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Clinical evaluation of the effectiveness of a new fixed combination antihypertensive drug based on brimonidine and brinzolamide in primary open-angle glaucoma

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Introduction. *Combined drug treatment of primary open-angle glaucoma (POAG) with several types of antihypertensive drops from different pharmacological groups is performed to enhance the hypotensive effect in cases when monotherapy does not always reduce intraocular pressure (IOP) to a tolerance level.*

Purpose. *Evaluation of the effectiveness and tolerability of a fixed combination antihypertensive drug, Glaubrinza, in the treatment of patients with POAG.*

Methods. *Depending on the treatment, 2 groups of patients were formed. The main group included 30 patients (60 eyes), who instilled the drug Glaubrinza, 1 drop 2 times a day. The comparison group consisted of 30 patients (60 eyes), whom the drug Simbrinza was instilled according to the same scheme as the drug Glaubrinza.*

All patients underwent a general ophthalmological examination and special research methods, including: computer static perimetry, pachymetry, and optical coherence tomography (OCT). The local and general tolerability of the drug was assessed within 10 days using a standard scale.

Results*. The effectiveness of the treatment in the main group was assessed as high in 85% and moderately high in 15% and averaged 3.8±0.1 points. The effectiveness of treatment in the comparison group was assessed as moderately high in 20% and high in 80% of patients and averaged 3.8±0.03 points.*

Conclusions. *Glaubrinza is a highly effective drug for treating POAG and is not inferior in all studied parameters to the reference drug and is also economically accessible to all segments of the population.*

Key words:
primary open-angle glaucoma, fixed combination antihypertensive drugs

Introduction. Glaucoma affects more than 70 million people worldwide. Approximately 10% of patients with this pathology have low vision or its complete absence, which allows us to consider glaucoma one of the leading causes of irreversible blindness worldwide [2, 12].

There are standards for diagnosing glaucoma, but the basic method for diagnosing the disease is tonometry, which measures intraocular pressure (IOP). Currently, there are a lot of equipment and methods for measuring IOP, but according to the authors, the most reliable method is Nesterov tonometry [1].

The goal of glaucoma treatment is to stabilize visual function and maintain an appropriate quality of life for the patient while ensuring that drugs are available at stable and reasonable prices. The cost of treatment should be considered and weighed carefully in combination, considering factors such as effectiveness as well as possible side effects of the drug used [15].

One of the main goals for treating patients with primary open-angle glaucoma (POAG) is to reduce IOP using medical or surgical approaches.

Combined drug treatment of POAG with several types of antihypertensive drops from different pharmacological groups is performed to enhance the hypotensive effect in cases in which monotherapy does not always reduce IOP to a tolerable level. However, such treatment creates difficulties for patients, reduces quality of life, and most often leads to disruption of the instillation regimen and, accordingly, to negative effects on visual function.

In order to reduce the number of daily instillations while maintaining maximum treatment effectiveness, clinical pharmacologists came to the conclusion about the need to create so-called fixed combination antihypertensive drugs. Today, in the arsenal of modern ophthalmologists, there are many antiglaucomatous antihypertensive drugs in the form of fixed combinations of drugs with different mechanisms of action. The authors have conducted many observational and clinical studies to assess the effectiveness and safety of combination drugs with different mechanisms of action [18, 19, 21, 22, 26, 29]. Medicines entered ophthalmology practice more than 20 years ago, and since then, their number has been steadily increasing. Research results indicate that the use of fixed combina-

tions is convenient, safer, and more economical than using non-fixed forms [10, 11, 12, 16, 29].

Clinical studies of GCP (Good Clinical Practice) aimed at determining the effectiveness of the drug, its possible complications, and side effects have been conducted in many clinics around the world [10, 30]. The need to conduct clinical trials in Uzbekistan is due to the climatic and geographical characteristics of the region and the corresponding manifestations of glaucoma; therefore, the effectiveness of the drug and its possible side effects and complications may have their own characteristics [4, 6, 7]. Moreover, in practice, ophthalmologists often encounter the fact that the standards developed for the European population are insufficient for the population of our region. Similar studies have previously been conducted in the republic [5], but the effectiveness and side effects of combined fixed antihypertensive drugs based on brinzolamide and brimonidine tartrate have not been studied in the region.

