# EFFICIENCY OF TRANSCRANIAL MAGNETIC STIMULATION IN THE TREATMENT OF PARTIAL OPTIC NERVE ATROPHY IN CHILDREN

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***Abstract****. This article is devoted to the problem of morbidity of the optic nerve, which is one of the main causes of blindness and visual impairment. Currently, the diagnosis, treatment and rehabilitation of patients with partial atrophy of the optic nerve are considered an important medical and social problem.*
***Keywords****: eye diseases; optic nerve; blindness; low vision.*

**Relevance**. Partial optic atrophy (PONA) is a severe pathology of the optic nerve leading to low vision, blindness and disability. The problem of treating this pathology is relevant and has great social significance due to the increasing prevalence and severity of the disease and its high disabling factor [1,3,4,17]. According to WHO, there are about 42 million blind and visually impaired people in the world. Diseases of the optic nerve are one of the main causes of blindness and low vision. 98% of visually impaired people with optic nerve atrophy need rehabilitation measures [2,5,6,10]. Currently, the diagnosis, treatment and rehabilitation of patients with partial atrophy of the optic nerve is considered an important medical and social problem. The increase in disability of the population due to partial atrophy of the optic nerve indicates the insufficient effectiveness of the basic rehabilitation system. Treatment of optic nerve atrophy is a complex problem due to the extremely limited ability to regenerate nerve tissue. Modern methods of treating patients with partial optic nerve atrophy provide for an integrated approach to therapy. Treatment methods for this pathology are being developed in the direction of improving blood circulation, increasing the level of tissue metabolism, creating biochemical, energetic and functional conditions to improve the conduction of rhythmic excitation along the optic nerve. According to various authors, the positive effect of “traditional” conservative therapy for PONA is observed in 21.4-63.4% of treated patients [4,7,8,18]. The problem of delivering drugs to the optic nerve and creating their sufficient concentration, taking into account the presence of histohematic barriers, remains a serious problem [5,19]. Complex therapy is the most effective, rationally combining methods of general and local influence on the body of several therapeutic factors that potentiate each other’s action at various levels of regulation of the body’s activity. In pharmacotherapy of partial optic nerve atrophy, the following are used: vasodilators: magnesium sulfate 25% [6,9,11]; angioprotectors: mildronate, emoxypine [8,12]; nootropics: Semax, Ceraxon, Cerebrolysin, glycine; neuroprotectors: cortexin; metabolic medications: actovegin, succinic acid; vitamin therapy: vitamins of group B, PP. These drugs enter the body in the form of periocular injections and through various irrigation systems [9,13,15]. In recent years, peptide bioregulators have been widely used in clinical practice for the prevention and treatment of various diseases of the organ of vision [6,16]. Retinalamine is a complex of peptides isolated from the retina of cattle. The drug has a specific effect on the retina: it stimulates photoreceptors and cellular elements of the retina, improves the functional interaction of the pigment epithelium of the outer segments of

photoreceptors, and accelerates the restoration of light sensitivity of the retina. Cortexin adequately affects the fibers of the optic nerve and helps normalize metabolism in the neurons of the retina and the corresponding parts of the optic tract, and also restores the functional activity of the optic nerve.

Optic nerve atrophy in children is one of the serious diseases leading to irreversible vision loss. It can be the outcome of various local and systemic processes in the body. Pathomorphologically, atrophy is characterized by the disintegration of nerve fibers and their replacement with glial tissue. Atrophic processes can occur as a result of inflammation or congestion in the optic nerve, as well as as a result of various toxic effects. The most common causes of partial optic nerve atrophy (PONA) in children are infectious inflammatory diseases of the central nervous system (up to 40% of cases), hydrocephalus of various origins, brain tumors, congenital diseases of the central nervous system, metabolic disorders, retinopathy of prematurity, head injury, etc. Partial atrophy optic nerve disorder (hereinafter referred to as PONA) can be congenital and hereditary, primary and secondary. In Uzbekistan, PONA occurs in 1.2–8.6% [2,14,20]. Among the visually impaired, up to 30.9%.

**The aim of research.**

To study the effectiveness of an integrated approach in the treatment of partial atrophy of the optic nerve of various origins using transcranial magnetic stimulation.

**Material and methods.**

We examined 36 children (64 eyes), hospitalized in the eye department of the TashPMI clinic and examined in the outpatient clinic of the centre neurosurgery. Of these, boys accounted for 53% (19 children), girls - 47% (17 children). The age of the studied patients varied from 2 to 17 years, the average age was 12 years. Of all requests, 17% (6 children, 9 eyes) are secondary atrophy of the optic disc. 15 children (42%) received transcranial magnetic stimulation as part of the complex treatment of partial atrophy, and 21 children (58%) received conservative treatment.

