Comparison of the Effects of Latanoprost 0.005%, Travoprost 0.004% and Bimatoprost 0.01% on Peripapillary and Macular Microcirculation

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ABSTRACT

Purpose: To compare the effects of three different prostaglandin analogs (PGAs) on optic nerve head (ONH) and macular vessel densities (VDs) in eyes with early-stage primary open-angle glaucoma (POAG).

Material and Methods: Ninety-five eyes from 95 patients with early-stage POAG (latanoprost 0.005% (n=35), travoprost 0.004% (n=30), bimatoprost 0.01% (n=30)) and a healthy control group (n=35) were included in this cross-sectional study. Retinal nerve fiber layer (RNFL) thickness and radial peripapillary capillary (RPC) VDs were measured using 4.5x4.5 mm ONH sections of the patients. Superficial capillary plexus (SCP) VDs, deep capillary plexus (DCP) VDs, and retinal thickness values were measured using 6x6 mm macular sections centered on the fovea.

Results: Peripapillary retinal thickness (ppRT), whole image VD (wiVD), and peripapillary VD (ppVD) measurements were significantly higher in the control group compared to the groups receiving PGA monotherapy (p=0.005, p=0.006, and p=0.002, respectively). SCP and DCP foveal VD (fVD) values were significantly higher in the bimatoprost 0.01% group (p=0.001 and p=0.010, respectively). No significant difference was observed between wiVD, parafoveal VD (pafVD), and perifoveal VD (pefVD) groups in both SCP and DCP (p>0.05). Additionally, in the bimatoprost 0.01% group, while foveal retinal thickness (fRT) was significantly thicker (p=0.005), whole image retinal thickness (wiRT) and perifoveal retinal thickness (pefRT) were significantly thinner (p=0.016, and p=0.009, respectively). Parafoveal retinal thickness (pafRT) was also thinner but not significantly so in the bimatoprost group (p=0.312).

Conclusion: The increased foveal blood flow in users of bimatoprost compared to those using latanoprost and travoprost may indicate that bimatoprost 0.01% positively affects ocular perfusion.

Key words: latanoprost 0.005%, travoprost 0.004%, bimatoprost 0.01%, primary open angle glaucoma, optical coherence tomography angiography

INTRODUCTION

Glaucoma presents a significant public health challenge, leading to vision loss and decreased visual acuity due to progressive damage to the optic nerve, ultimately resulting in blindness.[1-4] Primary open-angle glaucoma (POAG) is the most common clinical subtype, with a global prevalence of approximately 3.05% among individuals aged 40 and older.[1,2] The primary risk factors for POAG include elevated intraocular pressure (IOP), age, race, family history, and other variables.[1,3,4] Although IOP is the only known modifiable risk factor for POAG, keeping it within a target range remains the most effective treatment strategy to prevent optic neuropathy. [3-5] Achieving this target IOP can help minimize the loss of visual acuity and visual field by preserving the retinal nerve fiber layer (RNFL).[3,4] Medical treatment is usually recommended for the initial manage-

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ment of newly diagnosed POAG patients, according to international guidelines.[4]

While various classes of anti-glaucomatous agents have different mechanisms of action, topical prostaglandin analogs (PGAs) are recognized for their superior long-term reduction of IOP.[4-8] These medications decrease IOP by lowering outflow resistance and enhancing aqueous humor drainage through the uveoscleral pathway. [3,4,9] Administered once nightly, PGAs are highly effective and well-tolerated, making them the preferred choice for glaucoma therapy.[3,4,6-9] They also have a more favorable systemic side effect profile compared to other medications used in glaucoma treatment, despite the potential for local side effects such as conjunctival hyperemia, eyelash elongation, and iris darkening, etc.[3,9]

Although the importance of ocular blood flow (OBF) in the pathogenesis and management of glaucoma has long been recognized,[10] significant research in this area has accelerated with the introduction of optical coherence tomography angiography (OCTA).[11-16] As an innovative, non-invasive, and reproducible imaging technique, OCTA enables three-dimensional visualization of the optic nerve head (ONH) and retinal microvascular structures through sequential OCT scans.[11-14] While the role of OCTA in glaucoma diagnosis and management has yet to be fully established, it has the potential to become a valuable structural test for early diagnosis and monitoring of disease progression in the future.[11-16]

