Comparison of ophthalmic artery blood flow between open-angle glaucoma and nonglaucomatous eyes of Indian patients

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Abstract:
This study was undertaken to compare ophthalmic artery blood flow in eyes having primary open angle glaucoma (POAG) with age matched non glaucomatous eyes using the technique of Color Doppler imaging in Indian patients. One hundred patients of either sex over 40 years of age were divided into two groups of 50 patients each. Group 1 included 50 patients diagnosed with POAG whereas group 2 included patients who did not have POAG. Tests like visual fields and OCT RNFL were conducted and a radiologist assessed the ophthalmic artery blood flow using Color Doppler imaging. Hemodynamic calculations of ocular blood flow were done using the parameters of resistivity index (RI) and pulsatility index (PI). Statistically significant increase in the values of RI and PI were noted in patients with POAG as compared to those who did not have POAG.

Keywords:
Optical coherence tomography retinal nerve fiber layer, primary open-angle glaucoma, pulsatility index, resistivity index

Introduction

Studies demonstrate that in a significant number of patients, glaucomatous deterioration of visual fields continues despite adequate intraocular pressure (IOP) control. This evidence strongly suggests that although elevated IOP may contribute to the pathophysiology of glaucoma, it does not account for the disease process in its entirety. In recent decades, alterations in ocular blood flow and abnormal vascular autoregulation are emerging as key components to enhance our understanding of the disease process of glaucoma.[1]

Hayreh and Walker in 1967 studied the fluorescence pattern of the optic disc and its relationship to cupping of the optic disc and field defects. They observed a reduction in the fluorescence of the optic disc in a large number of patients with significant changes at the optic disc and visual field defects. This observation led them to the conclusion that there was a permanent interference in the blood supply of the optic disc in glaucoma.[2,3]

They emphasized the fact that the choroidal contribution to the blood supply of the optic disc and the peripapillary choroid is most susceptible to obliteration by the raised IOP. Hayreh postulated that this would go a long way toward explaining the pathogenesis of the nerve fiber bundle defects, cupping of the optic disc, and cavernous degeneration of the optic nerve in glaucoma.[4] This marked a new era of research into the field

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of glaucoma pathogenesis. With the tools of technology available to us today like color Doppler imaging (CDI), we can study the ophthalmic artery (OA) blood flow in real time noninvasively.

Optic disc changes have been correlated to alterations in ocular blood flow in the retinal and retrobulbar circulations using multiple measurement techniques. In patients of primary open-angle glaucoma (POAG) using laser Doppler flowmetry, blood flow was assessed, and a significant negative correlation has been found between blood flow in the neuroretinal rim and cup-to-disc ratio. However, no such relationship was seen in juxtapapillary blood flow.\cite{5,6}

Studies have shown that localized reduction of parapapillary blood flow is associated with neuroretinal rim damage in glaucoma patients, especially in the inferior temporal quadrant.\cite{7}

The present study was undertaken to establish the changes in hemodynamics of the OA blood flow in patients of POAG versus nonglaucomatous patients using CDI in Indian patients. Blood velocity parameters obtained with CDI, resistivity index (RI), and pulsatility index (PI) reflect OA blood flow, especially RI is an indicator of vascular resistance.

**Subjects and Methods**

The present hospital-based case–control study was conducted at a tertiary care center in Northern India from March 2016 to April 2017. After obtaining approval from the Hospital Ethics Committee, a written informed consent was obtained from the patients. One hundred patients above 40 years of age were divided into two groups. Group 1 included patients with POAG, whereas Group 2 included nonglaucomatous patients. There were 20 females and 30 males in Group 1 and 28 males and 22 females in Group 2. Patients with any retinal vein or artery occlusion, secondary glaucoma, cardiovascular abnormalities, or diseases affecting retinal nerve fiber layer thickness other than POAG were excluded from the study.

One hundred patients of either sex between 40 and 80 years of age were inducted in the study and divided into two groups. Group 1 included cases of POAG, whereas Group 2 included cases not having any evidence of POAG. Those having any cardiovascular illness, retinal venous, or arterial occlusion, secondary glaucoma or any disease affecting the retinal nerve fiber thickness such as high myopes, optic atrophy, or extensive retinal atrophy were excluded from our study. All patients were assessed for their visual acuity, and a detailed assessment of the anterior segment was done using a slit lamp, applanation tonometry, gonioscopy, and stereoscopic disc evaluation using a 90D lens. Visual field testing using 24-2 threshold was done in the Oculus visual field analyzer, followed by the assessment of retinal nerve fiber layer thickness using optical coherence tomography retinal nerve fiber layer (OCT RNFL) protocol in Cirrus HD OCT software 5.0.(of Carl Zeiss Meditec, Inc. in the United States of America) Those having an open angle after gonioscopic examination, reproducible visual field defects, and glaucomatous cupping of the optic disc were diagnosed as POAG patients.\cite{8} Then, the patients were taken to the department of radiology for CDI using GE P5 Logic Color Doppler with 4–11 MHz linear array electronic transducer. The radiologist would localize the OA behind the globe [Figure 1], while the patient was lying in supine position with his/her eyes closed.

