ORIGINAL ARTICLE

UDC: 616.13/.14:611.84]::617.7-007.681
DOI: 10.2298/VSP1412128M

Retrobulbar hemodynamic parameters in men and women with open angle glaucoma

Parametri retrobulbarne cirkulacije kod muškaraca i žena sa glaukomom otvorenog ugla

Ivan Marjanović*†, Marija Marjanović‡, Ranko Gvozdenović§, Dušica Risović†‖

†Faculty of Medicine, University of Belgrade, Belgrade, Serbia, *Institute of Ophthalmology, ‡Cardiology Clinic, Clinical Center of Serbia, Belgrade, Serbia; ‖Eye Clinic, University Medical Center Zvezdara, Belgrade, Serbia; §Ophtalmology Clinic "Perfect Vision", Subotica, Serbia

Abstract

Background/Aim. Several factors may have influence on systemic circulation. Additionally, peripheral circulation also demonstrates sex differences, in young women presenting significantly lower finger blood flow in comparison to men of the same age, a finding that disappears in women after menopause. The aim of this study was to compare the retrobulbar hemodynamic parameters measured by means of color Doppler imaging in women and men with open-angle glaucoma and elevated intraocular pressure. **Methods.** A total of 52 eyes from 52 open-angle glaucoma (OAG) patients, with elevated intraocular pressure (IOP), were included in this cross-sectional study. Peak-systolic velocity (PSV), end-diastolic velocity (EDV), and Pourcelot resistivity index (RI) were assessed in the ophtalmic artery (OA), central retinal artery (CRA), and posterior cilliary arteries (PCA). IOP was measured both with Goldmann Applanation tonometer (GAT) and with the dynamic contour tonometer (DCT), three times respectively. Ocular pulse amplitude (OPA) appeared during the DCT measurement. **Results.** The retrobulbar hemodynamic parameters did not show any difference between men and post-menopausal women. **Conclusion.** The results of our study did not find any difference between sexes in patients with open-angle glaucoma and elevated intraocular pressure.

Key words:
glaucoma, open-angle; men; women; intraocular pressure; ischemia; eye; diagnosis.

Apstrakt

Uvod/Cilj. Postoji nekoliko faktora koji utiču na sistemsku cirkulaciju. Osim toga, periferna cirkulacija pokazuje razlike među polovima, čineći znatno nižim protok krvi u prstu kod mladih žena nego kod muškaraca istih godina. Ova razlika nestaje kod žena u menopauzi. Cilj ovog rada bio je upoređivanje parametara retrobulbarne cirkulacije izmerenih kolor doplerom kod žena i kod muškaraca sa glaukomom otvorenog ugla. **Metode.** Istraživanjem je bilo obuhvaćeno 52 oka od 52 bolesnika (50 i više godina starosti) sa glaukomom otvorenog ugla i povišenim intraokularnim pritiskom (IOP). Vršni sistolni (PSV), završni dijastolni (EDV) i Pourcelotov indeks rezistencije (Ri) mereni su u oftalmičkoj arteriji (OA), centralnoj retinalnoj arteriji (CRA) i zadnjim kratkim cilijarnim arterijama (PCA). IOP je meren i Goldmannovim aplanacionim (GAT) i dinamičkim konturnim tonometrom (DCT), po tri puta uzastopno. Okularna pulsna amplituda je dobijana tokom merenja dinamičkim konturnim tonometrom. **Rezultati.** Analizom parametara retrobulbarne hemodinamike nije ustanovljena razlika između muškaraca i žena. **Zaključak.** Prema rezultatima ove studije ne postoji razlika u retrobulbarnoj cirkulaciji između muškaraca i žena sa glaukomom otvorenog ugla i povišenim IOP.

Ključne reči:
glaukom, otvorenog ugla; muškarci; žene; intraokularni pritisak; ishemija; oko; dijagnoza.

Introduction

The term glaucoma covers a wide range of chronic, multifactorial, and progressive optic neuropathies in which elevated intraocular pressure (IOP) is an important risk factor [1–3].

Nevertheless, there is increasing evidence suggesting that ocular blood flow disturbances are involved both in the

Correspondence to: Ivan Marjanovic, Institute of Ophthalmology, Clinical Center of Serbia, 11 000 Belgrade, Serbia.
E-mail: Ivanmarjanovic007@gmail.com

pathogenesis of glaucoma [4–9] and in progression of glaucomatous damage [10–12].

Several factors may have influence on systemic circulation. Additionally, peripheral circulation also demonstrates sex differences, in young women presenting significantly lower finger blood flow in comparison to men of the same age, a finding that disappears in women after menopause [13–14].

