Turkish Journal of Medical Sciences

Volume 44 | Number 3 Article 30

1-1-2014

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TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2014) 44: 524-529
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doi:10.3906/sag-1303-87

Pulsatile ocular blood flow changes after panretinal photocoagulation treatment in patients with proliferative diabetic retinopathy

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Received: 18.03.2013 • **Accepted:** 01.08.2013 • **Published Online:** 31.03.2014 • **Printed:** 30.04.2014

Background/aim: To prospectively assess the effects of panretinal photocoagulation (PRP) treatment on pulsatile ocular blood flow (POBF) in patients with proliferative diabetic retinopathy (PDRP).

Materials and methods: The study included 40 eyes with PDRP in 27 patients. The PRP treatments were completed in 3 sessions with 3-week intervals. The intraocular pressure (IOP), pulse amplitude (PA), pulse volume (PV), and POBF changes that arose during the sessions were recorded using a blood flow analyzer.

Results: The average age of the patients was 57.37 ± 11.14 years. The pre-PRP basal IOP, PA, PV, and POBF values were 20.44 ± 4.13 mmHg, 4.23 ± 1.73 mmHg, 6.89 ± 2.28 μL, and 21.86 ± 5.83 μL/s, respectively. One month after the completion of the PRP sessions, the values were 18.49 ± 4.44 mmHg, 2.78 ± 1.13 mmHg, 5.27 ± 2.08 μL, and 15.89 ± 5.05 μL/s, respectively, and the differences were significant ($P = 0.001$, $P < 0.0001$, $P < 0.0001$, and $P < 0.0001$, respectively).

Conclusion: PRP treatment reduces the choroidal blood flow and consequently causes significant decreases in IOP, PA, PV, and POBF.

Key words: Diabetic retinopathy, choroidal blood flow, intraocular pressure, laser coagulation, regional blood flow, retinal diseases

1. Introduction

Diabetes mellitus (DM), an important and common endocrine disorder, results in micro- and macrovascular complications in many organs in direct proportion to the duration and degree of hyperglycemia (1–3). Diabetic retinopathy (DRP), an important complication caused by the disease, is the main cause of acquired blindness (4,5). Panretinal laser photocoagulation (PRP) is still valid for the prevention of complications in DRP treatment (6).

Using the devices developed in recent years, many researchers have carried out studies related to ocular blood flow (7–11). Ocular blood flow is pulsatile and is affected by intraocular pressure (IOP) changes (12). The relationship between IOP changes during the cardiac cycle and ocular volume was reported for the first time in 1962 (13). In the ensuing years, an instrument was developed to measure ocular volume changes arising as a result of IOP (14). This instrument is a modified pneumotonometer for recording eye pulses. The rhythmic changes in IOP during the cardiac cycle are called pulse waves, and such waves are sent by the pneumotonometer to the instrument and converted into digital data therein. The currently used pulsatile ocular blood flow (POBF) analyzer (Paradigm Medical Industries, Inc., Salt Lake City, UT, USA) works with a similar principle (15).

It was reported that the impairment of ocular blood flow is a risk factor for the development of some ocular diseases such as glaucoma, age-related macular degeneration (ARMD), and cataracts (16–19). Therefore, measuring ocular blood flow and knowing the causes of ocular blood flow disturbances are very important issues. To date, many studies have been conducted on ocular blood flow in DM patients (7,20,21). In such a study, Savage et al. (7) reported lower POBF values in patients subjected to PRP treatment compared to patients who did not undergo PRP treatment. Their study included a comparison between PRP cases and non-PRP cases (7). However, POBF values can be affected by individual demographic factors such as age, sex, IOP, corneal thickness, refraction error, and systemic hypertension (22–27). Hence, this study was designed to evaluate the possible impact of PRP on POBF. Patients with high-risk proliferative DRP were prospectively evaluated for POBF before and after PRP sessions. Thus, the study design may provide advantages for better elucidating the effects of PRP on POBF within the same individual rather than a comparison of measurements obtained from different individuals.

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2. Materials and methods

This prospective study consisted of consecutive proliferative diabetic retinopathy (PDRP) patients and was carried out at the Department of Ophthalmology, School of Medicine, Karadeniz Technical University, Trabzon, Turkey. Consent of the medical ethics committee was obtained for the study protocol.