Studies investigating the effects of PGAs on OBF have primarily focused on their impacts on choroidal thickness, foveal thickness, and ocular perfusion pressure (OPP).[17-20] Although substantial research exists on the effects of medical anti-glaucomatous therapy on retinal microcirculation using OCTA,[21-27] there is still a gap in studies that investigate and compare the effects of different PGAs on the optic disc and retinal microvascular bed. The objective of the present study is to assess the effects of three different PGAs: latanoprost 0.005% (Xalatan, Pfizer Manufacturing Belgium, N.V./S.A., Puurs-Belgium), travoprost 0.004% (Travatan, Alcon Cusi, S.A., El Masnou, Barcelona, Spain), and bimatoprost 0.01% (Lumigan RC, Allergan Sales, LLC, Waco, Texas, USA) on ONH and macular vessel densities in patients with early-stage POAG.

MATERIAL AND METHODS

This prospective, single-center cross-sectional study was conducted at a tertiary reference glaucoma center. Written informed consent was obtained from all study participants, and the study protocol received approval from the Ankara Training and Research Hospital Ethics Committee (Ethics committee no: 507/2020). The study procedures followed the Declaration of Helsinki Principles and adhered to Good Clinical Practice Guidelines.

All participants underwent a comprehensive ophthalmological examination that included measuring best-corrected visual acuity (BCVA) with Snellen charts, performing an anterior segment and dilated fundus examination using slit-lamp biomicroscopy, evaluating the iridocorneal angle with a Goldmann three-mirror lens, measuring IOP using Goldmann applanation tonometry, conducting standard automated perimetry by utilizing the Humphrey Visual Field Analyzer (Carl Zeiss Meditec Inc., Dublin, CA, USA), applying the 24-2 Swedish Interactive Threshold Algorithm (SITA) Standard strategy and stimulus size III, analyzing peripapillary RNFL via optical coherence tomography (OCT; Spectralis, Heidelberg Engineering GmbH, Heidelberg, Germany), and measuring OCT angiography (OCTA) with the AngioVue device (RTVue-XR, Optovue, Inc.; Fremont; California, USA; software Version 2017.1.0.151).

Patient Selection

This study included ninety-five eyes from 95 patients diagnosed with early-stage POAG, treated with latanoprost (n=35), travoprost 0.004% (n=30), or bimatoprost 0.01% (n=30) as monotherapy, along with 35 eyes from 35 subjects in the control group. If both eyes of a subject were eligible for the study, data from the right eye were used for statistical analysis. A diagnosis of POAG was defined as having a grade 3 or higher open iridocorneal angle according to the Shaffer grading system during gonioscopic examination, along with evidence of glaucomatous ONH changes and corresponding RNFL and visual field (VF) loss. Early-stage POAG classification was based on the Hodapp-Parrish-Anderson criteria, which include a mean deviation (MD) of less than -6 dB, fewer than 25% of points below the 5% level, and fewer than 10 points below the 1% level on the pattern deviation plot. Additionally, no points within the central 5º should have sensitivity less than 15 dB.

The inclusion criteria for the PGA groups were as follows: (1) Patients aged 45 to 75 years; (2) BCVA of 0.4 logMAR or better; (3) Spherical equivalent between -5.0 D and +3.0 D, with cylindrical correction ranging from -3.0 D to +3.0 D; (4) Patients who have been exclusively treated with latanoprost 0.005%, travoprost 0.004%, or bimatoprost 0.01% as monotherapy since diagnosis, without evidence of progression.

The criteria for including participants in the control group were as follows: (1) Participants aged 45 to 75 years; (2) BCVA of 0.4 logMAR or better; (3) Spherical equivalent between -5.0 D and +3.0 D, with cylindrical correction between -3.0 D and +3.0 D; (4) Participants must have a completely normal ophthalmologic examination, aside from refractive error, and no family history of chronic eye diseases.

The exclusion criteria included: (1) Subjects whose treatment was discontinued for any reason, switched to another PGA or a different type of antiglaucomatous medication, or had an additional medication added; (2) A history of any antiglaucomatous medication other than latanoprost 0.005%, travoprost 0.004%, or bimatoprost 0.01%; (3) An MD value for the visual field worse than -6 dB; (4) A history of systemic diseases affecting the cardiovascular system, including ischemic heart disease or heart failure. Subjects with systemic hypertension and diabetes mellitus were included unless they had been diagnosed with diabetic or hypertensive retinopathy; (5) Those diagnosed with types of glaucoma other than POAG and those with coexisting ocular diseases affecting the retina, uvea, or optic nerve; (6) A history of ocular trauma or intraocular surgery, except for uncomplicated cataract surgery conducted at least 6 months prior; (7) Presence of an open posterior capsule in pseudophakic patients, whether noted during surgery or later by YAG laser capsulotomy; (8) A history of uveitis, intraocular infection, or inflammation; (9) Poor signal strength index (SSI) for OCTA scans, scoring less than 6 on a 10-point scale.