Many different methods are used to measure directly or calculate indirectly the ocular hemodynamic parameters in humans. Among them, the color Doppler imaging (CDI) combines B-scan grey scale imaging of tissue structure, color representation of blow flow based on Doppler shift and pulsed Doppler measurement of blood flow velocities. This method is used, in ophthalmology, to measure blood flow velocities in retrobulbar vessels [6, 15–17].

The aim of this study was to compare the retrobulbar hemodynamic parameters measured by means of color Doppler imaging in women and men (age 50 and more) with open-angle glaucoma and elevated intraocular pressure.

Methods

This prospective cross-over study was conducted on consecutive recruited patients who met inclusion and exclusion criteria, seen at the University Eye Clinic, Clinical Center of Serbia in Belgrade, from December 2009 to December 2010.

This study was approved by the Ethics Committee of the University Eye Clinic, Clinical Center of Serbia, and was conducted in accordance with Good Clinical Practice and the tenets of the Declaration of Helsinki. The patients signed an informed consent form before inclusion.

All the participants were required to meet the following inclusion criteria: age equal to or higher than 50 years, clinical diagnosis of open-angle glaucoma in early to moderate stage [18], IOP equal or higher than 25 mmHg without treatment and willingness to comply with the investigators and protocol indications.

The patients were excluded if they had other type of glaucoma different than open-angle glaucoma, previous treatment with ocular filtering surgery, the history of previous refractive surgery, any hormonal therapy, acute myocardial infarction or stroke within the past three month, diabetes, the history of progressive retinal or optic nerve disease of any cause, and asthma or any other obstructive pulmonary disease.

All the patients underwent complete ophthalmologic examination, Goldmann applanation (GAT) (Goldmann tonometer; Haag Streit AG, Koeniz, Switzerland) and dynamic contour tonometry (DCT) (Dynamic Contour tonometer; Ziemer Ophthalmic Systems, Port, Switzerland), central corneal thickness (CCT) with ultrasound pachymetry (Palm Scan AP 2000, Ophthalmic Ultrasound, Micro Medical Devices, Inc., Clabasas, CA, USA), visual field examination (Humphrey VFA, Carl Zeiss Meditec) and confocal scanning laser retinal tomography (HRT II) (Heidelberg Engineering Inc. Heidelberg, Germany). IOP was measured both with GAT and DCT, three times respectively. After a decrease of elevated IOP (IOP < 20 mmHg), both by medications or by surgery, we repeated GAT and DCT. Ocular pulse amplitude (OPA) appeared during the DCT measurement.

Hemodynamic parameters were measured in the ophthalmic artery (OA), central retinal artery (CRA), and posterior cilliary arteries (PCA). Peak systolic (PSV) and end-diastolic (EDV) velocities were measured. Peak systolic velocity and EDV were used to calculate the Pourcelot resistivity index (RI) using the following equation: RI = PSV - EDV/PSV [19]. All color Doppler imaging (CDI) examinations (model Antares; Siemens, Munich, Germany) were performed by the same experienced observer, who was masked to the diagnosis. Evaluations of blood pressure and radial pulse were obtained in a supine position after 10 min of rest. Systolic (SBP) and diastolic blood pressure (DBP) were measured in the upper right arm using a mercury sphygmomanometer and heart rate (HR) was measured by palpation of the radial pulse. These parameters were obtained every 10 min, during Doppler examination.

Descriptive statistics (mean and standard deviation) and 95% confidence intervals (95% CIs) were used to report demographic and ocular baseline characteristics. Data were tested for normal distribution using a D'Agostino-Pearson test [20]. As data were normally distributed, a two-tailed, independent samples Student's *t*-test was used to evaluate the IOP and the hemodynamic parameters by intergroup comparisons. Because of the large number of tests, simultaneous inference using the Bonferroni correction was used to correct the p -value ($\alpha/9$). Statistical significance was accepted for $p < 0.0055$.

Statistical analysis was performed using MedCalc11.5.1.0 (MedCalc software, Mariakerke, Belgium).

Results

Of the 60 patients who were screened, 52 (22 women and 30 men) fulfilled the respective demands of the inclusion and exclusion criteria. The mean (SD) [95% confidence interval (CI)] age was 70.7 (9.9) [66.6 to 74.8] and 68.3 (12.9) [63.7 to 72.9] years in women and men, respectively. The main clinical and demographic characteristics are summarized in Table 1.

Regarding the retrobulbar hemodynamic parameters, there were no significant differences between women and men (Table 2).

Discussion

The results of our study suggested no differences in the retrobulbar hemodynamic parameters between the women of 50 years and more and age-matched men with open-angle glaucoma and elevated IOP.

There are relatively few studies that evaluate possible differences in the retrobulbar hemodynamic parameters between sexes in open-angle glaucoma patients.