2.1. Inclusion and exclusion criteria for the study

The study included patients over 18 years old with DM (type I or type II) who were treated with oral hypoglycemics and/or insulin and were diagnosed with high-risk PDRP in the ophthalmic examination. Informed consent was provided by each patient included in the study. The exclusion criteria were as follows: patients with findings of uveitis, glaucoma, retinal vascular occlusion, vitreous hemorrhage, or exudative ARMD; patients treated with intravitreal injection or retinal laser photocoagulation; any prior intraocular surgery; media opacity inhibiting a retinal examination; patients with only 1 eye; any corneal pathology; or any other ocular problem, such as nystagmus, preventing POBF measurement.

A detailed medical history including the age of onset and duration of diabetes, existence of hypertension or any other systemic disease, and medications used was taken during the initial patient examination. All patients underwent a biomicroscopic ophthalmologic examination that included the anterior and posterior segments, and the pupils were dilated in both eyes. Normal and red-free fundus images (Canon 60UVi, Japan) were taken. The criteria for the Early Treatment Diabetic Retinopathy Study (ETDRS) (28) were taken into consideration for the diagnosis of diabetic retinopathy on the fundus images, and all ophthalmologic examinations were performed by the same researcher. The cases approved for PRP treatment as a result of the examinations were included in the study. The demographic and clinical findings of each case were recorded.

2.2. Ocular blood flow measurements

Ocular blood flow measurements were performed 4 times in total during the study. The first measurement was taken prior to the first PRP treatment (baseline, first visit), the second prior to the second PRP treatment (second visit), the third prior to the third PRP treatment (third visit), and the fourth 1 month after the completion of PRP (fourth visit). Systemic blood pressure was also recorded at each of the time points.

Because ocular blood flow is affected by body posture, the measurements were taken in a sitting position. Under local anesthesia, 1 drop of 0.5% proparacaine (Alcaine, Alcon Laboratories Inc., Fort Worth, TX, USA) was placed in the conjunctival sac of the eye to be measured, and POBF was measured after 5 min had elapsed. The same measurement device was used for all eyes (Paradigm DICON Blood Flow Analyzer, Paradigm Medical Industries Inc.). All measurements were performed by the same researcher using disposable probes in contact with the central cornea. Five consecutive ocular blood flow measurements of approximately 20 s each were recorded by the instrument, and detailed instrument printouts were taken. The mean intraocular pressure (IOP; mmHg), pulse amplitude (PA; mmHg), pulse volume (PV; μL) and pulsatile ocular blood flow (POBF; μL/s) values of each measurement were recorded.

2.3. Application of panretinal photocoagulation

The PRP application was completed in 3 sessions with 3-week intervals. The laser treatment was performed with a 532-nm wavelength argon laser device (Viridis, Quantel Medical, Clermont-Ferrand, France). During the laser treatment, 1500–2000 burns were applied in 3 sessions, so as not to exceed the temporal retinal vessel arcades surrounding the macula. The fovea was approached for a maximum of 2 disk diameters in the temporal region and the optic disk for a maximum of a half-disk diameter in the nasal region. The posterior pole retina surrounding the macula was laser etched in the first session, the midperipheral and inferior retina in the second session, and the remaining part of the retina in the third session. The spot diameter, duration, and power were adjusted to 200–500 μm, 0.10–0.15 s, and 250–500 mW, respectively, during the PRP applications. The laser was used to create an effective retinal burn. Care was taken not to burn the macular area within the major vessel arcades or the major vessels and papilla during the laser sessions.

The aforementioned measurements were repeated in all cases before each laser session and 1 month after the completion of the laser treatments.

2.4. Statistical analysis

The results were expressed as the mean ± standard deviation. Statistical analyses were performed using SPSS 13.0.1 (SPSS Inc., Chicago, IL, USA; License no: 9069728, KTÜ, Trabzon, Turkey). The data were evaluated for normality with the single-sample Kolmogorov–Smirnov test. A repeated measures of variance analysis (with least significant difference) was used to compare the subsequently measured systemic blood pressures with the IOP, PA, PV, and POBF values calculated using the POBF analyzer device. In the statistical analysis, $P < 0.05$ was considered significant.

