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# FEATURES OF NEUROPROTECTIVE TREATMENT OF CHILDREN WITH PRIMARY CONGENITAL GLAUCOMA

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***Summary***

*Normalization of intraocular pressure is an indispensable condition, but it does not guarantee stabilization of the glaucomatous process. Neuroprotective therapy aimed at maintaining the active function of axons of ganglion cells is of great importance.*

***The aim** of the study was to study the effectiveness of the neuroprotective effect of the Cortexin drug in congenital glaucoma.*

***Material and methods.** Thirty-two (64 eyes) children with congenital glaucoma in the compensation stage were included in the study. Of these, 18 children (36 eyes) were included in the main group that received the neuroprotectant Cortexin. The remaining 14 children (28 eyes) were included in the control group and received standard treatment. Research methods: Visometry, ophthalmoscopy, perimetry, tonometry, tonography, ocular ultrasound, gonioscopy.*

***Results.** All patients underwent antiglaucomatous surgery and, in the absence of negative dynamics during the year, neuroprotective treatment with Cortexin was performed every three months. To study visual acuity in young children, a computer program was developed and used to determine visual acuity. The computer program «Scale for assessment of visual functions» was certified (No. DGU 11841). Next, the parents of the child were explained how to score. After 1 month and after 3 months of treatment, the parents filled in the table and deducted points. After completion of neuroprotective treatment within one year, we collected data from the questionnaire filled out by the parents and analyzed visual acuity. Data analysis in the main group showed an increase in visual acuity in all stages of glaucoma except the final stage. In children in the control group, visual acuity before surgery was identical to that in the main group. After one year of observation, the increase in visual acuity in the control group was much less than in the main group.*

***Conclusion.** Thus, the dynamics of visual acuity improvement was significantly more pronounced in the main group, which indicates the usefulness of including drugs with neuroprotective effect in the complex treatment of glaucomatous neuropathy.*

***Key words:** Treatment; Congenital Glaucoma; Neuroprotective therapy.*

## Introduction

Pediatric glaucoma is rightly considered to be a difficult disease to cure, mainly due to the peculiarities of the pathology and the specificity of the course of the disease in this group of patients. Primary congenital glaucoma is the most common form of pediatric glaucoma, occurring with an incidence of 1 case per 10,000 newborns, with every 10th blind child permanently losing vision due to glaucoma [1-4].

Signs of the disease can be detected in 60 % of children within the first 6 months of life and in 80 % within the first year of life. When newborns are examined in maternity hospitals, 90 % of them can be diagnosed because of early signs of the disease. The urgency of the glaucoma problem is illustrated by the following facts: only 50 % of glaucoma patients living in developed countries are aware of their disease; 50 % of glaucoma patients in developed countries are untreated and 95 % in developing countries; 50 % of people worldwide have never had their intraocular pressure measured. Studies in recent years have clearly shown that there is no single cause of primary congenital glaucoma, but many «different glaucomas» [5-9]. Most authors believe that this disease is multifactorial with a complex etiopathogenesis that is not fully understood [10-12].

Surgical treatment is the main pathogenetically based treatment aimed at lowering IOP. Therefore, after surgical treatment, during rehabilitation, the main attention is paid to IOP control and eye growth. The condition of the optic nerve – glaucomatous neuropathy – remains unattended. This in turn leads to loss of visual acuity. As a result, more and more ophthalmic researchers have paid attention to the investigation of biomolecular mechanisms behind neuronal survival and the development of further neuroprotective therapies as an adjunct to IOP lowering treatment [13-17].