The purpose of this study was to evaluate the effectiveness and tolerability of the fixed combination antihypertensive drug glaubrinza for treating POAG.

Methods

Data from patients who were treated and observed in the ophthalmology department of the Tashkent Medical Academy (TMA) between June 2023 and January 2024 were analyzed. Patients who participated in the study provided written informed consent. The study included 60 patients with primary open-angle glaucoma. The distribution of patients by gender was as follows: men, 34; women, 26. The age of patients ranged from 38 to 65 years. The average age of the patients was 51+0.4 y.o.

Depending on the treatment, 2 groups of patients were formed. The main group consisted of 30 patients (60 eyes) who were instilled with Glaubrinza (1 drop 2 times a day). The comparison group consisted of 30 patients (60 eyes) who received Simbrinza according to the same regimen as Glaubrinza. The distribution of POAG patients in the study groups was homogeneous according to the stages of glaucoma, IOP level, corneal thickness, age, and sex (Table 1). Patients were treated for 10 days at the TMA ophthalmology department, then after 1, 3, and 6 months, they were re-examined.

Patients underwent an acute drug test (ADT) at baseline. Glaubrinza was instilled 1 drop 2 times a day. In 2 patients using Glaubrinza and in 4 patients using the comparison drug, side effects were observed in the form of itching and hyperemia of the conjunctiva, and they were excluded from the study. Further prospective, comparative studies were conducted on 60 patients (120 eyes) diagnosed with POAG, in whom local and systemic side effects were not observed.

The Pharmaceutical Committee of the Republic of Uzbekistan sent the drug Glaubrinza (S.C. ROMPHARM COMPANY S.R.L, Romania) to the TMA for a clinical trial (target program protocol No. 29/11-00943 dated May 4, 2023). A combined fixed antihypertensive drug, simbrinza eye drops (ALCON-COUVREUR N.V., S.A., Belgium) was proposed as a comparison drug according to the decisions of the Pharmaceutical Committee of the Republic of Uzbekistan (protocol No. 29/03-291 of 03/07/2023) and the Bioethics Committee of the Ministry of Health of the Republic of Uzbekistan (protocol No. 1/1-1726 dated February 23, 2023). The TMA management approved the study and assigned the test to the Department of Ophthalmology under the leadership of Prof. Bakhritdinova. The manufacturer gave us the drops for study and its analog for research. After the study, we submitted a report on the test results to the pharmaceutical committee. Based on the results of our research, the Pharmaceutical Committee allowed Glaubrinza's use in practical ophthalmology in the Republic of Uzbekistan. Registration number: DV/X 10597/02/24.

The active ingredients of the studied drugs are brinzolamide (10 mg/ml) and brimonidine tartrate (2 mg/ml).

Brinzolamide is a substance from the group of carbonic anhydrase inhibitors and a catalyst for the reversible reaction in the hydration of carbon dioxide and the dehydration of carbonic acid. The effect of reducing IOP when using brinzolamide, is achieved by reducing intraocular liquid production by the ciliary body.

Brimonidine tartrate is an α2-adrenergic receptor agonist with dual effects. As a result of its selective action, the production of intraocular fluid is reduced, and its uveoscleral outflow is simultaneously improved, leading to a decrease in intraocular pressure. Criteria for inclusion of patients in the study: POAG patients aged >18 years.

The exclusion criteria were age under 18 years; central corneal thickness (CCT) of less than 410 μm and more than 625 μm; patients with other eye pathologies; severe somatic diseases; pregnancy, breastfeeding; hypotension or severe hypertension; asthma and obstructive pulmonary diseases; patients with hypersensitivity to the active substance(s) or any of the excipients; patients receiving therapy with monoamine oxidase inhibitors (MAOIs), antidepressants that affect noradrenergic transmission; patients with severe renal failure; and patients with hyperchloremic acidosis.

Depending on the treatment, 2 groups of patients were formed. The main group included 30 patients (60 eyes), who were instilled Glaubrinza (1 drop 2 times a day). The comparison group consisted of 30 patients (60 eyes), whom Simbrinza was instilled according to the same scheme as Glaubrinza. The distribution of POAG patients in the study groups was homogeneous according to the stages of glaucoma, IOP level, corneal thickness, age, and sex (Table 1).

