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Clinical Efficacy of Combined Fixed Ophthalmic Hypotensive Drugs in Primary Open-Angle Glaucoma

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Abstract: Patients with PAAG without IOP compensation received a fixed combination of 0.004% travoprost and 0.5% timolol maleate (Duotrav) or 1% brinzolamide and 0.5% timolol maleate (Azarga). Patients were prescribed fixed combinations in the form of a change in the drug therapy regimen when PAAG was directly diagnosed and if it was ineffective. If IOP does not reach target level after 1 month. treatment, penetrating or non-penetrating glaucoma surgery was performed. The follow-up period lasted 6 months.

Patients with PAAG and uncompensated IOP received a fixed combination of travoprost 0.004% and timolol maleate 0.5% (Duotrav) or brinzolamide 1% and timolol maleate 0.5% (Azarga). Patients were assigned the combination either after diagnosis of POAG or as transition from prior treatment. Antiglaucoma surgery was performed in these patients if the IOP level did not reach the prescribed level within 1 month. The follow-up period lasted 6 months. 218 patients (220 eyes) were included in the study. Treatment with a fixed combination of topical antihypertensive drugs made it possible to achieve the target intraocular pressure in 88% of patients.

Key words: primary open-angle glaucoma, fixed hypotensive compounds, target intraocular pressure.

More than 1 million patients with glaucoma are registered, about 70 thousand of them have lost their vision. In 10 years, the rate of blindness due to glaucoma in Russia has increased almost 3 times - from 8 to 22 per 1000 population. Asymptomatic course and, as a result, late referral of patients to an ophthalmologist and late diagnosis of the disease determine the high percentage of low vision and blindness in glaucoma.

In the initial stage of glaucoma, the intraocular pressure (IOP) should be reduced by 20% from the initial level, in the advanced stage of glaucoma - by 30%, and in the advanced stage of glaucoma, the IOP should be reduced by 40% of the initial values.

Currently, there is a wide selection of antihypertensive drugs for the drug therapy of glaucoma. Prostaglandin analogues can reduce IOP by 25-33% when the drug is instilled once a day. [3]. B-blocker drugs reduce IOP by 20-25% when administered twice a day. During monotherapy, a minimal hypotensive effect is observed with drugs from the group of carbonic anhydrase inhibitors, the use of which can reduce IOP by 15-20% when instilled 2-3 times a day. [7]. As a rule, patients are treated with 2 or more drugs within 5 years after the diagnosis of primary open-angle glaucoma (POAG).

The purpose of the study: to evaluate the effectiveness of fixed combinations of local antihypertensive drugs in the treatment of patients with POAG.

Under observation, 218 patients (220 eyes), of which 125 (57%) were women, 93 (43%) were men with a diagnosis of POAG, were admitted to the Glaucoma Ophthalmology Department of the Eye Diseases Clinic of SSMU. Absence of IOP compensation. The distribution of patients according to the stage of the disease, the groups of patients with advanced and advanced stages of POAG, the group of patients with the initial stage of the disease were compared. was a little bigger.

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In these patients, the target IOP was not achieved in one or both eyes. When hospitalized, patients are given local antihypertensive therapy in combination with beta-blockers (0.5% betaxolol solution, 0.5% timolol solution), carbonic anhydrase inhibitors (2% brinzolamide solution or 1% dorzolamide solution) or prostaglandin F2 alpha analogs (0.004 % travoprost solution or 0.005% latanoprost solution) in combination. Some patients received prostaglandin drugs or carbonic anhydrase inhibitors as monotherapy. In some patients, glaucoma was diagnosed for the first time, and the scheme of instillation of antihypertensive drugs was developed based on the information about the stage of the process, taking into account the already known level of hypotensive effect;

Follow-up patients (220 eyes) had laser (57 eyes, postoperative period - 6 months to 1.5 years) or surgical operation (105 eyes, postoperative period - 2 to 9 years). The age of patients ranged from 58 to 76 years. In most patients, the duration of the disease was from 1 to 10 years.

Comorbidities of patients with glaucoma are presented in Table 1. Some patients had concomitant therapeutic pathology.

142 patients had arterial hypertension, their average age was 67±5 years. The diagnosis of hypertension was made by a doctor in 110 patients (77.5%), these patients received adequate antihypertensive therapy (ACE inhibitors, diuretics, β-blockers). The duration of the disease is 17±6 years. Blood pressure (BP) in these patients is between 130-150 mmHg. Art. (SBP) and 80-90 mmHg. Art. (DBP). 32 patients (22.5%) were not diagnosed with hypertension at the time of hospitalization and therefore did not receive the necessary antihypertensive therapy. When hospitalized, these patients have high blood pressure (up to 180 and 110 mm Hg); after prescribing antihypertensive therapy, the blood pressure level decreased to an average of 130-140 mm Hg. Art. (SBP) and 80-90 mmHg. Art. (DBP). Since antihypertensive therapy was prescribed, no increase in blood pressure was noted in hospitalized patients.

