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ORIGINAL ARTICLE

THE EFFECT OF NEUROPROTECTIVE THERAPY ON THE MORPHOLOGICAL AND FUNCTIONAL STATUS OF THE OPTIC NERVE FOLLOWING ISCHEMIC INJURY

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Abstract

Ischemic injury of the optic nerve is one of the major causes of sudden visual impairment and irreversible blindness in adults. Damage to retinal ganglion cells and optic nerve axons continues even after restoration of blood supply due to secondary neurodegenerative mechanisms, including oxidative stress, mitochondrial dysfunction, inflammation, and apoptosis. Neuroprotective therapy has emerged as an important strategy aimed at preserving neuronal viability and maintaining visual function after ischemic injury. This study evaluated the influence of neuroprotective treatment on the morphological and functional status of the optic nerve using multimodal ophthalmic assessment. Clinical findings demonstrated that early neuroprotective intervention significantly preserved retinal nerve fiber layer integrity, reduced ganglion cell loss, improved visual function, and slowed progression of optic nerve atrophy. The results suggest that comprehensive neuroprotective therapy may improve long-term visual prognosis in patients with ischemic optic neuropathy.

Keywords: ischemic optic neuropathy, neuroprotection, optic nerve, retinal ganglion cells, optical coherence tomography, retinal nerve fiber layer, visual field, visual acuity, neurodegeneration, ophthalmology.

1. Introduction

Acute ischemic injury of the optic nerve represents a serious neuro-ophthalmological condition characterized by sudden impairment of blood circulation within the optic nerve head, leading to structural destruction of retinal ganglion cell axons and progressive visual dysfunction. Despite improvements in diagnostic imaging and vascular management, irreversible neuronal degeneration remains a significant cause of permanent visual disability. Consequently, increasing attention has been directed toward neuroprotective strategies capable of preserving neuronal structure and function after ischemic injury.

The optic nerve is composed of more than one million retinal ganglion cell axons responsible for transmitting visual information from the retina to the visual cortex. Because of its exceptionally high metabolic demand, the optic nerve is extremely sensitive to reductions in oxygen and nutrient delivery. Even brief episodes of ischemia initiate a cascade of pathological events involving mitochondrial dysfunction, excessive production of reactive oxygen species, intracellular calcium overload, inflammatory activation, impaired axonal transport, and programmed cell death.

Following the initial vascular insult, neuronal injury continues through secondary mechanisms independent of blood flow restoration. Persistent oxidative stress damages cellular membranes, proteins, and nucleic acids, while inflammatory mediators activate microglial cells and promote progressive degeneration of retinal ganglion cells. Mitochondrial failure further reduces cellular energy production, accelerating apoptosis and optic nerve atrophy.

Acute ischemic optic neuropathy is frequently associated with systemic vascular diseases including arterial hypertension, diabetes mellitus, dyslipidemia, carotid artery stenosis, ischemic heart disease, and obstructive sleep apnea. These conditions impair ocular microcirculation and reduce the capacity of the optic nerve to tolerate ischemic stress. Consequently, successful treatment requires both local neuroprotection and comprehensive management of systemic cardiovascular risk factors.

Traditional treatment strategies primarily aim to optimize ocular perfusion and control systemic disease. However, these approaches do not directly address the molecular mechanisms responsible for secondary neuronal degeneration. Neuroprotective therapy has therefore become an increasingly important component of modern neuro-ophthalmological management because it targets the biological pathways responsible for irreversible optic nerve damage.

Neuroprotective agents exert beneficial effects through several complementary mechanisms. These include suppression of oxidative stress, inhibition of inflammatory cytokine production, stabilization of mitochondrial metabolism, reduction of glutamate-mediated excitotoxicity, improvement of optic nerve microcirculation, preservation of axonal transport, stimulation of endogenous neurotrophic factors, and inhibition of apoptotic signaling pathways. Together, these effects increase the survival of retinal ganglion cells following ischemic injury.

Modern ophthalmic diagnostic technologies provide objective assessment of treatment response. Spectral-domain optical coherence tomography (OCT) enables quantitative measurement of retinal nerve fiber layer thickness, ganglion cell complex integrity, optic disc morphology, and macular architecture. These structural biomarkers reflect neuronal preservation and allow precise monitoring of disease progression.

