GLAUCOMA OPTIC NEUROPATHY: MODERN METHODS OF EARLY DIAGNOSIS AND PREDICTION OF PROGRESSION

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Abstract. *The article presents an analysis of long-term monitoring of the condition of a patient with primary open-angle glaucoma. The features of this clinical observation are long-term observation based on a single clinic and the use of standardized diagnostic methods. In addition, it should be noted that in this case, dynamic observation was carried out using the same equipment to assess morphological and functional changes in the retina and optic nerve. This practice allows minimizing measurement errors in the study of morphofunctional changes in the retina and optic nerve. It was found that various groups of factors influence the prognosis and dynamics of the development of a chronic progressive neurodegenerative disease that leads to irreversible loss of visual functions. Such factors include early (timely) detection of the disease, a convenient and effective system of medical examination, rational tactics of patient treatment with changing medications to avoid a decrease in the therapeutic effect, patient compliance with treatment with an explanation of the causes and features of the development of the disease, possible complications if recommendations are not followed, as well as the need to establish contact with the patient.*

Keywords: *primary open-angle glaucoma, glaucomatous optic neuropathy (GON), compliance, diagnosis, monitoring, visual functions.*

Introduction: The difficulties in diagnosing primary open-angle glaucoma (POAG) at an early stage are associated with the lack of patient complaints and the difficulty of differential diagnosis between the norm and the initial manifestations of the disease. This is supported by the presence of suspicious and inconsistent fluctuations in intraocular pressure (IOP), clinically insignificant asymmetry, preserved anterior segment of the eye, and the absence of morphometric and functional changes according to additional imaging methods. In addition, specific problems of this category of patients include lack of motivation for treatment and low compliance with the recommended treatment regimen [1].

Many authors agree that better strategies for the treatment and diagnostic process should be recommended for patients with POAG to improve treatment adherence. Knowledge of prognostic factors characterizing the development and risk of glaucomatous optic neuropathy (GON) is important for all those involved in the management of the treatment and diagnostic process. The most vulnerable risk groups for poor adherence to medical recommendations are middle-aged patients (50-59 years) and those over 80 years of age, patients with long-term POAG and requiring external care, and those with three or more severe somatic diseases in addition to glaucoma. In this regard, the need to develop and implement effective personalized tools that help increase patient awareness of the disease and the awareness of healthcare professionals in the tactics of managing different groups of patients becomes obvious.

Below is an analysis of clinical observation, which clearly demonstrates the effectiveness of the diagnosis and the prescribed treatment, provided that the patient correctly followed the doctor's recommendations. Ophthalmostat was as follows: best-corrected visual acuity (BCVA) OU=1.0; IOP level (P t) - 23 mm Hg. Art. and 24 mm Hg. Art. Accordingly, biomicroscopy data showed the presence of a small amount of pseudoexfoliative material located along the pupillary border (mainly in the right eye), and ophthalmoscopy data revealed a difference in the state of the optic nerve discs (OND): marginal excavation - of medium size (excavation to OND) - greater ratio (E/D) on the right. Additional examination methods were used. Thus, according to the results of standard automatic perimetry (SAP) using the 24-2 program (Humphrey Field Analyzer 740, Carl Zeiss, Germany), the mean deviation (MD) of OD / OS was + 0.16 / -0.53 dB; the sample standard deviation (PSD) of OD / OS was 1.49 / 1.26 dB.

Retinotomographic morphometric results (Heidelberg Retina Tomograph, HRT, version 3.0.2/2078, Heidelberg Engineering, Germany): neuroretinal zone area (NRP) - 1.03/1.08 mm3, NRP volume - 0.19/0.24 mm3, average nerve fiber - mm2.0.N. thickness tricuspid profile - -0.16/-0.18, retinal surface elevation - 0.29/0.30 mm, E/D - 0.66/0.62. When studying the results of Moorfields Regression Analysis (MRA), a marginal decrease in the RNFL profile was detected in the temporal, nasal and lower nasal sectors of the right eye, and in the upper temporal, upper nasal and lower nasal sectors of the left eye.