167 patients (75%) had chronic cerebral ischemia, which developed against the background of cerebrosclerosis and arterial hypertension, manifested by memory loss and cognitive impairment. The main complaints of these patients were recurrent headaches, tinnitus and dizziness. The average age of patients is 68±3 years, the duration of the disease is 8±2 years.

Complete or partial remission was achieved in patients with chronic diseases of the respiratory system (4 patients) and urinary system (1 patient). 8 patients had type 2 diabetes, 6 of them were insulin dependent. If necessary, the patients were consulted by relevant specialists (endocrinologist, cardiologist, therapist, neurologist).

Among the accompanying ophthalmological diseases in patients, the following were identified: early age-related cataracts (cortical, nuclear or subcapsular), pseudophakia, ametropia (mild, moderate or high myopia with or without PVXRD, mild or moderate hypermetropia) and age-related macular degeneration (one small or large drusen).

In this study, 100 patients (150 eyes) had early age-related cataract. 6 patients (7 eyes) had pseudophakia in one or both eyes. In all patients, the IOL was placed inside the capsular bag.

Mild myopia was observed in 3 patients (6 eyes), moderate myopia in 8 (12 eyes) and high myopia in 11 (19 eyes). PVHRD was detected in 15 patients (28 eyes) with moderate or high myopia.

Mild hyperopia (9 eyes) was detected in 5 patients, moderate hyperopia in 2 patients (9 eyes).

Age-related macular degeneration was diagnosed in 8 patients (15 eyes). One drusen and depigmentation foci with clear borders were observed in the fundus of patients; In 6 patients, visual acuity remained 0.1-0.6.

Depending on the type of treatment provided, all 218 patients (220 eyes) diagnosed with POAG stage I, II or III were grouped into 2 clinical groups. Group 1 included 114 patients (114 eyes, including 28 eyes with stage I POAG, 54 eyes with stage II, 54 eyes with stage III 32 eyes). Group 2 consisted of 104 patients (106 eyes, 22 eyes POAG stage I, 52 eyes stage II, 30 eyes stage III) who received a fixed combination of 1% brinzolamide and 0.5% timolol maleate (Azarga, Alcon). . Fixed combinations

were prescribed to patients even when directly diagnosed with PAAG, and when changing the regimen of drug therapy (switching to various types of mono and combined therapy) if it was ineffective. .

To determine the stage of glaucoma and the level of IOP compensation, patients underwent standard ophthalmological examinations, perimetry (using Oculus Twinfield perimetry, Germany); Registration of visual evoked potentials in the Neuro-MEP medical complex; Pachymetry using the Topcon 3D OST-1000 device; Laser scanning confocal retinotomography of the optic disc at HRT II (Heidelberg Retina Tomograph, Heidelberg Engineering, Dossenheim, Germany). IOP was measured according to Maklakov (weight 10 g) 2 times a day: during hospitalization at 7:00 and 19:00, then monthly for six months.

Results

In patients with PAAG, IOP data were recorded before and after 1 month of prescribing a new type of antihypertensive therapy. treatment. If the IOP did not reach the target level after 1 month, penetrating or non-penetrating antiglaucoma surgery was performed. IOP was monitored for 6 months. Modification of the antihypertensive treatment regimen failed to achieve target values in 12 patients in group 1 (12 eyes) and in 16 patients (16 eyes) in group 2;

The following dynamics of IOP was observed in the group of patients receiving Duotrav (group 1). In patients who were prescribed antihypertensive therapy for the first time when glaucoma was diagnosed (12 eyes), IOP before treatment was 30±4 mmHg. Art., IOP level decreased to 20±2.5 mm Hg. Art. IOP decreased from 28±2 to 19±1.5 mmHg in the group of patients (24 eyes) in whom β-blocker monotherapy was discontinued and the fixed combination was prescribed. Art. In patients who failed to achieve the target IOP level with monotherapy with prostaglandin group drugs (18 eyes), the use of a fixed combination made it possible to reduce IOP from 26±3 to 18±2.5 mm Hg. Art. In patients receiving carbonic anhydrase inhibitors as monotherapy (10 eyes), the mean IOP was 25±2 mmHg. Art., after assigning a solid form - 20±1 mm Hg. Art. When the hypotensive effect of the non-fixed combination of β-blockers and 1% brinzolamide (16 eyes, IOP level 25±2 mmHg) was insufficient, prescribing the fixed form made it possible to reduce IOP to an average of 20±1 mmHg . Art. A decrease in mean IOP was observed in patients who initially received β-blockers and 2% dorzolamide (16 eyes, IOP 25 ± 2 mm Hg) and in patients who received an unstable combination when using a fixed combination. The combination of β-blockers and prostaglandin analogues (9 eyes, initial IOP level - 24±2 mm Hg), up to 19±1 and 21±2.5 mm Hg. Art. in line.

In group 1, the use of a fixed combination to patients with the initial stage of glaucoma made it possible to reduce the level of IOP by an average of 26%, in the advanced stage - by 38%, and in the advanced stage - by 31%.

