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The effects of beta-blockers on ocular blood flow in patients with primary open angle glaucoma: a color doppler imaging study

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PURPOSE. *To evaluate the effects of four commonly used beta-blockers on ocular blood flow in patients with primary open angle glaucoma (POAG).*
METHODS. *Eighty eyes of 40 subjects with POAG were included in the study. Subjects were randomly divided into four groups given timolol maleate 0.50%, betaxolol HCl 0.50%, carteolol 1% or levobunolol 0.50% drops, applied twice daily (one drug to each group). Before beginning the treatment and at the end of the first month ocular blood flow velocity was measured using the color Doppler imaging (CDI) method. In the ophthalmic artery (OA), central retinal artery (CRA) and temporal posterior ciliary artery (TPCA) the peak systolic (PS) and end-diastolic (ED) blood flow velocities were measured and resistive index (RI) values were calculated. The results within each group were analysed using the matched paired student's t-test. The data between groups was compared with one-way analysis of variance (ANOVA) and Tukey-Kramer multiple comparison tests.*
RESULTS. *The timolol group showed a significant increase in RI values of TPCA. In the betaxolol group RI decreased significantly in CRA and TPCA, whereas in the carteolol group there was a significant decrease only in CRA. In the levobunolol group there was no change in any artery.*
CONCLUSIONS. *Betaxolol seemed to have a greater vasodilator effect than carteolol, and levobunolol had no effect on the retinal and choroidal vasculature. Timolol may have some vasoconstrictive effect in the ciliary vasculature. (Eur J Ophthalmol 2001; 11: 37-46)*

KEY WORDS. *Primary open angle glaucoma, Ocular blood flow, Color doppler imaging, Beta-blockers*

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INTRODUCTION

Primary open angle glaucoma (POAG) is accepted today as the most important cause of irreversible blindness in developed countries. It is defined as a progressive multifactorial optical neuropathy, which causes structural damage to the optic nerve, and characteristic visual field defects (1). Despite many studies the pathogenesis of POAG has remained obscure. There are several risk factors for glaucoma: high intraocular pressure (IOP) age, race, family history, myopia (2), systemic hypertension, diabetes, migraine and vasospastic syndromes (3, 4). High IOP and vascular insufficiency are involved in the etiology of glaucoma (5, 6). Formerly the aim of therapy in glaucoma was to lower the IOP, but now it is recognised that lowering IOP alone cannot prevent the progression of nerve fiber loss.

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Hemodynamic changes in the retrobulbar vasculature can be observed before the glaucomatous changes develop (7). Color Doppler imaging (CDI) is one of the most commonly used techniques to assess ocular blood flow. CDI uses an ultrasound device that combines traditional B-scan gray-scale imaging with a color-coded image of flow (8). The blood velocity is calculated from the Doppler frequency shifts, which are displayed as the spectral waveform and are angle-dependent. The resistive index (RI) is a ratio and is angle-independent (9).

In the treatment of POAG the clinical aims are to lower IOP, increase ocular blood flow and protect ganglion cells and nerve fibers, so as to preserve visual field and function (4). Topical beta-blockers are the most widely used ocular hypotensive agents and their effects on ocular blood flow are under investigation. Timolol maleate 0.50%, betaxolol HCl 0.50%, carteolol 1% and levobunolol 0.50% are the most widely used beta-blockers. We planned this study to investigate and compare the effects of these beta-blockers on ocular blood flow.

METHODS

Subjects were enrolled in the study after giving a full history. No patient had a history of a systemic illness which might limit the use of any beta-blocker. Patients with systemic hypertension were controlled with diuretics only and on carotid Doppler ultrasonography no patient had more than 50% constriction. Subjects with a cup/disc ratio of 0.4-0.5 and glaucomatous defects on visual field examination were selected for the study.

