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Original Article

A Color Doppler Imaging Study of Ocular Haemodynamic Parameters in Primary Open Angle Glaucoma (POAG)

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Abstract

Aims: *To study retrobulbar haemodynamics in primary open angle glaucoma (POAG) patients.*

Methods: *It was a hospital based cross-sectional study carried out in Medical College Out Patient Department (OPD). A total of 26 patients with newly diagnosed POAG and 23 controls were randomly selected for the study. The haemodynamic parameters i.e. Peak systolic velocity (PSV), End diastolic velocity (EDV) and resistivity index (RI) were studied in ophthalmic artery (OA), central retinal artery (CRA) and short posterior ciliary arteries (SPCA) measured using Color Doppler imaging (CDI). Mean, standard deviation (SD) and Independent t- test was applied to compare the results between the two group.*

Results: *The mean intraocular pressure (IOP) for the POAG group and control group was 26.31±4.51 mmHg and 17.04±1.26 mmHg, respectively (P < 0.001). The mean PSV for both OA and CRA, the mean EDV for all OA, CRA and SPCA were significantly lower whereas the mean RI in the CRA and SPCA were significantly higher in POAG than controls.*

Conclusions: *Retrobulbar blood flow was significantly lower in POAG as compared to controls, thereby suggesting the importance of measuring the retrobulbar blood flow in POAG patients.*

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Keywords: *Color Doppler imaging (CDI), Primary open angle glaucoma (POAG), End diastolic velocity (EDV), Peak systolic velocity (PSV), Resistivity index (RI), Retro bulbar blood flow, Ocular Haemodynamic Parameters*

Introduction

CDI is an important non- invasive tool for measuring retrobulbar flow which can play an important role in assessing ocular haemodynamic parameters in diagnosing & monitoring treatment effect in POAG. As the definition of glaucoma has changed, raised intra ocular pressure has been distinguished as one of the main risk factors for primary open angle glaucoma. Growing evidence from clinical studies suggested that circulatory abnormalities can be involved in the pathogenesis of glaucomatous optic nerve disease, which indicates that vascular factors likely play a role.[1,2] These observations support the idea that the eye being treated for glaucoma could possibly be a part of wider systemic dysfunction, particularly of blood flow regulation. This hypothesis is further backed up by observation of progression of disease in certain patients despite the IOP control.[3]

Now many non-IOP factors have also been identified as contributing to primary open-angle glaucoma progression, including lower ocular perfusion pressure, reduced ocular blood flow, cardiovascular disease, and low systolic blood pressure. Impaired optic nerve blood flow is considered a potential causative factor in the development of glaucoma optic atrophy.[4]

New technologies for ocular blood flow evaluation have been introduced to clinical ophthalmology, and Color Doppler imaging (CDI) has been particularly useful because of its non-invasiveness and the reliability of its results. Color Doppler imaging has been widely used in glaucoma to study pathogenic aspects of the disease and the vascular effects of its treatment. Color Doppler Imaging is an established method for qualitative assessment of blood flow in retrobulbar vessels (Ophthalmic artery, Central Retinal and Short Posterior Ciliary Artery). The fact that the optic nerve head perfusion is directly related to retrobulbar circulation, that is directly accessible to ultrasound study makes Color Doppler imaging a potential tool for the evaluation of early changes in vascular flow related to glaucoma.[5] Therefore, this study has been conducted to with the objectives to study retrobulbar haemodynamics in primary open angle glaucoma (POAG) patients and compare it with healthy control group.

Materials and Methods

This was a hospital based cross-sectional study carried out in a outpatient department of a tertiary eye care centre for a period of one year i.e. from July 2014 to June 2015. A total of 26 patients with established POAG and 23 matched controls were randomly selected for the study. Inclusion criteria for the POAG group were raised IOP >21 mmHg, gonioscopically open angles with characteristic optic disc appearance and visual field defects. Patients with lenticular and other media opacities, uveitis, myopia or hyperopia of more than or equal to 5 Dioptres, retinal disorders other than glaucoma, and those with systemic diseases or on systemic drugs for example diabetes, systemic hypertension, any cardiovascular disease, any neurological problem were excluded from the study.

