQR) time from initial symptoms to the diagnosis of 700 (150–1440) days. The average patient age was 37.8 ± 11.3 years (mean ± standard deviation). The control group was composed of 27 volunteers of matched age without ocular disease or general medical condition.

The study followed the ethical standards stated in the Declaration of Helsinki, the European Convention on Human Rights and Biomedicine and relevant laws of Ukraine. Written informed consent was obtained from

all participants. Measures were taken to preserve the anonymity of patients.

Patients underwent a clinical ophthalmological examination, which included assessment of visual acuity, tonometry, slit-lamp biomicroscopy, ophthalmoscopy through a dilated pupil, axial length of the eye, current threshold for eliciting phosphenes, critical flicker fusion frequency, and Humphrey 24-2 SITA visual field testing (Carl Zeiss Meditec). In addition, OCT of the macula area, optic nerve and peripapillary area was performed if required to clarify the diagnosis. Patients were consulted by a neuropathologist and underwent magnetic resonance imaging (MRI) and computed tomography (CT) of the brain. Patients with MS were excluded from the study. Patients underwent ophthalmic rheography (ORG) and rheoencephalography (REG) with Reocom (KHAI-Medika, Kharkiv, Ukraine), the computerized rheography apparatus.

The ORG included measurements of ocular pulse blood filling (OPBF, expressed as RQ, ‰ rheographic coefficient) and tonicity (expressed as alpha/T percentage index). The REG included assessment of relative pulse blood filling (expressed as relative rheographic index RI, i.e., ratio of the patient's rheographic index to that of age-matched normals, taken as 100%) of brain vessels, and the tonicity in large-caliber vessels and dicrotic index (DCI) and diastolic index (DSI) in small-caliber vessels in the internal carotid system (ICS) and vertebral-basilar system (VBS).

Statistical analysis

Statistical analyses were conducted using Statistica 8.0 (StatSoft, Tulsa, OK, USA) software. Nominal data are presented as absolute numbers and percentages. The normal distribution of data was tested using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Mean (M), standard deviation (SD), and 95% confidence interval (CI) values were calculated for normally distributed data. Student's t test was used to compare mean values of normally distributed data. The median (IQR) values were calculated for non-normally distributed data. Mann-Whitney U test was used for the comparison of two samples when the underlying distributions were not normal. The level of significance $p \leq 0.05$ was assumed. The percentage coefficient of variation v_Q (%) was calculated. Spearman and Pearson correlation coefficients were calculated to assess correlations. Odds ratio (OR) was used as a measure of risk that compares the frequency of exposure to a putative causal factor in the individuals with the health outcome (cases) versus those individuals without the health outcome (controls). The 95% CI was calculated to extend the results to the general population. Contingency tables were used to calculate odds ratios and 95% CI.

Results

Frequency analysis found no significant difference in the frequency of unilateral/bilateral ON in groups 1 and 2 (primary process) and in groups 3 and 4 (disease outcome). Therefore, no effect of laterality of optic neuritis was found. In addition, no difference in the disease duration between groups 3 and 4 was noted. BCVA varied widely, from 0.12 to 1.0 (v_Q = 70%) in acute ON, and from 0.3 to 0.5 (v_Q = 50%) in prolonged ON, and from 0.04 to 0.6 (with a v_Q as large as 112%) in two groups with clinical signs of complete resolution of inflammation (Table 1). This means that mechanisms of effect on baseline function vary. BCVA was twofold to threefold lower in ON eyes with the involvement of the central retina (group 4) than for the eyes with acute ON (group 1) or prolonged ON (group 2), and this difference was significant ($p < 0.05$) (Table 1).

BCVA showed mild direct correlation with OPBF expressed as RQ ($r = 0.24$; $p < 0.05$), and negative correlation with the presence of complications following ON ($r = -0.35$; $p < 0.05$). RQ values in patients of group 1 were 15.5% higher than in controls ($p < 0.05$) and 35% and 31% higher than in patients of group 3 and group 4, respectively ($p < 0.05$). In addition, RQ values in patients with POA were 23.6% lower than in controls ($p < 0.05$), which reflected regional ischemic process (Table 2).