All children underwent neuro-ophthalmological (visiometry, biomicroscopy, perimetry, ophthalmoscopy, optical coherent tomography, visually evoked potentials), clinical and laboratory research methods, as well as consultations with related specialists (ENT, pediatrician, neurosurgeon).

Transcranial magnetic stimulation (TMS) is a noninvasive form of brain stimulation in which a changing magnetic field is used to induce an electric current at a specific area of the brain through electromagnetic induction. An electric pulse generator, or stimulator, is connected to a magnetic coil connected to the scalp. The stimulator generates a changing electric current within the coil which creates a varying magnetic field, inducing a current within a region in the brain itself

Transcranial magnetic stimulation is a method based on stimulating brain neurons with an alternating magnetic field and recording responses to stimulation using electromyography. Its essence lies in the depolarization of nerve cell membranes under the influence of a strong magnetic field. Rhythmic TMS (rTMS) is a type of stimulation that generates a series of pulses that range in frequency from 1 to 100 Hz. There are two main rTMS modes: low-frequency (<1 Hz) and high-frequency (>5 Hz). Low-frequency magnetic stimulation causes a decrease in the excitability of neurons in the cerebral cortex, which leads to an inhibitory aftereffect, and high-frequency magnetic stimulation causes its increase, which has a stimulating effect. There are also “pattern” stimulation modes (intermittent theta burst stimulation - iTBS, continuous theta burst stimulation

- cTBS), in which stimuli are presented in the form of specific clusters. The duration of the rTMS aftereffect is proportional to the duration of stimulation, the total number of stimuli and the frequency of sessions [4]. The physiological (therapeutic) effect of rTMS and long-term (up to 3 months) aftereffect are traditionally associated with changes in synaptic plasticity due to the phenomena of long-term potentiation and depression.

**Results.**

The main group consisted of 21 patients (35 eyes) with PONA, the control group - 15 patients (29 eyes). Patients in each of the two groups were divided into three subgroups according to the etiology of PONA: subgroup I consisted of patients with PONA due to pathology of the central nervous system (consequences of intoxication, traumatic brain injury, demyelinating processes, neurosurgical interventions, congenital disorders); Subgroup II consisted of patients with PONA due to retinal pathology (central chorioretinal dystrophy, retinal pigment abiotrophy); In subgroup III we combined patients with pathology of the optic nerve that developed in the long term after acute disorders of the blood supply to the optic nerve and retina (anterior ischemic neuropathies, posterior ischemic neuropathies, thrombosis of the central retinal vein and its branches, occlusion of the central retinal artery and its branches).

Treatment was carried out as pathogenetically as possible, taking into account the underlying disease and was aimed at improving blood circulation and stimulating the vital activity of surviving but depressed nerve fibers.

In the main group, traditional therapy was used to treat patients with PONA, consisting of: 1) nootropics (piracetam, etc.); 2) vasodilators (no-spa, papaverine, nicotinic acid, cavinton, etc.); 3) antioxidants (lipoic acid, blueberry forte, etc.); 4) angioprotectors (emoxipin, etc.); 5) polypeptides (cortexin, retinalamine); 6) neurotrophics (taufon, cerebrolysin).

In the control group, treatment was carried out in combination with transcranial magnetic stimulation. Patients were monitored on an outpatient basis throughout the entire treatment period. The session of transcranial magnetic stimulation lasted 10 days for 30 minutes.

We carried out dynamic monitoring of patients with PONA who were treated. The results obtained were assessed 1 and 3 months after treatment.

Assessing the results of the treatment, one can note better functional results according to the “visual acuity” criterion in subgroups II and III of the control group compared to patients of the main group. In patients with PONA due to pathological changes in the retina and circulatory disorders of the retinal vessels and optic nerve, it was possible to achieve an improvement in visual acuity by 60 and 47%, respectively.