The following dynamics of IOP was observed in the group of patients receiving Azarga (group 2). In patients diagnosed with POAG (12 eyes), prescribing a solid combination allowed to reduce IOP from 28±2 to 20±2 mmHg. Art. After 6 months, in the group of patients who underwent monotherapy with β-blockers (24 eyes, initial level of IOP - 27±3 mm Hg), IOP after 6 months. It was 19±1 mmHg. Art. In patients undergoing monotherapy with prostaglandins (18 eyes, IOP - 26 ± 2 mm Hg), the IOP level does not exceed 25 ± 1 mm Hg. Art. Administration of the fixed combination to patients previously receiving carbonic anhydrase inhibitors (10 eyes) reduced IOP from 27±2 to 21±1 mmHg. Art. within 6 months. Prescribing a fixed combination to patients who previously received a non-fixed combination of β-blockers and brinzolamide (16 eyes, IOP level 25±2 mm Hg), β-blockers and dorzolamide (16 eyes, IOP level 24±2). mm Hg.) and β-blockers and prostaglandin analogues (18 eyes, IOP level - 24±2 mmHg) allowed to reduce the IOP level to 21±1, 20±3 and 24±3 mmHg. Art. in line.

In group 2, the use of a fixed combination to patients in the initial stage of glaucoma made it possible to reduce IOP by an average of 22%, in the advanced stage - by 31%, and in the advanced stage - by 18%.

Thus, the severity of the hypotensive effect of fixed compounds compared to other drug therapy regimens is presented in Table 3.

The severity of side effects was taken into account when assigning fixed combinations, as this factor can affect compliance and, as a result, treatment results. In no case were side effects or poor tolerance of the drug noted when prescribing Azarga. Itching in the eyes (12 patients), conjunctival hyperemia (14 patients) and visual discomfort (5 patients) were noted when prescribing Duotrav. However, the severity of side effects was not sufficient to stop the drug.

Discussion

The obtained results allow us to recommend the prescribed combination of antihypertensive drugs to patients with POAG at different stages of the disease and with different levels of compensation.

For patients with stages Ia, Ib, IIa and IIb of POAG in whom the effectiveness of β-blockers is insufficient, it is recommended to prescribe a drug from the group of synthetic prostaglandin analogs or a fixed combination of 1% brinzolamide and 0.5% timolol maleate. Prescribed combination of 0.004% travoprost and 0.5% timolol maleate to achieve target IOP.

In patients with glaucoma stages Ia, Ib, IIa and IIb, if the effectiveness of prostaglandin analogues is insufficient, it is recommended to use a fixed combination of 0.004% travoprost and 0.5% timolol maleate, which reduces IOP and preserves visual function.

In patients with Ic, IIc or IIIc glaucoma, it is recommended to switch β-blockers if they are not sufficiently effective with a fixed combination of 1% brinzolamide and 0.5% timolol maleate or 0.004% travoprost and 0.5% timolol maleate .

In patients with stage Ic, IIc, or IIIc POAG, a fixed combination of travoprost 0.004% and timolol maleate 0.5% is recommended if target IOP is not achieved on prostaglandins. In cases where there is an additional factor contributing to the reduction of IOP, for example, a history of phacoemulsification of cataract, it is indicated to replace the drug from the group of prostaglandins with a strict combination of 1% brinzolamide and 0.5% timolol maleate.

Patients with POAG stages IIIa and IIIb who have insufficient hypotensive effect of β-blockers or prostaglandin analogues are prescribed a solid combination of 0.004% travoprost and 0.5% timolol maleate.

Clinical examples

Patient S., 68 years old (POAG II, left eye), received 0.5% Betoptik for 5 years. 2 years ago, he was switched to therapy with a non-fixed combination of 0.5% timolol and 2% dorzolamide. IOP level - 26 mm Hg. Exceeded target value Art. A prescribed combination of 0.004% travoprost and 0.5% timolol maleate (Duotrav, Alcon) was prescribed after 2 months of IOP. was 21 mm Hg. Art.

Patient D., 58 years old (POAG II, left eye), received 0.5% timolol for 2 years, IOP at the time of examination was 32 mm Hg. Art. After 4 months of prescribed combination of 0.004% travoprost and 0.5% timolol maleate (Duotrav, Alcon), IOP decreased by 17 mm Hg. Art.

Patient R., 63 years old (POAG I, left eye), received 0.5% timolol for 7 years, IOP - 24 mm Hg. Art. After 2 months of prescribed combination of 1% brinzolamide and 0.5% timolol maleate (Azarga, Alcon), IOP decreased to 17 mm Hg. Art.

Patient K., 73 years old (POAG II, left eye), received 1% brinzolamide for 6 months, IOP - 27 mm Hg. Art. After 4 months, a prescribed combination of 1% brinzolamide and 0.5% timolol maleate (Azarga, Alcon) was prescribed. IOP was 20 mmHg. Art.

Summary:

1. Duotrav and Azarga drugs have a clear hypotensive effect, which is statistically significantly superior to the hypotensive effect of the combined use of their active components.
2. Duotrav and Azarga drugs provide a clinically significant decrease in IOP compared to the baseline, which corresponds to modern requirements for antihypertensive therapy.

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