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IMPORTANCE OF CITICOLINE IN THE TREATMENT OF ISCHEMIC DISEASES OF THE ORGAN OF VISION IN ATHEROSCLEROSIS

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Resume

The aim of study was to evaluation of efficacy and safety of neuroprotector (Citicolin) – OMK II in patients with ischemic diseases of organ of vision in atherosclerosis. The average age of patients was 59,3 ± 5,61 y., including 11 women and 16 men. 12 patients entered in the basic group (I) that received standard treatment in combination with topical application of the drug OMK II. 15 patients in the control group (II) who received standard treatment.

The use of standard therapy in combination with OMK II in the treatment of IDOV has a positive effect on the course of the disease, thereby, increase of visual acuity, a decrease in sectoral loss in vision fields, the positive dynamics OCT parameters, improving hemodynamic parameters at Doppler imaging in dynamics. Application OMK II in patients with IDOV is safe because, in patients of the main group were not recorded statistically significant indicators of adverse events and violations of the blood pressure and heart rate.

Keywords: *ischemic diseases of organ of vision, treatment of ischemic diseases of the eye, atherosclerosis, citikolin, OMK II.*

ЗНАЧЕНИЕ ЦИТИКОЛИНА В ЛЕЧЕНИИ ИШЕМИЧЕСКИХ ЗАБОЛЕВАНИЙ ОРГАНА ЗРЕНИЯ ПРИ АТЕРОСКЛЕРОЗЕ

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Резюме

Целью исследования явилась оценка эффективности и безопасности нейропротектора (Цитиколина) - ОМК II у пациентов с ишемическими заболеваниями органа зрения. Средний возраст пациентов составил 59,3 ± 5,61 лет, из них 11 женщин и 16 мужчин. 12 пациентов вошли в основную группу (I), которая получала стандартное лечение в сочетании с местным применением препарата ОМК II в виде глазных капель. 15 пациентов контрольной группы (II) получали стандартное лечение.

В результате использования стандартного лечения в сочетании с нейропротектором ОМК II в терапии ишемических заболеваний органа зрения при атеросклерозе выявили положительную динамику в течении заболевания, в частности, отмечалось повышение остроты зрения, уменьшение секторального выпадения полей зрения, а также положительная динамика параметров оптической когерентной томографии, улучшение гемодинамических показателей при допплерографии. Применение ОМК II у пациентов с ишемическими заболеваниями органа зрения при атеросклерозе является безопасным, так как у пациентов основной группы не было выявлено достоверно значимых показателей, приводящих к возникновению каких-либо осложнений и возникновению нарушений показателей артериального давления и сердечных ритмов.

Ключевые слова: *ишемические заболевания органа зрения, лечение ишемических заболеваний органа зрения, атеросклероз, цитиколин, ОМК II.*

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АТЕРОСКЛЕРОЗДА КЎРУВ АЪЗОСИНИНГ ИШЕМИК КАСАЛЛИКЛАРИНИ ДАВОЛАШДА ЦИТИКОЛИННИНГ АҲАМИЯТИ

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Резюме

Тадқиқотнинг мақсади - атеросклерозда кўрув аъзосининг ишемик касалликлари бўлган беморларда нейропротектор (Цитиколин) - ОМК IIнинг самарадорлиги ва ҳавфсизлигини баҳолаш. Ушбу тадқиқот ўтказилган беморларнинг ёши 59,3 ± 5,61 ташкил этиб, улардан 11 нафари аёллар, 16 нафари эркаклардан ташкил этди. Тадқиқотнинг асосий гуруҳига 12 бемор киритилиб, уларга стандарт даволаш билан биргаликда ОМК II препарати кўз томчилари шаклида махалий буюрилди. Назорат гуруҳидаги беморларга эса фақат стандарт даволаш буюрилди ва уларнинг сони 15 тадан иборат бўлди.

Атеросклерозда кўрув аъзосининг ишемик касалликлари бўлган беморларда стандарт даволаш билан биргаликда ОМК II нинг қўлланилиши касалликнинг кечишида ижобий динамика аниқланди, жумладан, кўриш ўткирлигининг ошиши, кўриш майдонининг секторал торайишининг камайиши, оптик когерент томография кўрсаткичлари ва допплерографиядаги гемодинамик параметрларнинг ижобий динамикаси кузатилди.

