Srp Arh Celok Lek. 2013 Nov-Dec;141(11-12):728-731
ОРИГИНАЛНИ РАД / ORIGINAL ARTICLE
DOI: 10.2298/SARH1312728M
UDC: 617.7-007.681-085

Changes in the Retrobulbar Arterial Circulation after Decrease of the Elevated Intraocular Pressure in Men and Women with Primary Open Angle Glaucoma

Ivan Marjanović[1,2], Antonio Martinez[3], Marija Marjanović[1,4], Djordje Kontić[1,2], Paraskeva Hentova-Senćanić[1,2], Vujica Marković[1,2], Marija Božić[1,2]

[1]School of Medicine, University of Belgrade, Belgrade, Serbia;
[2]Clinic of Eye Diseases, Clinical Center of Serbia, Belgrade, Serbia;
[3]Instituto Gallego de Oftalmologia, Clinical Research Department, Science Research and Sports, Santiago de Compostela, La Coruna, Spain;
[4]Clinic of Cardiology, Clinical Center of Serbia, Belgrade, Serbia

SUMMARY

Introduction An altered perfusion of the optic nerve head has been proposed as a pathogenic factor of glaucoma.

Objective The aim of this study was to evaluate the changes of the hemodynamic parameters in the retrobulbar arterial circulation after decrease of the elevated intraocular pressure (IOP) in women and men with primary open angle glaucoma.

Methods The study included 60 patients (33 males and 27 females) older than 50 years, with diagnosed and treated primary open angle glaucoma (77 eyes of 39 patients had increased IOP, >25 mm Hg). They were examined at the Clinic of Eye Diseases (complete ophthalmologic exam) and Clinic of Neurology, Clinical Center of Serbia, Belgrade, from December 2009 to December 2010. Imaging of hemodynamic parameters of three retrobulbar arterial vessels: ophthalmic, central retinal and posterior ciliary arteries with color Doppler was performed.

Results Among women, hemodynamic arterial parameter of the peak-systolic velocity was increased in the central retinal artery and decreased in the ophthalmic artery and posterior ciliary arteries; end-diastolic velocity was increased in all three retrobulbar vascular levels; Pourcelot resistivity index was increased, but pulsatility index was decreased in all three vessels. Among men, peak-systolic velocity, end-diastolic velocity and pulsatility index were decreased in all three vessels; resistivity index was increased in the ophthalmic artery, but decreased in the central retinal artery and posterior ciliary arteries. There was a significant change of the ophthalmic artery pulsatility index in women, and the end-diastolic velocity of the ophthalmic artery in men.

Conclusion There was a difference of the retrobulbar arterial circulation between women and men with primary open angle glaucoma after decrease of the elevated intraocular pressure. The role of vascular factors in the supply of the optic disc neuroretinal rim is important.

Keywords: elevated intraocular pressure; retrobulbar arterial circulation; color Doppler imaging; primary open angle glaucoma

INTRODUCTION

Although an elevated intraocular pressure (IOP) is among the major risk factors of glaucoma progression [1, 2, 3], an impaired ocular blood flow is also an important and independent risk factor [4, 5, 6]. Different risk factors are predominant in different types of glaucoma. A stage of disease is also significant. It is reported that ocular blood flow is reduced in normal tension glaucoma patients and patients with primary open angle glaucoma with the advanced visual field impairment [6, 7, 8]. Several disturbances in ocular blood flow have been also reported in patients with pseudoexfoliative glaucoma [9, 10].

Color Doppler imaging (CDI) is well established as a technique that can be used to measure blood flow velocities in the retrobulbar vessels [11, 12]. However, the approach has not been fully validated in the eye diseases such as glaucoma, because little is known about its reproducibility within these specific patient populations.

