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Assessment of the optic nerve head, peripapillary, and macular microcirculation in the newly diagnosed patients with primary open-angle glaucoma treated with topical tafluprost and tafluprost/timolol fixed combination

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Abstract:

RELEVANCE: The ability of antiglaucoma drugs to improve ocular hemoperfusion is an important aspect of their action. Tafluprost is the first preservative-free prostaglandin analog. The efficacy and safety of tafluprost, as well as tafluprost/timolol fixed combination (FC), were demonstrated in randomized multicenter trials. However, there is no literature on the effect of tafluprost and its FC on the peripapillary and macular blood flow.

PURPOSE: To determine the changes of microcirculation in the optic nerve head (ONH), peripapillary retina, and macula in patients with newly diagnosed primary open-angle glaucoma (POAG) under the topical tafluprost and tafluprost/timolol FC treatment.

MATERIALS AND METHODS: Optical coherence tomography angiography (OCT-A) was performed in dynamics with an interval of a week in 36 patients (36 eyes) with a newly diagnosed initial stage of POAG: 12 eyes with tafluprost, 12 – tafluprost/timolol FC, and 12 – no topical treatment (the control group). The change in intraocular pressure (IOP), mean ocular perfusion pressure (MOPP) of the eye, and vessel density (VD) inside the ONH (inside disc), as well as in the peripapillary retina and macula, was evaluated by comparing paired repeated observations using the median growth analysis.

RESULTS: In the tafluprost group, there were a decrease in IOP by 19.4% and an increase in MOPP by 8.7% from the reference level. In the tafluprost/timolol group, these figures were 43% and 30.1%, respectively. OCT-A values did not change reliably, except for VD inside disc: the median growth of the tafluprost group was 2.28 ($P = 0.02$) and of the tafluprost/timolol group was 1.82 ($P = 0.03$). These changes were obtained in 11 of 12 patients in each group under treatment. In control group, all indicators remained unchanged.

CONCLUSIONS: A significant increase of MOPP and a decrease of VD in the ONH in patients with initial glaucoma occurred within a week under the topical tafluprost or its FC. This can be explained by the restoration of autoregulation of the ocular blood flow in conditions of pronounced hypotensive effect of the drugs.

Keywords:

Ocular blood flow, optical coherence tomography -angiography, preservative-free prostaglandin analog, primary open-angle glaucoma

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Introduction

Relevance

Tafluprost (Saflutan®/Taflotan®) is the first preservative-free prostaglandin analog (PGA). Being a fluorinated PGA F2α, or an ether of tafluprost acid, the medicinal product has the expressed features of the selective agonist of human FP-receptors, exceeding those of other PGAs, in particular, of latanoprost.[1] The fixed dose combination of prostaglandin/timolol (PTFC) – tafluprost/timolol – contains 15 mg/ml of tafluprost and 5 mg/ml of timolol maleate.[2] It should be noted that this PTFC is one of the first preservative-free PGAs.[2] The prospective application of PTFC to reduce intraocular pressure (IOP) was repeatedly discussed in the literature.[3]

The efficacy and safety of tafluprost, as well as of its PTFC, were demonstrated in randomized multicenter trials.[4-9] Some experimental and clinical studies revealed that tafluprost improves retinal and optic nerve hemoperfusion.[10-16] The role of vascular disorders in the pathogenesis of glaucoma has repeatedly been discussed in the literature.[17,18] According to the literature, the parameters of ocular blood flow can play a role in the early diagnosis of glaucoma[19,20] and serve as predictors of its progression.[21]

Optical coherence tomography angiography (OCT-A) is a new method that allows to study the ocular microvascular bed and to obtain information on retinal and optic disc microcirculation without using contrast agents.[22] Our recent studies have shown that the method can be useful for early diagnosis of glaucoma and its monitoring.[23,24] However, it is not clear if the topical hypotensive eye drops affect the OCT-A parameters.