The OR for the presence of a reduced RQ value (a) in the eye with POA following ON compared to the eye with acute ON was 9.2 ($P < 0.05$, 95% confidence interval 2.0–42.4), and (b) in the eye developing macular lesion following ON compared to the eye with acute ON was 4.3 ($P < 0.05$, 95% CI, 1.2–14.7).

In all groups, RQ showed mild negative correlations with ROG characteristics such as pulse blood filling as assessed by RI in the right and left internal carotid systems ($r=-0.38$, $p < 0.05$ and $r=-0.29$, $p < 0.05$, respectively), tonicity (alpha/T) of the vessels in the right and left internal carotid systems ($r=-0.37$, $p < 0.05$ and $r=-0.40$, $p < 0.05$, respectively) and VBS ($r=-0.49$, $p < 0.05$). This phenomenon is likely to reflect the mechanisms of compensation of reduced ocular blood filling by an increased brain vessel blood flow with an increase in vessel tonicity and increased blood deposit on the vascular bed.

Pulse blood filling as assessed by RI in the ICS was actually normal in patients with acute ON and 44% increased in patients with prolonged ON or outcome of ON compared to controls ($p < 0.05$) (Table 3). Pulse blood filling as assessed by RI in the VBS was stable and at average 30% increased in patients than in controls ($p < 0.05$) (Table 3).

Tonicity of large vessels in the ICS and VBS as assessed by alpha/T was normal in group 1 and at average 15% higher in patients of groups 3 and 4 than in controls ($p < 0.05$) (Table 4).

There was no significant difference in the tonicity of small-caliber vessels in the ICS and VBS as assessed by the dicrotic index (DCI) and diastolic index (DSI) between the groups. In addition, there was no significant difference in the tonicity of small-caliber vessels as assessed by the DCI and DSI between the ICS and VBS ipsilaterally.

Table 1. Best-corrected visual acuity in patients with optic neuritis and patients with complications of optic neuritis

Characteristic	Acute ON, n=36		Prolonged ON, n=14		POA following ON, n=14		Complications other than POA following ON, n=18	
	1		2		3		4	
	Median (Q_{l-u})	v_e	Median (Q_{l-u})	v_e	Median (Q_{l-u})	v_e	Median (Q_{l-u})	v_e
Visual acuity	0.6 (0.12–1.0)	70.0%	0.4 (0.3–0.5)	51.0%	0.12 (0.04–0.6)	103.0%	0.12 (0.04–0.3)	112.0%
Significance of difference between groups (p)	$p_{1-4} = 0.009$ $p_{2-4} = 0.01$							

Note: IQR, interquartile range (25–75%); n, number of eyes; ON, optic neuritis; v_e, percentage coefficient variation; POA, partial optic atrophy

Table 2. Ocular pulse blood filling (expressed as RQ, ‰ rheographic coefficient of ophthalmic rheogram) in patients with optic neuritis and patients with complications of optic neuritis (M ± SD)

Characteristic	Acute ON, n=35	Prolonged ON, n=11	POA following ON, n=13	Complications other than POA following ON, n=9	Controls n=27
	1	2	3	4	5
RQ‰	4.5±1.7	3.7±1.6	2.9±1.3	3.1±1.3	3.8±1.7
Significance of difference between groups (p)	p_{1-5}=0.05; p_{3-5} =0.05 p_{1-3}=0.027; p_{1-4}=0.045				

Note: M, mean value; SD, standard deviation; n, number of eyes; ON, optic neuritis; v_e, percentage coefficient variation; POA, partial optic atrophy

Moreover, DCI and DSI values were at average 32.2% and 55%, respectively, higher in patients than in controls (Table 5).