Ocular ischaemia, acting independently or because of elevated IOP, may trigger glutamate-mediated toxicity, attenuate ganglion cell function and contribute to retinal nerve fiber loss [13]. In some patients with glaucoma, disease progression continues despite significant IOP reduction. Large population-based studies provide strong evidence of the associations of ocular ischaemia and glaucoma progression [14] or its severity [15]. Improvement of ocular and retrobulbar perfusion may, therefore, be effective in addition to IOP reduction in preventing the glaucoma progression.

OBJECTIVE

The aim of this study was to compare the value of CDI measurements, peak-systolic velocity

Correspondence to:
Ivan MARJANOVIĆ
Clinic of Eye Diseases
Clinical Center of Serbia
Pasterova 2, 11000 Belgrade
Serbia
ivanmarjanovic007@yahoo.com

(PSV), end-diastolic velocity (EDV), Pourcelot resistivity index (RI) and pulsatility index (PI) in the ophthalmic artery (OA), central retinal artery (CRA) and posterior ciliary arteries (PCA), after decrease of the elevated IOP in glaucoma patients.

METHODS

This prospective interventional study included 60 patients (33 males and 27 females) older than 50 years, with diagnosed and treated primary open angle glaucoma (77 eyes of 39 patients had increased IOP, >25 mm Hg), examined from December 2009 to December 2010, at the Clinic of Eye Diseases and Clinic of Neurology, Clinical Center of Serbia, Belgrade; they all met the inclusion/exclusion criteria and signed a written consent form in accordance with the principles of the Declaration of Helsinki and local Ethics Board approval. All patients were selected upon the regular ophthalmic physical examination at the Clinic of Eye Diseases, Clinical Center of Serbia.

All subjects had a complete ophthalmologic examination at the Clinic of Eye Diseases, including visual acuity (Snellen chart), slit-lamp biomicroscopy, gonioscopy, IOP measurement with Goldmann applanation and Dynamic Contour tonometers (DCT), central corneal thickness (CCT) measurement with ultrasound pachymeter and fundus examination using the Volk Superfield lens. Some examinations were done under topical anaesthesia (1% tetracaine sol.). First, CCT was measured three times consecutively with ultrasound pachymetry. IOP was determined three times consecutively using DCT and Goldmann tonometry, between 9 and 11 a.m., always by the same examiner. For DCT examination, tip preservative was changed before every exam. Ocular pulse amplitude (OPA) appeared during the DCT measurement. Diagnostic observation also included automated perimetry (Humphrey) and scanning laser ophthalmoscopy-Heidelberg retinal tomography (with HRT II) exam at least once a year.

Hemodynamic parameters were measured in OA, CRA and PCA. PSV and EDV were measured, and RI and PI were calculated using the ultrasound machine Aloka Alpha 10 (7.5–10 MHz linear probe). Imaging of the retrobulbar arterial circulation was performed with CDI at the Clinic of Neurology, Clinical Center of Serbia by an experienced neurologist.

After decrease (IOP<20 mm Hg) of the elevated IOP, achieved by medications (prostaglandin analogues and beta blockers, independently or as fixed drug combination) or by surgery (glaucoma filtering surgery-trabeculectomy), we repeated Goldmann tonometry and DCT and CDI of the retrobulbar arterial vessels.

Inclusion criteria were patients older than 50 years, with diagnosed and treated primary open angle glaucoma.

Glaucoma is a chronic, degenerative optic neuropathy that can be distinguished from most forms of the acquired optic neuropathy by its characteristic appearance of the optic nerve .The main clinical features of primary open-angle glaucoma are open iridocorneal angle and cupping of the optic-nerve head (or optic disk), with corresponding loss of visual field and elevated intraocular pressure.

Patients were excluded from the study if they had any of the following: 1) A history of the significant vascular and/or neurological disease (previous cerebrovascular insult), patients with vasospastic syndromes, advanced stage of D. Mellitus, previous operations on the heart and magistral vessels); 2) astigmatism >2D or corneal abnormalities (such as edema, scars, or dystrophy, which may prevent contour matching on the DCT); 3) history of the intraocular surgery/refractive surgery.