In a cross sectional study Harris et al. [21] evaluated the influence of age on retrobulbar circulation assessed with color Doppler. Based on the results of this study, it seemes

Table 1

Baseline demographic and clinical characteristics of the patients

Characteristics	Women (n = 22) mean (SD) [95% CI]	Men (n = 30) mean (SD) [95% CI]	*p*-value
Age (years)	70.7 (9.9) [66.6 – 74.8]	68.3 (12.9) [63.7 – 72.9]	0.367
CCT (μ)	558.5 (36.3) [543.3 – 573.7]	550.3 (40.3) [535.9 – 564.7]	0.447
IOP (mm Hg)	30.8 (7.9) [27.7 – 33.9]	31.2 (9.2) [27.4 – 35.0]	0.850 0.715
OPA (mm Hg)	4.2 (1.4) [3.6 – 4.8]	4.1 (1.2) [3.7 – 4.5]	0.515
MD (dB)	-3.2 (3.3) [-4.6 – -1.8]	-2.8 (3.2) [-3.9 – -1.7]	0.681
PSD (dB)	2.6 (1.9) [1.8 – 3.4]	2.6 (2.1) [1.8 – 3.4]	0.958

SD – standard deviation; 95% CI – 95% confidence interval; CCT – central corneal thickness; IOP – intraocular pressure; OPA – ocular pulse amplitude; MD – mean defect; PSD – pattern standard deviation.

***p*-values were calculated comparing the parameters at baseline between the two study groups (one-way ANOVA test); *p*-values were considered statistically significant if lower than 0.05.**

Table 2

Comparison of the retrobulbar hemodynamic variables between the women and men

Parameter	Women (n = 22)		Men (n = 30)		*p* value
	Mean (SD)	95% CI	Mean (SD)	95% CI	
PSV OA	54.9 (29.9)	42.4 – 67.4	57.5 (21.4)	48.6 – 66.4	0.733
EDV OA	16.6 (11.9)	11.6 – 21.6	17.5 (12.2)	12.4 – 22.6	0.785
RI OA	0.72 80.12)	0.67 – 0.77	0.71 (0.10)	0.67 – 0.75	0.903
PSV CRA	24.7 (9.5)	20.9 – 28.5	28.6 (10.2)	24.3 – 32.9	0.266
EDV CRA	7.3 (2.4)	6.3 – 8.3	9.9 (3.9)	8.3 – 11.5	0.377
RI CRA	0.68 (0.14)	0.62 – 0.74	0.67 (0.11)	0.63 – 0.71	0.878
PSV PCA	27.7 (12.9)	22.3 – 33.1	33.1 (13.3)	27.5 – 38.7	0.173
EDV PCA	9.0 (3.7)	7.5 – 10.5	9.4 (4.5)	7.5 – 11.3	0.713
RI PCA	0.64 (0.13)	0.59 – 0.69	0.68 (0.14)	0.62 – 0.74	0.294

SD – standard deviation; 95% CI – 95% confidence interval; PSV – peak systolic velocity; EDV–end-diastolic velocity; RI – resistivity index; OA – ophthalmic artery; CRA – central retinal artery; PCA – posterior cilliary artery.

Unpaired Student's *t*-test (*p*-values were considered statistically significant if lower than 0.05).

that women and men show different behavior. In women not receiving estrogen replacement therapy older age is associated with reduced EDV, constant PSV, and elevated resistivity index in posterior cilliary arteries. Although our study did not evaluate the impact of age on the retrobulbar hemodynamic, we did not find any difference between men and women in these parameters.

It is well-known that peripheral and central circulations respond differently to the status of sexual hormones. Harris-Yitzhak et al. [22] examined the role that estrogen may play on retrobulbar arteries. This study reports that estrogen-replacement therapy in postmenopausal women apparently helps to reduce vascular resistance distal to the ophthalmic artery to the levels matching those of young women. Similarly, Centofanti et al. [23] and Kavroulaki et al. [24], observed higher choroidal blood flow in premenopausal women. In our study women did not take estrogen replacement therapy and that fact might justify the lack of differences in retrobulbar circulation among them.

In our study we did not evaluate hormonal involvement in men and women, nor its correlation with retrobulbar circulation. Hormonal therapy was one of the exclusion criteria for our study.

Conclusion

The results of our study show no difference between sexes in patients with open-angle glaucoma and elevated intraocular pressure. Further investigations are needed in this field to clarify these results.