Keratopyximetric indices OD/OS were in the average normal range (554/552 μm). Taking into account the above examination results, the patient was given the following clinical diagnosis: "Suspected glaucoma of both eyes". The patient was recommended to undergo quarterly monitoring, which he carefully followed. During 2007, changes in IOP (P t) were noted several times, with a predominance of ophthalmotonus in the right eye (up to 23 mm Hg).

Other changes detected in the anterior and posterior segments of the eye (presence of pseudoexfoliative material, increased E/D ratio with loss of retinal tissue in the inferotemporal border zone, and a significantly reduced RNFL profile in the inferotemporal segment) allowed us to make a final diagnosis of glaucoma of both eyes." Initial local antihypertensive therapy was prescribed using prostaglandin analogues (PGA) - 0.005% latanoprost in both eyes. 2 days after the introduction of antihypertensive therapy (P t), monitoring of the IOP level showed a decrease of 19/16 mm Hg. Art.

Methods and materials of the study: During the dynamic observation period from 2007 to 2009, the characteristics of the morphometric structure of the optic nerve head and vitreous humor did not have clinically significant negative dynamics. During the specified period, the level of IOP (P 0) OU was within 19 mm Hg. Art. In January 2010, negative dynamics were noted (cluster analysis data showed a decrease in RNFL thickness in the inferotemporal sector of the right eye, but according to MRA, changes in RNFL thickness were detected in the upper and lower nasal segments), which indicated the development of GON. In March 2010, significant changes in IOP (P 0) were again noted in the right eye (subcompensation up to 25 mm Hg) [3]. Taking into account these findings, a change in drug therapy was made with the appointment of a combination of a selective beta-blocker (BB) and APG. After that, the level of ophthalmotonus was normalized within a year.

Against the background of the above-mentioned hypotensive therapy, observed for 1.5 years, in July 2011, further episodes of subcompensation of the IOP level (P 0) were detected in the left eye (>25 mm Hg). It was decided to change the antihypertensive regimen to combined local antihypertensive therapy using a fixed combination (FC) containing a local carbonic anhydrase inhibitor (CAI) and a non-selective BB (timolol maleate). Against the background of the indicated instillations, the patient almost immediately began to complain of hyperemia and itching of the eyelids, which intensified over several months. This condition was assessed as an individual intolerance to the components of local antihypertensive drugs, possibly their preservatives. At the same time, the IOP (P 0) level was compensated in this regimen and was within 20 mm Hg. Art. Due to individual intolerance, the treatment regimen was changed and BB + APG combination therapy was prescribed. According to HRT (Topographic Change Analysis, TCA), a gradual thinning trend of the NRP in the inferotemporal segment in the right eye was noted starting in July 2011. Similar progressive changes in the function of the optic nerve in the left eye were detected in May 2015.

This type of analysis reflects changes in the morphometric parameters of the optic nerve head. Areas of depression indicate negative dynamics, areas of expression indicate an improvement in morphometric parameters after changing the mode.

These findings were the reason for changing drug therapy - once again, the combined BB + ICA regimen was used, which had a sufficient hypotensive effect (despite the patient's increased sensitivity to the drug). The IOP level (P 0) in the prescribed regimen was in the range of 19-20 mm Hg. Art. According to the analysis of the development of perimetric changes (Analysis of the Probability of Glaucoma - GPA Conclusion) (SAP, program 24-2), no statistically significant decrease in light sensitivity was detected during the observation period from 2006 to 2014 (the perimetric light sensitivity index in both eyes MD from 86 to 82 -12 dB).