The following measuring devices were used: ultrasound pachymeter (Palm Scan AP 2000, ophthalmic ultrasound, Micro Medical Devices, Inc. Clabasas, CA, USA), dynamic contour tonometer (DCT), developed by Swiss Microtechnology AG (Port, Switzerland), automated perimetry (Humphrey Zeiss Meditec, Dublin, CA, USA), scanning laser ophthalmoscopy performed with the Heidelberg Retinal Tomograph (HRT; Heidelberg Engineering, GmbH, Dossenheim, Germany).

Retrobulbar blood flow velocities and calculated vascular resistive (RI) and pulsatility indices (PI) were measured with the Antares CDI device (Siemens, Munich, Germany). CDI measurements were carried out in OA, CRA and PCA. In each vessel, PSV and EDV were determined, and RI and PI were calculated (RI=(PSV-EDV)/PSV).

Statistical analysis was performed using the Med-Calc 11.5.1.0 (MedCalc software, Mariakerke, Belgium).

Descriptive statistics [mean (standard deviation)] and 95% confidence intervals (95% CIs) were used to report demographic and ocular baseline characteristics. Data were tested for normal distribution using the Kolmogorov–Smirnov test. As data were normally distributed, a two-tailed, paired Student's t-test was used to evaluate the IOP and the hemodynamic parameters by intragroup comparisons made between the values obtained under the baseline and treatment conditions.

To analyze the correlation between the changes in the retrobulbar hemodynamics and changes in IOP assessed with both GAT and DCT, Pearson's correlation coefficients were calculated for every parameter.

RESULTS

After IOP decrease in women, PSV was increased in CRA (34.87; 27.7 to 43.6 vs 39.27; 31.1 to 46; p=0.09), decreased in OA (52.41±22.05 vs 51.28±23.8; p=0.73) and in PCA (28.54±12.51 vs 28.28±11.87; p=0.89). EDV was increased in all observed arterial vessels: OA (16.59±10.18 vs 17.99±11.24; p=0.33), CRA (11.74±6.84 vs 12.29±6.2; p=0.13) and PCA (9.18±3.37 vs 9.52±3.83; p=0.52), but without statistical significance. RI was increased in all observed arterial vessels: OA (0.73±0.14 vs 0.75±0.24; p=0.52), CRA (0.72±0.18 vs 0.76±0.21; p=0.13) and PCA (0.71±0.2 vs 0.76±0.31; p=0.21), also without statistical significance. PI was decreased only in the OA with statistical significance (1.34±0.54 vs 1.14±0.42; p=0.006; p<0.05), and no statistical significance in the CRA (1.24±0.45 vs

1.23±0.5; p=0.96) and PCA (1.19±0.51 vs 1.05±0.41; p=0.08).

Among men, after IOP reduction, PSV was decreased in all three observed retrobulbar arteries: OA (62.72±26.29 vs 54.21±23.01; p=0.095), CRA (39.39±11.71 vs 38.97±20.93; p=0.86) and PCA (29.19±12.49 vs 26.28±10.17; p=0.12). EDV was significantly decreased in the OA (22.35±15.57 vs 17.81±10.47; p=0.01; p<0.05), without changes in the CRA (10.95; 7.9 to 16.1 vs 11.01; 7.9 to 14.8; p=0.37) and PCA (8.57; 7.1 to 10.1 vs 8.85; 7.4 to 10.9; p=0.98). RI was without changes in the OA (0.68±0.15 vs 0.69±0.16; p=0.66) and the CRA (0.69±0.1 vs 0.69±0.15; p=0.98), but slightly decreased in the PCA (0.66±0.13 vs 0.62±0.12; p=0.063). Similar changes of PI were found, without changes in the OA (1.2±0.5 vs 1.22±0.53; p=0.71) and in the CRA (1.25±0.40 vs 1.23±0.41; p=0.81), but slightly decreased in the PCA (1.19±0.43 vs 1.08±0.36; p=0.08).