OCTA Imaging

The OCTA assessment was performed using the AngioVue device (RTVue-XR, Optovue, Inc.; Fremont, California, USA; software Version 2017.1.0.151). This system, which utilizes the SSADA algorithm, achieves a scanning speed of 70,000 A-scans per second with an 840 nm light source and requires consecutive B-scan images. Consequently, at least two repeated B-scans can be obtained at a single point without altering resolution, imaging angle, or acquisition time. Volumetric A-scanning with 304×304 A-scans is accomplished in approximately 3 seconds.

The OCTA software generates standard vitreous, superficial, radial peripapillary capillary (RPC), and choroidal sections for the optic nerve head. The boundaries for RPC vascularity analysis are defined as being between the internal limiting membrane (ILM) and the posterior border of the RNFL. The disc analysis includes 2 mm and 4 mm rings centered on the disc, with the 2 mm central ring representing the intrapapillary area, while the area between the two rings constitutes the peripapillary area (Figure 1). The entire image of the 4.5 x 4.5 mm disc scan is referred to as whole image vessel density (wiVD). The software calculates the whole image vessel density (wiVD), intrapapillary vessel density (iVD), peripapillary vessel density (ppVD), superior hemi vessel density (shVD), and inferior hemi vessel density (ihVD) values for the optic nerve head.

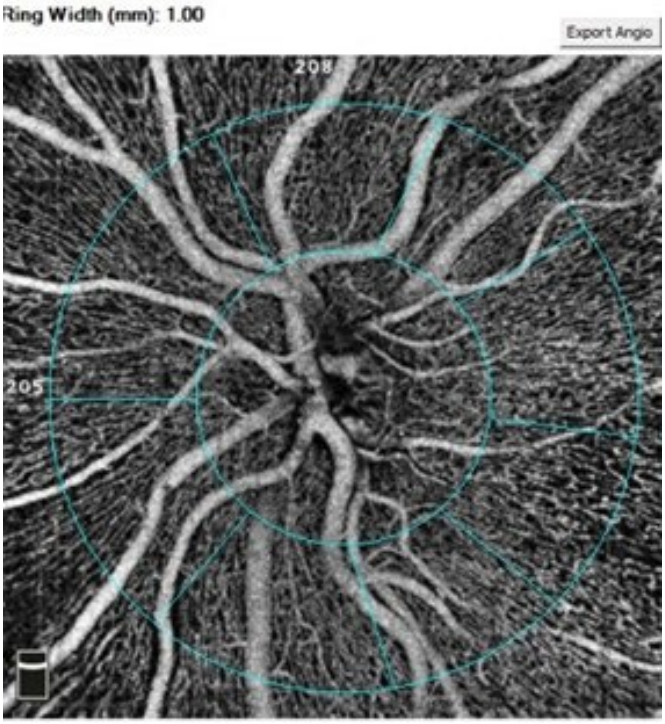

Figure 1. *For disc analysis, the area between two circles with diameters of 2 mm and 4 mm from the center is divided into eight quadrants by the device.*

The evaluation of macular vascular density is performed using a 6x6 mm scan, with the device software automatically determining the vascular density values for the superficial capillary plexus (SCP) and deep capillary plexus (DCP). For SCP assessment, the upper boundary is set at the inner limiting membrane (ILM), while the lower boundary is defined as 9 µm below the inner plexiform layer. In the case of DCP assessment, the upper boundary is set at 9 µm below the inner plexiform layer, and the lower boundary is defined as 9 µm above the inner plexiform layer. Quadrants are automatically generated based on the Early Treatment Diabetic Retinopathy Study (ETDRS) 9-zone map centered on the fovea (Figure 2). In this study, vascular density and retinal thickness values for the entire area, fovea, parafovea, and perifovea were obtained for the macula. The foveal avascular zone (FAZ) area was automatically determined by the device software, and relevant parameters were calculated. To standardize the measurements, all OCTA scans were performed between 9:00 AM and 12:00 PM by an experienced technician who was unaware of the group assignments.