Purpose

The purpose of this study is to determine the changes of microcirculation in the optic nerve head (ONH), peripapillary retina, and macula in patients with newly diagnosed primary open-angle glaucoma (POAG) under the topical tafluprost and tafluprost/timolol fixed combination (FC) treatment.

Materials and Methods

Thirty-six patients (36 eyes) with a newly diagnosed initial stage of POAG were studied.

Glaucoma was diagnosed on the basis of typical changes in the optic disc detected during ophthalmoscopy (abnormal proportions of neural rim, glaucomatous excavation of optic disc, peripapillary atrophy, retinal nerve fiber layer [RNFL] wedge-shaped defects close to the edge of the optic disc, and hemorrhage at the optic disc edges). The diagnosis of glaucoma according to ophthalmoscopy was confirmed by two independent glaucoma specialists. The results of standard automated perimetry (SAP) performed at Humphrey perimeter (Carl Zeiss Meditec, Dublin, CA, USA) were abnormal. Glaucomatous visual field defects were determined as having a cluster of three or more nonedge points with P <5% and at least 1 point with P < 1% in the pattern deviation probability plot; pattern standard deviation (PSD) of <5%; or glaucoma hemifield test results outside normal limits. All the participants underwent SAP at least twice before this study.

The following inclusion criteria were used: presence of emmetropic refraction and open anterior chamber angle, which was confirmed by OCT of the anterior segment (Visante OCT, Zeiss), and at the same time the acceptable angle of the anterior chamber was not <30°. All patients were Caucasians.

Exclusion criteria were the presence of the following: large refractive errors (outside of ± 6.00 D sphere or 2.00 D cylinder), pupil diameter <3 mm, systemic administration of beta-blockers and calcium-channel blockers, concomitant ocular disease (except early-stage cataract), chronic autoimmune diseases, diabetes mellitus, acute circulatory disorders in the past medical history, and any concomitant disease involving the administration of steroid drugs. A history of ocular arterial or venous obstruction (branch or central occlusion), as well as systemic conditions associated with venous congestion (e.g., heart failure), was also considered as an exclusion criterion. The analysis included only patients who had previously no ophthalmic surgeries. The patients were instructed to avoid caffeine intake, smoking, and exercise for 5 h before the study visit.

The ophthalmic examination included viscometry, tonometry using the analyzer of biomechanical ocular features (ocular response analyzer, Reichert Ophthalmic Instruments Inc., Depew, NY, USA), biomicroscopy, gonioscopy, measurement of anterior-chamber angle (Visante OCT), pachymetry (SP-100, Tomey, GmbH), SAP (Humphrey, Carl Zeiss Meditec, Dublin, CA, USA), and OCT (OCT RTVue-100, Optovue, Inc., Fremont, CA, USA) in the region of macula and optic disc. The thickness of the RNFL was estimated by sectors, and the thickness of the ganglion cell complex and its characteristics – global loss volume and focal loss volume – were measured as described by us earlier.[21]

Optical coherence tomography-angiography imaging of the optic disc, peripapillary region, and macula

OCT-A scans were collected using the spectral-domain system (RTVue XR Avanti, Optovue Inc., Fremont, CA, USA): AngioVue, 2016.1.0.26.

The optic disc scan covers an area of 4.5 mm × 4.5 mm. The following parameters of vessel density (VD) were investigated: whole *en face* image VD disc scan. It included VD inside disc and peripapillary VD (750-µm-wide elliptical annulus extending from the optic disc boundary). The software automatically fits an ellipse to the optic disc margin and calculates the average VD within the ONH (referred to as the inside disc VD). The peripapillary region is divided into six sectors based on the Garway-Heath map, and the VDs are calculated in each sector (nasal, inferonasal, inferotemporal, superotemporal, superonasal, and temporal sectors), as described by us earlier.[24]

The peripapillary VDs were analyzed in superficial retinal layers from the radial peripapillary capillary (RPC) segment. The RPC segment extends from the internal limiting membrane (ILM) to the posterior boundary of the RNFL.