Discussion

In patients with ON, visual loss usually progresses over a period of hours to days; in the untreated course of the disease, visual acuity generally reaches its nadir in one to two weeks.[13, 14] In the current study, in patients with acute ON, BCVA varied widely from 0.12 to 1.0. This is in agreement with others, who found the BCVA in the affected eyes to vary from count fingers to 20/20.[15] Inflammation in the optic nerve and impaired axonal transport (implied by retinal nerve fibre layer swelling) are associated with visual dysfunction and demyelination (long visual evoked potential latency) during acute ON.[16] The Optic Neuritis Study Group assessed visual function more than 10 years after an episode of ON [17] and 15 years after acute unilateral ON [18] in patients enrolled in the Optic Neuritis Treatment Trial. Visual acuity in the affected eyes was > or = 20/20 in 74% [17] and 72% [18]. On average, visual function was slightly worse among patients with MS than among those without MS.[17,18] Visual functions were, however, found to decrease in the eyes with optic atrophy after neuritis if more than half of nerve fibers running to the macula were damaged. After weeks of follow-up, some degree of optic atrophy was common despite recovery of visual acuity.[19] In the current study, visual acuity values were twofold to threefold lower for the eyes with optic atrophy after ON or those with macular involvement in ON than for the eyes with acute ON or prolonged ON. Trip and colleagues [20] described relationships among RNFL thickness and visual acuity, visual field, color vision, and visual-evoked potential amplitude. Retinal nerve fiber layer (RNFL) thickness has been shown to decrease by ~10–40 μm in the 3–6 months following an episode of acute optic neuritis.[21] RNFL degeneration may result in a decrease in the macular volume, partially due to the loss of retinal ganglion cells secondary to retrograde axonal degeneration.[22] Walter and colleagues [23] demonstrated that ganglion cell layer/inner plexiform layer (GCL+IPL) thinning is most significantly correlated with visual

Table 3. Relative pulse blood filling (expressed as relative rheographic index RI, against a norm of 100%) of brain vessels in the internal carotid system (ICS) and vertebral-basilar system (VBS), based on rheoencephalography in patients with optic neuritis (M ± SD)

Vascular system	Acute ON, n=25	Prolonged ON, n=7	POA following ON, n=7	Complications other than POA following ON, n=11	Significance of difference between groups (p)
	n=25	2	3	4	
Right internal carotid system	88.5±38.0	145.7±40.5	157.7±30.9	147.2±57.5	p_{1-2}=0.02 p_{1-3}=0.006 p_{1-4}=0.05
Left internal carotid system	102.7±46.2	141.8±49.2	132.5±54.5	140.2±88.6	p_{1-2}=0.03 p_{1-4}=0.04
Right vertebral-basilar system	130.1±30.5	171.6±28.7	120.0±44.8	135.3±100.5	p_{1-2}=0.001 p_{2-3}=0.01
Left vertebral-basilar system	143.2±33.9	157.2±14.1	134.8±36.5	122.7±21.9	p_{2-4}=0.03

Note: M, mean value; n, number of eyes; ON, optic neuritis; POA, partial optic atrophy; SD, standard deviation

Table 4. Tonicity in large-caliber vessels (expressed as alpha/T; against a norm of 100%) in the internal carotid system (ICS) and vertebral-basilar system (VBS), based on rheoencephalography in patients with optic neuritis (M ± SD)

Vascular system	Acute ON, n=25	Prolonged ON, n=7	POA following ON, n=7	Complications other than POA following ON, n=11	Significance of difference between groups (p)
	1	2	3	4	
Right internal carotid system	104.4±32.2	122.2±30.4	140.6±29.3	122.2±26.8	p_{1-3}=0.02
Left internal carotid system	103.5±37.6	106.4±30.4	141.5±72.8	113.3±38.4	p_{1-3}=0.04
Right vertebral-basilar system	105.5±26.3	99.8±18.0	118.3±37.9	121.9±25.4	p_{2-4}=0.03
Left vertebral-basilar system	103.5±29.3	97.7±20.9	130.6±38.4	122.7±21.9	p_{1-3}=0.01 p_{2-3}=0.03

Note: M, mean value; n, number of eyes; ON, optic neuritis; POA, partial optic atrophy; SD, standard deviation

function, and may serve as a useful structural marker of disease. Neuroretinitis can be a manifestation of idiopathic neuritis with progressive macular lesions, with macular exudate in a star-shaped pattern emerging 1-2 weeks after disease onset. The pathogenesis involves localized inflammation of the optic nerve vessels with increased vascular permeability and consequent leakage of liquid that accumulates in the macular region, with subsequent resorption and deposition of hard exudate. In most cases, neuroretinitis is a self-limiting disease associated with mild or moderate visual function impairment.[24]