3. Results

The study included 27 patients with DM, 15 females (55.6%) and 12 males (44.4%), with an average age of 57.37 ± 11.14 (26–75) years. The average DM duration of the patients was 14.33 ± 5.07 (2–25) years, and 23 (85.2%) patients were also diagnosed with hypertension. The

systolic and diastolic blood pressure values of all patients measured during the 4 visits are shown in the Table. The systolic and diastolic blood pressures did not significantly differ between visits.

The study included a total of 40 eyes from 27 patients with DM; 22 (55%) were right eyes and 18 (45%) were left eyes. The IOP values of the eyes measured with the POBF analyzer device prior to the laser treatment (first visit) and during the subsequent visits are provided in the Table. The IOP values significantly differed between the first visit and any other visit ($P < 0.05$ for each), but they did not significantly differ between the other visits ($P > 0.05$ for each).

The PA, PV, and POBF values of the 40 eyes included in the study as measured prior to the laser treatment (first visit) and at the subsequent visits are provided in the Table and Figures 1–3. The PA values between the first visit and any other visit ($P < 0.0001$ for each) and between the second visit and the fourth visit ($P = 0.022$) were significantly different. However, PA did not significantly differ between the second visit and the third visit or the third visit and the fourth visit ($P = 0.22$ and 0.095, respectively).

The PV values were significantly different between the first visit and any other visit ($P < 0.05$ for each) and between the second visit and the fourth visit ($P = 0.026$). However, the PV was not significantly different between the second visit and the third visit or the third visit and the fourth visit ($P = 0.151$ and 0.137, respectively).

The POBF values also significantly differed between the first visit and any other visit ($P < 0.05$ for each) and between the second visit and the fourth visit ($P = 0.016$). However, they were not significantly different between the second visit and the third visit ($P = 0.478$) or the third visit and the fourth visit ($P = 0.084$).

One month after the completion of PRP (fourth visit), signs of PDRP were improved to a large extent in 33 out of 40 patients (82.5%), while a rather limited improvement in the remaining patients was also present.

4. Discussion

By investigating pulsatile ocular blood flow changes after panretinal photocoagulation treatment in patients with PDRP, it was found that PRP treatment reduces the choroidal blood flow and consequently causes significant decreases in IOP, PA, PV, and POBF.

In a study examining the values of ocular blood flow in healthy adult subjects, POBF values were reported as 1512 ± 347 mL/min in females and 1193 ± 312 mL/min in males (29). In the same study, PA values were reported as 3.8 ± 1.3 mmHg in females and 3 ± 1.1 mmHg in males, and PV values were reported as 9.4 ± 2.7 mL in females and 7.1 ± 2.9 mL in males (29).

Previous studies have reported varied results with respect to the POBF values in DM patients. A study by Geyer et al. (30) showed decreases in the PA and POBF values in the early phases of DRP when compared to normal cases and increases in the POBF values in the subsequent phases of retinopathy without any significant difference in PA. Langham et al. (20) stated that the POBF values in DM patients without DRP were 12% lower compared to the nondiabetic control group. A study by Savage et al. (7) found no significant change in POBF in cases with early-phase DRP compared to the normal population, but the POBF values were significantly increased in cases with mid- or late-phase nonproliferative DRP. The same study reported lower POBF values in patients with PDRP who were treated with laser photocoagulation compared to other cases. Although our study did not involve a control group, we also found reduced POBF values following PRP procedure in patients with DRP.

In a study performed by MacKinnon et al. (31), the average POBF values were 818 μL/min, 1015 μL/min,

Table. Comparison of data obtained from 4 examinations of patients with proliferative diabetic retinopathy who were treated with panretinal photocoagulation.