ОМК II нинг кўриш аъзоси ишемик касалликларида қўлланилиши беморлар учун ҳавфсиз бўлиб, асосий гуруҳдаги беморлар артериал қон босими ҳамда юрак уриш ритмлари бузилишига олиб келувчи ишончли муҳим асоратлар аниқланмади.

Калит сўзлар: *кўрув аъзосининг ишемик касалликлари, кўрув аъзосининг ишемик касалликларини даволаш, атеросклероз, цитиколин, ОМК II.*

Introduction

Ischemic diseases of organ of vision (IDOV) is called a violation of the intraocular blood circulation as a result of limiting or preventing the inflow of arterial blood to the eye while maintaining the normal outflow of venous blood. As a result of circulatory disorders of the eye is the development of local ischemia and hypoxia. One of the common pathogenetic factor is a violation of autoregulation of blood vessels, which is extremely important to consider in the pathogenesis of the disease [4, 5, 9, 10].

Therefore, in the treatment of IDOV to eliminate hypoxic and ischemic processes, and improve perfusion of an organ of vision it is advisable to conduct courses of conservative treatment with drugs that increase the outflow of aqueous humor, at the same time without affecting the production of the latter, thus reducing hypoxic manifestations in organs and tissues of the eye. Thus the drug is OMK II, refers to citicoline, which gives a useful and beneficial structural support in restoring the integrity of cell membranes also damaged by degenerative ophthalmic diseases.

Citicoline stimulates the biosynthesis of structural phospholipids of neuronal membranes, which improves the function of membranes, including the functioning of ion-exchange pumps and neuroreceptors. Due to the stabilizing effect on the membrane, citicoline has a decongestant property and reduces brain edema.

Citicoline reduces the severity of symptoms of cerebral dysfunction after pathological processes such as traumatic brain injury or acute cerebrovascular accident.

Citicoline reduces amnesia, improves cognitive, sensory and motor impairment, and also reduces the severity of symptoms that occur with hypoxia and cerebral ischemia, including memory impairment, emotional lability, impaired ability to perform normal self-care actions. Citicoline is a natural compound contained in the human body, therefore, classical pharmacokinetic studies cannot be carried out due to the complexity of the

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quantitative determination of exogenous and endogenous citicoline.

During the pharmacokinetic study, its almost complete absorption in the gastrointestinal tract was determined - less than 1% of the accepted dose was detected in feces within 5 days after taking the drug. There were also 2 peaks of radioactivity in blood plasma due to metabolism in the liver and intestines: the first after 1 hour, the second after 24 hours.

The bioavailability of the oral and parenteral routes of administration are almost identical. Excretion is very slow, mainly through the respiratory system and with urine. After 5 days of administration, about 16% of the dose was revealed, which indicates the inclusion of the rest of the dose in metabolic processes

Purpose. To study the significance of Citicoline in the treatment patients with ischemic diseases of organ of vision in atherosclerosis, and evaluation of efficacy and safety of Citicolin – OMK II.

Materials and methods

The material for this study were the results of a comprehensive examination and treatment of 27 patients with ischemic diseases of organ of vision (IDOV). The study was conducted with the Declaration of Helsinki approved by the National Ethics Committee of the Republic of Uzbekistan at the Ministry of Health of the Republic of Uzbekistan. Patients introduced and signed a written informed consent.

The study was conducted on the basis of the Republican Clinical Eye Hospital of the Ministry of Health of the Republic of Uzbekistan (Tashkent) from 2018 to 2019 y.

The average age of patients was 58,5 ± 5,69 y., including 14 women and 18 men. 17 patients in the control group (II) who received standard treatment. 12 patients entered in the basic group (I) that received standard treatment in combination with topical application of the drug OMK II.

For patients of the main group the drugs of OMK II instilled – 1 drop into the conjunctival sac of one or both eyes affected by the pathological process, twice a day – in the morning and evening. When adverse effects or allergic reactions, drug instillation was stopped.