Some authors hypothesized that various central and local vascular factors may be involved in the pathogenesis of ON. Thus, cardiovascular dysfunction (CD) in MS is related to involvement of reflex pathways in the brainstem. [25] The pathophysiology of ON has not been fully described, but thickening of the nerve in association with demyelination and inflammation may compress the blood vessels within the optic canal. Alternatively, vasospasm due to an increased plasma level of endothelin-1, a potent vasoconstrictor, may result in vasospasm and vascular dysregulation.[5] This could cause an increase in resistance

Table 5. Dicrotic index (DCI) and diastolic index (DSI) in small-caliber vessels in the internal carotid system (ICS) and vertebral-basilar system (VBS) (against a norm of 100%), based on rheoencephalography in patients with optic neuritis (M ± SD)

Vascular system	Characteristic of rheo-encephalography	Acute ON, n=25	Prolonged ON, n=7	POA following ON, n=7	Complications other than POA following ON, n=11	Total n=50
		1	2	3	4	1-4
Right internal carotid system	DCI (%)	147.2±49.0	98.2±33.9	142.8±54.9	148.3±39.2	137.2±48.0
	DSI (%)	160.2±45.0	161.1±6.0	148.3±39.2	164.3±40.6	156.5±42.0
Left internal carotid system	DCI (%)	145.2±39.0	103.2±26.4	142.8±54.9	139.5±38.2	134.6±42.1
	DSI (%)	161.8±46.2	129.1±27.2	164.3±39.9	158.1±45.1	154.4±43.0
Right vertebral-basilar system	DCI (%)	134.6±36.1	115.6±27.0	133.6±54.9	148.5±39.2	133.7±35.4
	DSI (%)	155.2±39.3	148.2±29.9	167.3±25.1	175.1±35.1	159.7±35.3
Left vertebral-basilar system	DCI (%)	136.2±29.4	102.8±29.4	118.4±53.9	127.1±53.9	124.2±40.2
	DSI (%)	154.2±31.8	136.0±32.7	154.0±30.4	150.0±36.8	149.7±33.4

Note: DCI, dicrotic index; DSI, diastolic index; M, mean value; n, number of eyes; ON, optic neuritis; POA, partial optic atrophy; SD, standard deviation

to flow in the artery and through ischemia lead to eventual exoplasmic stasis and visual loss.[7] In the current study, OPBF expressed as RQ values in patients with acute ON were 15.5% higher than in controls ($p < 0.05$) and 35% and 31% higher than in patients with POA following ON (group 3) and patients developing macular lesion following ON (group 4), respectively ($p < 0.05$). RQ values, however, were low in the outcome of complicated neuritis. Thus, RQ values in patients with POA were 23.6% lower than in controls, which reflected regional ischemic process.

Colour Doppler imaging (CDI) is one of the most widely used and well-established techniques for assessing ocular blood flow velocities in the retrobulbar vessels. [15] Although studies vary in their reports on abnormal hemodynamics in the orbital vessels in ON, most reports are generally in agreement with our findings. Some authors [6, 26] reported increased blood flow velocities in the ophthalmic artery in acute ON, but noted that these changes do not persist over a long period. Others [27], however, reported that the mean retrobulbar blood flow velocities in the ophthalmic artery in the eyes with ON were not significantly different from the unaffected fellow eyes and healthy control eyes, but mean resistivity indices in the central retinal and posterior ciliary arteries were higher in the eyes with ON than in the control eyes.[27] Modrzejewska and colleagues [28] evaluated blood flow velocity in ophthalmic artery, central retinal artery and short posterior ciliary artery in affected and unaffected eyes in patients with past retrobulbar ON in the course of MS. They concluded that reduction in blood flow parameters in the examined arteries occurred both, in the eyes previously affected by past optic neuritis and in contralateral, unaffected eyes. The inconsistencies between findings of different study groups may be explained by differences in patient characteristics, instru-mentation and technique of blood flow velocity measurements and the amount of time elapsed between the acute attack and examination. Accurate assessment of or¬bital blood flow is critical in understanding the dysregula¬tion that occurs during ON.[15]

The features of regional hemodynamics presented warrant that neuroprotective and anti-ischemic therapy should be applied taking into account the disease duration, course pattern and presence of complications in ON.

Conclusion

First, BCVA values were twofold to threefold lower for the eyes with macular involvement in ON than for the eyes with acute ON or prolonged ON.