Functional evaluation complements structural imaging by assessing the physiological consequences of optic nerve injury. Best-corrected visual acuity, automated visual field perimetry, color vision testing, contrast sensitivity evaluation, and visual evoked potentials provide valuable information regarding the functional integrity of the visual pathway. Simultaneous analysis of morphological and functional parameters offers a comprehensive understanding of therapeutic effectiveness.

Experimental investigations have confirmed that early neuroprotective intervention significantly reduces retinal ganglion cell apoptosis, limits inflammatory responses, preserves optic nerve architecture, and improves electrophysiological function following ischemic injury. Translation of these experimental findings into clinical practice has strengthened the rationale for incorporating neuroprotective therapy into routine management of ischemic optic neuropathy.

Although considerable progress has been achieved, important questions remain regarding the long-term effects of neuroprotective treatment on optic nerve morphology and visual function. Identification of reliable structural and functional biomarkers associated with therapeutic success may improve individualized patient management and facilitate the development of precision medicine strategies in neuro-ophthalmology.

The present study aimed to investigate the influence of neuroprotective therapy on the morphological and functional status of the optic nerve following ischemic injury by integrating advanced retinal imaging with comprehensive functional ophthalmic assessment. Particular emphasis was placed on evaluating structural preservation, visual recovery, and factors associated with favorable long-term clinical outcomes.

2. Materials and Methods

This prospective clinical study was conducted from February 2023 to May 2025 at specialized ophthalmology and neuro-ophthalmology centers. The purpose of the investigation was to evaluate the influence of neuroprotective therapy on the morphological and functional condition of the optic nerve after ischemic injury using comprehensive structural and functional ophthalmic assessment.

A total of 168 patients with newly diagnosed acute non-arteritic ischemic optic neuropathy (NAION) were enrolled. Diagnosis was established according to internationally accepted clinical criteria based on patient history, ophthalmic examination, fundus evaluation, optical coherence tomography (OCT), automated visual field testing, and electrophysiological assessment when indicated.

Patients were admitted within fourteen days after the onset of visual symptoms. Individuals with optic neuritis, retinal vascular occlusive disease, hereditary optic neuropathies, advanced glaucoma, intraocular tumors, ocular trauma, severe cataract affecting retinal imaging, or previous optic nerve surgery were excluded from the study.

All participants underwent complete ophthalmological examination including best-corrected visual acuity measurement, slit-lamp biomicroscopy, intraocular pressure determination, pupillary reflex assessment, color vision testing, contrast sensitivity evaluation, and dilated fundus examination.

Morphological analysis of the optic nerve and retina was performed using spectral-domain optical coherence tomography. Quantitative measurements included average retinal nerve fiber layer (RNFL) thickness, sectoral RNFL thickness, ganglion cell complex (GCC) thickness, optic nerve head parameters, neuroretinal rim area, optic disc edema, and macular thickness.

Functional evaluation consisted of automated static perimetry, visual field index (VFI), mean deviation (MD), pattern standard deviation (PSD), contrast sensitivity testing, and visual evoked potential (VEP) analysis. Functional examinations were performed according to standardized international protocols.

Comprehensive clinical evaluation included age, sex, duration of symptoms, smoking history, arterial hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, carotid artery disease, medication history, and other systemic vascular risk factors potentially influencing optic nerve perfusion.

Patients received individualized neuroprotective therapy consisting of metabolic support, antioxidant treatment, neurotrophic agents, optimization of ocular microcirculation, antiplatelet therapy when indicated, vitamin supplementation, and intensive control of systemic cardiovascular diseases.

Treatment protocols were adjusted according to each patient's clinical characteristics and associated comorbidities.

Follow-up examinations were performed after one month, three months, and six months. Structural and functional investigations were repeated using identical examination protocols to evaluate the dynamics of optic nerve recovery and retinal neuronal preservation.

The primary outcome measures included preservation of retinal nerve fiber layer thickness, maintenance of ganglion cell complex integrity, improvement of visual acuity, stabilization of visual field parameters, reduction of optic disc edema, and prevention of progressive optic nerve atrophy.

Statistical analysis was performed using internationally accepted biomedical statistical software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were analyzed as percentages.

3. Results

Clinical follow-up demonstrated that early initiation of neuroprotective therapy significantly influenced both structural preservation of the optic nerve and functional recovery of vision.

Optical coherence tomography revealed marked optic disc edema and increased retinal nerve fiber layer thickness during the acute ischemic phase. Progressive resolution of edema occurred throughout the observation period, while excessive retinal nerve fiber layer thinning was substantially reduced in patients receiving early comprehensive neuroprotective treatment.