Registration of patient study parameters was performed in 30 minutes, and 1, 2, 6 and 12 hours after instillation of the drugs. If the patient was instilling any antihypertensive drug before the test, it was discontinued 2 weeks before the start of the study in order to avoid false results (a method of washing out the previous antihypertensive drug, according to the requirements of the study). In addition, IOP was measured on days 3, 7, and 10 of treatment.

Table 1. Distribution of patients by sex, age, glaucoma stage, and IOP level

Groups	Gender (male/female)	Average age	Stages of glaucoma		IOP level, mm Hg	Corneal thickness, μm
			II	III		
Main group (n=30)	18/12	43±0,17	21	9	31,18±2,17	457±12,17
Comparison group (n=30)	16/14	41±1,24	23	7	31,12±2,15	462±14,11

Subsequently, the examined patients were registered at the dispensary, and all patients before treatment and 1, 3, and 6 months after treatment, in addition to a general ophthalmological examination, also underwent color duplex scanning of the orbital vessels supplying the optic nerve.

Evaluation of the effectiveness of the treatment was performed based on the results of ophthalmological examination methods, including visometry, biomicroscopy, gonioscopy, perimetry, computer static perimetry, and tonometry. IOP was measured with a standard Maklakov tonometer. Daily tonometry was performed according to the method proposed by Yu. S. Astakhov et al. Ophthalmoscopy, pachymetry, and optical coherence tomography (OCT) using a HUVITZ device (Korea) were performed in all patients according to the protocol of the Pharmaceutical Committee and the Ethical Committee of the Republic of Uzbekistan. All patients provided informed consent to participate in the study. Patients were also examined at day 10 and at months 1, 3, and 6.

The local and general tolerability of the drug was assessed at the end of 10 days of use by a standard scale (no ocular discomfort, moderate discomfort, moderate discomfort, severe discomfort, very severe discomfort).

The cost and effectiveness of drug treatment were analyzed using the formula by Stewart W.C., Stewart J.A. and Mychaskiw M.A. : sum/% reduction in IOP from baseline during the treatment period (3 months)[28].

The data obtained during the study were subjected to statistical processing on a Pentium-IV personal computer using Microsoft Office Excel-2012 software, including the use of built-in statistical processing functions. Methods of variational parametric and nonparametric statistics were used with the calculation of the arithmetic mean of the studied indicator (M), standard deviation (б), standard error of the mean (m), relative values (frequency, %), the statistical significance of the obtained measurements when comparing average values was determined by the Student's criterion (t) with the calculation of the error probability (P) when checking the normality of the distribution (according to the kurtosis criterion) and the equality of general variances (F - Fisher's criterion). A significance level of P <0.05 was considered statistically significant.

Results

One of the important indicators of the effectiveness of treatment for glaucoma is the reduction in IOP, which before treatment exceeded the limits of normal values in all patients and averaged 31.15±2.16 mmHg 30 minutes after instillation of the drugs, the IOP level in patients of both groups began to decrease and after 1 hour reached normal values (24.7±2.8 and 24.3±2.34 mmHg, respectively, in the main and comparison groups). The maximum decrease in IOP was observed 6 hours after instillation, and the average values were: in the comparison group – 20.4±2.52 and 20.8±2.61 mmHg in the main group. 12 hours after instillation, a slight increase in IOP was noted in both groups, but the values remained within normal limits (22.8 and 23.2 mmHg, respectively, in the main and comparison groups). On the 10th day of treatment, the IOP level in almost all patients with stage POAG was stabilized (Table 2); (Figure 1).

On the 3rd treatment, the IOP values in both study groups averaged 21.6±1.18 mmHg and were significantly

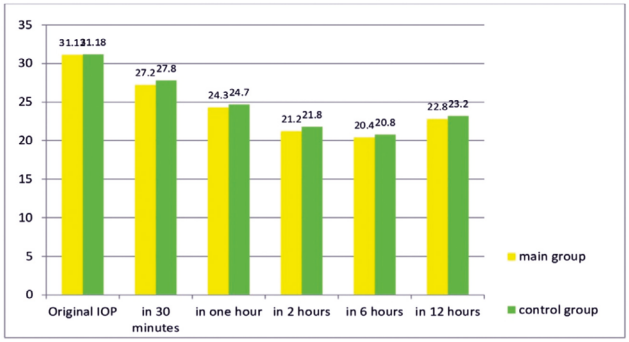

Figure 1. Change in IOP

Table 2. Dynamics of IOP (mmHg) during treatment

Groups	Initial IOP	In 30 minutes	In 1 hour	In 2 hours	In 6 hours	In 12 hours
Main group (n=30)	31,12±2,15	27,2±3,64	24,3±2,34*	21,2±2,46*	20,4±2,52*	22,8±2,12*
Comparison group (n=30)	31,18±2,17	27,8±3,72	24,7±2,8*	21,8±2,54*	20,8±2,61*	23,2±2,24*