DISCUSSION

Our study failed to find any difference between retrobulbar circulation among men and women after IOP reduction in glaucoma patients. Among women, IOP lowering caused PSV increase in CRA and PI decrease in OA; among men, lowering of the IOP led to decrease of PSV and EDV in OA and RI and PI in PCA. Despite difference in the peripheral circulation between men and women [16, 17, 18] we could not find but one published study on difference in the retrobulbar circulation between men and women with glaucoma [19].

This study compared retrobulbar circulation in men and women according to their age, and found decrease of EDV and RI in OA in both sexes; further on, EDV of OA was increased in females and decreased in males; all other observed parameters were similarly changed in the abovementioned as well as in our study.

The results of this study were compatible with the results of our previous studies [20, 21].

Majority of studies used some kind of scleral suction to increase IOP, mostly in healthy population with normal IOP [22, 23] or they lowered IOP for 10-20 mm Hg, with some kind of vacuum, also among healthy individuals [24].

Our study analyzed the lowering of pathologically elevated IOP, in glaucoma patients, with previously impaired retrobulbar circulation due to disease itself. Similar to our study, other studies analyzed retrobulbar circulation in glaucoma [25, 26, 27]. None of the mentioned studies analyzed particularly retrobulbar circulation in men and women.

Incidental finding in our research was a fact that a half of all patients had 50% obstruction of the internal carotid artery (ICA); 4 of them had more than 70% obstruction of the ICA, and 2 of them bilateral, so they were operated on by vascular surgeon immediately. In our study, this was a side effect, but very important, and we believe that it is a good argument that glaucoma patients are also vascular and neurological patients, so their examination is also important. We found similar recommendations in other studies [28-31].

Important limitation of our study was a fact that all our patients were under topical antiglaucoma therapy for IOP lowering, so it might have some influence on the retrobulbar outflow. There was no correlation between IOP difference measured by Goldmann applanation or DCT, as well as parameters of the retrobulbar circulation between males and females.

CONCLUSION

Our study showed a difference between women and men in the retrobulbar arterial circulation after decrease of the elevated intraocular pressure in primary open angle glaucoma. Major goal of our study was to present a significance of vascular theory in glaucoma pathogenesis and importance of CDI for tracking patients with glaucoma. Changes in retrobulbar circulation are important for approach and treatment, but the role of vascular factors in the supply of the optic disc neuroretinal rim could be a key for progression backlash of glaucoma and the basis of neuroprotection.

REFERENCES

1. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120:714-20.
2. Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller JP, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120(6):701-13.
3. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B,Hussein M. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002; 120(10):1268-79.
4. Galassi F, Sodi A, Ucci F, Renieri G, Pieri B, Baccini M. Ocular hemodynamics and glaucoma prognosis: a color Doppler imaging study. Arch Ophthalmol. 2003; 121(12):1711-5.
5. Satilmis M, Orgul S, Doubler B, Flammer J. Rate of progression of glaucoma correlates with retrobulbar circulation and intraocular pressure. Am J Ophthalmol. 2003; 135:664-9.
6. Martinez A, Sanchez M. Predictive value of color Doppler imaging in a prospective study of visual field progression in primary open-angle glaucoma. Acta Ophthalmol Scand. 2005; 83:716-23.
7. Flammer J, Orgul S, Costa VP, Orzalesi N, Krieglstein GK, Serra LM, et al. The impact of ocular blood flow in glaucoma. Prog Retin Eye Resea. 2002; 21:359-93.
8. Gherghel D, Orgul S, Gugleta K, Gekkieva M, Flammer J. Relationship between ocular perfusion pressure and retrobulbar blood flow in patients with glaucoma with progressive damage. Am J Ophthalmol. 2000; 130(5):597-605.
9. Sobour G, Finazzo C, Boles Carenini A. Monolateral Pseudoexfoliation capsulae: a study of choroidal blood flow. Acta Ophthalmol Scand. 1997; 75(Suppl 224):13-4.
10. Repo LP, Suhonen MT, Terasvirta ME, Koivisto KJ. Color Doppler imaging of the ophthalmic artery blood flow spectra of patients who have had a transient ischemic attack. Correlations with generalized iris transluminance and pseudoexfoliation syndrome. Ophthalmology. 1995; 102:1199-205.