Over the next 2 years, the IOP level (P 0) was in the range of 19-20 mm Hg. Art. against the background of the use of the above-mentioned FK (BB + ICA). Given the duration of its use (and in this regard, the high probability of developing impaired tolerance), it is recommended to plan a change in local antihypertensive therapy to a single instillation of timolol maleate 0.5% + bimatoprost 0.03%. In this regimen, the IOP level (P 0) even decreased slightly and did not exceed 16 mm Hg over the next year. Art.

Since June 2014, optical coherence tomography (OCT) Spectralis Tracking Laser Tomography, Heidelberg Engineering, Germany, with the glaucoma module, has been used to detect the development of GON. Its use allowed us to detect a decrease in the average thickness of the RNFL in the upper part of the right eye (up to 79 μm, -14%). The average RNFL thickness values of the right eye on OCT corresponded to the changes in RNFL thickness according to the results of HRT, while the RNFL thickness of the left eye, according to both devices, did not change and remained within the age norm (92 μm).

Results: During the observation period from 2014 to 2016, while maintaining the previous antihypertensive regimen, the IOP level (P 0) was in the range of 16-17 mm Hg. st., according to HRT, OCT and SAP, no statistically significant negative dynamics were found. After 2 years of strict adherence to this hypotensive regimen, the patient developed and slightly increased complaints of eye hyperemia and foreign body sensation. This condition was assessed as another manifestation of the individual reaction to the use of the components of the antihypertensive regimen. As a result, in the fall of 2016, drug therapy was changed: a preservative-free drug (timolol maleate 0.5% and tafluprost 0.0015%) was prescribed in the PK. As a result of the change in therapy, the IOP level (P 0) was compensated within the range of 17-19 mm Hg. Art.

At the same time, according to OCT data (in November 2018), a statistically insignificant progressive decrease in RNFL thickness was noted in the upper sector, to which changes were added in the lower nasal sector of the right eye (up to 77 μm). These changes were reflected in the OCT analysis (Retinal Nerve Fiber Layer Thickness (RNFL) Assessment Protocol, Vector Analysis). Also, suspicious negative morphometric dynamics were noted in both eyes according to Heidelberg tomography data (Fig. 2), and according to the results of SAP (Protocol 24-2), the indicators remained within the age norm and the development of GON was not detected. The detected changes explained the development of primary cataract in the patient, their differential changes according to different diagnostic methods, which are characterized by structural changes of the optic disc using OCT and Heidelberg tomography, local spot is being examined.

Dynamics of optic nerve head condition indicators, Trend analysis protocol, HRT3 Spectralis (2006–2019) Fig. 2. Changes in ONH morphology (HRT3 Spectralis, Trend analysis, 2006–2019)

Given the above data, it was decided to maintain the previous regimen, since the patient had an individual intolerance to the components of FC BB + ICA. At the next medical examination in January 2019, the development of cataracts was confirmed by an increase in myopic refraction and a decrease in visual acuity (BCVA OD/OS with sph -2.0 D = 0.5/0.6). In March 2019, during glaucoma monitoring, due to the fact that negative dynamics were detected according to OCT and HRT analyzes, and the stage of glaucoma according to SAP (protocol 24-2) still corresponded to the initial stage, it was decided to perform selective laser trabeculoplasty in both eyes. After 1 month, the IOP level (P 0). after this operation, while maintaining the previous hypotensive regimen, it was 16 mm Hg. Art., and it remained the same after 3 months.

During the observation period from March to November 2019, the IOP level (P 0) was in the range of 17–19 mm Hg. Art. against the background of a previous hypotensive regimen. Cluster and vector analyses using HRT and OCT devices did not reveal areas of RNFL thickness depression. During the SAP examination (GPA Summary protocol) in 2019, no focal changes in retinal light sensitivity were detected in OD/OS (MD index status - -1.22/-2.13 dB, PSD - 1.68/1.64 dB) (Fig. 3). Taking into account the presence and characteristics of cataract development, as well as the stabilization of the glaucoma process, the patient is recommended for planned surgical treatment - phacoemulsification of cataracts with implantation of an intraocular lens.