Standard treatment consisted to use of drugs that improve the microcirculation, anticoagulants, antiplatelet agents, neuroprotective agents, as well as drugs stabilizing blood glucose and blood pressure within 3 months.

The criterion for evaluating the effectiveness of therapy was to compare the visual fields, visual acuity, parameters of hemodynamics and OCT in the main vessels of the eye between the two groups.

Safety was evaluated by the number of adverse events during treatment. Adverse events were divided into two groups: a life-threatening events included in group 1, non-threatening in the 2nd group.

For life-threatening events attributed conditions leading to disability or death of the patient. To a non-threatening life conditions include: dyspepsia, dizziness, headaches, feeling the tide, pulsation, "tingling" in the limbs, as well as allergic reactions.

The diagnosis IDOV was based on the clinical and instrumental investigations and violations of hemodynamic parameters in the internal carotid and ophthalmic arteries, as well as clinical manifestations in the form of anterior ischemic neuropathy, central retinal artery occlusion, ischemic central retinal vein thrombosis and glaucoma. Patients with concomitant diseases of the eye, such as diabetic retinopathy, diseases of the inflammatory genesis of the optic nerve and retina, congenital abnormalities of the optic nerve and retina is not included in this study.

General examination of patients consisted of complaints, medical history, as well as the measurement of blood pressure, heart rate.

In all patients was performed a comprehensive ophthalmologic examination, including visometry, tonometry, computerized static perimetry, gonioscopy, biomicroscopy, fundus ophthalmoscopy. Special methods of investigation include ultrasound dopplerography of vessels of the organ of vision and the brachiocephalic trunk.

Visometry according to EN ISO 8596 (European standard) conducted on Snellens table (20/200) or Landolt rings. Tonometry was performed by the method of Goldman. Biomicroscopy of the eyeball conducted slit lamp company «Carl Zeiss».

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Fundus ophthalmoscopy were performed by ophthalmoscope «Kiler» and fundus-camera «Carl Zeiss».

Computer static perimetry was performed using the perimeter of Humphrey Field Analyzer 740i (Carl Zeiss Meditec inc.) by programme central threshold test 30-2 and peripheral test 60-4. All results were recorded using a digital marking with the general analysis of indexes MD (mean deviation sensitivity of the retina) and PSD (pattern standard deviation). The distance between the test points was 6°.

To estimate the parameters of the optic nerve (optic disk) all patients underwent examination optical coherence tomography (OCT) Cirrus HD - OCT (Zeiss, Spectral Domain Technology). Explored the area of the optic nerve (protocol ONH) and the area of the retina (RNFL).

Ultrasound examination with color Doppler mapping in 3D mode was performed by transpalpebral contact method using multiultrasonic instrument («VOLUSON 730 PROGE»). Doppler of the extracranial and intracranial segments of the main vessels of the brachiocephalic trunk was performed to analyze the state, caliber, patency and hemodynamics at the internal, external and common carotid arteries. In order to visualize blood flow in the ophthalmic artery, central retinal artery and its branches used ophthalmodopplerography.

The studies were conducted in the dynamics: before treatment, after treatment and 3 months after treatment.

All patients were randomized by the method of stratification by diagnosis, age, sex, visual function, and concomitant diseases.

We used a variational methods of parametric and nonparametric statistics with the calculation of the arithmetic mean of the studied parameter (M), standard deviation (σ), standard error of the mean (m) and relative values (frequency,%).

The statistical significance of the measurements by comparing the mean values was determined by Student's test (t) with the calculation of the probability of error (P) when checking normality of distribution (by the excess) and the equality of the population variance (F - Fisher's exact test). For statistically significant changes have taken level of confidence P <0.05.

Results and discussion

According to the study in 8 patients the diagnosis IDOV were based on central retinal artery occlusion combined with anterior ischemic optic neuropathy. In 6 patients was observed pseudoexfoliative syndrome in combination with occlusion of the central retinal artery and cataract. In 4 patients central retinal vein thrombosis combined with anterior ischemic neuropathy. In 8 patients occlusion of the central retinal artery developed in conjunction with anterior ischemic neuropathy and open-angle glaucoma. 6 patients had occlusion of the central retinal artery in combination with open-angle glaucoma and cataract. All patients with the above nosologies were evenly divided in the main and control groups for therapeutic measures.

