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

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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
Glaucoma are open iridocorneal angle and cupping of the optic nerve. The main clinical features of primary open-angle optic neuropathy by its characteristic appearance 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. Mellaunus, 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.

Statistical analysis was performed using the Med-Calc 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 twotailed, 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.

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 (33 males and 27 females) older than 50 years, with diagnosis 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 ophthalmologic 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 appplanation and Dynamic Contour tonometers (DCT), central corneal thickness (CCT) measurement with ultrasound pachymet and fundus examination using the Volk Superfield lens. Some examinations were done under topical anesthesia (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-tracteculectomy), 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.

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 (52.4±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
REFERENCES


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 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.
**КРАТАК САДРЖАЈ**

**Увод** Претпоставља се да је поремећај перфузии у главном крвном грађу патоген фактор код похорда.

**Циљ рада** Циљ је био да се процене промене у хемодинамским параметарма ретробулбарне артеријске циркулације након снижења претходно повећаног интроокуларног притиска (ИОП) код мушкараца и жена с примарним глуком са отвореним углом након снижења повишеног интроокуларног притиска.

**Методе рада** Истраживање је обухватало 60 испитаника (33 мушкарца и 27 жена) старијих од 50 година са дигностико- ваним и леченим РОАГ. На 77 очи 39 болесника забележен је повишен ИОП (>25 мм Hg). Испитивање је обављено од децембра 2009. до децембра 2010. године на Клиници за очне болести (комплетан офталмологијски преглед) и на Клиници за неурологију Клиничког центра Србије у Београду. Кролор допером су испитани хемодинамски параметаре три ретробулбарне артеријске крвне суда: офталмичке артерије, централне ретиналне артерије и кратких цилијарних артерија.

**Резултати** Код жена хемодинамски артеријски параметар вршине систолне брзине протока крви порастао је у централној ретиналној артерији, али смањено се у офталмичкој и краткој зданим цилијарним артеријама. Завршна дијастолна брзина протока крви је порасла у свим трима ретробулбарним крвним судама. Пурсеплов (Purcelot) индекс резистентности се повећао, док се индекс пулзатилности снизио у свим крвним судама. Код мушкараца су се вршине систолна и завршна дијастолна брзине протока крви и индекс пулзатилности снизили у свим трима крвним судама. Индекс резистентности се повећао у офталмичкој артерији, али смањено у централној ретиналној артерији, која се у офталмичкој артерији резистентност смањена у свим трима крвним судама. Кролор допером се испитани хемодинамски параметаре три ретробулбарне артеријске крвне суда: офталмичке артерије, централне ретиналне артерије и кратких цилијарних артерија.

**Кључне речи:** повећање интроокуларног притиска; ретробулбарна артеријска циркулација; кролор допер; примарни глазом отвореног угла.

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