Srp Arh Celok Lek. 2011 Nov-Dec;139(11-12):718-721
ОРИГИНАЛНИ РАД / ORIGINAL ARTICLE
DOI: 10.2298/SARH1112718M
UDC: 617.7-007.681-07

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

Ivan Marjanović[1], Ana Šundić[2], Milija Mijajlović[2] Nadežda Čovičković-Šternić[2], Djordje Kontić[1], Paraskeva Hentova-Senćanić[1], Vujica Marković[1], Marija Božić[1], Miroslav Knežević[1]

[1]Clinic of Eye Diseases, Clinical Centre of Serbia, Belgrade, Serbia;
[2]Clinic of Neurology, Clinical Centre of Serbia, Belgrade, Serbia

SUMMARY

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

Objective To evaluate changes of haemodynamic parameters in the retrobulbar arterial circulation after a decrease of elevated intraocular pressure (IOP) in patients with primary open angle glaucoma (POAG).

Methods Twenty-six patients were examined, 14 men and 12 women, 21 up to 50 years old and 5 below, all with previously diagnosed and treated POAG, and all examined at the Eye Clinic, Clinical Centre of Serbia. IOP was measured both with a Goldmann aplanation tonometer and dynamic contour tonometer. Central corneal thickness was measured with ultrasound pachymeter. Imaging of the retrobulbar arterial circulation by colour Doppler was performed at the Neurology Clinic, Clinical Centre of Serbia. It involved measuring of haemodynamic parameters of the ophthalmic artery, central retinal artery, and posterior ciliary arteries. Peak systolic velocity (PSV) and end-diastolic velocity (EDV) were measured, and resistive index (RI) and pulsatility index (PI) were calculated.

Results Haemodynamic arterial parameters PSV and EDV in the ophthalmic and central retinal artery after decrease of IOP were lower, while RI and PI were higher. In the posterior ciliary arteries PSV, EDV and PI were lower, and RI was higher.

Conclusion Changes of the retrobulbar arterial circulation after elevated IOP in POAG patients are important for approach and treatment, while the role of vascular factors in the supplement of the optic disc neuroretinal rim could be a key for progression backlash of glaucoma and the radix of neuroprotection.

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

INTRODUCTION

Primary open angle glaucoma (POAG) is a common optic neuropathy that appears to have a multifactorial origin. A central debate has focused on the potential disordered perfusion of the optic nerve head [1].

Elevated intraocular pressure (IOP) has been defined as the most important risk factor in the pathogenesis of glaucomatous optic neuropathy. Over the past several decades evidence has grown that vascular factors also contribute to the pathogenesis of glaucoma [2-5]. Numerous techniques have been developed in an attempt to quantify ocular blood flow in the different ocular vascular beds [3, 4].

The observation of the retrobulbar circulation after IOP elevation in POAG yielded an improved understanding of glaucomatous optic neuropathy associated with IOP elevation [6].

Reduction in ocular blood flow parameters in glaucoma has been reported using various techniques to measure blood flow velocity, blood vessel diameter, or oxidative tissue status within or around the eye [7, 8]. Previous studies using the Langham pulsatile ocular blood flow device have indeed shown that pulsations were reduced in patients with glaucoma, but whether this is only true for patients with normal tension glaucoma or also in POAG is controversial [5, 9].

Colour Doppler Imaging (CDI) of the retrobulbar orbit allows real-time imaging of individual vessels in this region. These individual vessels can be investigated, and the Doppler frequency shifts are received from a specific sample volume. This sample volume is placed over a vessel of interest, and the frequency shifts received can be assembled into a spectral waveform. This spectral waveform represents the cumulative frequency shifts present and can be displayed as a time-velocity waveform. The velocities present in the sample volume follow the cardiac cycle, allowing measurements to be taken at the peak of systole (peak systolic velocity – PSV) and at the lowest point of diastole (end-diastolic velocity – EDV). Both of these measurements are dependent on the angle subtended between the probe and the vessel, the Doppler angle. The Doppler formula used to compute blood velocity takes this angle into consideration. Because the PSV and EDV are both dependent on the Doppler angle, they are both regarded, to a degree, as operator-depen-

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

dent. To relate the systolic and diastolic velocities to each other, a ratio, the resistive index (Pourcelot's index), is used [10]. This ratio is angle-independent and is regarded as a good method to quantify the vascular resistance of the circulation, particularly in the cephalic region. The velocity and resistive index have been studied in the ophthalmic artery, the central retinal artery, and the short posterior ciliary arteries of patients with glaucoma. These measurements have been shown to be reproducible [11] and investigators have followed up by comparing disease populations and normal subjects to ascertain the basic findings of CDI within these groups.

OBJECTIVE

The aim of this study was to evaluate changes in the retrobulbar arterial vessels circulation before and after decrease of the elevated IOP in patients with POAG.