doi: 10.2298/SARH1312728M

11. Kagemann L, Harris A. The clinical utility of colour Doppler imaging. Eye. 2007; 21(7):1015.
12. Polska E, Polak K, Luksch A, Fuchsjager-Mayrl G, Petternel, Findl O, et al. Twelve hour reproducibility of choroidal blood flow parameters in non-glaucomatous subjects. Br J Ophthalmol. 2004; 88:533-7.
13. Osborne NN, Wood JP, Chidlow G, Bae JH, Melena J, Nash MS. Ganglion cell death in glaucoma: what do we really know? Br J Ophthalmol. 1999; 83:980-6.
14. Zeitz O, Galambos P, Wagenfeld L, Wiermann a, Wlodarsch P, Praga R, et al. Glaucoma progression is associated with decreased blood flow velocities in the short posterior ciliary artery. Br J Ophthalmol. 2006; 90:1245-8.
15. Plange N, Kaup M, Arend O, Remky A. Asymmetric visual field loss and retrobulbar haemodynamics in primary open-angle glaucoma. Graefes Arch Clin Exp Ophthalmol. 2006; 244:978-83.
16. Lally EV. Raynaud's phenomenon. Curr Opin Rheumatol. 1992; 4(6):825-36.
17. Goundry B, Bell L, Langtree M, Moorthy A. Diagnosis and management of Raynaud's phenomenon. BMJ. 2012; 344:e289.
18. Aiba Y, Yamamoto K, Ohshiba S, Ikeda K, Morioka I, Miyashita K, et al. A longitudinal study on Raynaud's phenomenon in workers using an impact wrench. J Occup Health. 2012; 54(2):96-102.
19. Harris A, Harris M, Biller J, Garzozi H, Zarfty D, Ciulla TA, at al. Aging affects the retrobulbar circulation differently in women and men. Arch Ophthalmol. 2000; 118(8):1076-80.
20. Marjanovic I, Milic N, Martinez A. The impact of intraocular pressure reduction on retrobulbar hemodynamic parameters in patients with open-angle glaucoma. Eur J Ophthalmol. 2012; 22(1):77-82.
21. Marjanovic I, Milic N, Martinez A, Benitez-del-Castillo J. Retrobulbar hemodynamic parameters in open-angle and angle-closure glaucoma patients. Eye (Lond). 2012; 26(4):523-8.
22. Regillo CD, Sergott RC, Brown GC. Successful scleral buckling procedures decrease central retinal artery blood flow velocity. Ophthalmology. 1993; 100:1044-9.
23. Harris A, Joos K, Kay M, Evans D, Shetty R, Sponsel WE, et al. Acute IOP elevation with scleral suction: effects on retrobulbar haemodynamics. Br J Ophthalmol. 1996; 80(12):1055-9.
24. Findl O, Strenn K, Wolzt M, Menapace R, Vass C, Eichler HG, et al. Effects of changes in intraocular pressure on human ocular hemodynamics. Curr Eye Res. 1997; 16:1024-9.
25. Liu CJ, Chou YH, Chou JC, Chiou HJ, Chiang SC, Liu JH. Retrobulbar haemodynamic changes studied by colour doppler imaging in glaucoma. Eye. 1997; 11:818-26.
26. Chiou HJ, Chou YH, Liu CJ, Hsu CC, Tiu CM, Teng MM, et al. Evaluation of ocular arterial changes in glaucoma with colour Doppler ultrasonography. J Ultrasound Med. 1999; 18:295-302.
27. Klingmuller V, Schmidt KG, von Ruckmann A, Koch B, Stein A. Doppler sonography of the short posterior ciliary artery in patients with primary open-angle glaucoma. Ultraschall Med. 2000; 21:32-7.
28. Dimitrova G, Kato S. Color Doppler imaging of retinal diseases. Surv Ophthalmol. 2010; 55(3):193-214.
29. Januleviciene I, Sliesoraityte I, Siesky B, Harris A. Diagnostic compatibility of structural and haemodynamic parameters in open-angle glaucoma patients. Acta Ophthalmol. 2008; 86(5):552-7.
30. Harris A, Jonescu-Cuypers C, Martin B, Kagemann L, Zalish M, Garzozi HJ. Simultaneous management of blood flow and IOP in glaucoma. Acta Ophthalmol Scand. 2001; 79:336-41.
31. Harris A, Jonescu-Cuypers C, Kagemann L, Ciulla T, Krieglstein GK. Atlas of Ocular Blood Flow. Philadelphia: Elsevier Science; 2003.