Measurements	First visit	Second visit	Third visit	Fourth visit	P-value
Systolic arterial pressure (mmHg)	150.74 ± 25.56 (100–200)	147.41 ± 31.08 (100–200)	150 ± 21.84 (120–200)	155.56 ± 21.9 (110–190)	0.243
Diastolic arterial pressure (mmHg)	87.04 ± 11.03 (70–120)	84.63 ± 12.93 (60–120)	87.78 ± 10.86 (70–110)	86.48 ± 8.06 (80–110)	0.321
Intraocular pressure (mmHg)	20.44 ± 4.13 (9–30)	18.02 ± 4.75 (7.9–30.2)	17.97 ± 4.48 (10.3–30.1)	18.49 ± 4.44 (9–27)	<0.0001
Pulse amplitude (mmHg)	4.23 ± 1.73 (1.6–9.6)	3.19 ± 1.6 (0.9–7.5)	2.97 ± 1.32 (0.8–6.1)	2.78 ± 1.13 (1.1–5.3)	<0.0001
Pulse volume (μL)	6.89 ± 2.28 (3.4–13)	6.09 ± 2.66 (2.2–11.4)	5.62 ± 2.23 (1.7–9.9)	5.27 ± 2.08 (2.5–9.2)	<0.0001
Pulsatile ocular blood flow (μL/s)	21.86 ± 5.83 (9.7–36.4)	18.1 ± 6.67 (8.2–36.3)	17.42 ± 6.29 (8.3–36)	15.89 ± 5.05 (8.3–28.1)	<0.0001

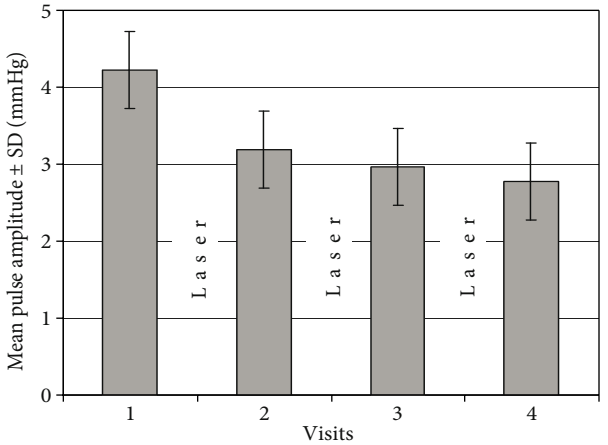

Figure 1. A comparison of the baseline pulse amplitude (PA) values with the average PA values in eyes with proliferative diabetic retinopathy following treatment with panretinal photocoagulation.

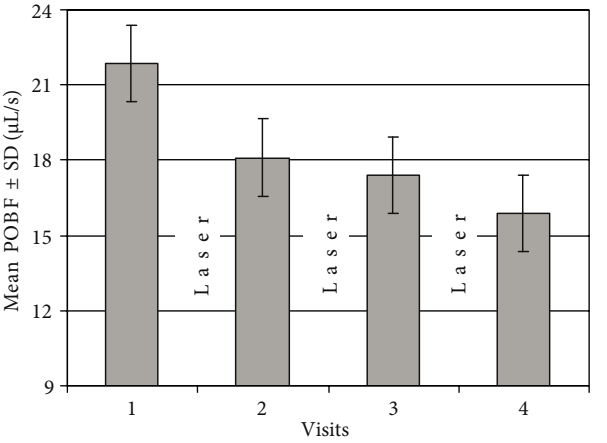

Figure 3. A comparison of the baseline pulsatile ocular blood flow (POBF) values with the average POBF values in eyes with proliferative diabetic retinopathy following treatment with panretinal photocoagulation.

1097 µL/min, and 644 µL/min in diabetic patients without retinopathy, patients with baseline DRP, in preproliferative/proliferative patients, and in the healthy control group, respectively. Perrott et al. (10) found POBF values of 893 µL/min in diabetic patients without retinopathy and 953 µL/min in patients with nonproliferative DRP. Although the number of patients in the current study is not sufficient to document normal ranges of POBF in patients with proliferative DRP, the average pre-PRP POBF value was 1311.6 µL/min (21.86 µL/s). These POBF values were higher than those reported, and this may be due to the fact that all the involved patients had high-risk PDRP. The reduction of POBF values to 953.4 µL/min (15.89 µL/s) in parallel to the regression of PDRP findings following PRP intervention provides further evidence for this assumption.

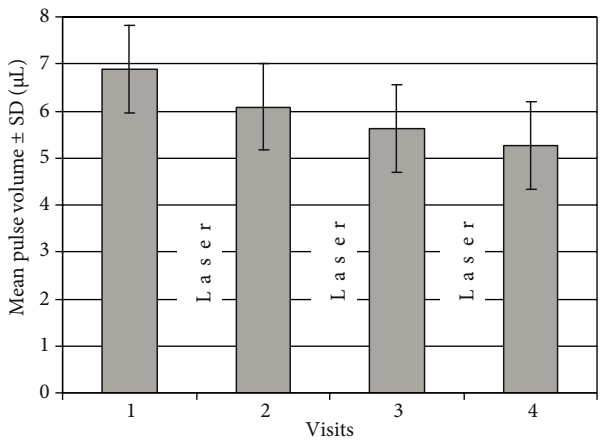

Figure 2. A comparison of the baseline pulse volume (PV) values with the average PV values in eyes with proliferative diabetic retinopathy following treatment with panretinal photocoagulation.