METHODS

The research followed the tenets of the Declaration of Helsinki, and informed consent was obtained after explanation of the nature and possible consequences of the study.

All patients were examined at the Institute of Eye Diseases and at the Institute of Neurology, Clinical Centre of Serbia, Belgrade, between December 2009 and March 2010. All patients were obtained from the General Ambulatory Ophthalmology Unit.

We examined 26 patients, 14 men and 12 women, 21 up to 50 years old and 5 below, all with diagnosed and treated POAG. All patients had elevated IOP (>25 mm Hg) in one (18 patients) or both eyes (8 patients). IOP was measured both with a Goldmann Aplanation tonometer (GAT) and Dynamic Contour tonometer (DCT) developed by Swiss Microtechnology AG (Port, Switzerland). Central corneal thickness was measured by ultrasonic pachymetry. Imaging of the retrobulbar arterial circulation using CDI was performed at the Neurology Clinic of the Clinical Centre of Serbia. After a decrease (compensation, IOP<20 mm Hg) of the elevated IOP by medication (21 patients) or surgery (5 patients) we repeated Goldmann and Dynamic contour tonometry and CDI of the retrobulbar arterial vessels.

Haemodynamic parameters were measured in the ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary arteries (PCA). PSV and EDV were measured, and resistive index (RI) and pulsatility index (PI) were calculated using ultrasound machine Aloka Alpha 10; 7.5–10 MHz, linear probe.

Table 1. Relation between haemodynamic parameters in the ophthalmic artery after IOP compensation

Parameter	r (mm Hg)		p		Δr
	GAT I	GAT II	GAT I	GAT II	
PSV I/II (cm/min)	0.44	0.04	0.001	0.74	↓
EDV I/II (cm/min)	0.23	0.16	0.11	0.24	↓
RI I/II	0.16	(-)0.21	0.27	0.14	↑
PI I/II	0.05	(-)0.17	0.71	0.24	↑

Excluded criteria were: 1) narrow/closed angle on gonioscopy (grades 0, 1, and 2 using the Scheie classification); 2) astigmatism >2D or corneal abnormalities (such as oedema, scars, or dystrophy, which may prevent contour matching on the DCT); 3) history of intraocular surgery/previous refractive surgery.

Statistics

Data are presented as mean value with standard deviation. Normal distribution and homoscedasticity of continuous variables were tested by means of the Kolmogorov-Smirnov test. Statistical evaluations were performed by running the SPSS/PC +software package (SPSS, Chicago, IL) on a personal computer. P values of less than 0.05 were regarded as statistically significant.

RESULTS

IOP measurements, before and after compensation, had normal data distribution. In the ophthalmic artery (Table 1) and in the central retinal artery (Table 2), PSV and EDV decreased after IOP compensation, but RI and PI increased. In the posterior ciliary arteries, PSV, EDV and PI decreased and only RI increased (Table 3). Statistical significance appeared only in RI after the IOP decrease (Table 4).

DISCUSSION

Our study confirmed that retrobulbar circulation changed after IOP lowering in the POAG patients. PSV and EDV velocities were decreased in all the observed arterial retrobulbar vessels (OA, CRA and PCA) and RI and PI were increased in OA and CRA; RI increased in CRA also, but PI in CRA decreased. Our results are in an agreement with other studies.

Various studies have compared the vascular parameters in POAG and normal tension glaucoma with those of normal control subjects.

Table 2. Relation between haemodynamic parameters in the central retinal artery after IOP compensation

Parameter	r (mm Hg)		p		Δr
	GAT I	GAT II	GAT I	GAT II	
PSV I/II (cm/min)	(-)0.31	(-)0.1	0.03	0.48	↓
EDV I/II (cm/min)	0.32	0.06	0.02	0.65	↓
RI I/II	(-)0.14	(-)0.19	0.33	0.17	↑
PI I/II	(-)0.17	(-)0.21	0.22	0.13	↑

Table 3. Relation between haemodynamic parameters in the posterior ciliary arteries after IOP compensation

Parameter	r (mm Hg)		p		Δr
	GAT I	GAT II	GAT I	GAT II	
PSV I/II (cm/min)	0.35	(-)0.16	0.01	0.25	↓
EDV I/II (cm/min)	0.42	0.08	0.002	0.58	↓
RI I/II	(-)0.09	(-)0.24	0.52	0.08	↑
PI I/II	(-)0.13	(-)0.04	0.35	0.8	↓

Table 4. Statistical significance of change in haemodynamic parameters in the posterior ciliar arteries (PCA), the central retinal artery (CRA) and the ophthalmic artery (OA) after IOP compensation

Parameters			II											
			PCA				CRA				OA			
			PSV	EDV	RI	PI	PSV	EDV	RI	PI	PSV	EDV	RI	PI
I	PCA	PSV	0.84											
		EDV		0.99										
		RI			0.39									
		PI				0.11								
	CRA	PSV					0.5							
		EDV						0.88						
		RI							<0.001					
		PI								0.65				
	OA	PSV									0.44			
		EDV										0.11		
		RI											0.33	
		PI												0.75

Early studies of retrobulbar circulation in glaucoma patients reported a significant reduction in the EDV and an increase in the RI [12, 13, 14]. Galassi et al [13] also identified a reduced PSV in the OA in glaucoma patients as compared with normal subjects. A subgroup of patients with uncontrolled IOP showed significant reduction in EDV and an elevated RI in the CRA and PCA after IOP compensation.