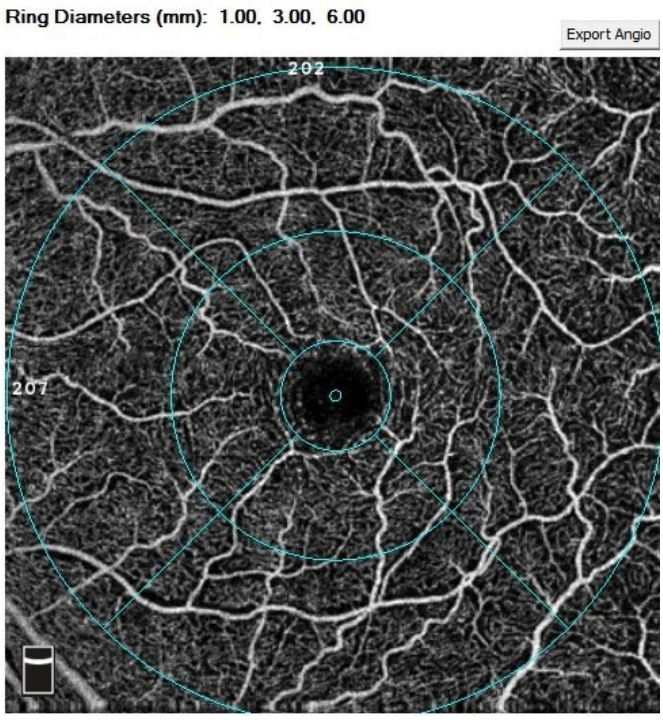

Figure 2. *Retinal angiography showing the quadrant map of the Early Treatment Diabetic Retinopathy Study (ETDRS)*

Statistical Analysis

SPSS Software (IBM SPSS for Windows Version 22.0; SPSS Inc., Chicago, IL, USA) was used to analyze the data obtained from the study and generate tables. The normality of the data was assessed using the Kolmogorov-Smirnov test. For normally distributed data, comparisons among the four groups were conducted using ANOVA, with the Bonferroni correction applied for pairwise comparisons between groups. For data showing a non-parametric distribution, comparisons were performed using the Kruskal-Wallis test, and pairwise comparisons between groups were conducted with the Mann-Whitney U test. The data were presented as mean ± standard deviation (SD). P-values less than 0.05 were considered statistically significant.

RESULTS

Demographics

There were no intergroup differences in age (p=0.658). The average duration of medication use was similar across groups (p=0.603), with 22.4±6.4 months for latanoprost 0.005%, 23.7±8 months for travoprost 0.004%, and 21.9±7.1 months for bimatoprost 0.01%. No significant difference was observed between the three groups in terms of IOPs before starting PGAs, IOPs after using PGAs, and IOP changes (p=0.492, p=0.490, and p=0.209, respectively). MD values were significantly better in the control group (p<0.001), though other clinical data showed no significant differences. Demographic and ocular characteristics for each group are summarized in Table 1.

Peripapillary VD

The radial peripapillary nerve fiber layer thickness (ppRT (µm)), whole image radial peripapillary capillary vessel density (wiVD (%)), and peripapillary vessel density (ppVD (%)) were significantly greater in the control group (p=0.005, p=0.006, and p=0.002, respectively). No differences were observed in intrapapillary vessel density values (iVD (%)) among the four groups (Table 2). In pairwise comparisons, while the bimatoprost 0.01% group showed higher ppRT, wiVD, iVD, ppVD, shVD, and ihVD values compared to the groups receiving other PGAs, these differences were not statistically significant (p>0.05).

Table 1: *Demographic variables, systemic characteristics, and ocular characteristics*

Variables		Control	Latanoprost 0.005%	Travoprost 0.004%	Bimatoprost 0.01%	P value
Age		61.3±10.1	60±7.9	61.9±7.7	59.1±11	0.658
Gender	Female	18 (%51.4)	17 (%48.5)	19 (%63.3)	13 (%43.3)	0.457[&]
	Male	17 (%48.5)	18 (%51.4)	11 (%36.6)	17 (%56.6)	
SBP (mmHg)		138.2±8.9	139.2±9.3	137.9±9.5	140.6±8.3	0.644
DBP (mmHg)		71.4±5.9	71.7±7.2	73.4±6.9	71.8±6.6	0.677
BCVA (Logmar)		0.056±0.05	0.073±0.06	0.076±0.08	0.098±0.7	0.124
CCT (µm)		555.37±38.2	545.77±30.8	544.2±28.1	551.2±36.3	0.482
Pre-treatment IOP (mmHg)		-	25.3 ± 3.3	25.7 ± 2.8	26.3 ± 3.7	0.492
Post-treatment IOP (mmHg)		18.1±2.8	16.5±2.5	17.2±2.3	16.5±3.4	0.070
IOP changing (mmHg)			8.5 ± 2.9 (34.3%)	8.6 ± 2.9 (32.8%)	9.8 ± 2.8 (37.3%)	0.209
MD (dB)		-1.3±0.7[a]	-2.8+1.6[b]	-3.1±1.4[b]	-2.9±1.5[b]	**<0.001**
Follow-up period (month)		-	22.4±6.4	23.7±8	21.9±7.1	0.603