R E F E R E N C E S

1. *Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA,* et al. The Ocular Hypertension Treatment Study: baseline fac–rs that predict the onset of primary open-angle glaucoma. Arch Ophthalmol 2002; 120(6): 714−20; discussion 829−30.
2. *Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller PJ*, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that –pical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol 2002; 120(6): 701−13.
3. *Heijl A, Leske CM, Bengtsson B, Hyman L, Bengtsson B*, et al. Reduction of Intraocular Pressure and Glaucoma Progression: Results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002; 120(10): 1268−79.
4. *Carter CJ, Brooks DE, Doyle LD, Drance SM*. Investigations in– a Vascular Etiology for Low-tension Glaucoma. Ophthalmology 1990; 97(1): 49−55.
5. *Hayreh SS*. Progress in the understanding of the vascular etiology of glaucoma. Curr Opin Ophthalmol 1994; 5(2): 26−35.
6. *Flammer J, Orgül S, Costa VP, Orzalesi N, Krieglstein GK, Serra LM, Stefánsson E*. The impact of ocular blood flow in glaucoma. Prog Retin Eye Res 2002; 21(4): 359−93.
7. *Harris A, Kagemann L, Ehrlich R, Rospigliosi C, Moore D, Siesky B*. Measuring and interpreting ocular blood flow and metabolism in glaucoma. Can J Ophthalmol 2008; 43(3): 328−36.
8. *Werne A, Harris A, Moore D, BenZion I, Siesky B*. The Circadian Variations in Systemic Blood Pressure, Ocular Perfusion Pressure, and Ocular Blood Flow: Risk Fac–rs for Glaucoma. Surv Ophthalmol 2008; 53(6): 559−67.
9. *Weinreb RN, Harris A*. Ocular Blood Flow in Glaucoma: The 6th Consensus Report of the World Glaucoma Association. Section II: Clinical Measurement of Ocular Blood Flow. Amsterdam: Kugler Publications; 2009. p. 59
10. *Galassi F, Sodi A, Ucci F, Renieri G, Pieri B, Baccini M*. Ocular hemodynamics and glaucoma prognosis. Arch Ophthalmol 2003; 121(12): 1711−5.
11. *Satilmis M, Orgül S, Doubler B, Flammer J*. Rate of progression of glaucoma correlates with retrobulbar circulation and intraocular pressure. Am J Ophthalmol 2003; 135(5): 664−9.
12. *Martínez A, Sánchez M*. Predictive value of colour Doppler imaging in a prospective study of visual field progression in primary open-angle glaucoma. Acta Ophthalmol Scand 2005; 83(6): 716−22.
13. *Bartelink ML, de Wit A, Wollersheim H, Theeuwes A, Thien T*. Skin vascular reactivity in healthy subjects: influence of hormonal status. J Appl Physiol (1985) 1993; 74(2): 727−32.
14. *Bollinger A, Schlumpf M*. Finger blood flow in healthy subjects of different age and sex and in patients with primary Raynaud's disease. Acta Chir Scand 1976; 465(Suppl): 42−7.
15. *Weinreb RN, Harris A*. Ocular Blood Flow in Glaucoma: The 6th consensus report of the World Glaucoma Association. Section II: Clinical Measurement of Ocular Blood Flow. Amsterdam: Kugler Publications; 2009. p. 21−2.
16. *Lieb WE*. Color Doppler ultrasonography of the eye and orbit. Curr Opin Ophthalmol 1993; 4(3): 68−75.
17. *Butt Z, O'Brien C, McKillop G, Aspinall P, Allan P*. Color Doppler imaging in untreated high- and normal-pressure open-angle glaucoma. Invest Ophthalmol Vis Sci 1997; 38(3): 690−6.
18. *Hodapp E, Parrish R, Anderson D*. Clinical Decisions in Glaucoma. St Louis, Missouri: Mosby-Year Book, Inc; 1993.
19. *Pourcelot L*. Indications de l'ultrasonographie Doppler dans l'etude des vaisseaux peripheriques. Rev Prat 1975; 25: 4671−80.
20. *Sheskin DJ*. Handbook of parametric and nonparametric statistical procedures. 5th ed. Boca Ra–n: Chapman & Hall /CRC; 2011.
21. *Harris A, Harris M, Biller J, Garzozi H, Zarfty D, Ciulla TA,* et al. Aging affects the retrobulbar circulation differently in women and men. Arch Ophthalmol 2000; 118(8): 1076−80.
22. *Harris-Yitzhak M, Harris A, Ben-Refael Z, Zarfati D, Garzozi HJ, Martin BJ*. Estrogen-replacement therapy: effects on retrobulbar hemodynamics. Am J Ophthalmol 2000; 129(5): 623−8.
23. *Centofanti M, Bonini S, Manni G, Guinetti-Neuschüler C, Bucci MG, Harris A*. Do sex and hormonal status influence choroidal circulation. Br J Ophthalmol 2000; 84(7): 786−7.
24. *Kavroulaki D, Gugleta K, Kochkorov A, Katamay R, Flammer J, Orgul S*. Influence of gender and menopausal status on peripheral and choroidal circulation. Acta Ophthalmol 2010; 88(8): 850−3.

Received on May 8, 2013.
Revised on September 22, 2013.
Accepted on December 27, 2013.