Punjabi's [15] study of retrobulbar circulation in glaucoma reported a significant reduction in the EDV and increase in the RI of the vessels of this region in patients with glaucoma.

Several studies support the idea that circulatory abnormalities represent risk factors for glaucoma [16]. With the use of Doppler ultrasound of the orbit, a non-invasive examination of the retrobulbar circulation is possible. Several studies using orbital CDI have revealed altered orbital haemodynamics in patients with glaucoma [17, 18].

The RI is a factor related to blood flow resistance in the vascular system downstream to the measurement point [19].

Akarsu and Bilgili [20] found lower EDV and higher RI in the posterior ciliary artery in open-angle glaucoma than in ocular hypertension.

As already known, the main blood supply of the anterior optic nerve derives from the posterior ciliary arteries [21].

Cheng's study had controlled factors, which are known to affect ocular blood-flow velocity, such as IOP [22], age [8], systemic blood pressure [23], and anti-glaucoma medications [24]; therefore, they hoped to eliminate the effect of these variables and to give a more useful comparison between glaucoma and ocular hypertensive patients.

CONCLUSION

Changes in the retrobulbar arterial circulation after elevated IOP in POAG patients are of importance for approach and treatment, but the role of vascular factors in the supplement of the optic disc neuroretinal rim, could be a key for progression backlash of glaucoma and the radix of neuroprotection. CDI of the blood flow in the retrobulbar vessels is a valuable method in the diagnosis of the vascular mechanism in glaucoma.

NOTE

This work was presented at the Serbian National Congress in Subotica in September 2010, as a short oral presentation.

REFERENCES

1. Simon J, Rankin A. Color Doppler imaging of the retrobulbar circulation in glaucoma. Surv Ophthalmol. 1999; 43(Suppl 1):S176-82.
2. 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(2):133-8.
3. Cioffi G, Alm A. Measurement of ocular blood flow. J Glaucoma. 2001; 10(Suppl):62-4.
4. Flammer J, Orgül S, Costa VP, Orzalesi N, Krieglstein GK, Metzner Serra L, et al. The impact of ocular blood flow in glaucoma. Prog Retin Eye Res. 2004; 21(4):359-93.
5. Schwenn O, Troost R, Vogel A, Grus F, Beck S, Pfeiffer N. Ocular pulse amplitude in patients with open angle glaucoma, normal tension glaucoma, and ocular hypertension. Br J Ophthalmol. 2002; 86(9):981-4.
6. Salimis 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.
7. Harris A, Chung HS, Ciulla TA, Kagemann L. Progress in measurement of ocular blood flow and relevance to our understanding of glaucoma and age-related macular degeneration. Prog Retin Eye Res. 1999; 18:669-87.
8. Williamson TH, Lowe GDO, Baxter GM. Influence of age, systemic blood pressure, smoking, and blood viscosity on orbital blood velocities. Br J Ophthalmol. 1995; 79:17-22.
9. Schmidt KG, von Rückmann AV, Mittag TW, Hessemer V, Pillunat LE. Reduced ocular pulse amplitude in low tension glaucoma is independent of vasospasm. Eye (Lond). 1997; 11(Pt 4):485-8.
10. Planiol T, Pourcelot L, Pottier J-M, Degiovanni E. Etude de la circulation carotidienne par les methodes ultrasoniques et al thermographie. Rev Neurol. 1972; 126:127-41.
11. Harris A, Williamson TH, Martin B, Shoemaker JA, Sergott RC, Spaeth GL, et al. Test/retest reproducibility of color Doppler imaging assessment of blood flow velocity in orbital vessels. J Glaucoma. 1995; 4:281-6.
12. Baxter GM, Williamson TH, McKillop G, Dutton GN. Color Doppler ultrasound of orbital and optic nerve blood flow: effects of posture and timolol 0.5%. Invest Ophthalmol Vis Sci. 1992; 33:604-10.