In the main group visual acuity of patients before treatment was 20/340 on average. In the control group the visual acuity of patients before treatment was 20/320 on average.

Ophthalmoscopy of the fundus: optic disk was round shape in 14 patients, oval - in 15 patients, palely - pink in 3 patients, pale - 21 patients, hyperemic - 4 patients.

The boundaries of the optic disc are distinct in 1, indistinct - in 23, were not detected in 5 patients. Papilledema was observed in 25, peripapillary edema in 20 cases. Narrowed artery in 19, normal-caliber veins in 6, the veins are narrowed in 15, expanded in 6 patients. In 19 patients were visualized locuses of hemorrhages. Cotton-like locuses were observed in 17 patients. Spontaneous pulsation of the arteries was observed in 9 patients.

Analysis of the data computed perimetry showed an absolute scotoma in 13, concentric narrowing of the visual field in 11 patients. In the main group the mean deviation of retinal sensitivity (MD) before treatment was – -14,34±1,21 dB (p<0.05), pattern standard deviation (PSD) – 6,52±0,61 dB (p <0.05). In the control group before treatment MD was – 13,88±1,38 dB (p <0.05), PSD – 6,73±0,27 dB (p <0.05).

At Doppler ultrasound of the eyes revealed hemodynamically significant asymmetry of the

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velocity parameters of blood flow in the central retinal artery in 14 patients, the posterior short ciliary arteries in 18 in the ophthalmic artery in 42 19 patients . In 17 patients had a decrease in blood flow velocity parameters by ophthalmic artery with signs spasm of the peripheral arterioles.

In these patients the aforementioned changes combined with an increase of resistivity index by the central retinal artery and posterior short ciliary arteries varying degrees, indicating that the deterioration of the blood supply in the organ of vision. The coefficient of ischemia averaged 0.63 ± 0.012. It was also showed a reduction in the velocity parameters of venous outflow through the central retinal vein in 14 patients.

In the study group before treatment hemodynamic parameters averaged: ophthalmic artery - Vmax 36,9 + 2,14 cm / s, Vmin 9,2 + 1,17 cm / s, Vmed 17,3 + 2,14 cm / s ($p < 0.05$) in the control group: ophthalmic artery - Vmax 36,9 + 1,85 cm / s, Vmin 10,3 + 1,19sm / s, Vmed 18,4 + 2,21 cm / s ($p < 0.05$).

In patients of both groups after treatment was a decrease in edema of the optic disc and peripapillary zones, areas of hemorrhage and cotton-like locuses.

After treatment in the main group visual acuity of patients in the affected eye improved by 30,8%, the intraocular pressure in the normal range. In the control group the visual acuity in the affected eye improved by 8,2%, intraocular pressure in the normal range.

After treatment in patients of the main group MD and PSD increased: -8,47±1,232 dB, 3,59±0,128 dB ($p < 0.05$) respectively, while in the control group MD and PSD increased by 9.2% and amounted: -9,73±1,869 dB, - 5,15±0,183 dB ($p < 0.05$). On optical coherence tomography papilledema and peripapillary zone in dynamics decreased in both groups. On the computed perimetry absolute scotoma in dynamics decreased in both groups.

After treatment in the study group noted improvement in blood circulation in the ophthalmic artery by 36.9%, after treatment 37.1%, at 1 months by 38.2% from baseline. In the control group, hemodynamic parameters in the ophthalmic artery after treatment has improved by 9.2%, after treatment 9.7% and at 1 months by 9.8%.

In evaluating the safety of the OMK II in both groups, adverse events that threaten the patient's life was not registered. Events that do not threaten the life of the patient in the main group were 3: eye irritation – in 1 patient, conjunctival hyperemia – at 2, in the control group recorded three cases: skin rash – in 2, conjunctival hyperemia – at 1, indicating that the statistical unreliability of the occurrence of adverse events.

Today the IDOV is an urgent problem of ophthalmology, despite numerous works on the development of diagnostic and therapeutic measures performed in different countries.

The most frequent clinical manifestations of IDOV were combination of anterior ischemic neuropathy, central retinal artery occlusion, ischemic central retinal vein thrombosis and glaucoma. In comparison with literature data the average age of patients was lower than 5.5 years.