Eighty eyes of 40 subjects who were diagnosed as having POAG at our clinic and had no history of medical or surgical treatment for glaucoma were included in the study. Informed consent was obtained from them all. Before beginning treatment IOPs were measured daily for one week. Every subject had a mean IOP of more than 22 mmHg. Ocular blood flow velocity was measured using the CDI method. The subjects were randomized into four groups of 10 (20 eyes per group). The first group was given timolol maleate 0.50%, the second betaxolol 0.50%, the third carteolol 1% and the fourth levobunolol 0.50% topical ocular drops twice daily. At the end of the first month ocular blood flow measurements were repeated.

Blood flow velocity was evaluated using a 7.5 MHz linear transducer probe and ATL-Ultramark 9 device (Advanced Technology Laboratories) at the Radiodiagnostic Department of our faculty. All measurements were made by the same physician (S.A.) who was unaware of the clinical diagnosis and the treatment modalities of the patients.

During the procedure patients rested for 5 minutes in the supine position and were asked to close their eyes. Methylcellulose gel was applied onto the eyelid, and patients were asked not to open their eyes and to look forward, without moving, during the procedure. Care was given not to put pressure on the eye during the measurement. For optimal visualization of the orbital vasculature the procedure began on a transverse plane. Then for spectral analysis the probe was angled to the longest axis of the artery. To observe the ophthalmic artery (OA) the pattern interval was directed to the nasal side of the optic nerve where it crosses the artery. For central retina artery (CRA) the optic nerve was found with the B-mode and the optic disc located. Then we moved to the Doppler-mode and the retinal artery and vein, and optic nerve were visualized. On the left and right sides of the optic nerve the nasal and temporal short posterior ciliary arteries (PCA) were visualized. Since it is reported that 60% of the watershed zones are on the temporal side we mesured only the temporal PCA (TPCA). The spectral waveform of each artery was evaluated three times. The strongest detecable signal as three consecutive identical waveforms was accepted as the ideal signal and chosen as the spectral example.

The peak systolic (PS) and end-diastolic (ED) blood flow velocities were measured in each artery. The RI was calculated automatically using the Pourcelot formula: (PS-ED)/PS.

The results were analysed using the Graphped INSTAT V2.O2 software. The before and after treatment CDI values within each group were compared individually with the matched paired Student's t-test. To identify differences between groups in the CDI measurements one month after beginning the treatment one-way analysis of variance (ANOVA)

was done. If the difference between groups was significant then the Tukey-Kramer multiple comparison test was used to establish significant differences.

RESULTS

The patients' sex and age are shown in Table I. There were no differences between groups ($p>0.05$). In each group the IOP values were less than 21 mmHg at the end of the first month. The blood flow velocity waveforms in OA and TPCA were similar to small resistant arteries as regards the fast systolic velocity rise and high diastolic flow. In CRA the waveform showed a slow ascending systolic velocity followed by a systolic peak without a dicrotic notch.

The pre-treatment and first month after treatment CDI values in each group were compared with the matched paired Student's t-test. The measurements for the timolol maleate 0.50% group are shown in Table II. The differences in blood flow velocities in OA were insignificant. In CRA there was a significant increase in PS blood flow velocity but the increase in ED blood flow velocity and the difference in RI were insignificant. In TPCA although the rise in PS blood flow velocity was insignificant, the decrease in ED blood flow velocity and increase in RI values were highly significant (Tab. II).

In the betaxolol 0.50% group the differences in OA measurements were insignificant (Tab. III). Although the decrease in PS blood flow velocity in CRA was insignificant the increase in ED blood flow velocity and decrease in RI values were significant. In TPCA the increase in PS and ED blood flow velocities and the decrease in RI were significant as well (Tab. II).

In the carteolol 1% group there was a significant increase in OA, PS and ED blood flow velocieites but the decrease in RI was insignificant (Tab. III). In CRA the increase in PS and ED blood flow velocities and the decrease in RI values were also significant. The differences in TPCA were insignificant (Tab. III).

In the levobunolol 0.50% group the differences in PS and ED blood flow velocities and RI in OA and TPCA were statistically insignificant. In CRA the decrease in PS blood flow velocity was significant but the decreases in ED flow velocity and RI were insignificant (Tab. III).