Note: * – reliable relative to the initial indicators (p<0.05); n – number of patients.

Table 3. Dynamics of IOP (mmHg) during treatment

Groups	Initial IOP	3-day	7-day	10-day
Main group (n=30)	31,12±2,15	21,4±1,14*	21,1±1,11*	20,6±1,2*
Comparison group (n=30)	31,18±2,17	21,7±1,22*	21,3±1,16*	20,9±1,1*

Note: the indicators of both groups are unreliable (p>0.05); * – reliable relative to the initial indicators; n – number of patients.

lower than the values before treatment. On the 7th day of treatment, a slight decrease in IOP was observed in both groups. The IOP values of patients who received Glaubrinza and Simbrinza did not differ significantly and were 21.3±1.16 and 21.1±1.11 mmHg, respectively. By the 10th day of treatment, the indicators in the main and comparison groups were, respectively, 20.9±1.1 mmHg and 20.6±1.2 mmHg (Table 3); (Figure 2).

The effectiveness of the treatment in the main group was assessed as high in 85% and moderately high in 15% and averaged 3.8±0.1 points (Table 4).

The effectiveness of treatment in the comparison group was assessed as moderately high in 20% and high in 80% of patients and averaged 3.8±0.03 points (Table 4).

When instilling drugs into six patients in the main group and 9 patients in the comparison group, a local reaction was noted in the form of a burning sensation and discomfort, which was relieved within 1-2 minutes and did not require discontinuation of the drugs. The tolerability of the drugs was generally rated by patients as very good in 65% and good in 35% of cases; in patients in the comparison group, the figures were 60% and 40%, respectively (Table 4).

The use of drugs during all periods of observation led to a slight decrease in blood pressure in patients (due to the general hypotensive effect of brimonidine), which had a beneficial effect on the general condition of patients with high blood pressure.

IOP indicators after 1 month against the background of instillation of drugs decreased by 22% and 23%, respectively, in the comparison and main groups (p <0.05). By the 3rd month of treatment, IOP decreased to an average of 21-22 mmHg The indicators of both groups did not significantly differ from each other (p<0.05). By the 6th month, IOP decreased significantly compared with the values before treatment (by 35 and 34%, respectively, in the comparison group and the main group) and on average amounted to: 20.4±2.3 mmHg in the group that instilled Simbrinza and 20.7±2.12 mmHg in the group that used Glaubrinza (Table 5); (Figure 3).

