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МЕТОДЫ СОВЕРШЕНСТВОВАНИЕ КОМПЛЕКСНОГО ЛЕЧЕНИЯ ДИАБЕТИЧЕСКОЙ РЕТИНОПАТИИ

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Аннотация. А**ктуальность.** Сахарный диабет и его осложнения являются одной из серьезнейших медико-социальных и экономических проблем современного здравоохранения. **Цель исследования.** Оценить эффективность метода адресной доставки препарата к сетчатке при лечении препролиферативной диабетической ретинопатии препаратом Ретиналамин в сочетании с препаратом Вобэнзим. **Материалы и методы.** Оценка эффективности лечения ретиналамином проведена у 73 пациентов с диабетической ретинопатией. Пациенты были разделены на 2 группы. В основной группе препарат в верхне–наружный квадрант под конъюнктиву (0,5 мл раствора) в течени 10 дней. Применяли также внутрь Вобэнзим по 3-6 таблеток 3 раза в день в течении 3 месяцев. **Результаты и заключение.** После лечения в основной группе острота зрения улучшилась на 0, 35 по сравнению с 0, 12 в контрольной группе. Также было улучшение реографических показателей и состояния глазного дна в обеих группах. Стабилизация зрительной функции была достигнута у 71% пациентов в результате комплексного метода лечения.

Ключевые слова: препролиферативная диабетическая ретинопатия, ретинальные геморрагии.

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DIABETIK RETINOPATIYANI KOMPLEKS DAVOLASH USULINI TAKOMILLASHTIRISH

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Annotatsiya. Dolzarbligi. Qandli diabet va uning asoratlari zamonaviy sog'liqni saqlashning eng jiddiy tibbiy, ijtimoiy va iqtisodiy muammolaridan biridir. **Tadqiqot maqsadi.** Preproliferativ diabetik retinopatiyani Retinalaminni maqsadli etkazib berish usuli bilan va Vobenzim dori vositalari birgalikda qo'llaganda davolash samaradorligini baholash. **Materiallar va usullari.** Preproliferativ diabetik retinopatiyali 73 nafar bemorda Retinalamin bilan davolash samaradorligini baholash amalga oshirildi. Bemorlar 2 guruhga bo'lingan. Asosiy guruhda Retinalamin kon'yunktiva ostiga, yuqori tashqi kvadrantda (0,5 ml eritma) 10 kun davomida yuborildi. Bundan tashqari, 3 oy davomida kuniga 3 marta 3-6 tabletka Vobenzim ichishga buyurildi. **Natijalar va xulosa.** Davolanishdan so'ng asosiy guruhdagi bemorlarining ko'rish o'tkirligi 0, 35 ga kontrol guruxda esa 0, 12 ga sezilarli darajada yaxshilandi. Ikkala guruxning ko'z tubi reologik ko'rsatkichlari xam yaxshilandi. Asosiy guruxda davolanganlaring ko'ruv faoliyatining stabillashishi 71% bemorlarda kuzatilgan.

Kalit so'zlari: preproliferativ diabetik retinopatiya, retinal gemorragiyalar.

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METHODS FOR IMPROVING COMPLEX TREATMENT OF DIABETIC RETINOPATHY

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Annotation. Relevance. Diabetes mellitus and its complications are one of the most serious medical, social and economic problems of modern healthcare. **Purpose of the study.** To evaluate the effectiveness of the method of targeted delivery of the drug to the retina in the treatment of preproliferative diabetic retinopathy with the drug Retinalamin in combination with the drug Wobenzym. **Material and methods.** The effectiveness of treatment with retinalamin was evaluated in 73 patients with diabetic retinopathy. The patients were divided into 2 groups. In the main group, the drug is in the upper – outer quadrant under

the conjunctiva (0.5 ml of solution) for 10 days. Also used internally Wobenzym 3-6 tablets 3 times a day for 3 months. **Results and conclusions.** After treatment in the main group, visual acuity improved by 0, 35 compared to 0, 12 in the control group. There was also an improvement in eographical indicators and the state of the fundus in both groups. Stabilization of visual function was achieved in 71% of patients as a result of a complex treatment method. Conclusion: a comprehensive method can be recommended for use in patients with preproliferative diabetic retinopathy to achieve stabilization of visual functions.