Second, ocular pulse blood filling expressed as ophthalmic rheography index (RQ) values in patients with acute ON were 15.5% higher than in controls ($p < 0.05$) and 35% and 31% higher than in patients with POA following ON and patients developing macular lesion following ON, respectively ($p < 0.05$). In addition, RQ values in patients with POA were 23.6% lower than in controls ($p < 0.05$), which reflected regional ischemic process.

Third, pulse blood filling in the internal carotid system as assessed by RI index was actually normal in patients with acute ON and half-time increased in patients with prolonged ON or outcome of ON compared to controls ($p < 0.05$). In addition, tonicity of large vessels in the ICS and VBS as assessed by α/T (%) was normal in patients with acute ON and at average 15% higher in patients

with outcome of ON. Moreover, tonicity of small-caliber vessels as assessed by the DCI and DSI values was at average 32.2% and 55%, respectively, higher in patients than in controls.

References

1. Beck RW, Cleary PA, Anderson MM Jr, Keltner JL, Shults WT, Kaufman DI, Buckley EG, et al. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. N Engl J Med. 1992 Feb 27;326(9):581-8. doi: 10.1056/NEJM199202273260901.
2. Hickman SJ, Petzold A. Update on Optic Neuritis: An International View. Neuroophthalmology. 2021 Aug 31;46(1):1-18. doi: 10.1080/01658107.2021.1964541.
3. Bennett JL. Optic Neuritis. Continuum (Minneap Minn). 2019 Oct;25(5):1236-64. doi: 10.1212/CON.0000000000000768.
4. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, et al. International Panel for NMO Diagnosis. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul 14;85(2):177-89. doi: 10.1212/WNL.0000000000001729.
5. Pache M, Kaiser HJ, Akhalbedashvili N, Lienert C, Dubler B, Kappos L, et al. Extraocular blood flow and endothelin-1 plasma levels in patients with multiple sclerosis. Eur Neurol. 2003;49(3):164-8. doi: 10.1159/000069085.
6. Hradílek P, Zapletalova O, Dolezil D, Skoloudik D. Acute optic neuritis in multiple sclerosis: evaluation of haemodynamics in the ophthalmic artery with colour Doppler imaging. Neuroophthalmology. 2005;29:161–4.
7. McLeod D, Marshall J, Kohner EM. Role of axoplasmic transport in the pathophysiology of ischaemic disc swelling. Br J Ophthalmol. 1980 Apr;64(4):247-61. doi: 10.1136/bjo.64.4.247.
8. Lightman S, McDonald WI, Bird AC, Francis DA, Hoskins A, Batchelor JR, et al. Retinal venous sheathing in optic neuritis. Its significance for the pathogenesis of multiple sclerosis. Brain. 1987 Apr;110 (Pt 2):405-14. doi: 10.1093/brain/110.2.405.
9. Lee TH, Ji YS, Park SW, Heo H. Retinal ganglion cell and axonal loss in optic neuritis: risk factors and visual functions. Eye (Lond). 2017 Mar;31(3):467-74. doi: 10.1038/eye.2016.253.
10. Khramenko NI, Konovalova NV. [Ocular hemodymanics in optic neuritis]. In: [Proceedings of the Filatov Memorial Lectures conference with international speakers. 23-24 May; 2019. Odesa. p. 127. Russian.
11. Khramenko NI, Konovalova NV, Velichko LN, Bogdanova AV. [Immunological status in optic neuritis]. In: [Proceedings of the Filatov Memorial Lectures conference with international speakers. 23-24 May; 2019. Odesa. p. 126. Russian.
12. Jonzzon S, Suleiman L, Yousef A, Young B, Hart J, Peschl P, et al. Clinical Features and Outcomes of Pediatric Monophasic and Recurrent Idiopathic Optic Neuritis. J Child Neurol. 2020 Jan;35(1):77-83. doi: 10.1177/0883073819877334.
13. Balcer LJ. Clinical practice. Optic neuritis. N Engl J Med. 2006 Mar 23;354(12):1273-80. doi: 10.1056/NEJMcp053247.