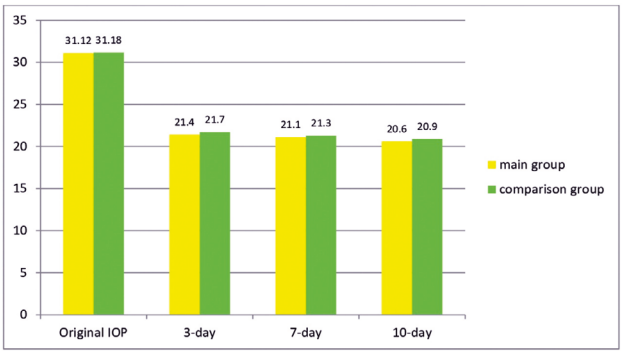

Figure 2. Change in IOP

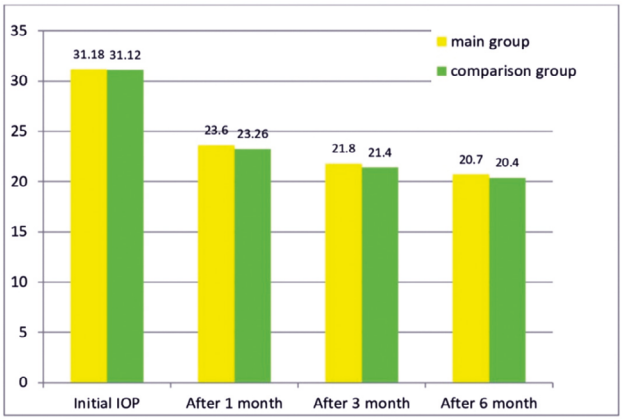

Figure 3. Change in IOP

OCT indicators. In both study groups, as early as 1 month after the start of treatment, there was an improvement in the dynamics of changes in the thickness of retinal nerve fiber layer (RNFL) (p<0.05) and by the 6th month of observation, RNFL data were significantly higher than the initial values and averaged 78.24±4. 31 µm and 78.52±4.12 µm, respectively, in the main and comparison

Table 4. Evaluation of efficacy and tolerability in patients in both groups in relation to side

Indicators assessed	Main group (n=30)				Comparison group (n=30)			
	1 point	2 points	3 points	4 points	1 point	2 points	3 points	4 points
Efficiency	0	0	15	85	0	0	20	80
Tolerability	0	0	35	65	0	0	40	60

Note: n – number of patients.

Table 5. Dynamics of IOP (mmHg) over the long term

Groups	Initial IOP	After 1 month	After 3 month	After 6 month	Average decrease in IOP	In %
Main group (n=30)	31,18±2,17	23,6±2,28*	21,8±2,22*	20,7±2,12*	10,15±2,2	34%
Comparison group (n=30)	31,12±2,15	23,26±2,34*	21,4±2,16*	20,4±2,33*	10,72±2,26	35%

Note: * – significant relative to the initial indicators (p<0.05); n – number of patients.

groups (Table 7). In the comparison group, the indicators were higher than those of the main group, but did not differ significantly.

The dynamics of perimetric indicators indicate an expansion of the visual field by an average of 14-18 o in 56% and 58% of cases, respectively, in the main group and control groups (p <0.05) (Table 6). In the main and comparison groups, the average visual field values by the 3rd month of observation significantly increased relative to the initial values to 384.8±24.21 degrees and 387.3±22.48 degrees, in the main and comparison groups, respectively. By the 6th month the indicators were, respectively, 402.3±31.62 and 403.5±32.26 degrees (Table 8).

Computer static perimetry data showed that the use of drugs in both groups of patients led to a gradual significant increase in the total photosensitivity of the retina (MS) by the 3rd month of observation to 13.8±1.16 and 14.2±1.24 dB, respectively, in the main and group comparisons. By the 6th month the indicators were, respectively, 15.3±1.17 and 15.8±1.41 dB. A significant decrease in the mean deviation from the age norm (MD) to 10.6±1.22 and 11.3±1.26 dB, respectively, in the main and comparison groups was noted by the 3rd month of observation. By the 6th month the indicator was 9.1±1.36 and 10.6±1.33 dB respectively (Table 8).

The cost and effectiveness of treatment with the studied drugs were calculated using the following formula by

Table 6. Orbital hemodynamic data (cm/sec) in the study groups

Groups	Vessels	Before treatment	1 month.	6 month
Main (n=30)	CV	0,84±0,04	0,78±0,02*	0,76±0,02*
	ShPCA	0,78±0,02	0,69±0,02*	0,66±0,01*
Comparison group (n=30)	CA	0,82±0,03	0,76±0,04*	0,73±0,01*

Note: CV – cerebral vessels; ShPCA – short posterior ciliary arteries. * – significant relative to the initial indicators (p<0.05).

Table 7. Dynamics of changes in the thickness of the retinal nerve fiber layer (RNFL-G) on OCT in patients with POAG (in μM)

Groups	Before treatment	After 1 month	After 3 month	After 6 month
Main group (n=30)	67,23±5,81	70,14±6,12	75,33±5,28	78,24±4,31*
Comparison group (n=30)	67,51±5,41	70,47±6,1	76,42±5,11	78,52±4,12*

Note: * – significant relative to the initial indicators (p<0.05).

