Correlation between Ocular Pulse Amplitude Measured by Dynamic Contour Tonometer and Colour Doppler Flow Imaging of the Arteric Retrobulbar Vessels

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INTRODUCTION

Glaucoma is one of the leading causes of vision loss worldwide. The number of people with primary glaucoma in the world in 2000 was estimated at nearly 67 million [1].

This syndrome of progressive optic neurological damage to the nerve fibres, characterized by optic nerve head excavation, has been known for many years. However, the exact mechanisms leading to this specific type of damage is not yet well understood. Elevated intra-ocular pressure 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].

Pascal Dynamic Contour Tonometry (DCT), developed by Swiss Microtechnology AG (Port, Switzerland), was used in this study to quantify one of the parameters of ocular blood flow — ocular pulse amplitude (OPA).

DCT is a non-applanation contact tonometer [6] designed to be largely independent of the structural properties of the cornea, especially central corneal thickness (CCT) [7]. This device has a contour-matched pressure-sensing tip applied to the corneal surface for a few seconds with a small constant force allowing direct continuous transcorneal intraocular pressure (IOP) measurements. While in contact with the eye, it records the systolic and diastolic IOPs and their difference to determine OPA [8].

By recording the pulsatile component of the ocular blood flow (heart pulse as a function of time), OPA may provide an indirect measurement of the choroidal perfusion and reflects the ocular blood flow. It has been suggested that this parameter could be an independent risk factor for glaucoma and possibly for normal tension glaucoma [8, 9].

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 [10, 11]. We hypothesized that OPA might also be reduced in patients with glaucoma. 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 (NTG) or also in primary open angle glaucoma (POAG) is controversial [5, 12].

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 the 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-dependent. To relate the systolic and diastolic velocities to each other, a ratio, the resistive index (Pourcelot’s index), is used [13]. 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 [14] 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 the correlation between OPA, measured by DCT and CDI of the retrobulbar vessels, in patients with normal tension glaucoma, ocular hypertension and suspected glaucoma.

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 2008 and March 2009. All patients were obtained from the General Ambulatory Ophthalmology Unit.

We examined 20 patients (40 eyes), four male and 16 female. All patients were older than 50 years and were divided into two equal groups. The first group comprised patients with normal tension glaucoma, with topical antiglaucomatous therapy. The diagnosis of NTG was based on normal intraocular pressure (≤22 mm Hg), open angle on gonioscopy, glaucomatous visual field defects, and glaucomatous cupping of the optic disk. The second group included patients with ocular hypertension and suspected glaucoma without any antiglaucomatous therapy. The diagnosis of ocular hypertension was based on elevated intraocular pressure (>22 mm Hg), normal visual fields, and normal appearing optic nerve heads. Normal controls involved subjects with normal visual fields, intraocular pressures, and appearance of optic nerve heads. This group consisted primarily of the spouses of the patients.

Patients were excluded from the study if they had any of the following: 1) narrow/closed angle on gonioscopy (grades 0, 1, and 2 using the Scheie classification); 2) astigmatism >2 D 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.

Ocular pulse amplitude was measured after topical anaesthesia (Sol. Tetracaine 1%), with the DCT by one investigator. Colour Doppler imaging (CDI) was also performed by one investigator.

We measured haemodynamic parameters of the internal carotid artery (ICA), ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary arteries (PCA). Peak systolic (PSV), end-diastolic (EDV) velocities were measured, and resistance index (RI) and pulsatility index (PI) were calculated using ultrasound machine Aloka Alpha 10; 7.5–10 MHz, linear probe.

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

In both observed groups OPA had normal data distribution. In the first observed group mean was 2.31 mm Hg and SD ±0.98 (p<0.05) (Graph 1).

In the second observed group, mean was 4.16 mmHg, and SD ±1.63 (p<0.05) (Graph 2).

In the first observed group, correlation between OPA and PCA was direct in all parameters: OPA=PCA-PSV, with ρ=+0.29 (p>0.05); OPA=PCA-EDV, with ρ=+0.06 (p>0.05); OPA=PCA-RI, with ρ=+0.1 (p>0.05); OPA=PCA-PI, with ρ=+0.12 (p>0.05). Correlation between OPA and ICA was direct in three parameters: OPA=ICA-PSV with r=+0.12 (p>0.05); OPA=ICA-RI, with r=+0.43 (p<0.05); and OPA=ICA-PI, with r=+0.13 (p>0.05); but indirect in OPA=ICA-EDV, with r=−0.02 (p>0.05) (Graph 3).
Graph 1. OPA data distribution in the first observed group

Graph 2. OPA data distribution in the second observed group

Graph 3. Correlation between OPA in ICA and EDV, in the first observed group

Graph 4. Correlation between OPA and CRA, through RI

Graph 5. Correlation between OPA and CRA, through PI

Graph 6. Second observed group, correlation between OPA and PCA, through RI
Correlation between OPA and OA was direct in all parameters: OPA∞OA-PSV, with \( r = +0.12 \) (p>0.05); OPA∞OA-EDV, with \( r = +0.07 \) (p>0.05); OPA∞OA-RI, with \( r = +0.06 \) (p>0.05); and OPA∞OA-PI, with \( r = +0.10 \) (p>0.05).