The measurements one month after beginning treatment were compared by one-way analysis of variance (ANOVA). If the groups were significantly different, indicative groups were designated using the Tukey-Kramer multiple comparison test. The measurements in OA are shown in Table IV. The differences in PS blood flow velocities in the four groups were significantly greater than expected ($F= 3.697$, $p=0.0153$). This was because of the difference between the betaxolol and carteolol groups ($p<0.05$). Differences between ED blood flow velocities were insignificant ($F= 0.8737$, $p= 0.4586$). For RI in OA the variance was significant between groups ($F= 5.237$, $p= 0.0024$) because of the difference between the timolol and carteolol, and the betaxolol and carteolol groups (Tab. IV).

In CRA the PS blood flow velocities were significantly different between groups ($F= 7.823$, $p= 0.0001$) (Tab. V). The significance was due to the differences between the betaxolol and carteolol groups, and the carteolol and levobunolol groups. The ED blood flow velocities were significantly different as well ($F= 5.093$, $p = 0.0029$). The carteolol group

TABLE I - MAIN CHARACTERISTICS OF POAG PATIENTS

	Female	Male	Total	Mean age (±SD)
Timolol maleate 0.50%	6	4	10	56.9 ± 5.43
Betaxolol 0.50%	6	4	10	58.9 ± 5.28
Carteolol 1%	5	5	10	56.8 ± 10.05
Levobunolol 0.50%	7	3	10	55.6 ± 10.3

was significantly different from the timolol and levobunolol groups. The RI in CRA were significantly different between groups (F= 11.598, p= 0.0001), an account of the difference between the timolol and the other three groups.

The results in TPCA are shown in Table VI. The PS blood flow velocities in TPCA at the end of first month showed significant difference between groups (F= 5.571, p= 0.0016), mainly because the carteolol group was different from the other groups. The ED blood flow velocities were significantly different too (F= 5.350, p= 0.0021), because of the difference between the timolol and carteolol groups. In TPCA the RI were significantly different as well (F= 4.848, p= 0.0039), because of the difference between the timolol and betaxolol grups (Tab. VI).

DISCUSSION

Studies on POAG were used to focus only on the IOP, but today it is accepted that the pathogenesis of glaucoma cannot be explained only by the mecahnical theory (10, 11). It is thought that ischemia of the optic nerve head autoregulation defects in retrobulbar blood flow and nocturnal hypotension are more important than the mechanical compression of nerve fibers in the pathogenesis of glaucomatous optic nerve head changes

TABLE II - MEAN BLOOD FLOW VELOCITY (cm/sec) MEASUREMENTS AND RESISTIVE INDEXES IN PATIENTS GIVEN TIMOLOL MALEATE 0.50% AND BETAXOLOL 0.50%

	Ophthalmic artery (OA)		Central retinal artery (CRA)		Temporal posterior short ciliary artery (TPCA)	
	BT	**AT**	**BT**	**AT**	**BT**	**AT**
Timolol maleate 0.50%						
PS	44.31 ± 2.60 t= 0.937	43.59 ± 1.62 p= 0.360	12.75 ± 0.69 t= 3.692	13.58 ± 0.81 p= 0.002**	13.68 ± 1.17 t= 0.425	13.81 ± 0.89 p= 0.675
ED	12.20 ± 1.45 t= 1.606	11.49 ± 1.05 p= 0.125	3.21 ± 0.33 t= 1.222	3.41 ± 0.60 p= 0.237	5.03 ± 0.56 t= 6.896	4.03 ± 0.68 p<0.0001***
RI	0.72 ± 0.02 t= 1.838	0.73 ± 0.02 p= 0.082	0.74 ± 0.02 t= 0.060	0.74 ± 0.03 p= 0.953	0.63 ± 0.03 t=7.071	0.70 ± 0.04 p<0.0001***
Betaxolol HCl 0.50%						
PS	44.62 ± 1.72 t= 1.085	45.05 ± 1.61 p= 0.291	12.26 ± 0.56 t= 2.013	11.87 ± 0.89 p= 0.059	13.37 ± 1.25 t= 2.870	14.64 ± 1.11 p=0.0098**
ED	12.04 ± 1.19 t= 0.882	12.29 ± 1.01 p= 0.389	3.60 ± 0.48 t= 2.982	4.04 ± 0.47 p= 0.008**	4.20 ± 0.57 t= 5.133	5.35 ± 0.59 p<0.0001***
RI	0.73 ± 0.02 t= 1.371	0.72 ± 0.02 p= 0.186	0.70 ± 0.03 t= 4.695	0.65 ± 0.03 p=0.0002***	0.68 ± 0.03 t= 5.300	0.63 ± 0.03 p<0.0001***