BCVA: Best Corrected Visual Acuity; CCT: Central Corneal Thickness; DBP: Diastolic Blood Pressure; IOP: Intraocular Pressure; MD: Mean Deviation; SBP: Systolic Blood Pressure.
Different lowercase letters indicate statistically different groups.
&: p-value calculated with the chi-square test.

Table 2: *Comparison of radial peripapillary nerve fiber layer thickness and radial peripapillary capillary vessel densities*

	control	latanoprost 0.005%	travoprost 0.004%	bimatoprost 0.01%	P value
ppRT (µm)	110.17±11.1[a]	100.8±10.4[b]	102.7±12.3[b]	102.9±11.4[b]	**0.005**
wiVD (%)	50.3±2.3[a]	48.1±2.8[b]	47.8±4.1[b]	48.1±3.7[b]	**0.006**
iVD (%)	47.8±3.8	47.8±6.7	46.6±4.9	49.3±4.9	0.252
ppVD (%)	53.6±2.6[a]	51.1±3.7[b]	50.7±4.3[b]	51.3±2.9[b]	**0.002**
shVD (%)	53.6±2.5[a]	51.7±3.3[b]	51.4±4.6[b]	51.3±3.6[b]	**0.037**[*]
ihVD (%)	53.5±3.0[a]	50.9±3.6[b]	50.8±5.0[b]	51.2±3.7[b]	**0.010**

iVD: intrapapillary vessel density; ppRT: peripapillary retinal nerve fiber layer thickness; ppVD: peripapillary vessel density; wiVD: whole image vessel density; shVD: superior hemi vessel density; ihVD: inferior hemi vessel density.
Different lowercase letters indicate statistically different groups.
*: Kruskal-Wallis test for nonparametrically distributed data.

Macular VD

Both macula SCP and DCP vascular densities in the foveal zone (fVD (%)) were significantly higher in the bimatoprost 0.01% group (p=0.001 and p=0.010, respectively) (Figure 3). An assessment of retinal thickness in the macula indicated that foveal retinal thickness (fRT (µm)) was significantly greater in the bimatoprost 0.01% group compared to the latanoprost 0.005%, travoprost 0.004%, and control groups (p=0.005). Whole image retinal thickness (wiRT (µm)) and perifoveal retinal thickness (pefRT (µm)) were notably lower in the bimatoprost 0.01% group compared to both the latanoprost 0.005% and travoprost 0.004%, and control groups (p=0.016 and p=0.009, respectively). Parafoveolar retinal thickness (pafRT (µm)) measurements showed no difference between the groups (p=0.312) (Table 3). No significant difference was noted in foveal avascular zone parameters (p>0.05). No significant correlation was observed between mean deviation, visual acuity, IOP value, IOP change and fVD values of SCP and DCP.