Automated perimetry was performed using Humphery's Field Analyser. An ISTYLE (TOSHIBA Company) machine with 6-12 mHz linear high frequency probe was used for Color Doppler Imaging in the Medical College Radiodiagnosis Department. The examination was performed by a single experienced sonographer, who was unaware of subject's clinical status. The test was performed with undilated pupil. Patient was asked to lie supine with the eye closed and gaze directed to the ceiling. The ultrasound transducer was applied with sterile ophthalmic methylcellulose as a coupling agent, through the closed upper lid. The examiner's hand rested on the orbital margin to minimise the pressure over globe. Each eye was initially examined with B-scan in both transverse and sagittal planes. The right eyes of both groups were used for the study to avoid variability between right and left side circulation that may confound the result.

This non-invasive method is based on the back-scattering of ultrasound by the formed elements in the blood vessels. Doppler effect results in frequency shifts, the measurement of which helps to assess blood velocity. In orbital CDI blood flow towards the transducer (usually arterial) is encoded as red and flow away from the transducer (usually venous) is encoded as blue. The anatomy of the eye followed by that of the optic nerve head were identified using the grey scale images in the B-scan mode. Color Doppler was used to visualize the flow within the vessels and allowed for identification of the appropriate vessels. Care was taken to place the sample volume in the centre of the vessel and to set the angle parallel to the vessel to account for the Doppler angle. Pulsed Doppler with spectral analysis is used in conjunction with the colour Doppler image for accurate quantification of the flow characteristics of vessels.

The sample volume depth was set at about 40 mm when imaging the ophthalmic artery (OA). The Doppler sample gate (≤2 mm) was then placed at the centre of the detected vessel to image the spectral pattern. The parameters of OA flow was measured nasally and superior to optic nerve soon after it crosses the optic nerve.[6] The flow velocity wave form of the ophthalmic artery (OA) is similar to that of the internal carotid artery, showing a high maximum peak systolic flow and low diastolic flow velocity. A dicrotic notch because of aortic valve closure is usually present and a window indicate relatively uniform blood velocity. (Figure 1)

The central retinal artery (CRA) leaves the second part of the OA and enters the inferior surface of the optic nerve about 12 mm behind the globe.[7] It possess straighter course in optic nerve and lie in close proximity to the central retinal vein. With orbital CDI the CRA and CRV are easily identified within the optic nerve and their colour images are immediately adjacent to each other with artery on the nasal side and the vein to the temporal side. CRA waveform shows pulsatile arterial flow with a steep systolic peak suggesting a high-resistance distal vascular bed. (Figure 2)

The nasal and temporal short posterior ciliary arteries (NPCA and TPCA) are located on each side of the optic nerve and need to be measured at a position that is close to the optic nerve.[8] It should also be as anterior as possible to avoid receiving noise from the choroid. Color Doppler imaging could not distinguish individual short posterior ciliary vessels. Therefore, the obtained waveform represented the mass effect produced by bundle of vessels rather than from individual ciliary vessels. The waveform in these vessels are almost similar to CRA but often with a sharper PSV. (Figure 3)

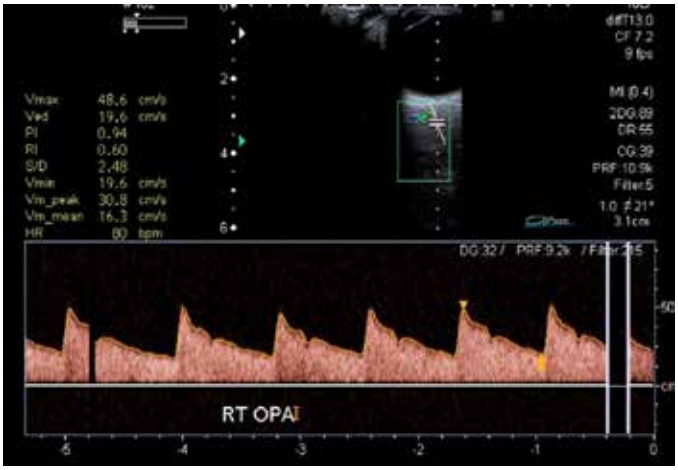

Figure 1: *Color doppler image of vessel and corresponding waveform of ophthalmic artery*