13. Galassi F, Nuzzaci G, Sodi A, Casi P, Vielmo A. Color Doppler imaging in the evaluation of optic nerve blood supply in normal and glaucomatous subjects. Int Ophthalmol. 1992; 16:273-6.
14. Lieb WE, Cohen SM, Merton DA. Color Doppler imaging of the eye and orbit: technique and normal vascular anatomy. Arch Ophthalmol. 1991; 109:527-32.
15. Punjabi OS, Ho HK, Kniestedt C, Bostrom AG, Stamper RL, Lin SC. Intraocular pressure and ocular pulse amplitude comparisons in different types of glaucoma using dynamic contour tonometry. Curr Eye Res. 2006; 31:851-62.
16. Flammer J, Orgul S. Optic nerve blood-flow abnormalities in glaucoma. Prog Ret Eye Res. 1998; 17:267-89.
17. Kaiser HJ, Schötzau A, Stumpfig D, Flammer J. Blood-flow velocities of the extraocular vessels in patients with high tension and normal-tension primary open-angle glaucoma. Am J Ophthalmol. 1997; 123:320-7.
18. 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; 38:690-6.
19. Williamson TH, Harris A. Color Doppler ultrasound imaging of the eye and orbit. Surv Ophthalmol. 1996; 40:255-67.
20. Akarsu C, Bilgili MY. Color Doppler imaging in ocular hypertension and open-angle glaucoma. Graefes Arch Clin Exp Ophthalmol. 2004; 242:125-9.
21. Onda E, Cioffi GA, Bacon DR, Van Buskirk EM. Microvasculature of the human optic nerve. Am J Ophthalmol. 1995; 120:92-102.
22. Joos KM, Kay MD, Pillunat LE, Harris A, Gendron EK, Feuer WJ, et al. Effect of acute intraocular pressure changes on short posterior ciliary artery haemodynamics. Br J Ophthalmol. 1999; 83:33-8.
23. Nicolela MT, Walman BE, Buckley AR, Drance SM. Ocular hypertension and primary open-angle glaucoma: a comparative study of their retrobulbar blood flow velocity. J Glaucoma. 1996; 5:308-10.
24. Harris A, Jonescu-Cuypers CP. The impact of glaucoma medication on parameters of ocular perfusion. Curr Opin Ophthalmol. 2001; 12:131-7.

Промене у ретробулбарној артеријској циркулацији након смањења повишеног интраокуларног притиска код особа с примарним глаукомом отвореног угла

Иван Марјановић[1], Ана Шундић[2], Милија Мијајловић[2], Надежда Човичковић-Штернић[2], Ђорђе Контић[1], Параскева Хентова-Сенћанић[1], Вујица Марковић[1], Марија Божић[1], Мирослав Кнежевић[1]

[1]Клиника за очне болести, Клинички центар Србије, Београд, Србија;
[2]Клиника за неурологију, Клинички центар Србије, Београд, Србија

КРАТАК САДРЖАЈ

Увод Поремећена перфузија главе очног живца је патогенетски фактор код глаукома.

Циљ рада Циљ рада био је да се установи како се мењају хемодинамски параметри у ретробулбарној артеријској циркулацији након смањења повишеног интраокуларног притиска (ИОП) код пацијената с примарним глаукомом отвореног угла.

Методе рада Истраживање је обухватило 26 испитаника (14 мушкараца и 12 жена), од којих је 21 пацијент био старији од 50 година, са претходно дијагностикованим и леченим примарним глаукомом отвореног угла. Сви пацијенти су прегледани на Клиници за очне болести КЦС. Поред мерења ИОП Голдмановим (*Goldmann*) апланационим тонометром (*GAT*), односно динамичким контурним тонометром (*DCT*), испитаницима је измерена и централна дебљина рожњаче ултразвучним пахиметром. Преглед ретробулбарне артеријске циркулације колор доплером обављен је на Клиници за неурологију КЦС. Он је обухватио хемодинамске промене у офталмичкој артерији, централној ретиналној артерији и задњим цилијарним артеријама. Посматрани су следећи параметри: вршни систолни волумен (*PSV*), завршни дијастолни волумен (*EDV*), индекс резистенције (*RI*) и индекс пулсатилности (*PI*).

Резултати Хемодинамски артеријски параметри *PSV* и *EDV* у офталмичкој и централној ретиналној артерији након смањења ИОП су се смањили, док су се *RI* и *PI* повећали. Код кратких задњих цилијарних артерија *PSV*, *EDV* и *PI* су се смањили, док се *RI* повећао.

Закључак Промене у ретробулбарној артеријској циркулацији током повећања ИОП код особа с примарним глаукомом отвореног угла значајне су за приступ и лечење, док улога васкуларних фактора у исхрани неуроретиналног обода главе очног живца може бити кључ у успоравању прогресије глаукома и основа неуропротекције.

Кључне речи: повишен интраокуларни притисак; ретробулбарна артеријска циркулација; примарни глауком отвореног угла

Примљен • Received: 15/10/2010 **Прихваћен • Accepted:** 01/02/2011