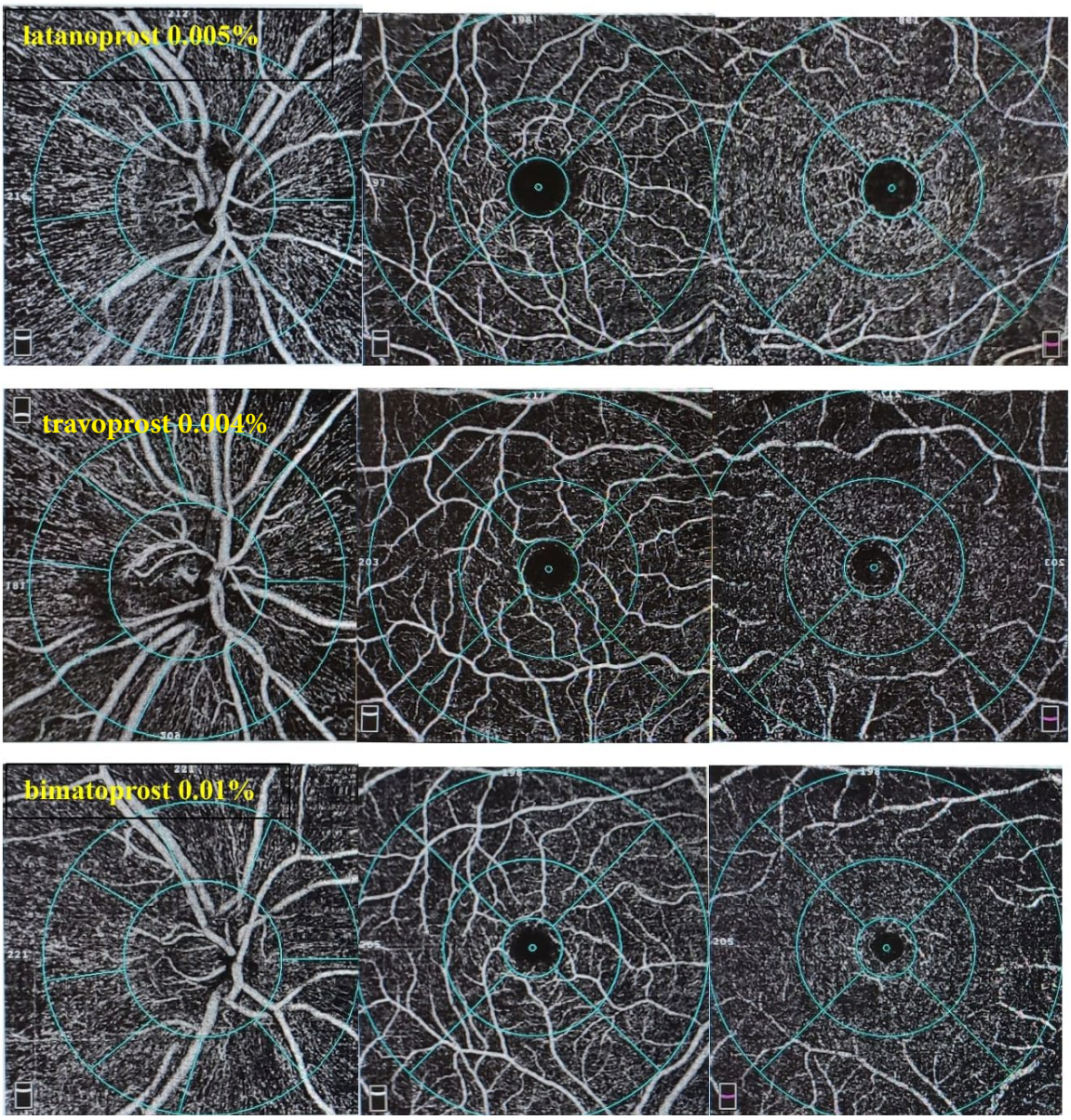

Figure 3. *Optical coherence tomography angiography images of patients treated with latanoprost 0.005%, travoprost 0.004%, and bimatoprost 0.01%, showing the radial peripapillary capillary plexus, superficial retinal capillary plexus, and deep retinal capillary plexus, respectively.*

Table 3: *Comparison of superficial capillary plexus and deep capillary plexus vessel densities, as well as retinal thickness in the macula*

	Control	latanoprost 0.005%	travoprost 0.004%	bimatoprost 0.01%	P value
Superficial capillary plexus					
wiVD (%)	49.5±3.0	48.0±4.0	48.4±4.6	49.4±3.7	0.319
fVD (%)	18.3±6.0[a]	18.2±6.5[a]	17.7±6.8[a]	23.3±4.4[b]	**0.001**
pafVD (%)	51.8±4.2	50.4±4.8	51.0±4.5	51.6±4.8	0.582
pefVD (%)	50.3±3.2	48.4±4.0	49.0±4.9	50.2±3.8	0.141
Deep capillary plexus					
wiVD (%)	49.6±5.2	49.2±6.6	48.5±6.6	49.4±7.0	0.909
fVD (%)	36.2±5.8[a]	35.9±7.8[a]	34.6±6.4[a]	40.4±7.4[b]	**0.010**
pafVD (%)	54.6±4.1	53.9±4.5	53.4±5.6	53.9±4.7	0.790
pefVD (%)	51.1±5.7	50.2±7.3	49.4±7.4	50.8±8.0	0.924
Retinal thickness					
wiRT (µm)	281.2±10.4[a]	280±13.1[a]	279.6±11.1[a]	273.1±7.3[b]	**0.016**
fRT (µm)	243.1±14.2[a]	245.2±21.8[a]	246.6±22.8[a]	258.5±14.7[b]	**0.005**
pafRT (µm)	320.2±12.3	321.1±15.9	317.7±17.4	314.7±13.7	0.312
pefRT (µm)	279.6±11.1[a]	277.6±14.1[a]	277.7±11.4[a]	270.4±6.5[b]	**0.009**