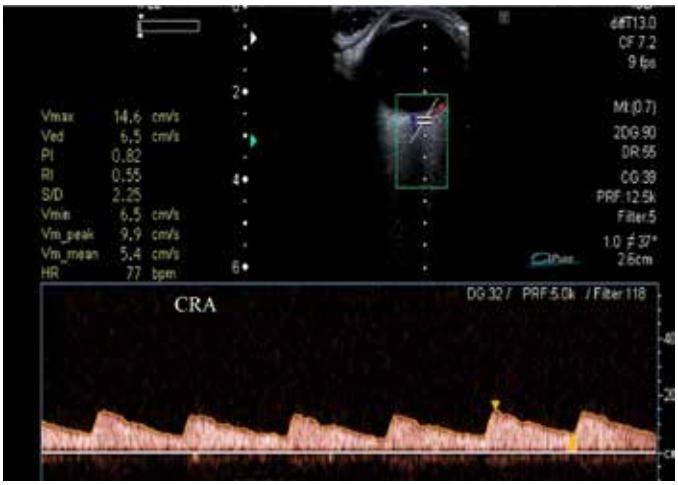

Figure 2: *Color doppler image of vessel and corresponding waveform of central retinal artery*

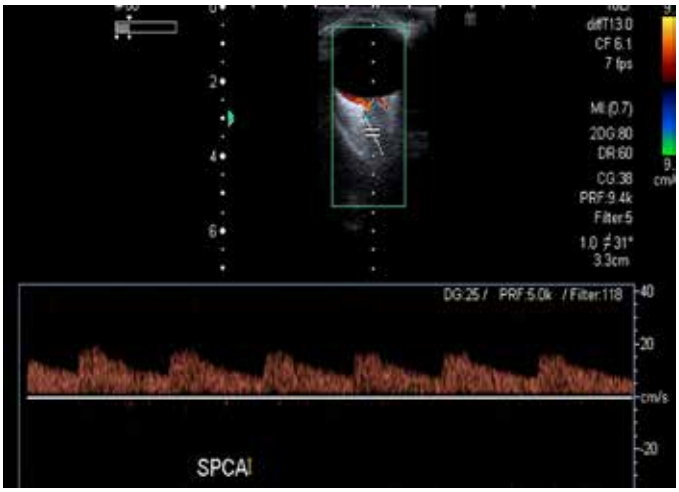

Figure 3: *Color doppler image of vessel and corresponding waveform of posterior ciliary artery*

The Peak Systolic Velocity (PSV) and End Diastolic Velocity (EDV) values were obtained by taking the velocity reading at the peak of the spectral wave pattern and that at the wave trough, respectively. Three readings of each artery were obtained and the average was taken, this was to minimize intra observer error. Resistive index (RI) was calculated as (PSV − EDV)/ PSV.

A written informed consent was taken from each participant after explaining them about the nature & consequence of study. Privacy & confidentiality was assured. The study protocol was approved by the institutional ethics committee of the Medical College.

Statistical Analysis

Data was entered and analyzed using SPSS software ver 20. Data normalcy was checked using Shapiro-Wilks test. Descriptive analysis in the form of mean and SD was done. Inferential analysis in the form of independent t- test was used to compare the difference in haemodynamic parameters of retrobulbar flow between POAG and control group. P value less than 0.05 was considered statistically significant.

Results

Baseline characteristics of study population

Table 1 shows the baseline characteristics of study population. The study population comprised of 26 males (POAG- 14, control- 12) & 23 females (POAG- 09, control- 14) (p= 0.393). The mean age of POAG group was 49.39±9.56 years while that of control group was 52.00±13.64 years (p= 0.448). The mean IOP of POAG patients (26.31±4.51 mm Hg) was significantly higher than controls (17.04±1.26 mm Hg).