Table 8. Dynamics of changes in functional indicators among patients with POAG

Группы	Main group				Comparison group			
Indicators assessed	Before treatment	1 month	3 month	6 month	Before treatment	1 month	3 month	6 month
Line of sight, degrees	330,8± 31,31	352,8± 28,16	384,8± 24,21 *	402,3 ± 31,62 *,**	328,2 ± 36,21	356,4 ± 26,15	387,3 ± 22,48 *	403,5 ± 32,26 *,**
Comp. stat. perimetry, MS, dB	11,2±1,14	12,5±1,23	13,8±1,16 *	15,3±1,17 *,**	10,8±1,48	12,1±1,19	14,2±1,24 *	15,8±1,41 *,**
Comp. stat. perimetry, MD, dB	13,2±1,25	11,4±1,34	10,6±1,22 *	9,1±1,36 *	13,2±1,21	12,3±1,27	11,3±1,26 *	10,6±1,33 *

Note: Significant difference p<0.05: * – from the initial indicators, ** – from the comparison group.

Stewart W.C., Stewart J.A. and Mychaskiw M.A.: sum/% reduction in IOP from baseline during the treatment period (3 months) [2].

Main group: Glaubrinza 85,000 UZS x 3 = 255,000 / 27.8% = 9,172 UZS

Control group: Simbrinza 125,000 UZS x 3 = 375,000 / 26.3% = 14,258 UZS

Discussion

Our study examined the effectiveness of a fixed combination of brimonidine and brinzolamide (FCBB) in 60 patients with POAG. The use of fixed combinations of brinzolamide + brimonidine had high antihypertensive efficacy in POAG in both the comparison and main groups. The administration of the proposed fixed combination drugs contributed to a significant reduction in IOP due to the suppression of the formation of aqueous humor by brinzolamide and the additional vasoconstrictor effect of brimonidine, which had an impact on the preservation of visual functions and improvement of hemodynamic parameters of the organ of vision in both groups of patients.

Kóthy and Holló [11] have studied the effect of FCBB in 52 cases of POAG and ocular hypertension (OHT) and reported a significant reduction in IOP in most eyes included in the study. Gandolfi et al. have compared treatment regimens using brinzolamide 1% and brimonidine 0.2%, administered as a fixed combination and in separate vials, in patients with POAG and OHT and found that FCBB was as effective in lowering IOP as treatment alone.

One of the indicators of the effectiveness of antihypertensive therapy is the restoration of the function of visual neurons and light sensitivity, which is very important in the initial stages of glaucoma when there is no change in functional indicators. In the later stages of the disease, it is necessary to monitor the effectiveness of the treatment. In our study, using data obtained from perimetry, static perimetry, and OCT, we studied the neuroprotective activity of the drugs.

Treatment adherence is low in patients with glaucoma, partly due to the asymptomatic nature of the condition during the early stages. The results of Lachlan S. W. Knight et al. [14] have showed that a decrease in IOP for every 1 mm Hg reduced the progression of glaucoma by 10%. 5 In our study, the mean reduction in IOP was 4.1 mmHg. Art. throughout the group.

Non-adherence to treatment is a major contributor to glaucoma treatment failure, with nearly 80% of patients failing to take their prescribed medications [20]. This condition may contribute to disease progression, requiring frequent specialist visits and increasing costs. Several factors, such as inadequate patient education, complexity of treatment regimens, medication side effects, and problems with regular and correct eye drop administration, have been identified as potential barriers to optimal adherence [25]. Studies have shown that persistence in taking glaucoma medications is also low when multiple medications are required [24].

Currently, first-line treatment for glaucoma is mainly based on topical application of one or more antiglaucoma drugs to lower IOP. Before resorting to surgical treatment, treatment with multiple drugs is necessary to achieve the target IOP. Studies have shown that use of more than two drops per day negatively affects patient compliance and, consequently, treatment success [12].

Fixed combination therapy, including FCC, can potentially alleviate several of these problems. However, one challenge is the objective assessment of long-term adherence. Adherence to various topical treatment regimens in clinical trials may not reflect the real clinical practice scenario and may be an overestimate.

Gandolfi et al. [9] have conducted a study with brinzolamide 1% and brimonidine 0.2% (in two separate vials); both drugs were taken twice daily. Overall, 890 patients with POAG or OHT were randomized (1:1) to BBFC or concomitant therapy. The percentage of patients with IOP <18 mmHg during the study visits was 68.9%–71.6% for those receiving FCBB and 65.8%–71.6% for those receiving the combination regimen.