In a study by Takahashi et al. (9), the choroidal blood flow in the fovea of the PRP-treated DM patients was examined using a laser Doppler flowmeter. They found that PRP increased the choroidal blood flow in the fovea. In a study by Mendivil and Cuartero (32) carried out using color Doppler ultrasonography, retinal blood flow was reduced following PRP in 25 eyes with PDRP. Hessemer and Schmidt (33) measured the ocular pulse amplitude in 10 eyes with PDRP using an oculo-oscillo-dynamometer and reported a significant decrease after PRP. Savage et al. (7) found that the POBF values measured in 54 eyes in 28 patients with PDRP after PRP were 22% lower than in the control group. Post-PRP, Grunwald et al. (34) observed statistically significant decreases in retinal blood flow in eyes with PDRP. In parallel with the latest studies we found significantly decreased POBF, PA, and PV values after PRP treatment. This is despite the fact that we used a different device in measurement of ocular blood flow compared to those reports.

The exact mechanism of ocular blood flow changes in diabetic patients is not yet known. In a POBF analysis, Savage et al. (7) noted that the POBF does not significantly differ between patients with early-phase DRP and healthy controls. They related this observation to the thought that the general choroidal circulation is not affected by vasoconstrictors, such as protein kinase C and endothelin I released by retinal cells, produced as a result of DRP-induced ischemia. The same study suggested that the vascular endothelial growth factors released in the subsequent phase of DRP may affect the choroidal circulation and cause an increase in blood flow. Even if the biochemical mechanism is not completely clear, Savage et al. (7) stated that the POBF values in PRP-treated patients are lower than normal. The vascular endothelial

growth factors released as a result of ischemia cause vasodilatation, and this results in an increase in blood flow (35,36). This suggests that the perfusion disorders caused by diabetes induce a blood flow reduction in the early phase and that the ischemia-induced release of vasodilator and angiogenic agents in the subsequent phases causes an increase in blood flow. The blood flow is again reduced as a result of a decrease in the release of the vasodilator and angiogenic agents by the cells necrosed by PRP in the late phases. A reduction in ocular blood flow due to the development of a choriocapillary closure following PRP treatment is another possible explanation (33). We think that all the above-mentioned mechanisms may be among the cause(s) of the determined decreased POBF values after PRP therapy.

Ocular blood flow can be affected by the systemic arterial pressure. A study performed by Esgin et al. (26) stated that systemic hypertension may increase POBF in diabetic patients. A study by Perrott et al. (37) reported no significant correlation between the systemic tension values and POBF in diabetic patients. In addition to systemic arterial pressure, various local and neurohormonal factors are thought to affect blood flow regulation (38). In our study, the systemic blood pressure values did not significantly differ between the 4 sessions when POBF was measured. Therefore, the possible effects of the systemic blood pressure on the POBF measurements were excluded.

The IOP values measured in our study prior to PRP were significantly increased compared to the post-PRP values. Previous studies on the effect of PRP on IOP have reported varied results. Blondeau et al. (39) reported temporary IOP increases that recovered within a few hours in PRP-treated DM patients. Schiødte et al. (40) found significantly decreased IOP values in diabetic patients in the first month after PRP. Similarly, in our study, a significant decrease was found in the IOP levels 3 weeks after the first PRP session. One possible cause of the late-period decreases in IOP is the reduction in the post-PRP uveal blood flow.

Due to the limited number of cases involved, both eyes of 13 out 27 patients were used for evaluations in the study, and this represents a limitation of our study. In conclusion, we demonstrated that PRP treatment significantly and progressively decreases POBF. The ocular blood flow reduction due to PRP observed in our study is in agreement with the literature. During our study, the PA, PV, and POBF values were also reduced following PRP treatment. We also suggest that history of retinal laser therapy should be taken into consideration when evaluating the ocular blood flow of patients.