The mean systolic blood pressure (SBP), diastolic blood pressure (DBP) & pulse rate (PR) of POAG patients were 128.38±8.06 mm Hg, 79.54±5.10 mm Hg & 81.31±6.74 beats per minute respectively while that of controls were 128.96±5.18 mm Hg, 80.35±3.98 mm Hg & 79.65±5.89 beats per minute respectively (p> 0.05, non- significant). (Table 1)

The mean axial length (AXL) & anterior chamber depth (ACD) among POAG patients were 23.02±0.71 mm & 3.71±0.59 mm respectively while that of controls were 22.99±0.70 mm & 3.48±0.53 respectively (p> 0.05, non- significant). (Table 1)

Table 1: Baseline characteristics of study population

PARAMETERS	CONTROLS (n=23)	POAG (n=26)	P value
Sex (male/female)	14/09	12/14	0.393
	MEAN ± SD	**MEAN ± SD**	
Age (years)	49.39±9.56	52.00±13.64	0.448
IOP (mmHg)	17.04±1.26	26.31±4.51	**<0.001**
PR (beats/min)	79.65±5.89	81.31±6.74	0.368
SBP (mmHg)	128.96±5.18	128.38±8.06	0.772
DBP (mmHg)	80.35±3.98	79.54±5.10	0.543
AXL (mm)	22.99±0.70	23.02±0.71	0.932
ACD (mm)	3.48±0.53	3.71±0.59	0.174

IOP- intraocular pressure, PR- pulse rate, SBP- systolic blood pressure, DBP- diastolic blood pressure, AXL- axial length, ACD- anterior chamber depth

Comparison of haemodynamic parameters of retro bulbar flow using Color Doppler imaging (CDI)

Table 2 compares haemodynamic parameters between POAG & control using CDI. In ophthalmic artery (OA), the mean peak systolic velocity (PSV) & end diastolic velocity (EDV) was significantly lower in POAG patients as compared to controls whereas no significant difference in mean resistive index (RI) was seen in POAG patients & controls. (Table 2)

In central retinal artery, the mean peak systolic velocity (PSV) & end diastolic velocity (EDV) was significantly lower in POAG patients as compared to controls whereas the resistive index (RI) in POAG patients was significantly higher than controls. (Table 2)

In short posterior ciliary arteries (SPCA), end diastolic velocity (EDV) was significantly lower in POAG patients as compared to controls; the resistive index (RI) in POAG patients was significantly higher than controls whereas no significant difference in mean peak systolic velocity (PSV) was seen in POAG patients & controls. (Table 2)

Table 2: Comparison of ocular haemodynamic parameters of control and primary open angle glaucoma patients

PARAMETERS	CONTROL (n=23) MEAN ± SD	POAG(n=26) MEAN ± SD	P value
OA-PSV	38.79±9.07	17.60±6.57	**<0.001**
OA-EDV	13.70±6.26	5.04±2.68	**<0.001**
OA-RI	0.64±0.11	0.69±0.12	0.147
CRA-PSV	11.37±2.68	9.62±2.79	**0.031**
CRA-EDV	4.05±1.49	2.75±1.23	**0.002**
CRA-RI	0.63±0.12	0.76±0.25	**0.028**
SPCA-PSV	12.28±2.22	11.05±3.80	**0.178**
SPCA-EDV	5.05±1.69	3.87±2.08	**0.035**
SPCA-RI	0.58±0.11	0.68±0.20	**0.047**

PSV = Peak Systolic Velocity, EDV = End Diastolic Velocity, RI =Resistive Index

Discussion

The problem in the optic nerve circulation resulting from localized organic changes in the blood vessels of the nerve with or without a low perfusion pressure has been implicated as one of the likely mechanisms in the pathogenesis of glaucomatous damage. The OA, CRA and SPCA are vessels in providing evidence of the influence of vascular factors in pathogenesis of glaucomatous optic neuropathy.[9] Color Doppler Imaging is a reproducible technique for evaluation of ocular vessels.[10] The blood flow velocities in these vessels in glaucomatous and non-glaucomatous eyes were the focus of this study.