Correlation between OPA and CRA was direct in OPA∞CRA-PSV, with \( r = +0.26 \) (p>0.05) and OPA∞CRA-EDV, with \( r = +0.5 \) (p<0.05, with statistical significance). Indirect correlation was in OPA∞CRA-RI, with \( r = -0.02 \) (p>0.05) (Graph 4); and OPA∞CRA-PI, with \( r = -0.13 \) (p>0.05) (Graph 5).

In the second observed group correlation between OPA and PCA was direct in OPA∞PCA-PSV, with \( r = +0.07 \) (p>0.05); OPA∞PCA-EDV, with \( r = +0.08 \) (p>0.05) and OPA∞PCA-PI, with \( r = +0.05 \) (p>0.05); and indirect was in OPA∞PCA-RI, with \( r = -0.03 \) (p>0.05) (Graph 6).

Correlation between OPA and ICA was indirect in OPA∞ICA-PSV, with \( r = -0.01 \) (p>0.05) (Graph 7), and OPA∞ICA-EDV, with \( r = -0.19 \) (p>0.05) (Graph 8); direct in OPA∞ICA-RI, with \( r = +0.01 \) (p>0.05) and OPA∞ICA-PI, with \( r = +0.51 \) (p<0.05, with statistical significance).

Correlation between OPA and OA was direct in OPA∞OA-PSV, with \( r = +0.21 \) (p>0.05) and OPA∞OA-EDV, with \( r = +0.06 \) (p>0.05); but indirect in OPA∞OA-RI, with \( r = -0.14 \) (p>0.05) (Graph 9) and OPA∞OA-PI, with \( r = -0.06 \) (p>0.05) (Graph 10).

Correlation between OPA and CRA was direct in OPA∞CRA-PSV, with \( r = +0.25 \) (p>0.05) and OPA∞CRA-PI, with \( r = +0.1 \) (p>0.05), but indirect in OPA∞CRA-EDV, with \( r h o = -0.19 \) (p>0.05) (Graph 11) and OPA∞CRA-RI, with \( r = -0.02 \) (p>0.05) (Graph 12).

**DISCUSSION**

In our study, with normal data distribution, OPA was found to be higher in the second (4.2 mm Hg) than in the first (2.3 mm Hg) observed group, and among the patients in the second group it was higher among OHT patients (4.8 mm Hg) than in the healthy subjects (3.3 mm Hg). Other studies also found that OPA was highest in the OHT group (3.60 mm Hg) and lowest in healthy controls group (2.86 mm Hg) and was found to increase with GAT and DCT IOP in all the groups, except in the OHT group [15]. Schmidt et al. [16] studied OPA in different types of glaucoma and found ocular hypertensives to have a significantly higher OPA than other groups.

OPA may be affected by the nature and dosage of medication used differently in the groups, which is something that would be very difficult to control [15].

Various studies have compared the vascular parameters in primary open-angle glaucoma and normal tension glaucoma with those of normal control subjects. This conclusion correlates with our results. In most of these studies, patients’ IOPs were controlled by treatment, so there was no significant difference between IOP in the groups under study.

In our study increase of the OPA was followed by the increase of the PSV in the PCA, ICA, OA and CRA; EDV in the PCA, OA and CRA; RI in the PCA, ICA and OA; and PI in the PCA, ICA and OA, in the normal tension glaucoma patients.

Other studies of retrobulbar circulation in glaucoma reported a significant reduction in the end diastolic velocity and an increase in the resistive index of the vessels of this region in patients with glaucoma [9].

Harris et al. [16] compared 10 normal-tension glaucoma patients with nine age and sex-matched controls and found a significant reduction of the end diastolic velocity and an elevation of the resistive index of the ophthalmic artery in the glaucoma group. These changes were not evident in the central retinal or short posterior ciliary arteries. Butt et al. [17] confirmed this finding in the ophthalmic arteries of 34 patients with normal-tension glaucoma and also identified an elevated resistive index in the central retinal artery as compared with normal controls.

In our study, among the OHT patients and normal controls, the increase of the OPA was followed by the increase of the PSV in the PCA, OA and CRA; EDV in the PCA and OA; RI in the ICA; and PI of the PCA, ICA and CRA.

Several studies support the idea that circulatory abnormalities represent risk factors for glaucoma [18]. With the use of Doppler ultrasound of the orbit, a non-invasive examination of the retrobulbar circulation is possible. Several studies using orbital colour Doppler imaging have revealed altered orbital haemodynamics in patients with glaucoma [19, 20].

Resistivity index is a factor related to blood flow resistance in the vascular system downstream to the measurement point [21].

According to our results, in the correlation between OPA and observed parameters, data distribution was mostly normal, except between OPA and EDV of the PCA in the first observed group, and OPA and EDV of the CRA in the second observed group.