Differences before and after treatment are shown as "t"; "p" is the probability (p>0.05 insignificant, p<0.05* significant, p<0.01** moderately significant, p<0.001*** very significant)
(BT: Before treatment, AT: After treatment, PS: Peak systolic blood flow velocity, ED: End-diastolic blood flow velocity, RI: Resistive index)

(7). The latest studies have focused on the vasogenic mechanisms and neuroprotection (3). Hayreh was the first to show choroidal and papillary filling defects in patients with POAG and suggested that these changes were responsible for the glaucomatous visual field defects (12). A study comparing glaucomatous and normal subjects reported that the blood flow and flow velocities were significantly diminished in the lamina cribrosa and superior temporal nerve fiber layer.

CDI is a quantitative and qualitative method for detecting ocular blood flow with an ultrasonic probe, which was introduced into ophthalmologic practice in 1989 (13). It is an easy, valuable, non-invasive and reproducible method (9). CDI was first used to evaluate the vascular anatomy of the eye and orbit (13). Later it was found useful in detecting blood flow velocities and resistance to blood flow in patients with POAG (14). Since CDI measurements may differ with the patient's position or among physicians, several indices have been developed which are independent of any factor (13). One of these indices is the RI, which does not change with the position of the probe in small arteries like ciliary arteries (15). Flow velocities in ocular arteries decline while RI increases with age in normal subjects (16). Glaucomatous eyes with uncontrolled IOP have a significant decrease in ED flow velocities and an increase in the RI in ciliary arteries (16). Several studies reported that in glaucoma pa-

TABLE III - MEAN BLOOD FLOW VELOCITY (cm/sec) MEASUREMENTS AND RESISTIVE INDEXES IN PATIENTS GIVEN CARTEOLOL 1% OR LEVOBUNOLOL 0.50%

	Ophthalmic artery (OA)		Central retinal artery (CRA)		Temporal posterior short ciliary artery (TPCA)	
	BT	**AT**	**BT**	**AT**	**BT**	**AT**
Carteolol 1 %						
PS	31.98 ± 13.46 t= 3.159	39.84 ± 9.52 p= 0.005**	12.12 ± 3.59 t= 2.114	15.29 ± 5.46 p= 0.048*	18.12 ± 5.61 t= 0.392	17.35 ± 4.70 p= 0.699
ED	9.43 ± 4.92 t= 2.941	12.96 ± 4.69 p= 0.008**	3.04 ± 1.32 t= 3.024	4.87 ± 2.19 p= 0.007**	5.70 ± 2.18 t= 0.435	6.03 ± 2.59 p= 0.669
RI	0.71 ± 0.08 t= 1.836	0.68 ± 0.07 p= 0.082	0.75 ± 0.06 t= 2.536	0.70 ± 0.06 p= 0.020*	0.70 ± 0.08 t= 1.281	0.67 ± 0.08 p= 0.216
Levobunolol 0.50%						
PS	39.49 ± 4.61 t= 1.990	41.73 ± 3.89 p= 0.061	12.73 ± 2.19 t= 2.454	11.29 ± 1.46 p= 0.024*	14.83 ± 3.49 t= 0.418	14.48 ± 3.31 p= 0.681
ED	12.87 ± 2.74 t= 0.313	12.62 ± 3.48 p= 0.758	3.92 ± 0.96 t= 0.761	3.68 ± 0.97 p= 0.456	5.15 ± 1.55 t= 0.854	4.71 ± 1.86 p= 0.404
RI	0.67 ± 0.04 t= 1.595	0.70 ± 0.07 p= 0.127	0.69 ± 0.07 t= 0.666	0.67 ± 0.07 p= 0.514	0.65 ± 0.07 t= 0.983	0.67 ± 0.07 p= 0.338