In applying the OMK II combined with comprehensive therapy in the main group resulted in increased of visual acuity by 29.9%, parameters of retinal sensitivity by 38.8%, reducing the area of scotomas compared with patients of the control group. This is confirmed by computed perimetry. Optical coherence tomography registered significant changes in the dynamics in patients of the main group - reducing the edema and restoration of RNFL and ONH. Recovery of visual function may have contributed neuroprotective activity of the drug OMK II by a protective effect on nerve tissue.

Were registered hemodynamic improvement by 38,2% in the main vessels of eye in patients of the main group, which corresponded to the literature data.

Considering the improvement of visual function and hemodynamic parameters in the main vessels of the eye in patients of the main group, as well as statistically insignificant indicators of adverse events in both groups, it may be noted about the safety and efficacy of the drug OMK II.

Conclusions

The use of standard therapy in combination with OMK II in the treatment of IDOV has a positive

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effect on the course of the disease, thereby, increase of visual acuity, a decrease in sectoral loss in vision fields, the positive dynamics OCT parameters, improving hemodynamic parameters at Doppler imaging in dynamics.

Application OMK II in patients with IDOV is safe because, in patients of the main group were not recorded statistically significant indicators of adverse events and violations of the blood pressure and heart rate.

REFERENCES:

1. Akmaeva I.I., Bogdanov T.Y., Zolotarev A.V., Manoilov I.K., Smolenkova I.I. Modern aspects of clinic with acute circulatory disorders in the eye in elderly and senile patients //Actual problems of ophthalmology. - M. - 2003.
2. Vlasov S.K. Changes in the organ of vision in pathological tortuosity and stenotic carotid atherosclerosis // West. oftalm. - 2010.- №5. - S.58-62.
3. Zhaboedov G.D., Skrypnyck R.L. Lesions of the optic nerve. /Kiiv. 2006.- 427.
5. Kiseleva T.N., Tarasova L.N., Fokin A.A. Bogdanov A.G. Blood flow in vessels of the eye in two types of ocular ischemic syndrome // Vestn. oftalmol. – 2001; 22-24.
6. Legeza S.G. The diagnostic capabilities of ultrasound, computed tomography and nuclear magnetic resonance in the pathology of the optic nerve // Oftalmol. magazine. – 2009; - №3.
7. Makkaeva S.M., Features ocular ischemic syndrome with vascular encephalopathy) // Author. dis. Dr. med. Sciences. - M. - 2010.
8. Ponomarev M.N. Diagnostics and drug correction of hemodynamic disorders in ischemic optic neuropathy in patients with cardiovascular disease " //Author. Dis., Dr. med. Sciences - Moscow, 2010.
10. Maurice E. Langham. Ischemia and loss of autoregulation in ocular and cerebral diseases. - "Springer" 2009. - c. 121-125.
11. Hayreh S.S. Ischemic optic neuropathies. - "Springer" 2011.- c. 389-395.
12. Boskovic, Z., Milne, M.R., Qian, L., Clifton, H.D., McGovern, A.E., Turnbull, M.T., Mazzone, S.B., Coulson, E.J., 2018. Cholinergic basal forebrain neurons regulate fear extinction consolidation through p75 neurotrophin receptor signaling. Transl. Psychiatry 8, 199.

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DEFINITIONS OF PSYCHOPATHOLOGICAL AND NEUROCOGNITIVE PROFILES IN PATIENTS WITH POST-SCHIZOPHRENIC DEPRESSION

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Resume

For justification of the place of a post-schizophrenic depression in dynamics of the basic schizophrenic disease determination of its psychopathological structure and clinical essence was carried out. During the research dissociation between insignificant weight of actually depressive symptoms and subjective perception by patients of the state as burdensome, its duration and resistance to the carried-out medication therapy is revealed. Post-schizophrenic depressions were observed in the presence of 1-4 psychotic episodes in the anamnesis and an experience of a disease of incidental paranoid schizophrenia till 10 years authentically more often.

Key words: *paranoid schizophrenia, post-schizophrenic depression, cognitive frustration, recursive depression, schizophrenia.*

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