***Table 1.***

***Dynamics of average visual acuity values before and after treatment, 3 months. (N±n)***

| | **Main group** | | | **Control group** | | |
|---|---|---|---|---|---|---|
| | I | II | III | I | II | III |
| before treatment | 0,17 ± 0,05* | 0,25 ± 0,09* | 0,17 ± 0,15* | 0,16 ± 0,05 | 0,31 ± 0,15* | 0,16 ± 0,03* |
| before treatment | 0,23 ± 0,07* | 0,4 ± 0,15* | 0,25 ± 0,05* | 0,19 ± 0,06 | 0,39 ± 0,02* | 0,21 ± 0,02* |

| | | | | | | |
|---|---|---|---|---|---|---|
| Enhancement Gradient | 0,06 | 0,15 | 0,08 | 0,03 | 0,08 | 0,05 |
| % improvement | 35,3 | 60 | 47 | 18,7 | 25,8 | 31,2 |
| *$p < 0,05$, significant differences before and after treatment | | | | | | |

Computer perimetry was carried out on an Octopus-900 computer perimeter (Haag-Streit AG, Switzerland) using screening programs to determine the photosensitivity of the retina in 120 areas of the visual field, the threshold level of photo sensitivity of the retina in the foveal zone was determined, average levels of photosensitivity of the central zone of the retina and the periphery of the visual field. The number of relative and absolute scotomas was assessed, their quantitative characteristics were determined, and a profile program was carried out to determine the size of the blind spot. One of the objective methods for assessing functional changes in visual functions was the quantitative assessment of the reduction in the number of absolute and relative scotomas when performing computer perimetry. We were able to achieve the highest results in the third experimental subgroup, where the number of absolute scotomas decreased by an average of 25%, and relative scotomas of the 1st and 2nd orders - by 58.4%.

Computer tomography (CT) of the optic nerve head (OND) was performed on a CirrusHD-OST tomograph (CarlZeiss, Germany). The thickness of the optic fibers, changes in ganglion cells and their axons forming the optic nerve, the depth of excavation, and the profile of the optic disc were assessed.

The examination of visually evoked potentials (VEP) was carried out using an EP-1000 PC-Electrophysiological Testing device (Tomey, Japan). An increase in visual acuity and electrical lability indicators indicated an improvement in the functioning of the axial fascicle of the optic nerve. An increase in the average amplitude values, a decrease in the average latency values of the P100 VEP wave, along with an increase in the average lability values, indicated an improvement in the parameters of the conduction of rhythmic excitation along the optic nerve. Visual evoked potentials were recorded per flash. In patients with high functioning VEPs were recorded for the reversal of chess patterns with a cell size of 14 min. The number of patients with visual acuity of 0.5 and higher in the main group was 10% and in the control group - 6%. Potentials recorded on patterns are more stable in time and amplitude characteristics, are well reproducible and are very sensitive to pathological changes in the visual pathways. For patients with low visual acuity up to 0.09 and from 0.5 and above, VEPs were recorded per flash, although flash biopotentials are less stable, more variable and less sensitive to pathological changes in the visual pathways. In both cases, VEPs were assessed according to the following criteria: 1 - significant decrease in the amplitude of biopotentials and their complete absence; 2 – prolongation of the latency of the positive P100 peak, as less variable, more stable; 3 – symmetry in amplitude and latency during light stimulation of the right and left eyes. Changes in VEP in PAI were characterized by a decrease in the amplitude of biopotentials, an increase in latency, and asymmetry in a monocular pathological process. Changes in VEP increased with the progression of the pathological process. Moreover, in cases with unilateral damage to the visual analyzer, a very significant difference in the latency of the P100 peak was recorded (up to 20 ms).

The differences turned out to be statistically significant according to the paired Student's test ($p < 0.05$) when determined before and after treatment in both groups.

In general, functional indicators were significantly higher in patients treated with the combined treatment method compared to the group treated with the traditional method. There was an improvement in the functioning of the axial bundle of the optic nerve (increase in the average value of visual acuity, improvement in electrolability indicators), improvement in the functioning of optic nerve fibers coming from the periphery of the retina (decrease in the average value of absolute and relative scotomas, improvement in the amplitude and temporal characteristics of the VEP).

**Conclusion**.

Thus, the data presented in our work convincingly confirm the fairly high effectiveness of the developed method of treating PONA, based on transcranial magnetic stimulation of the optic nerve, which allows for controlled stimulation treatment on an outpatient basis. The original method of treating patients with various forms of PONA that we have developed ensures the achievement of good results in a complex category of patients with pathology of the optic nerve and retina and determines the prospects for the further development of this method of treatment and the widespread introduction of the original method into clinical practice. Combined treatment of partial optic nerve atrophy in children can improve visual functions and stabilize the process.

It should be noted that patients in control group, visual functions remained unchanged after 6 months and (or) decreased slightly after treatment, while in the main group, visual functions returned to the initial data before treatment.

The effectiveness of complex treatment depended on the stage, etiology of the disease, and the age of the patient. At the initial stages of CAP, the therapeutic effect was more pronounced; the greatest effectiveness was observed in cases of optic nerve atrophy of glaucomatous and vascular origin. The effectiveness of treatment depended on the etiology and stage of the disease, concomitant pathology, its timely correction and the competence of the patient.

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