The differences before and after treatment are shown as "t"; "p" is the probability (p>0.05 insignificant, p<0.05* significant, p<0.01** moderately significant, p<0.001*** very significant)
(BT: Before treatment, AT: After treatment, PS: Peak systolic blood flow velocity, ED: End-diastolic blood flow velocity, RI: Resistive index)

tients the PS and/or ED blood flow velocities were lower and RI higher than in normal subjects (9, 15, 17).

In the treatment of glaucoma the ideal drug should lower the IOP, increase the blood flow to the optic nerve head and prevent retinal nerve fiber loss (4). Nowadays beta-blockers are the drugs of first choice in POAG. They lower the IOP by inhibiting the β-receptors on the ciliary body epithelium, thus reducing aqueous humor production (18). However, these drugs may reach the choroidal vasculature and cause vasoconstriction.

Studies of the effects of different beta-blockers have worked mostly with timolol and betaxolol. To our knowledge there are few reports on levobunolol and carteolol. We designed our study to investigate the effects of four widely used beta-blockers on ocular blood flow, using the easy, non-invasive, reproducible CDI method to measure blood flow in POAG.

We found that timolol 0.50% did not change the flow parameters in OA. There was a significant rise in PS blood flow velocity in CRA with no difference in RI. However in TPCA there was a significant decrease in ED blood flow velocity and increase in RI. It thus seemded that timolol has a vasoconstrictive effect on the ciliary vasculature, with no effect on OA and CRA. Martin and Rabineau measured the retinal vessel diameters using photographic enlargements and suggested that timolol 0.50% may have a vasoconstrictive effect on the retinal circulation in normal subjects (19). Van Buskirk et al also reported that timolol had vasoconstrictive effects, which lasted even after seven weeks (20). These findings are comparable to our results. However, several studies report that timolol had no significant effect on ocular blood

TABLE IV - MEAN (±SD) BLOOD FLOW VELOCITY IN THE OPHTHALMIC ARTERY (OA) AT THE END OF THE FIRST MONTH IN THE FOUR TREATMENT GROUPS

	OA PS		OA ED		OA RI	
	Mean ± SD	**p**	**Mean ± SD**	**p**	**Mean ± SD**	**p**
Timolol	43.59 ± 1.62		11.49 ± 1.05		0.73 ± 0.02	
		p>0.05		p>0.05		p>0.05
Betaxolol	45.05 ± 1.61		12.29 ± 1.01		0.72 ± 0.02	
Timolol	43.59 ± 1.62		11.49 ± 1.05		0.73 ± 0.02	
		p>0.05		p>0.05		p<0.01 **
Carteolol	39.84 ± 9.52		12.96 ± 4.69		0.68 ± 0.07	
Timolol	43.59 ± 1.62		11.49 ± 1.05		0.73 ± 0.02	
		p>0.05		p>0.05		p>0.05
Levobunolol	41.73 ± 3.89		12.62 ± 3.48		0.70 ± 0.07	
Betaxolol	45.05 ± 1.61		12.29 ± 1.01		0.72 ± 0.02	
		p<0.05*		p>0.05		p<0.05*
Carteolol	39.84 ± 9.52		12.96 ± 4.69		0.68 ± 0.07	
Betaxolol	45.05 ± 1.61		12.29 ± 1.01		0.72 ± 0.02	
		p>0.05		p>0.05		p>0.05
Levobunolol	41.73 ± 3.89		12.62 ± 3.48		0.70 ± 0.07	
Carteolol	39.84 ± 9.52		12.96 ± 4.69		0.68 ± 0.07	
		p>0.05		p>0.05		p>0.05
Levobunolol	41.73 ± 3.89		12.62 ± 3.48		0.70 ± 0.07	

p is the probability (p>0.05 insignificant, p<0.05* significant, p<0.01** moderately significant, p<0.001*** very significant)
(PS: Peak systolic blood flow velocity, ED: End-diastolic blood flow velocity, RI: Resistive index)

flow and it seemed that the drug did not even reach the choroidal vasculature to produce measurable vasoconstriction (21-24).