Neuroprotection is a therapeutic approach aimed at preserving neural structure and function [18-22]. In glaucoma, neuroprotection refers to non-IOP related interventions that can prevent or delay RGC apoptosis independent of IOP. Although it may be difficult to identify a single causative factor for the development of glaucoma, a reasonable approach to glaucomatous optic neuropathy remains to target possible underlying mechanisms of glaucomatous damage, including neurotrophic factor (NTF) deprivation, reactive oxygen species (ROS) generation, oxidative stress, glutamate excitotoxicity, ischemia, glial activation, and genetic determinants. Therefore, understanding the pathogenic factors in glaucoma may further pave the way for the development of more practical neuroprotective methods and subsequent clinical translation. In the field of glaucoma, neuroprotection is defined as any treatment, independent of IOP lowering, that prevents RGC death [23-25]. Glutamate antagonists, Ginkgo biloba extract, neurotrophic factors, antioxidants, calcium channel blockers, brimonidine, anti-glaucoma medications, and nitric oxide synthase inhibitors are among the compounds with possible neuroprotective activity in preclinical studies. A few agents (such as brimonidine or memantine) with neuroprotective effects in experimental studies have progressed to clinical trials; however, the results of clinical trials for these agents have been inconclusive. Nevertheless, the lack of convincing clinical evidence has not prevented the off-label use of some of these agents in glaucoma practice. Stem cell transplantation has been reported to halt experimental neurodegenerative disease processes in the absence of cell replacement. It has been hypothesized that transplantation of certain types of stem cells activates multiple neuroprotective pathways through the secretion of various factors. The advantage of

this approach is a prolonged and targeted effect. Important concerns in this field include secretion of unwanted harmful mediators, graft survival issues, and tumorigenesis [26]. Neuroprotection in glaucoma, whether pharmacological or by stem cell transplantation, is an interesting topic that awaits broad and multidisciplinary collaborative studies to better elucidate its role in clinical practice.

Thus, at the level of IOP control, ocular growth, treatment of glaucomatous neuropathy remains a rather urgent aspect of pediatric ophthalmology. In this regard, the study of the efficacy of neuroprotective drugs in children is of particular importance.

**Aim** of the research was to study the efficacy of neuroprotective effect of the drug «Cortexin» in congenital glaucoma.

**Material and Methods.** 32 (64 eyes) children with congenital glaucoma in the compensation stage were observed. Of these, 18 children (36 eyes) were included in the main group treated with the neuroprotective drug Cortexin. 14 children (28 eyes) were included in the control group and received standard treatment.

All patients underwent standard ophthalmologic examination including visometry, perimetry, ophthalmoscopy, tonometry, tonography, gonioscopy, ocular ultrasound (A, B-scan). In all patients IOP was lowered to a tolerable level and 18 (36 eyes) patients received 10mg of Cortexin in a volume of 1ml injected into the periocular space. The groups were matched for age, stage of disease and degree of IOP decompensation.

**Results and discussion.** All patients underwent antiglaucomatous surgery and were discharged home after IOP normalization under the supervision of a local ophthalmologist. Repeat examination was performed after one month. Tonometry and slit-lamp biomicroscopy were performed. Neuroprotective treatment was recommended in children with normal IOP and age-related eye growth. IOP and eye size were examined every month. In the absence of negative dynamics during the year, neuroprotective treatment with Cortexin was performed every three months. Due to the lack of objective methods for testing visual acuity in young children, a computer program for determining visual acuity was developed and used. The computer program «Scale for Assessment of Visual Functions» was certified (No. DGU 11841). The software product allows to determine visual acuity in children under three years of age with congenital glaucoma. As a basis for the calculations, the indicators of the scale of the questionnaire for evaluation of visual functions in children up to three years of age were used, taking into account the significance of these data.

After surgery, the questionnaire was completed by an ophthalmologist during the first 5 days. Parents were then instructed on how to complete the questionnaire. After 1 month and after 3 months of treatment, the parent completed the chart and derived the scores. At repeated visits at the same time, the parents and the ophthalmologist reviewed the scores and determined visual acuity.

The scale for evaluation of visual functions in infants consists of seven evaluation signs: recognizes his mother, imitates some adult movements, looks at toys in proximity, recognizes a favorite toy in proximity, follows objects, recognizes parents in a photo, the angle of strabismus and the caliber of nystagmus decrease. In the absence of a sign the score is not determined, in the appearance of a moderate degree 1 point, in the pronounced manifestation of the sign 2 points. The maximum score was 14 points.

When analyzing the stage of glaucoma in the main group it was found: initial stage – in 4 eyes (11,2 %), developed – in 8 eyes (22,7 %), very advanced – in 18 eyes (50,1 %) and final stage – in 6 eyes (16,7 %).

Analyzing the stage of glaucoma in the control group it was found: early stage – in 4 eyes (14,3 %), advanced – in 5 eyes (17,9 %), very advanced – in 15 eyes (53,6 %) and final stage – 14,2 %, 4 eyes.