Keywords: preproliferative diabetic retinopathy, retinal hemorrhages, Retinalamin preparations, Wobenzym.

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Relevance. Diabetes mellitus and its complications are one of the most serious medical, social and economic problems of modern healthcare. In the structure of disability of patients suffering from diabetes, its late complications occupy a leading position. The problem of treating patients with diabetic retinopathy is complex and not fully resolved. Quite a few drugs and surgical methods have been proposed to eliminate pathological phenomena on the retina in diabetic retinopathy [1,2,5]. However, the problem of increasing the effectiveness of treatment of patients with diabetic retinopathy remains extremely relevant, since most methods affect the consequences of retinal damage, and not the pathogenetic links in the development of retinopathy.

Neuroprotection can be defined as a set of therapeutic measures aimed at preventing, reducing, and in some cases reversing the processes of neuronal cell death. One of the significant groups of neuroprotectors is biogenic peptides.

Retinalamin , which is a representative of this group of drugs, is a complex of water-soluble polypeptide fractions. Retinalamin has a stimulating effect on photoreceptors and cellular elements of the retina, helps improve the functional interaction of the pigment epithelium and outer segments of photoreceptors in dystrophic changes, accelerates the restoration of light sensitivity of the retina. Against this background, vascular permeability is normalized, reparative processes are activated in diseases and dystrophic lesions of the cells of the retina and optic nerve [2.7-10].

Thus, the drug has indications for use for both prophylactic and therapeutic purposes.

In patients with diabetic retinopathy, the disease occurs with vascular lesions of the retina, including retinal hemorrhages. The severity of hemorrhages and the time it takes to resolve largely depend on the amount of blood spilled and the methods of its resolution [2-4.6] .

Pathogenetically justified method of treatment of hemorrhage is enzymatic treatment. Enzymes are applied both locally - parabulbar , under the conjunctiva or known physiotherapeutic methods, and internally in the treatment of hemorrhage is the use of enzymes [2,7] .

Wobenzym is a combination of natural highly active enzymes of plant (bromelain and papain) and animal origin (amylase, lipase, trypsin and chymotrypsin) with rutin. Entering the body, enzymes are absorbed in the small intestine by resorption of intact molecules and, binding to blood transport proteins, enter the bloodstream. Subsequently, enzymes migrate through the vascular bed. Accumulate in the area of the pathological process [3,5].

Wobenzym has a positive effect on the course of the inflammatory process, has fibrinolytic and thrombolytic effects, limits pathological manifestations of autoimmune and immune complex reactions, optimizes reparative processes, and has a positive effect on the indicators of the body's immunological reactivity. Numerous clinical studies have proven its effectiveness, safety, and compatibility with various drugs [3].

Existing methods of treating diabetic retinopathy, along with a number of advantages (absence of a traumatic factor, general availability and universality), have their drawbacks, and the main one is the inability to act directly on the lesion, which reduces the effectiveness of the treatment.

In this regard, there is an urgent task of developing an effective method for treating diabetic retinopathy, which would combine the method of targeted delivery of the drug directly to the retina, contribute to the improvement of visual functions and stabilization of the process over a long period of time [1,4].

In this regard, special attention should be paid to the further search and detailed development of a comprehensive approach for the treatment of this severe pathology, based on a combined mechanism of action.

The aim of the work. To evaluate the effectiveness of the method of targeted delivery of the drug to the retina in the treatment of preproliferative diabetic retinopathy with the drug Retinalamin in combination with the drug Wobenzym.