Van Buskirk et al studied the retinal arterioles of rabbits and discovered that one drop of betaxolol caused vasoconstriction but tolerance developed to its effect in a few weeks (20). In a previous study Turaçli et al reported a decrease in RI in OA in patients with POAG (25). We found no significant effect of betaxolol on arteriolar hemodynamics in OA. In CRA there was a significant rise in ED blood flow velocity and a significant decrease in RI. There was a significant increase in PS and ED blood flow velocities and a decrease in RI in TPCA as well. We therefore conclude that betaxolol increases the blood flow to the capillary circulation of the eye. Several studies report the vasodilator effect of betaxolol which could be by reason of its calcium channel blocking effect or its increasing effect on perfusion pressure (24, 26, 27).

Studies using different methods have found carteolol can either cause vasodilatation in the retinal capillary vasculature (28, 29) or have no effect (30). However we were unable to find any study on the effects of carteolol using the CDI method. We observed no effect of carteolol on OA and TPCA, whereas the PS and ED blood flow velocities increased and RI decreased significantly in CRA. We concluded that carteolol causes some vasodilatation specifically in CRA.

Using the CDI method we found significant effect of levobunolol 0.50% in OA and TPCA blood flow velocities, and RI. In CRA, although there was a significant decrease in PS blood flow velocity the ED blood flow velocity and RI did not change. Since the RI indicates the resistance to blood flow

TABLE V - MEAN (±SD) BLOOD FLOW VELOCITY IN THE CENTRAL RETINAL ARTERY (CRA) AT THE END OF THE FIRST MONTH IN THE FOUR TREATMENT GROUPS

	CRA PS		CRA ED		CRA RI	
	Mean ± SD	**p**	**Mean ± SD**	**p**	**Mean ± SD**	**p**
Timolol	13.58 ± 0.81		3.41 ± 0.60		0.74 ± 0.03	
		p>0.05		p>0.05		p<0.001***
Betaxolol	11.87 ± 0.89		4.04 ± 0.47		0.65 ± 0.03	
Timolol	13.58 ± 0.81		3.41 ± 0.60		0.74 ± 0.03	
		p>0.05		p<0.01**		p<0.001***
Carteolol	15.29 ± 5.46		4.87 ± 2.19		0.70 ± 0.06	
Timolol	13.58 ± 0.81		3.41 ± 0.60		0.74 ± 0.03	
		p>0.05		p>0.05		p<0.05*
Levobunolol	11.29 ± 1.46		3.68 ± 0.97		0.67 ± 0.07	
Betaxolol	11.87 ± 0.89		4.04 ± 0.47		0.65 ± 0.03	
		p<0.01**		p>0.05		p>0.05
Carteolol	15.29 ± 5.46		4.87 ± 2.19		0.70 ± 0.06	
Betaxolol	11.87 ± 0.89		4.04 ± 0.47		0.65 ± 0.03	
		p>0.05		p>0.05		p>0.05
Levobunolol	11.29 ± 1.46		3.68 ± 0.97		0.67 ± 0.07	
Carteolol	15.29 ± 5.46		4.87 ± 2.19		0.70 ± 0.06	
		p<0.001**		p<0.05*		p>0.05
Levobunolol	11.29 ± 1.46		3.68 ± 0.97		0.67 ± 0.07	

p is the probability (p>0.05 insignificant, p<0.05* significant, p<0.01** moderately significant, p<0.001*** very significant)
(PS: Peak systolic blood flow velocity, ED: End- diastolic blood flow velocity, RI: Resistive index)

we conlcuded that levobunolol has no significant effect on ocular blood flow. We were able to find only a few studies concerning the effects of levobunolol on ocular hemodynamics. Bosem et al measured ocular pulsatile blood flow two hours after levobunolol and found that blood flow was significantly increased (31). In a subsequent study levobunolol seemed to increase the ocular blood flow after one week as well (32). The difference between our results and these studies could be due to differences in methods.