Macular scans covered a 6.0 mm × 6.0 mm area, in which the microvasculature VD was measured. VD is defined as the percentage area occupied by the large vessels and microvasculature in a particular region. Two vascular plexuses were studied in the macula: (1) a superficial plexus located in a layer with the upper limit 3 µm below the surface of the ILM and lower limit 15 µm below the inner plexiform layer (IPL) and (2) a deep plexus located in the retina layer at a depth of 15–70 µm below the IPL. Measurements were performed in the fovea and parafovea. The average value of the vascular density for these two zones was also measured – whole *en face* image VD macula scan [Figure 1]. The parafoveal region was divided into four sectors of 90° each (nasal, inferior, superior, and temporal sectors). Image quality was assessed for all OCT-A scans.

Only images with optimal image quality (signal strength index >50), no motion artifacts, vitreous floaters, or other artifacts were selected.

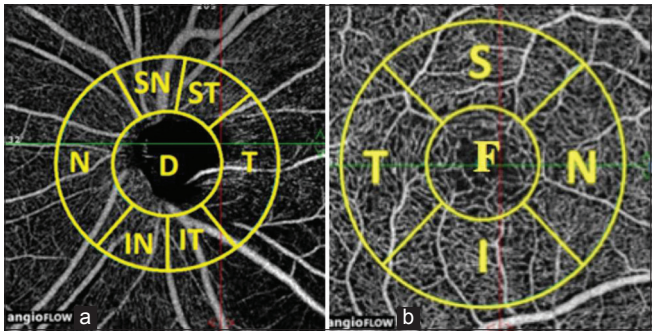

Figure 1: Optic disc, peripapillary retina (a) and macular area (b) studied during OCT-A. (a) ONH and circumpapillary VD map measurement region defined: D – ONH (Inside Disc), SN –superonasal, ST – superotemporal, N – nasal T – temporal, IN – inferornasal, IT – inferotemporal. Peripapillary area: SN + ST + T + IT + IN + N. wiVD Disc: D + Peripapillary area. (b) Fovea (F) and circumparafovea VD map measurement region defined: S – superior, N – nasal, I – inferior, T – temporal. wiVD Macula: F+ circumparafovea

Mean ocular perfusion pressure

Mean ocular perfusion pressure (MOPP) was calculated from IOP and arterial blood pressure (BP) measurements immediately before the OCT scanning and investigation of retrobulbar blood flow, after a 10-min resting period in the sitting position. Systemic BP was measured using the Riva-Rocci technique. MOPP was calculated using the formula: MOPP = (2/3 diastolic BP + 1/3 systolic BP) × 2/3 – IOP.

Study design

The study was approved by the Institutional Review Board of the Federal Medical and Biological Agency of Russia and was conducted in accordance with the provisions of Declaration of Helsinki.

Patients were recruited if they fulfilled the inclusion criteria.

Before enrollment, the patients were made aware of the procedures and the aim of the study following which they signed written consent form. Subsequently, the patients were divided, in a random and double-blind manner, into three groups: Group A – 12 patients who were administered a single evening dose of tafluprost 0.0015%, Group B – 12 patients who were administered a single evening dose of tafluprost/timolol FC (comprises 15 µg/ml tafluprost and 5 mg/ml timolol maleate in a single-dose container), and Group C – 12 patients who were administered a single evening dose of water for injection (placebo group). Following the baseline visit, follow-up examination was conducted by an ophthalmologist blind to the treatment group at 1 week.

All patients underwent a full complex of ophthalmological examinations, as well as measurement of BP before OCT-A. Then, the patients took tafluprost or its FC in the dosage of 1 drop per night daily. The repeated examination was carried out at the same day time 1 week later by the same specialist.

Statistical data processing

We used the analysis methods to compare paired repeated observations with a small statistical sample. A typical value of difference was estimated using an incremental median. An increment was understood as the difference between the value of the compared parameter at the time of the last patient's examination and its initial value. Too large or too small number of positive increments meant a systematic parameter change.[25] An exact one-sided sign test was evaluated. The parameters with $P < 0.05$ were considered statistically significant.