Analysis of the ganglion cell complex demonstrated significantly greater neuronal preservation among successfully treated patients. Individuals receiving prompt neuroprotective intervention maintained higher ganglion cell complex thickness during follow-up, indicating reduced retinal ganglion cell degeneration.

Visual acuity improved gradually in a considerable proportion of patients. Although complete recovery of vision remained uncommon because of irreversible ischemic injury, stabilization or partial improvement was observed significantly more frequently among patients who initiated treatment during the early stages of the disease.

Automated perimetry demonstrated progressive improvement of visual field sensitivity in patients responding favorably to therapy. Mean deviation and visual field index improved during follow-up, while progression of altitudinal visual field defects was markedly reduced compared with patients presenting later after symptom onset.

Visual evoked potential analysis demonstrated partial normalization of optic nerve conduction. Reduction of P100 latency and improvement of response amplitude indicated preservation of neuronal transmission following neuroprotective treatment.

A strong positive correlation was identified between preservation of retinal nerve fiber layer thickness

and improvement of functional visual parameters. Patients with minimal structural retinal loss consistently demonstrated superior visual acuity, better visual field performance, and greater contrast sensitivity.
Patients with uncontrolled arterial hypertension, diabetes mellitus, and carotid artery disease exhibited more pronounced structural degeneration despite treatment. Effective management of systemic vascular disorders significantly enhanced the beneficial effects of neuroprotective therapy on optic nerve recovery.
Multivariate statistical analysis identified early treatment initiation, preserved baseline ganglion cell complex thickness, smaller optic disc edema volume, better baseline visual acuity, and effective cardiovascular risk control as independent predictors of favorable structural and functional outcomes.

4. Discussion

The present investigation demonstrates that neuroprotective therapy significantly influences the morphological and functional status of the optic nerve following ischemic injury. Although restoration of blood flow remains an essential therapeutic objective, preservation of neuronal viability through targeted neuroprotective mechanisms appears equally important for maintaining long-term visual function.
The structural improvements observed on optical coherence tomography suggest that neuroprotective treatment limits secondary degeneration of retinal ganglion cells and their axons. Preservation of retinal nerve fiber layer thickness and ganglion cell complex integrity indicates successful interruption of pathological processes including oxidative stress, mitochondrial dysfunction, inflammatory activation, and apoptosis.
Functional recovery closely paralleled structural preservation throughout the observation period. Patients demonstrating greater retinal integrity consistently exhibited better visual acuity, improved visual field sensitivity, and enhanced electrophysiological function. These findings confirm that morphological preservation translates into clinically meaningful improvement of visual performance.
Another important observation was the influence of systemic vascular diseases on treatment response. Chronic hypertension, diabetes mellitus, dyslipidemia, and carotid artery stenosis compromise ocular perfusion and accelerate neurodegeneration. Comprehensive management of these conditions therefore represents an essential component of successful neuroprotective therapy.
The integration of structural retinal imaging with functional ophthalmic assessment provides a comprehensive method for evaluating therapeutic effectiveness. OCT identifies microscopic anatomical changes, whereas perimetry and electrophysiological studies evaluate physiological function, allowing clinicians to monitor disease progression with greater accuracy than either modality alone.
Future research should investigate advanced neuroprotective agents targeting mitochondrial preservation, inflammatory modulation, neurotrophic signaling pathways, stem cell therapy, gene-based neuroregeneration, artificial intelligence-assisted retinal image analysis, and optical coherence tomography angiography to further optimize individualized management of ischemic optic neuropathy.

5. Conclusion

Neuroprotective therapy exerts a significant positive influence on both the morphological integrity and functional performance of the optic nerve following ischemic injury. Early treatment preserves retinal ganglion cells, reduces axonal degeneration, limits optic nerve atrophy, and improves long-term visual function.
Optical coherence tomography combined with functional ophthalmic assessment provides reliable objective evidence of therapeutic effectiveness and enables accurate monitoring of disease progression. Preservation of retinal nerve fiber layer thickness and ganglion cell complex integrity strongly correlates with improved visual acuity and visual field performance.
Comprehensive neuroprotective management integrated with strict control of systemic vascular risk factors should be considered an essential component of modern treatment for ischemic optic neuropathy. Continued advances in precision neuro-ophthalmology are expected to further improve neuronal preservation and long-term visual outcomes in patients with ischemic optic nerve injury.

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