14. Foroozan R, Buono LM, Savino PJ, Sergott RC. Acute demyelinating optic neuritis. Curr Opin Ophthalmol. 2002 Dec;13(6):375-80. doi: 10.1097/00055735-200212000-00006.
15. Karami M, Janghorbani M, Dehghani A, Riahinejad M. Orbital Doppler evaluation of blood flow velocities in optic neuritis. Korean J Ophthalmol. 2012 Apr;26(2):116-22. doi: 10.3341/kjo.2012.26.2.116.
16. Henderson AP, Altmann DR, Trip AS, Kallis C, Jones SJ, Schlottmann PG, et al. A serial study of retinal changes following optic neuritis with sample size estimates for acute neuroprotection trials. Brain. 2010 Sep;133(9):2592-602. doi: 10.1093/brain/awq146.
17. Beck RW, Gal RL, Bhatti MT, Brodsky MC, Buckley EG, Chrousos GA, et al. Optic Neuritis Study Group. Visual function more than 10 years after optic neuritis: experience of the optic neuritis treatment trial. Am J Ophthalmol. 2004 Jan;137(1):77-83. doi: 10.1016/s0002-9394(03)00862-6.
18. Optic Neuritis Study Group. Visual function 15 years after optic neuritis: a final follow-up report from the Optic Neuritis Treatment Trial. Ophthalmology. 2008 Jun;115(6):1079-82.e5. doi: 10.1016/j.ophtha.2007.08.004.
19. Miller NR, Newman NJ, Biousse V, Kerrison JB. Walsh and Hoyt's Clinical Neuro-ophthalmology. Lippincott Williams & Wilkins: Philadelphia, PA;2005.
20. Trip SA, Schlottmann PG, Jones SJ, Altmann DR, Garway-Heath DF, Thompson AJ, et al. Retinal nerve fiber layer axonal loss and visual dysfunction in optic neuritis. Ann Neurol. 2005 Sep;58(3):383-91. doi: 10.1002/ana.20575.
21. Costello F, Coupland S, Hodge W, Lorello GR, Koroluk J, Pan YI, et al. Quantifying axonal loss after optic neuritis with optical coherence tomography. Ann Neurol. 2006 Jun;59(6):963-9. doi: 10.1002/ana.20851.
22. Burkholder BM, Osborne B, Loguidice MJ, Bisker E, Frohman TC, Conger A, et al. Macular volume determined by optical coherence tomography as a measure of neuronal loss in multiple sclerosis. Arch Neurol. 2009 Nov;66(11):1366-72. doi: 10.1001/archneurol.2009.230.
23. Walter SD, Ishikawa H, Galetta KM, Sakai RE, Feller DJ, Henderson SB, et al. Ganglion cell loss in relation to visual disability in multiple sclerosis. Ophthalmology. 2012 Jun;119(6):1250-7. doi: 10.1016/j.ophtha.2011.11.032.
24. Viturino MGM, Moura FC. Recurrent idiopathic neuroretinitis as a spectrum of atypical optic neuritis: a case report and literature review. Arq Bras Oftalmol. 2018 Jan-Feb;81(1):70-2. doi: 10.5935/0004-2749.20180016.
25. Acevedo AR, Nava C, Arriada N, Violante A, Corona T. Cardiovascular dysfunction in multiple sclerosis. Acta Neurol Scand. 2000 Feb;101(2):85-8. doi: 10.1097/NRL.0000000000000064.
26. Karaali K, Senol U, Aydin H, Cevikol C, Apaydin A, Lüleci E. Optic neuritis: evaluation with orbital Doppler sonography. Radiology. 2003 Feb;226(2):355-8. doi: 10.1148/radiol.2262011915.
27. Akarsu C, Tan FU, Kendi T. Color Doppler imaging in optic neuritis with multiple sclerosis. Graefes Arch Clin Exp Ophthalmol. 2004 Dec;242(12):990-4. doi: 10.1007/s00417-004-0948-1.
28. Modrzejewska M, Karczewicz D, Wilk G. Assessment of blood flow velocity in eyeball arteries in multiple sclerosis patients with past retrobulbar optic neuritis in color Doppler ultrasonography. Klin Oczna. 2007;109(4-6):183-6.

Disclosures

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The study was conducted with human participants. This study was approved by the local bioethics committee. All patients gave informed consent to participate in the study. The study was conducted in accordance with the Declaration of Helsinki. This study did not include animal experiments.