There are several studies comparing the effects of different beta-blockers on ocular blood flow. Harris et al compared betaxolol and timolol using CDI and found that timolol did not significantly alter ocular blood flow, whereas betaxolol tended to increase ED velocity and decrease RI (24). Using oculo-oscillo-dynamography Pillunat and Stodtmeister reported a slight decrease in ocular perfusion pressure in carteolol-treated subjects but no difference with timolol and betaxolol (33). In pigs, Hester et al reported the intrinsic relaxant sensitivity of betaxolol was equal to that of nitroprusside, six times that of carteolol and ten times that of timolol (34). Measuring the fundus pulsation amplitudes, Schmetterer et al reported timolol reduced choroidal and optic disc blood flow, whereas levobunolol and betaxolol had no such effect. However, in the same study, CDI showed no effect on ocular hemodynamics with any of the drugs (35). Morsman et al reported that betaxolol significanlty reduced ocular blood flow, whereas timolol caused only an insignificant decrease. In the same study levobunolol significantly increased ocular blood flow (32). Using the oculo-cerebral vasculometer, Bucci et al measured ocular pulse amplitudes with different

TABLE VI - MEAN (±SD) BLOOD FLOW VELOCITY IN THE TEMPORAL POSTERIOR SHORT CILIARY ARTERY (TPCA) AT THE END OF THE FIRST MONTH IN FOUR TREATMENT GROUPS

	TPCA PS		TPCA ED		TPCA RI	
	Mean ± SD	**p**	**Mean ± SD**	**p**	**Mean ± SD**	**p**
Timolol	13.81 ± 0.89		4.03 ± 0.68		0.70 ± 0.04	
		p>0.05		p>0.05		p<0.01**
Betaxolol	14.64 ± 1.11		5.35 ± 0.59		0.63 ± 0.03	
Timolol	13.81 ± 0.89		4.03 ± 0.68		0.70 ± 0.04	
		p<0.01**		p<0.05*		p>0.05
Carteolol	17.35 ± 4.70		6.03 ± 2.59		0.67 ± 0.08	
Timolol	13.81 ± 0.89		4.03 ± 0.68		0.70 ± 0.04	
		p>0.05		p>0.05		p>0.05
Levobunolol	14.48 ± 3.31		4.71 ± 1.86		0.67 ± 0.07	
Betaxolol	14.64 ± 1.11		5.35 ± 0.59		0.63 ± 0.03	
		p<0.05*		p>0.05		p>0.05
Carteolol	17.35 ± 4.70		6.03 ± 2.59		0.67 ± 0.08	
Betaxolol	14.64 ± 1.11		5.35 ± 0.59		0.63 ± 0.03	
		p>0.05		p>0.05		p>0.05
Levobunolol	14.48 ± 3.31		4.71 ± 1.86		0.67 ± 0.07	
Carteolol	17.35 ± 4.70		6.03 ± 2.59		0.67 ± 0.08	
		p<0.05*		p>0.05		p>0.05
Levobunolol	14.48 ± 3.31		4.71 ± 1.86		0.67 ± 0.07	

p is the probability (p>0.05 insignificant, p<0.05* significant, p<0.01** moderately significant, p<0.001*** very significant)
(PS: Peak systolic blood flow velocity, ED: End- diastolic blood flow velocity, RI: Resistive index)

beta-blockers; carteolol caused a significant decrease, timolol and betaxolol insignificant decreases, whereas levobunolol significantly raised ocular pulse amplitudes (36).

We compared the results with four beta-blockers and concluded that betaxolol seemed to have a better vasodilator effect than carteolol, while levobunolol had no noticeable effect on the retinal and choroidal vasculature. Timolol may have some vasoconstrictive effect on the ciliary vasculature.

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