Results

The groups of patients were homogeneous in age, BP, IOP, and glaucoma stage [Table 1].

All the included patients successfully completed the study per protocol.

The results are summarized in Tables 2 and 3.

None of the treated patients experienced symptoms of photophobia or irritation as well as no signs of inflammation were noted during slit-lamp examination in 1 week of treatment.

A significant decrease in IOP compared with the baseline was detected in both groups of treated patients: by 19.4% in tafluprost and by 43% in tafluprost/timolol FC. Corneal hysteresis increased significantly in both groups [Table 2]. MOPP increased by 8.7% and 30.1% in tafluprost-treated patients and in tafluprost/timolol FC-treated patients, respectively. IOP and MOPP did not change in the placebo group.

Instillation of tafluprost and its PTFC during a week did not affect vascular density of the peripapillary retina and inner macular layers but caused a decrease in the density of microcirculatory bed in ONH (inside disc). These changes were observed in 11 of 12 patients in each group of patients treated with tafluprost or its PTFC. All OCT-A parameters remained unchanged in the placebo group [Table 3].

Table 1: Patient's characteristics

Parameters	Tafluprost group	Tafluprost/timolol FC group	Placebo group
Age (years)	64.7 (7.2)	60.5 (7.6)	62.6 (5.7)
BP systolic (mmHg)	125.0 (5.0)	126.7 (5.4)	129.2 (12.6)
BP diastolic (mmHg)	80.0 (3.2)	81.8 (4.1)	83.15 (8.2)
IOPcc (mmHg)	20.8 (3.7)	23.7 (5.1)	19.8 (5.3)
MOPP (mmHg)	42.5 (4.5)	41.0 (6.8)	45.2 (5.6)
Corneal thickness (μm)	535 (12.1)	538.5 (21.2)	541.1 (23.3)
Axial length (mm)	23.5 (1.2)	23.2 (2.3)	24.0 (1.9)
Visual field MD (dB)	–isual field	–1.91 (0.45)	–1.13 (0.2)
Visual field PSD (dB)	1.48 (0.29)	2.12 (1.82)	2.73 (1.59)
RNFL (μm)	92.9 (8.1)	93.5 (9.3)	94.3 (15.3)
GCC (μm)	86.3 (6.1)	87.2 (9.4)	89.5 (10.3)
FLV (%)	1.91 (1.25)	2.13 (1.05)	2.45 (1.68)
GLV (%)	4.61 (1.23)	5.33 (2.13)	4.91 (2.04)

MOPP=Mean ocular perfusion pressure, MD=Mean deviation, PSD=Pattern standard deviation Avg. RNFL=Average retinal nerve fiber layer, Avg. GCC=Average ganglion cells complex, FLV=Focal loss volume, GLV=Global loss volume, FC=Fixed combination, IOP=Intraocular pressure, BP=Blood pressure

Discussion

According to the results of this study, instillation of tafluprost and its PTFC during a week does not affect vascular density of the peripapillary retina and inner macular layers. At the same time, the density of microcirculatory bed in ONH (inside disc) was being decreased in the setting of treatment with both the tafluprost and its PTFC. At first sight, these findings seemed unexpected and contradictory to the literature. In fact, many authors noted both in animal experiments[10-12,14,15,17] and in clinical use that tafluprost increases the retinal blood flow even more than other PGAs.

According to Akaishi *et al.*,[15] the optic disc blood flow in rabbits increased by 11.9% after 28 days of treatment with tafluprost, by 7.2% with latanoprost, and by 6.7% with travoprost. Dong *et al.*[10] discovered the ability of tafluprost to induce drug concentration-dependent dilatation of isolated ciliary arterioles in rabbits, constricted in response to the administration of endothelin-1. The effect of tafluprost was more lasting than of other PGAs.