References

1. Fisher EB, Thorpe CT, Devellis BM, Devellis RF. Healthy coping, negative emotions, and diabetes management: a systematic review and appraisal. Diabetes Educ 2007; 33: 1080–1103.
2. Turk A, Nuhoglu I, Mentese A, Karahan SC, Erdol H, Erem C. The relationship between diabetic retinopathy and serum levels of ischaemia-modified albumin (IMA) and malondialdehyde (MDA). Retina 2011; 31: 602–608.
3. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27: 1047–1053.
4. Natali A, Ferrannini E. Hypertension, insulin resistance, and the metabolic syndrome. Endocrinol Metab Clin North Am 2004; 33: 417–429.
5. American Diabetes Association. Economic costs of diabetes in the U.S. in 2007. Diabetes Care 2008; 31: 596–615.
6. Erdol H, Turk A, Akyol N, Imamoglu HI. The results of intravitreal bevacizumab injections for persistent neovascularizations in proliferative diabetic retinopathy following photocoagulation therapy. Retina 2010; 30: 570–577.
7. Savage HI, Hendrix JW, Peterson DC, Young H, Wilkinson CP. Differences in pulsatile ocular blood flow among three classifications of diabetic retinopathy. Invest Ophthalmol Vis Sci 2004; 45: 4504–4509.
8. Kim SK, Cho BJ, Hong S, Kang SY, Kim JS, Kim CY, Seong GJ. Pulsatile ocular blood flow in healthy Koreans. Korean J Ophthalmol 2008; 22: 6–9.
9. Takahashi A, Nagaoka T, Sato E, Yoshida A. Effect of panretinal photocoagulation on choroidal circulation in the foveal region in patients with severe diabetic retinopathy. Br J Ophthalmol 2008; 92: 1369–1373.
10. Perrott RL, Drasdo N, Owens DR, North RV. Can pulsatile ocular blood flow distinguish between patients with and without diabetic retinopathy? Clin Exp Optom 2007; 90: 445–450.
11. Krepler K, Polska E, Wedrich A, Schmetterer L. Ocular blood flow parameters after pars plana vitrectomy in patients with diabetic retinopathy. Retina 2003; 23: 192–196.
12. Langham ME, Farrell RA, O'Brien V, Silver DM, Schilder P. Blood flow in the human eye. Acta Ophthalmol Suppl 1989; 191: 9–13.
13. Eisenlohr JE, Langham ME, Maumenee AE. Manometric studies of the pressure-volume relationship in living and enucleated eyes of individual human subjects. Br J Ophthalmol 1962; 46: 536–548.
14. Silver DM, Farrell RA, Langham ME, O'Brien V, Schilder P. Estimation of pulsatile ocular blood flow from intraocular pressure. Acta Ophthalmol Suppl 1989; 191: 25–29.
15. Silver DM, Farrell RA. Validity of pulsatile ocular blood flow measurements. Surv Ophthalmol 1994; 38: S72–S80.
16. Leske MC, Wu SY, Hennis A, Honkanen R, Nemesure B; BESs Study Group. Risk factors for incident open-angle glaucoma: the Barbados Eye Studies. Ophthalmology 2008; 115: 85–93.

17. Janulevičiene I, Ehrlich R, Siesky B, Nedzelskienė I, Harris A. Evaluation of hemodynamic parameters as predictors of glaucoma progression. J Ophthalmol 2011; 2011: 164320.

18. Mori F, Konno S, Hikichi T, Yamaguchi Y, Ishiko S, Yoshida A. Pulsatile ocular blood flow study: decreases in exudative age related macular degeneration. Br J Ophthalmol 2001; 85: 531–533.

19. Hopkins SD. Ocular haemodynamics in cataractous eyes. A pilot study. Acta Ophthalmol Suppl 1989; 191: 43–48.

20. Langham ME, Grebe R, Hopkins S, Marcus S, Sebag M. Choroidal blood flow in diabetic retinopathy. Exp Eye Res 1991; 52: 167–173.

21. Schmitt K, Hessemer V. Effect of panretinal photocoagulation on the ocular pulse curve. Klin Monbl Augenheilkd 1997; 210: 53–57 (article in German with abstract in English).