Dynamics of SAP indicators, Program 24-2, GPA Summary Protocol (2006–2019) Fig. 3. Changes in SAP 24-2 (GPA Summary, 2006–2019)

The described clinical observation indicates not only the importance of timely diagnosis of POAG and the appointment of a complex of treatment and diagnostic measures by the doctor, but also the need for the patient to fully comply with all recommendations.

Discussion

A study of the treatment of ocular hypertension has shown that topical antihypertensive therapy is effective in slowing the progression of POAG and also reduces the likelihood of developing glaucoma in people with elevated IOP (called ocular hypertension) without evidence of glaucomatous damage [4]. Long-term adherence to treatment for a chronic asymptomatic condition is difficult for many patients. Evaluating treatment for progressive glaucoma can also be challenging for physicians, as their assumptions about whether treatment is effective are based on the patient's adherence to all recommendations. Adherence is a complex multifactorial phenomenon that can be influenced by any number of variables, including patient-related, therapy-related, comorbid, healthcare system, and socioeconomic factors [5].

Despite increased awareness of the disease, poor adherence to chronic disease treatment remains a global problem. The World Health Organization defines adherence as "the extent to which a person's behavior—taking medication, following a diet, or making lifestyle changes—conforms to the agreed-upon recommendations of a healthcare provider" [6, 7]. Other studies have shown that only 50% of patients adhere to their doctor's recommendations. A retrospective analysis by TN. Malishevskaya et al. (2016) found that by the end of 5 years of follow-up, 15% of patients with advanced glaucoma remained compliant, 52% were noncompliant, and 33% were inadequately compliant and at risk for noncompliance [7]. In a retrospective study of RA.

Newman-Casey et al. (2015) found that adherence in the first year of treatment in patients with newly diagnosed glaucoma who were already receiving antihypertensive therapy was generally a good predictor of how well people would adhere to their doctor's prescriptions in the long term. Almost all of those who were good adherents during the first year maintained it for the next 4 years [8]. Various studies have consistently identified various reasons for barriers to treatment adherence, including: lack of patient knowledge about the long-term consequences of glaucoma, problems with reading instructions, difficulty or incorrect technique in instilling drops, polypharmacy, financial costs of drugs and side effects associated with drug components [9].

S.Yu. Casanova and V.V. Strakhov (2016) determined the rate of progression of the glaucoma process in groups with different options for patient non-compliance and found that, on average, the transition of the disease to one stage occurs in the worse eye within 2.5 years. In the other eye, the progression rate is lower and occurs every 6 years.

On the one hand, this highlights the asymmetry of the course of glaucoma, on the other hand, it indicates that POAG in paired eyes is diagnosed earlier and treated more actively (and the patient adheres better to the recommendations), as a negative example is poor vision [10]. Fixed-dose combinations in a single dosage form simplify administration and improve compliance with treatment. An individualized approach to the patient is necessary to ensure adherence to treatment regimens.

Achieving compliance can have a greater impact on improving treatment and prognosis than any other approach, and the health system should work to address this problem [11, 12].

Conclusion

The presented clinical observation shows a low rate of GON development, which is achieved by achieving a “target pressure” with long-term compensation of the GON level and timely medical examination, including timely changes in local hypotensive therapy regimens to prevent tolerance disorders. Strict adherence to the treatment regimen and sufficient information about the existing disease indicate a high level of qualification of the patient and good communication between him and the doctor. Most drugs used to reduce IOP in glaucoma contain preservatives. Long-term use of such drops leads to an increase in individual intolerance to the drugs in some patients. It should be noted that high adherence to treatment is associated with good tolerability by the patient of the preservative-free PK used (tafluprost 0.0015% + timolol maleate 0.5%), which has a sufficient hypotensive effect for a long time.

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