Materials and methods. The study included 70 patients (122 eyes) with type 2 diabetes mellitus, preproliferative diabetic retinopathy aged 34 to 71 years. In 82.3% of cases, the process was bilateral.

All patients with preproliferative diabetic retinopathy were divided into two groups, comparable by age, gender and duration of diabetes mellitus.

The 1st (main) group included 34 patients (59 eyes) who underwent conservative complex treatment, including the administration of Retinalamin at 0.5 ml. in the upper outer quadrant under the conjunctiva. The course of treatment is 10 days. Wobenzym was also used internally, 3-6 tablets 3 times a day for 3 months.

The 2nd (control) group included 42 patients (63 eyes) who underwent conservative drug treatment. Parabulbar injections of Retinalamin, 0,5 ml. The course of treatment was 10 days.

Ophthalmological examination included: visometry, computer static perimetry, ophthalmoscopy, rheoophthalmography, Dopplerography, electrophysiological examination.

Treatment results. The dynamics of visual acuity during observation are presented in the table. After the course of treatment in the main group, visual acuity improved by 0.35 (p <0.05). An increase in visual acuity was observed in 88.9%. By the 6th month, a gradual decrease in visual acuity indicators was noted by an average of 0.06 (p <0.05). After one year, the average level of visual acuity did not differ significantly from the initial level.

In the control group, after a course of drug therapy, visual acuity increased by 0.12 (p <0.01), which is 0,2 3 less than in the main group. In the long-term period (6–12 months), the average visual acuity decreased almost to the initial level (p >0.05).

The expansion of the visual fields in the main group occurred due to the disappearance of relative scotomas and the transition of absolute scotomas to relative ones. The number of normally perceived points increased by an average of 21%. (p <0.05). Visual fields immediately after treatment improved in 64% of patients, in 36% of cases visual fields did not change, and there were no cases of deterioration.

in the number of microaneurysms.

Analysis of rheograms showed a reliable increase in the rheographic coefficient in the main group immediately after the course of treatment by an average of 0.61±0.07 d. (p <0.05). Later control studies revealed a tendency for this indicator to stabilize within 3 to 6 months. After a year, the level of the rheographic coefficient exceeded the initial values by 0.44±0.06 d. (p <0.0 1).

In the control group, after a course of drug therapy, an increase in the rheographic coefficient was also noted on average for the group by 0.3±0.06 days. Further observation showed that this level of the rheographic coefficient was maintained from 1 to 6 months, then we noted a tendency for it to decrease (already 12 months after treatment, it practically does not differ from the initial one).

A significant decrease in linear blood flow velocities in the ophthalmic artery before treatment was detected in patients in the main group. After the course of treatment in the main group, the maximum blood flow velocity increased by 2.8±0.9 cm/s (p <0.05) . By the 6th month of dynamic observation, this indicator began to decrease, remaining, however, higher than the initial level. After a year, it approached the indicators recorded before treatment.

Table.1

Dynamics of visual acuity during observation observation periods

	visual acuity	
	Group I	II group
before treatment	0.57 + 0.07	0.56 + 0.03
after treatment (10 days)	0.82 + 0.07*	0.68 + 0.03**
in 1 month	0.84 + 0.06**	0.66 + 0.03***
in 3 months	0.84 + 0.06**	0.62 + 0.03***
in 6 months	0.78 + 0.07*	0.60 + 0.03***
in 12 months	0.64 + 0.07***	0.58 + 0.07***

Note: difference compared to baseline * p <0.05; **p <0.01; ***p>0.05

In the control group, immediately after treatment, the number of relative scotomas decreased to 13.4%. Then their number gradually increased and by the 6th month of observation was practically no different from the initial indicators.