fRT: foveal retinal thickness; fVD: foveal vessel density; pafRT: parafoveolar retinal thickness; pafVD: parafoveolar vessel density; pefRT: perifoveolar retinal thickness; pefVD: perifoveolar vessel density; wiRT: whole image retinal thickness; wiVD: whole image vessel density.
Different lowercase letters indicate statistically different groups.

DISCUSSION

Glaucoma is the leading cause of irreversible blindness worldwide.[1-4] Because the disease can be asymptomatic until later stages, early diagnosis and appropriate treatment are critically important.[3,5,7] Therefore, the primary goal of glaucoma management is to lower IOP, aiming to reach the target IOP with the fewest medications necessary while minimizing adverse effects.[4,5,7] Evidence from several multicenter clinical trials has shown that lowering IOP helps prevent the onset of glaucoma, slows its progression, reduces the rate of visual field loss, and potentially protects against further vision impairment and blindness.[28-30] However, glaucomatous optic nerve damage cannot be solely attributed to elevated IOP and its mechanical effects. The significance of OBF in the pathogenesis of glaucoma has been well-established over the years.[10] Consequently, investigating how changes in IOP affect microcirculation in the macula and peripapillary regions has grown in importance for understanding the development and progression of glaucoma. Numerous studies using OCTA have reported reduced microvascular structures in the peripapillary and macular areas of patients with glaucoma and ocular hypertension, even in the early stages, compared to healthy individuals.[11-16]

After establishing the detrimental effects of glaucoma on OBF and the peripapillary and macular microvascular networks, it became increasingly important to explore whether antiglaucoma drugs could have positive effects on OBF while also reducing IOP. Since OBF is regulated by autoregulation, investigating how these drugs impact ocular microvasculature is likely to provide more valuable insights. Several studies have demonstrated that PGAs enhance OBF in eyes with glaucoma.[17-19] Geyer et al.[17] observed a 20% increase in pulsatile OBF after topical latanoprost treatment compared to the control group. In a study by Koz et al.,[18] which examined the effects of PGAs on ocular circulation using color Doppler ultrasonography, it was shown that PGAs significantly increased OPP in patients with POAG or ocular hypertension. Similarly, Boltz et al.[19]

found that latanoprost improved OBF regulation during both increased and decreased OPP, concluding that this enhancement might be attributed to the drug's intraocular pressure-lowering effect. Duru et al.[20] reported that ocular perfusion pressure and subfoveal choroidal thickness increased after three months of topical latanoprost therapy. However, they associated this occurrence not with an increase in OBF but rather with the pathogenesis of central serous chorioretinopathy in patients undergoing latanoprost treatment.

As an advanced, non-invasive, and reliable imaging technique, OCTA shows promise as a valuable structural tool for the early detection and monitoring of glaucoma by enabling the visualization of the ONH and macular microvascular structures.[11-16] However, research on the effects of medical anti-glaucomatous therapy on retinal microcirculation using OCTA remains limited, with most studies featuring short follow-up durations and small sample sizes.[21-27] Chen et al.[21] observed that latanoprost treatment significantly reduced IOP by 26.3% and led to an increase in RPC VD following IOP reduction in patients with OHT, while macular microcirculation remained unaffected. In a study comparing the effects of topical tafluprost use and surgical treatment on vascular parameters, Weindler et al.[22] noted that tafluprost not only lowers IOP but may also enhance retinal blood flow even at normal IOP levels. In one notable study, Liu et al.[23] investigated the impact of latanoprost in treatment-naïve patients and found a 26.1% reduction in mean IOP, which was significantly correlated with the increase in RPC VD during a 3-week follow-up. They suggested that their findings might indicate a mechanism by which IOP reduction modulates the risk of glaucoma progression by improving ocular microperfusion. Similarly, we recently reported that topical latanoprost 0.005% treatment significantly increases RPC and macular VD values in the SCP during the first month after treatment, likely due to acute IOP reduction.[24] However, by the third month, these values stabilize, possibly due to compensatory adaptation in the ONH and retinal microvasculature.