Our work evaluates the efficacy and safety of FCBB, but there are certain limitations in previous studies. For example, most studies were short-term [23]. Thus, the long-term impact of FCBB on IOP and safety is unknown. Furthermore, IOP was not measured over a 24-hour period, and thus nocturnal IOP readings were not inferred. Each IOP-lowering drug exhibits significant peaks and troughs at various time points during the day and may not provide a consistent delivery system. To date, most studies have compared the efficacy of FCBB with its two monotherapeutic agents, and only one study has compared FCBB with a concomitant regimen. In addition, the FCBB dosing regimens have varied across studies, and a head-to-head comparison is lacking. Both brinzolamide and brimonidine have been approved for twice-daily administration in the European Union and many countries outside the European Union [8]. Given these and the comparable results with the three-time-daily dosing schedule, a trend toward twice-daily dosing is recommended. However, further studies are required to confirm the optimal dosing of FCBB.

When interpreting the indicators of color Doppler scanning of the orbital vessels of both groups, by the 3rd month of observation, there was a significant decrease in indicators by 14% and 15%, respectively, in the main and comparison groups (Table 6). The resistance index (Ri) in these groups averaged 1.0 and 1.1, respectively. It should be noted that in both groups, the hemodynamic indicators of ocular vascular resistance remained consistently low by the 6th month of observation. The results indicated the vasoconstrictor effect of brimonidine, which slows blood flow in the ciliary body and reduce the production of intraocular fluid [15].

Simbrinza has a more pronounced hypotensive activity compared to monotherapy drugs for patients with POAG. Despite this, it has more ocular side effects than each com-

ponent used separately due to the content of benzalkonium chloride in its composition. Simbrinza contains benzalkonium chloride (BAK; 0.03 mg/mL), which can have adverse effects on the ocular surface, including decreased tear film stability, increased 5corneal and conjunctival staining, and increased tear film osmolarity [27].

An alternative is the drug we are studying, Glaubrinza, which is based on brinzolamide and brimonidine and does not contain benzalkonium chloride. The use of preservative-free drugs significantly increases the tolerability of local hypotensive therapy, which has reduced the number and degree of subjective complaints and improved objective indicators of the state of the ocular surface. This approach reduces the need for the instillation of "artificial tears", which determines the economic benefit for patients. Glaucoma is an "expensive disease" requiring lifelong therapy, and minimizing the need for long-term drug use will reduce the economic burden on both the patient and the state.

Furthermore, Simbrinza and Glaubrinza are the first combination therapies for glaucoma that do not contain beta-blockers (beta-adrenergic antagonists (especially 0.5% timolol), which are the most commonly used agents in combination with other drug classes in fixed combination eye drops, can be used in the presence of beta-blocker use. Although they are generally well tolerated, their use may be contraindicated or should be avoided in patients with certain medical conditions, such as asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, impotence, depression, confusion, and memory loss. Additional studies with long-term follow-up will determine whether efficacy is maintained over longer periods.

Based on the results of the abovementioned studies, we found that the fixed combination reduced IOP to a greater extent than either component taken as monotherapy and was equivalent to the combination when dosed simultaneously. Moreover, this effect occurred at the beginning of the course of treatment and was maintained throughout the treatment period. Thus, drugs that act with fewer drops or fixed combinations containing two drugs in one bottle are preferable, which confirms the data obtained by us.

In conclusion, FCBB appears to be a promising new combination therapy for IOP lowering in patients with POAG and OHT. It has a more pronounced IOP-lowering effect compared to monotherapy agents and comparable side effects compared to the concomitant regimen. The development of these agents has provided a new option in the clinician's armamentarium for treating glaucoma.

Conclusions. Thus, the fixed combination drug Glaubrinza is highly effective in the treatment of POAG and not inferior in all studied parameters to the comparison drug. It is also economically accessible to all segments of the population, and therefore, its use in ophthalmological practice is advisable.

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Abbreviation. *POAG – primary open-angle glaucoma; IOP – intraocular pressure; GCP – good clinical practice; TMA – Tashkent Medical Academy; ADT – acute drug test; CCT – central corneal thickness; OCT – optical coherence tomography; RNFL – retinal nerve fiber layer; OHT – ocular hypertension; FCBB – fixed combination brinzolamide 1%/brimonidine 0.2%; MAOIs – monoamine oxidase inhibitors.*