Промене у ретробулбарној артеријској циркулацији код мушкараца и жена с примарним глаукомом отвореног угла након снижења повишеног интраокуларног притиска

Иван Марјановић[1,2], Антонио Мартинез[3], Марија Марјановић[1,4], Ђорђе Контић[1,2], Параскева Хентова-Сенћанић[1,2], Вујица Марковић[1,2], Марија Божић[1,2]

[1]Медицински факултет, Универзитет у Београду, Београд, Србија;
[2]Клиника за очне болести, Клинички центар Србије, Београд, Србија;
[3]Одељење за клиничка истраживања, Галицијски институт за офталмологију, Сантјаго де Компостела, Ла Коруња, Шпанија;
[4]Клиника за кардиологију, Клинички центар Србије, Београд, Србија

КРАТАК САДРЖАЈ

Увод Претпоставља се да је поремећај перфузије у глави очног живца патогени фактор код глаукома.

Циљ рада Циљ рада је био да се процене промене у хемодинамским параметрима ретробулбарне артеријске циркулације након снижавања претходно повишеног интраокуларног притиска (ИОП) код мушкараца и жена с примарним глаукомом отвореног угла (енгл. *primary open-angle glaucoma – POAG*).

Методе рада Истраживањем је обухваћено 60 испитаника (33 мушкарца и 27 жена) старијих од 50 година са дијагностикованим и леченим *POAG*. На 77 очију 39 болесника забележен је повишен ИОП (>25 *mm Hg*). Испитивање је обављено од децембра 2009. до децембра 2010. године на Клиници за очне болести (комплетан офталмолошки преглед) и на Клиници за неурологију Клиничког центра Србије у Београду. Колор доплером су испитани хемодинамски параметри три ретробулбарна артеријска крвна суда: офталмичке артерије, централне ретиналне артерије и кратких цилијарних артерија.

Резултати Код жена хемодинамски артеријски параметар вршне систолне брзине протока крви порастао је у централној ретиналној артерији, а смањио се у офталмичкој и кратким задњим цилијарним артеријама. Завршна дијастолна брзина протока крви је порасла у сва три ретробулбарна крвна суда. Пурселоов (*Pourcelot*) индекс резистенције се повећао, док се индекс пулзатилности снизио у сва три крвна суда. Код мушкараца су се вршна систолна и завршна дијастолна брзина протока крви и индекс пулзатилности снизили у сва три крвна суда. Индекс резистенције се повећао у офталмичкој артерији, а смањио у централној ретиналној и кратким задњим цилијарним артеријама. Статистичка значајност је забележена у индексу пулзатилности у офталмичкој артерији жена и у завршној дијастолној брзини протока крви у офталмичкој артерији мушкараца.

Закључак Утврђена је разлика у ретробулбарној артеријској циркулацији између мушкараца и жена са *POAG* након снижења ИОП. Улога васкуларних фактора у исхрани неуроретиналног обода главе очног живца је веома значајна.

Кључне речи: повећање интраокуларног притиска; ретробулбарна артеријска циркулација; колор доплер; примарни глауком отвореног угла

Примљен • Received: 05/04/2012 **Прихваћен • Accepted:** 24/12/2012