The increased optic disc blood flow induced by tafluprost was demonstrated by Mayama *et al.* in their experiment on monkeys.[14] These data were later confirmed in Tsuda *et al.*'s clinical study.[13] The authors suggested that tafluprost improves optic nerve microcirculation due to direct relaxation of the microcirculatory bed vessels and/or by improving the retrobulbar blood flow.

Most authors agreed that this relaxation effect of tafluprost is related to its ability to block the constricting effect of endothelin-1.[15]

Table 2: Values of intraocular pressure, corneal hysteresis, and perfusion pressure in three groups of glaucoma patients and their change in the setting of tafluprost and tafluprost/timolol fixed combination

Parameter	Tafluprost group				Tafluprost/timolol group				Placebo group			
	Baseline	At the end	Incremental median	*P**	Baseline	At the end	Incremental median	*P***	Baseline	At the end	Incremental median	*P****
IOPcc (mmHg)	20.8 (3.7)	16.8 (3.2)	-4.4	0.002	23.7 (5.1)	13.2 (3.9)	-8.6	0.016	19.8 (5.3)	20.1 (3.4)	0.9	0.86
Hysteresis (mmHg)	9.3 (2.6)	11.2 (2.8)	1.9	0.035	9.3 (3.0)	10.6 (3.2)	1.55	0.016	9.1 (2.0)	9.0 (1.0)	0.3	0.53
MOPP (mmHg)	42.5 (4.5)	46.2 (5.2)	3.7	0.001	41.0 (6.8)	52.1 (4.5)	9.9	0.000	45.2 (5.6)	44.1 (3.8)	0.28	0.67

An incremental median means the change of the value in the setting of treatment with tafluprost or tafluprost/timolol. **P*=Reliability of the incremental median with tafluprost, ***P*=With tafluprost/timolol FC, ****P*=In the control group (placebo group). FC=Fixed combination, IOP=Intraocular pressure

Table 3: Optical coherence tomography angiography values in three groups of glaucomatous patients and their change in the setting of tafluprost and tafluprost/timolol fixed combination