Present study observed statistically significant lower blood flow velocities; both mean peak systolic velocity (PSV) and mean end diastolic velocity (EDV) in Ophthalmic Artery (OA) and Central Retinal Artery (CRA) in 26 untreated patients of glaucoma when compared to 23 normal subjects. Mean end diastolic velocity (EDV) was significantly lower in Short Posterior Ciliary Artery (SPCA) in POAG patients when compared to normal subjects. Mean RI was increased in all the three vessels but statistically significant result was achieved only in CRA and SPCA. Similar to our outcome, Rojanapongpun et al observed significant reduction in mean PSV and mean EDV of Ophthalmic Artery in POAG patients

when compared to normal subjects.[11] Januleviciene et al observed statistically significant difference in mean EDV in ophthalmic artery and mean PSV in the central retinal artery between the OAG subjects and the control group.[12] Our findings are also supported by similar studies conducted by Akarsu et al who reported decreased EDV in all three vessels.[13] Kaiser et al showed significant decrease in EDV and a significant increase in RI in all arteries measured OA, CRA and SPCA.[14] Similarly, Brinci et al observed an association of decreased flow velocity and increased resistivity index in retro bulbar vasculature of patients suffering from primary open angle glaucoma.[15] Butt et al observed significantly reduced EDV of CRA and significantly higher RI of OA, CRA in POAG when compared to normal.[16] Likewise, Rankin et al observed statistically significant decrease in the mean EDV and an increase in the mean RI in all vessels studied OA, CRA and SPCA in POAG patients when compared to normal subjects.[17]

In the above mentioned clinical studies, increased RI has been reported in all the three vessels beside reduction in blood velocity. Polska et al reported in an experimental study that CDI observed RI in central artery of retina does not correspond to the actual resistance in retinal vasculature.[18] There has not been much data published on the reliability of RI in reference to ocular vessels. Many studies reported that RI depends on the amplitude of pulse pressure.[19,20] A reduction in pulse pressure amplitude induced by physiological stimuli was reported to be associated with a decrease in the RI in the OA as well as in posterior ciliary arteries (PCAs).[20] In our clinical study, no statistically significant difference was noted in RI in ophthalmic artery between POAG cases and controls. Thus, concluding that resistivity Index does not correlate with the vascular resistance in ophthalmic artery. Thus, these findings correlate more with experimental studies and less with the clinical studies mentioned earlier.[13-15]

In our study, no statistically significant difference was found in mean PSV of SPCA in POAG patients when compared to controls. Reproducibility of the value obtained by the CDI in SPCA are very poor. The most relevant of these factors are, on the one hand, the short length of the vessels, tortuous course and unknown number of vessels within probing volume which makes it very difficult to apply the correction angle and on the other the broad spectrum of waves that are recorded when measuring said vessels makes their identification more difficult. On the other hand, reproducibility of the OA and CRA with CDI are much better than SPCA because it can be easily identified in the optic nerve head and it has straighter course. Thus, the findings of the other studies are being reciprocated in this study also. Conclusions: The study results showed significant decreased flow and increased resistivity index in ocular vasculature in POAG as compared to healthy controls. CDI may provide a mean of measuring part of vascular component in glaucoma. This study suggests that in the diagnosis of glaucoma, it is necessary to know not only the IOP, but also the ocular blood flow.

Limitations

The limitation of this study was fewer number of patients. This study being a cross-sectional study on newly diagnosed POAG group yet to commence anti-glaucoma medications could not assess the effect of lowering IOP on the blood flow parameters studied. The other limitation was that CDI measures the flow within vessels that supply ocular tissues but not the flow within the retinal tissue or directly at the level of the ganglion retinal cells.

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