Akarsu and Bilgili [22] found that PSV and EDV were lower and RI was higher in all retrobulbar arteries in the ocular hypertensive patients than in the normal subjects. Previous studies showed significant differences in the ocular circulation between glaucomatous eyes and ocular hypertensive eyes [23]. They found lower end-diastolic velocity and higher RI in the posterior ciliary artery in open-angle glaucoma than in ocular hypertension [22].

As we previously mentioned, in our study the increase of OPA was followed by the increase of PSV in the PCA, ICA, OA and CRA; EDV in the PCA, OA and CRA; RI in the PCA, ICA and OA; and PI in the PCA, ICA and OA, among the normal tension glaucomatous patients. Among the OHT patients and normal controls, the increase of OPA was followed by the increase of PSV in the PCA, OA and CRA; EDV in the PCA and OA; RI in the ICA; and PI of the PCA, ICA and CRA.

Nicoletta et al. [23] found a reduction in the central retinal artery flow velocity in glaucoma patients compared with ocular hypertension. The present study also confirmed the study which reported no significant difference in pulsatile ocular blood flow between ocular hypertensive patients.
Graph 7. Second observed group, correlation between OPA and ICA, through PSV

Graph 8. Second observed group, correlation between OPA and ICA, through EDV

Graph 9. Second observed group, correlation between OPA and OA, through RI

Graph 10. Second observed group, correlation between OPA and OA, through PI

Graph 11. Second observed group, correlation between OPA and CRA, through EDV

Graph 12. Second observed group, correlation between OPA and CRA, through RI
and normal subjects [24]. The general agreement is that the main blood supply of the anterior optic nerve is from the posterior ciliary arteries [25].

Cheng’s study had controlled factors, which are known to affect ocular blood-flow velocity, such as intraocular pressure [26], age [11], systemic blood pressure [23], and anti-glaucoma medications [27]; therefore, they hoped to eliminate the effect of these variables and to give a more useful comparison between glaucoma and ocular hypertensive patients.

Clinically, it is not possible to accurately predict who will develop glaucomatous optic neuropathy. Based on the assumption that defective blood flow contributes to the development of glaucomatous optic neuropathy, it may be expected that one subgroup of ocular hypertensive patients with a lower blood-flow velocity could develop glaucomatous optic neuropathy, or at least these subjects may be at much higher risk for the development of damage.

**CONCLUSION**

Increase of OPA is mostly accompanied by the increase of the parameters of the retrobulbar vessels in normal tension glaucoma patients. In ocular hypertension and glaucoma suspected patients, the increase of OPA is in almost 50% of the parameters associated with their decrease. Statistical significance in our study appears in the correlation between OPA and EDV of the CRA, in normal tension glaucoma patients, and in the ocular hypertension and glaucoma suspected patients, in the correlation between OPA and PSV of the ICA. Colour Doppler imaging of the blood flow in retrobulbar vessels is a valuable method in the diagnosis of the vascular mechanism in optic neuropathy.

**NOTE**

This work was presented as a short oral presentation at the DOG congress (German Ophthalmic Society), Leipzig, September 2009.

**REFERENCES**

Корелација између окуларне пулсне амплитуде мерене динамичким контурним тонометром и протока крви кроз ретробулбарне артеријске крвне судове мереног колор доплером

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КРATAK САДРЖАЈ
Увод Перемећена перфузија главе очног живца је патогенетски фактор код глукома.
Циљ рада Циљ рада је био да се утврди корелација између окуларне пулсне амплитуде (енгл. ocular pulse amplitude – OPA) измерене динамичким контурним тонометром (енгл. dynamic contour tonometer – DCT) и налаза колор доплера артеријских ретробулбарних крвних судова.
Методе рада Испитано је 20 пацијената старијих од 50 година, који су сврстани у две једнаке групе. Прву групу чинили су испитаници с нормотензивним глукомом који су примали топикалну антиглаукомну терapiју, а другу групу пацијенти с очном хипертензијом и они код којих се сматрали на глуком. OPA је мерена динамичким контурним тонометром. Свим испитаницима је урађен колор доплер ретробулбарних артеријских крвних судова. Хемодинамски параметри су мерени у унутрашњој каротидној артерији, офталмичкој артерији, централној ретиналној артерији и задњим цилиарним артеријама. Мерени су параметри вршне систолне и завршне дијастолне фазе, те израчунавани индекси резистенције и пулзатилности.
Резултати У првој групи болесника корелација са OPA била је индиректна у индексу резистенције код унутрашње каротидне артерије, као и у индексима резистенције и пулзатилности код централне ретиналне артерије. У другој групи индиректна корелација постојала је између: вршне систолне и завршне дијастолне фазе унутрашње каротидне артерије, индекса резистенције и пулзатилности офталмичке артерије, завршне дијастолне фазе и индекса резистенције централне ретиналне артерије и индекса резистенције задњих цилиарних артерија.
Закључак Пораст OPA углавном је био праћен повећањем вредности посматраних параметара артеријских ретробулбарних крвних судова у првој групи, док је у другој пораст OPA у скоро 50% параметара био праћен њиховим смањењем.
Кључне речи: окуларна пулсна амплитуда; динамички контурни тонометар; колор доплер крвних судова

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