Parameters	Tafluprost group			Tafluprost/timolol FC group			Placebo group		
	Variable	Incremental median	*P**	Variable	Incremental median	*P***	Variable	Incremental median	*P****
Disc scan									
wiVD disc (disc scan)	46.6 (8.6)	−1.55	0.254	48.8 (8.3)	−0.16	0.5	49.3 (8.2)	−0.44	0.344
Inside disc VD	25.1 (9.3)	−2.58	0.020	37.2 (14.3)	−1.82	0.033	41.1 (14.4)	−1.145	0.656
Average peripapillary VD	55.3 (10,5)	1.25	0.746	56.4 (7.6)	−0.52	0.227	55.5 (9.9)	0.89	0.891
Nasal VD	54.2 (10.6)	0.5	0.746	54.9 (7.2)	−0.73	0.5	51.9 (8.7)	−0.25	0.656
Inferonasal VD	56.9 (11.4)	−0.56	0.500	59.5 (7.4)	3.05	0.773	56.7 (11.1)	0.2	0.656
Inferotemporal VD	56.0 (13.0)	1.71	0.746	58.5 (9.8)	−2.64	0.227	61.6 (10.9)	2.385	0.891
Superotemporal VD	58.2 (9.1)	−1.35	0.500	61.8 (5.7)	0.49	0.773	60.9 (10.5)	1.545	0.891
Superonasal VD	50.6 (12.1)	3.35	0.090	50.1 (10.0)	−1.47	0.227	49.9 (9.0)	−2.525	0.344
Temporal VD	56.1 (14.2)	−0.07	0.500	56.6 (11.4)	−1.26	0.227	56.1 (13.6)	3.495	0.891
Macula scan									
wiVD macula superficial	43.3 (8.3)	−2.53	0.254	46.2 (5.2)	3.42	0.773	47.0 (5.6)	−2.38	0.227
Foveal VD superficial	29.6 (6.6)	−0.5	0.500	30.6 (3.7)	0.79	0.227	34.6 (6.6)	−2.42	0.500
Parafoveal VD superficial	49.6 (6.8)	−2.95	0.500	49.7 (5.0)	2.33	0.773	50.3 (5.9)	−0.47	0.500
Temporal	48.9 (7.5)	−3.6	0.254	49.7 (5.5)	0.52	0.773	51.3 (6.3)	3.77	0.938
Superior	49.4 (5.3)	−1.52	0.254	49.2 (5.2)	−1.17	0.500	49.8 (7.1)	−2.21	0.500
Nasal	48.1 (8.8)	−1.25	0.500	49.4 (7.0)	1.83	0.773	50.9 (6.5)	−2.16	0.500
Inferior	50.0 (7.0)	−0.77	0.500	50.5 (3.9)	3.95	0.773	49.2 (5.4)	−3.53	0.500
wiVD macula deep	47.1 (10.8)	−1.11	0.254	54.7 (7.3)	5.58	0.773	54.1 (7.5)	−4.35	0.500
Foveal VD deep	31.0 (10.0)	2.47	0.746	32.3 (6.4)	1.63	0.773	32.8 (6.3)	2.32	0.063
Parafoveal VD deep	55.0 (9.8)	0.18	0.746	58.8 (7.5)	−0.31	0.500	57.8 (6.2)	−1.27	0.227
Temporal VD	53.2 (12.6)	−5.91	0.500	57.5 (7.0)	−1.13	0.500	56.4 (7.2)	−2.37	0.500
Superior VD	56.5 (10.0)	−2.41	0.500	58.4 (8.7)	−6.9	0.500	57.2 (8.2)	−1.88	0.227
Nasal VD	53.8 (11.1)	0.47	0.746	58.1 (9.4)	0.85	0.773	58.7 (5.6)	−0.35	0.500
Inferior VD	56.5 (7.5)	−1.64	0.500	61.3 (6.1)	2.48	0.773	59.0 (6.2)	−2.16	0.227

An incremental median means the change of the value in the setting of treatment with tafluprost or its PTFC. **P*=Reliability of the incremental median with tafluprost, ***P*=With tafluprost/timolol FC, ****P*=In the control group (placebo group). FC=Fixed combination

In some clinical studies, tafluprost was compared with other hypotensive eye drops, in particular, with dorzolamide/timolol FC. According to Seo and Ha,[16] tafluprost significantly improves ocular pulsation pressure better than dorzolamide/timolol FC in patients with normal tension glaucoma (NTG). Thus, the authors concluded that tafluprost is the drug of choice for NTG treatment. In experiments on cats, Kurashima *et al*. showed a positive effect of tafluprost on the ophthalmic artery blood flow by reducing of its resistive index.[12]

In our previous study, we found some regularities, which might be typical for the results of OCT-A in initial glaucoma.[26] Thus, an inverse correlation was found between the peak systolic velocity in ophthalmic artery and the density of capillary network in the superficial vascular plexus of macula, as well as between the end-diastolic velocity of the short posterior ciliary arteries and the VD in optic disc and peripapillary retina. In other words, in initial glaucoma, the more the blood comes to the retina and optic disc, the lower the OCT-A values are. The identified features were explained as the preservation of autoregulation of the retinal blood flow at the initial disease stage. This was also confirmed by the fact that normally, when autoregulation of the ocular blood flow *a priori* exists, there was an inverse correlation between the ocular perfusion pressure and foveal and parafoveal VD. There were no similar correlations at the advanced stages of glaucoma. The above-mentioned assumption is supported by the literature data on decrease in OCT-A retinal parameters in hyperoxia.[27] The authors also explained this fact with the existence of autoregulation of the retinal blood flow. The specified phenomenon is that the increased blood flow in retrobulbar vessels, for example, in response to a decrease in IOP or an increase in BP, is accompanied by a spasm of small arterioles and capillaries, which in its turn blocks the possibility of their OCT-A visualization. Based on the observation data, we believe that a pronounced IOP decrease in the setting of tafluprost and its PTFC leads to the same phenomenon. It is accompanied by a significant increase in the MOPP, especially in the setting of the treatment with tafluprost/timolol (there was an increase in MOPP by one-third of the initial). The decrease in OCT-A values in the setting of the treatment with these drugs does not indicate a deterioration of the blood supply to the optic disc. Most likely, this is just the effect of ocular blood flow autoregulation preserved at the initial stage of