22. Gunvant P, Baskaran M, Vijaya L, Joseph IS, Watkins RJ, Nallapothula M, Broadway DC, O'Leary DJ. Effect of corneal parameters on measurements using the pulsatile ocular blood flow tonograph and Goldmann applanation tonometer. Br J Ophthalmol 2004; 88: 518–522.

23. Ravalico G, Toffoli G, Pastori G, Crocè M, Calderini S. Age-related ocular blood flow changes. Invest Ophthalmol Vis Sci 1996; 37: 2645–2650.

24. Saleh TA, Adams M, McDermott B, Claridge KG, Ewings P. Effects of central corneal thickness and corneal curvature on the intraocular pressure measurement by Goldmann applanation tonometer and ocular blood flow pneumatonometer. Clin Experiment Ophthalmol 2006; 34: 516–520.

25. Benavente-Pérez A, Hosking SL, Logan NS, Broadway DC. Ocular blood flow measurements in healthy human myopic eyes. Graefes Arch Clin Exp Ophthalmol 2010; 248: 1587–1594.

26. Esgin H, Alimgil ML, Erda S. The effect of systemic hypertension on pulsatile ocular blood flow in diabetic patients. Acta Ophthalmol Scand 2001; 79: 160–162.

27. Fontana L, Poinoosawmy D, Bunce CV, O'Brien C, Hitchings RA. Pulsatile ocular blood flow investigation in asymmetric normal tension glaucoma and normal subjects. Br J Ophthalmol 1998; 82: 731–736.

28. Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. Ophthalmology 1991; 98: 823–833.

29. Agarwal HC, Gupta V, Sihota R, Singh K. Pulsatile ocular blood flow among normal subjects and patients with high tension glaucoma. Indian J Ophthalmol 2003; 51: 133–138.

30. Geyer O, Neudorfer M, Snir T, Goldstein M, Rock T, Silver DM, Bartov E. Pulsatile ocular blood flow in diabetic retinopathy. Acta Ophthalmol Scand 1999; 77: 522–525.

31. MacKinnon JR, O'Brien C, Swa K, Aspinall P, Butt Z, Cameron D. Pulsatile ocular blood flow in untreated diabetic retinopathy. Acta Ophthalmol Scand 1997; 75: 661–664.

32. Mendivil A, Cuartero V. Ocular blood flow velocities in patients with proliferative diabetic retinopathy after scatter photocoagulation. Two years of follow-up. Retina 1996; 16: 222–227.

33. Hessemer V, Schmidt KG. Influence of panretinal photocoagulation on the ocular pulse curve. Am J Ophthalmol 1997; 123: 748–752.

34. Grunwald JE, Riva CE, Brucker AJ, Sinclair SH, Petrig BL. Effect of panretinal photocoagulation on retinal blood flow in proliferative diabetic retinopathy. Ophthalmology 1986; 93: 590–595.

35. Caldwell RB, Bartoli M, Behzadian MA, El-Remessy AE, Al-Shabrawey M, Platt DH, Liou GI, Caldwell RW. Vascular endothelial growth factor and diabetic retinopathy: role of oxidative stress. Curr Drug Targets 2005; 6: 511–524.

36. Caldwell RB, Bartoli M, Behzadian MA, El-Remessy AE, Al-Shabrawey M, Platt DH, Caldwell RW. Vascular endothelial growth factor and diabetic retinopathy: pathophysiological mechanisms and treatment perspectives. Diabetes Metab Res Rev 2003; 19: 442–455.

37. Perrott RL, North RV, Drasdo N, Ahmed KA, Owens DR. The influence of plasma glucose upon pulsatile ocular blood flow in subjects with type II diabetes mellitus. Diabetologia 2001; 44: 700–705.

38. Caprioli J, Coleman AL; Blood Flow in Glaucoma Discussion. Blood pressure, perfusion pressure, and glaucoma. Am J Ophthalmol 2010; 149: 704–712.

39. Blondeau P, Pavan PR, Phelps CD. Acute pressure elevation following panretinal photocoagulation. Arch Ophthalmol 1981; 99: 1239–1241.

40. Schiødte SN, Scherfig E, Nissen OI. A pressure lowering effect of retinal xenon photocoagulation in normotensive diabetic eyes. Acta Ophthalmol (Copenh) 1980; 58: 369–376.