Analysis of visual acuity before surgical treatment showed that in children in the main group with the initial stage in 6 eyes – 57 % (8 points), in two patients visual acuity was 42 % (6 points).

In the advanced stage in five patients visual acuity was 42.8 % (6 points), in eight patients – 28 % (4 points).

Twenty-six children had a visual acuity of 36 % (5 points) in the advanced stage. In nine children it was 21 % (3 points). In the final stage all children had visual acuity below 14 % (2 points).

After antiglaucomatous surgery and neuroprotective treatment for one year, we collected questionnaire data completed by parents and analyzed visual acuity. The analysis of the visual acuity data of the children in the main group showed a sharp increase in visual acuity in 4 eyes in the initial stage, the values increased compared to before surgery and neuroprotective treatment and averaged 85 % (12 points). In the advanced stage, the average visual acuity was 76 % (11 points). In the most advanced stage, the average was 34 % (5 points). In the end stage, visual acuity did not change (14 % – 2 points).

In children in the control group, visual acuity before surgical treatment was identical to that in the main group. After one year of follow-up, the average visual acuity in the early glaucoma control group was 71 % (10 points).

In the advanced stage, visual acuity averaged 57 % (8 points). In the most advanced stage, visual acuity averaged 28 % (4 points). In the end stage, visual acuity did not change (14 % – 2 points).

**Conclusion.** Thus, the dynamics of visual acuity improvement was significantly more pronounced in patients of the main group, which indicates the expediency of including drugs with neuroprotective effect in the complex treatment of glaucomatous neuropathy.

The results of the questionnaire on visual acuity in small children objectively prove the improvement of visual functions with the use of Cortexin. The use of Cortexin in children with primary congenital glaucoma did not cause any complications or side effects.

**Conflict of interest:** The Authors declare no conflict of interest.

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# ОСОБЛИВОСТІ НЕЙРОПРОТЕКТОРНОГО ЛІКУВАННЯ ДІТЕЙ З ПЕРВИННОЮ ВРОДЖЕНОЮ ГЛАУКОМОЮ

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## Резюме.

Нормалізація внутрішньоочного тиску є обов'язковою умовою, але не гарантує стабілізацію глаукомного процесу. Важливе значення надається нейропротекторній терапії, спрямованої на збереження активної функції аксонів ганліонарних нервових клітин.

**Метою дослідження** стало вивчення ефективності препарату нейропротекторної дії «Кортексин» при вродженій глаукомі.

**Матеріал і методи дослідження.** Під спостереженням знаходилися 32 (64 очей) дитини з вродженою глаукомою в стадії компенсації. З них 18 дітей (36 очей) увійшли до основної групи, яким застосовувався нейропротектор Кортексин. Інші 14 (28 очей) дітей увійшли до групи контролю, яким проводилося стандартне лікування. Методи дослідження: візометрія, офтальмоскопія, периметрія, тонометрія, тонографія, УЗД очного яблука, гоніоскопія.

**Результати.** Всім пацієнтам була проведена антиглаукоматозна операція і за відсутності негативної динаміки протягом року кожні три місяці проводилось нейропротекторне лікування із застосуванням препарату Кортексин. Для дослідження гостроти зору у дітей молодшого віку було розроблено та використано комп'ютерну програму для визначення гостроти зору. Отримано свідчення комп'ютерної програми «Шкала оцінки зорових функцій» (№ DGU 11841). Далі батькам дитини пояснювали, як ставити бали. Батьки після 1 місяця та після 3-х місяців курсу лікування заповнювали таблицю та виводили бали.

Після завершення нейропротекторного лікування протягом одного року нами було зібрано дані опитувальника, заповнені з боку батьків, та проведено аналіз гостроти зору. Аналіз даних в основній групі показав підвищення гостроти зору на всіх стадіях глаукоми, окрім термінальної. У дітей контрольної групи гострота зору до хірургічного втручання була ідентична основний групі. Після одного року спостереження в контрольній групі зростання гостроти зору відзначалося набагато менше, ніж в основній групі.

**Висновок.** Таким чином, динаміка підвищення гостроти зору у пацієнтів основної групи була достеменно більш виражена, що свідчить про цілеобразність включення в комплексне лікування глаукомної нейропатії препаратів нейропротекторної дії.

**Ключові слова:** лікування; вроджена глаукома; нейропротекторна терапія.

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