glaucoma. However, it may be disturbed in advanced stages of the decease. Holló recently has published a case-reported study and speculated that a large reduction of IOP may lead to increase of the peripapillary VD in some glaucoma eyes.[28] More observations for patients with different stages of POAG are required to verify the effect of IOP reduction on retinal VD.

According to the results of the present study, OCT-A parameters significantly decreased only in optic disc, but not in the peripapillary retina or macula. It is difficult to explain this phenomenon. Probably, this is due to the greater lability of the optic disc tissues (in particular, a sieve-like scleral membrane) in response to changes in IOP compared with the tissues of peripapillary region and macula. Our data coincide with those in the literature. Thus, according to the OCT-A results obtained by Rao *et al*.,[29] VD depends on IOP, but only in inside optic disc. Rao *et al*. suggested that the OCT-A parameters in the macula and peripapillary retina are IOP independent.

Like other PGAs, the IOP decreased in the setting of tafluprost starts in 2–3 h after the instillation, reaching its peak in 8–12 h.[30] Timolol starts to decrease IOP just in 20 min after the instillation with the maximum effect in 2 h. Thus, the study of IOP and OCT-A parameters in a week after the start of treatment corresponds to the maximum possible effect of the studied eye drops.

The hypotensive efficacy of the new PTFC was demonstrated in two prospective, randomized, 6-month studies[7,8] and highlighted in the review by Hoy.[9] It ranges from 27% to 35%, depending on the initial IOP. In general, the authors suggest that this efficacy is comparable to that of PTFC with timolol. It is noteworthy that in our study, we did not find a single case of local hyperemia, while according to other authors, it is developed in 6.4%–8% cases.[2] We explain this difference with the fact that our study was performed with the participation of a small number of patients and was limited to 1 week, while the maximum number of cases of local hyperemia was registered by other authors in 2 weeks after the start of treatment.

Our study has several limitations that must be acknowledged. First, we had a limited sample size. Second, to study the effect of PGAs on the microcirculation in the ONH, peripapillary area, and macula, we included only patients with initial glaucoma stage. As it has been mentioned above, the autoregulation of retinal blood flow may be preserved only at the beginning of glaucoma process; hence, the assessment of retinal VD in the glaucoma patients with the advanced stages under the topical hypotensive treatment can differ from the results of the present study. Third, the follow-up period was limited to 1 week. We did not study the progression pattern of disease, and we did not study the progression pattern of the disease, and we did not analyze the link between visual fields deterioration and the change of OCT-A data.

We have assumed that a decrease in the density of microcirculatory bed in ONH (inside disc) might be a consequence of autoregulation of the retinal blood flow by a spasm of small arterioles and capillaries in response to increased blood flow in retrobulbar vessels after IOP reduction or BP elevation. The mechanism of autoregulation is one of the possibilities to explain the data observed from this study; however, it is difficult to use a single-shot time point to explain a dynamic autoregulation response. To support the hypothesis of autoregulation, further studies with prolonged follow-up period are needed.

Conclusions

The present study revealed a significant decrease of IOP, an increase of MOPP, and a decrease of VD in the ONH without any change in the vascular density of peripapillary retina and inner macular layers in patients with new diagnosed initial glaucoma within a week of treatment. A larger patient population and a longer follow-up period are required to obtain more accurate results and to understand the vascular density change under treatment.

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Nil.

Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

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