There are also studies in the literature comparing the effects of different anti-glaucomatous agents on the microvascular network. El-Nimri et al.[25] suggested that treatment with latanoprostene bunod 0.024% enhances macular VD in patients with POAG or OHT, but not in normal subjects. However, they reported that timolol maleate ophthalmic solution 0.5% was not associated with changes in VD. Chihara et al.[26] compared the effects of ripasudil, a topical Rho-associated protein kinase inhibitor, and brimonidine, an alpha-2 agonist, on RPC VD. Their findings revealed that ripasudil increased VD in patients with POAG and OHT, whereas brimonidine had no significant effect on VD. Similarly, another recent study examined the impact of brimonidine, dorzolamide, and carteolol on VD in patients with normal-tension glaucoma.[27] This study reported no changes in microcirculation with brimonidine. However, dorzolamide and carteolol produced contrasting outcomes: dorzolamide improved VD, while carteolol reduced VD in the aforementioned study.

As a result, all of the aforementioned studies highlight the growing interest in exploring the potential positive effects of antiglaucoma agents on ocular microvascular structures. However, there is no OCTA study comparing the effects of different PGAs on the ONH and retinal microvascular network. The present study aimed to compare the measurements of latanoprost 0.005%, travoprost 0.004%, and bimatoprost 0.01% on ONH and macular vessel densities in patients diagnosed with early-stage POAG. In this study, ppRT, wiVD, and ppVD in the peripapillary region were significantly lower in the three PGA groups compared to the control group. These vascular changes in the peripapillary region indicate that OBF in glaucoma does not reach the same level as in healthy individuals, despite the use of anti-glaucoma medications.

Among the PGAs, bimatoprost 0.01% showed higher ppRT, wiVD, iVD, and ppVD values compared to the other PGAs in pairwise comparisons; however, these differences were not statistically significant. On the other hand, fRT was found to be thickest in the bimatoprost group, and both SCP and DCP fVD values were significantly higher in this group compared to the other PGAs. The wiRT and pefRT values in the macular region were significantly thinner in the bimatoprost group. pafRT were also thinner but not significantly in the bimatoprost group. In contrast to these findings, wiVD, pafVD, and pefVD in both SCP and DCP were higher, although these differences were not statistically significant. Yeom et al.[31] also did not report significant differences in macular thickness after a 3-month follow-up in patients using bimatoprost 0.01%. However, their study

did not mention changes in ONH and macular microvascular parameters.

The observed increase in vascular density in the bimatoprost group in the present study may suggest that bimatoprost enhances microvascularity. However, this hypothesis remains speculative, and prospective studies comparing OCTA parameters of all three PGAs before and after treatment are needed to clarify this further. Meta-analyses, as in the present study, have shown that bimatoprost reduces IOP more effectively than latanoprost and travoprost, although the difference was not statistically significant. [6 7] In addition to the direct effects of bimatoprost, the reduction in IOP itself may influence optic disc or retinal perfusion. Nevertheless, the results of the present study support the need for further research with longer follow-up periods to better elucidate the potential effects of bimatoprost on ocular perfusion in eyes with glaucoma.

There are several limitations to the current study that require attention. First, the sample size was relatively small across all groups, which may limit the ability to detect significant differences. Second, the cross-sectional design of this study restricts its capacity to fully assess the effects of PGA treatment on the remodeling of the microvascular structure, as the initial pretreatment vascular parameters were not available. Longer longitudinal studies with larger cohorts are necessary to gain a better understanding of these effects. Another limitation is that this study only evaluated early-stage glaucoma, where microvascular changes may not be apparent yet, or vascular autoregulation may compensate for these changes. Further analysis is needed to investigate the effects of PGA treatments on the peripapillary and macular microcirculation in glaucoma patients at various stages. A further limitation of our study is the lack of axial length assessment. Although patients with high myopia and hyperopia were excluded based on predefined refractive thresholds, the absence of axial length measurements remains a noteworthy limitation. Lastly, since vessel density measured by OCTA does not directly reflect retinal perfusion velocity, future studies should explore potential changes in perfusion velocity in both large vessels and the microcirculation of the peripapillary region.

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