In the ophthalmoscopic picture of the fundus in patients with preproliferative diabetic retinopathy, an improvement in the picture of the fundus was noted due to the disappearance of hemorrhages and a decrease

In the control group, the systolic blood flow velocity in the ophthalmic artery after treatment increased by 1.8±0.6 cm/s (p <0.0 1). After 3 months of observation, the systolic blood flow velocity in the ophthalmic artery decreased to the initial values – 33.3±0.7 cm/s (p >0.05).

During the general electroretinogram: an increase in the amplitude of the "a" wave in the main group immediately after the course of treatment by an average of 11.8±2.1 μV. The state of stabilization of

the amplitude of the "a" wave was maintained for six months, when the average values of this indicator were determined at the level of 37.2±1.3 μV. At a later date (6 months) after treatment, the amplitude of the "a" wave tended to decrease somewhat (to 35.4±2.3 μV).

In the control group of eyes, an increase in the average amplitude of the "a" wave was noted immediately after treatment by 9.1±0.8 μV. However, after six months of observation, a decrease in the average amplitude of the "a" wave to 23.3±1.1 μV was detected. At later stages, a decrease in the amplitude of the "a" wave was found to be almost to the initial level.

After treatment, the average amplitude of the "b" wave increased significantly by 37.9±11.2 μV. A relatively high level of this indicator was also noted during further observation. In the long-term period after 12 months of observation, despite a slight decrease in the amplitude of the "b" wave to 233.8±10.1 μV, it still remained higher than the initial level.

In the control group, an increase in the average amplitude of the "b" wave was noted immediately after treatment by 33.2±10.1 μV. However, after six months of observation, a decrease in the amplitude of the "b" wave to 198.6±10.1 μV was detected. At later stages, a decrease in the amplitude of the "b" wave was found almost to the initial level.

Our study has shown that the effectiveness of hemophthalmos treatment directly depends on the location, volume and duration of vitreous hemorrhage. During the study, patients tolerated Wobenzym satisfactorily; we did not observe any allergic reactions. High therapeutic effectiveness of Wobenzym was noted in the treatment of relatively small hemorrhages, especially those located in the anterior vitreous. In these cases, visual acuity with correction increased on average from 0.1±0.03 to 0.3 ±0.02 (p <0.001) already one month after the start of treatment. A /B scanning of the eyes showed a decrease in the darkening characteristic of hemophthalmos up to complete acoustic transparency of the vitreous body. In the control group, resorption of hemophthalmos was practically not observed during the first month.

Thus, the use of Retinalamin and Wobenzym in the treatment of preproliferative diabetic retinopathy is pathogenetically justified. A significant improvement in visual functions has been achieved. In our opinion, this is due to the pharmacological action of the drugs, as well as the method of its administration. With targeted administration of the drug, it becomes possible to enhance the degree of penetration into the internal structures of the eyeball and achieve the maximum effect of Retinalamin .

Remote treatment results indicate that stabilization of the process in the fundus after parabulbar injections occurred in 39% of cases (control group) , after the complex method (main group) in 71% of patients .

This method of treatment allows for active drug therapy, achieving improvement of visual functions, which makes it possible to use the proposed treatment as a method of choice in the absence of stabilization of the process in patients with preproliferative diabetic retinopathy. The method of administering the drug can be repeated in any quadrant of the eyeball.

Conclusions.

1. The applied method of targeted delivery of the drug Retinolamine to the posterior segment of the eye in the treatment of preproliferative diabetic retinopathy and the combined oral use of Wobenzym provides stable stabilization of visual functions in 71% of patients within 12 months after treatment.

2. Ophthalmoneuroprotection using Retinalamin in patients with PDR provides not only an improvement in functional and electrophysiological parameters, a decrease in the permeability of the vascular wall, but also an improvement in regional hemodynamics of the eye (a decrease in compensatory increased linear parameters of blood flow velocity and a decrease in the resistance index). Timely initiation of neuroprotective treatment contributes to the long-term preservation of visual functions and the prevention of the development of proliferative DR.

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