The values of peak systolic velocity (PSV), end-diastolic velocity (EDV), and mean flow velocity (MFV) were obtained [Figure 2], and RI was calculated as PSV − EDV / PSV and PI as PSV − EDV / MFV. The data were then analyzed, and \( P \) value of <0.05 was considered statistically significant.
Results

The mean IOP in glaucomatous eyes was found to be statistically higher than nonglaucomatous eyes. The difference observed in the age and gender distribution in the two groups was statistically insignificant ($P < 0.05$).

The cup-to-disc ratio was higher in cases of POAG than others. Narrowing of the retinal nerve fiber layer as measured by the OCT RNFL thickness was more marked in cases of POAG.

The mean RI value in POAG patients was 0.80 in the right eye (standard deviation [SD] 0.059) and 0.79 in the left eye (SD 0.063), whereas in nonglaucomatous patients, it was 0.73 in the right eye and 0.74 in the left eye (SD 0.050). The $P$ value for the right eye was 0.005 and for the left eye was 0.002; both values being <0.05 were statistically significant [Figure 3].

The mean RI in the right eye of POAG patients in the age group 40–49 years was 0.79, whereas in nonglaucomatous patients, it was 0.71 and in the left eye, it was 0.78 and 0.74. Similarly, in the other age groups also, the RI in POAG patients was higher than in nonglaucomatous eyes [Figure 4].

The mean PI in POAG patients was 1.37 in the right eye with a SD of 0.204 and 1.36 in the left eye with a SD of 0.205. The mean PI in nonglaucomatous patients was 1.28 in the right eye (SD 0.110) and 1.25 in the left eye (SD 0.119) [Figures 5 and 6]. $P$ value for the right eye was 0.006 and for the left eye was 0.002; both being <0.05 were statistically significant. Thus, the PI is found to be significantly higher in POAG patients than in nonglaucomatous patients.

Discussion

There have been ample attempts to elucidate the etiology for the deterioration in glaucomatous optic neuropathy despite adequate IOP control. A variety of research publications have come up, but still, a lot needs to be done, particularly in the context to the Indian population, where significant research regarding the role of ocular blood flow and ocular perfusion is definitely lacking.[9]

The introduction of orbital CDI in 1989 by Erickson et al. presented the opportunity for assessment of orbital blood vessels.[6] A primary problem in the optic nerve circulation resulting from changes in the blood vessels of the nerve and possibly with a low perfusion pressure may be associated with the pathogenesis of glaucomatous damage.[10] The changes in blood flow to the OA, central retina artery (CRA), and the short posterior ciliary artery (SPCA) may be responsible for the pathogenesis of glaucomatous optic neuropathy.[11]

In 1997, Butt et al. studied 25 untreated patients with normal pressure glaucoma (NPG), 23 untreated patients with POAG, and 26 age-matched normal controls. CDI for the measurement of blood flow velocity in the CRA and OA was done.[12] The OA PSV was found to be significantly greater in patients with POAG than in those with NPG and normal individuals. The RI of both the OA and CRA was significantly greater in patients with POAG than in normal individuals. The CRA RI was also significantly higher in those with NPG than in normal individuals. In cases of POAG, the mean RI was 0.80, in NPG, it was 0.77, and in the normal population, it was 0.73.

In our study, RI in POAG patients was 0.795, which is comparable with this study. The RI in normal cases was 0.735, which is again comparable. However, we did not allot a group separately for NPG. They studied the RI of CRA also, whereas we studied the OA only. PI was not studied by Butt et al. In 2006, Sharma and Bangia studied the blood flow indices of 25 patients with POAG, 15 with PACG, and 15 normal cases using CDI of OA,
CRA, and SPCA. In cases of POAG, RI was found to be higher (0.81 ± 0.10) than normal controls (RI 0.55 ± 0.08). This study also reasserts the findings of decreased ocular blood flow in POAG as with other studies.

In 2010, Garhofer et al. studied retrobulbar flow velocities in POAG patients and their association with the mean arterial pressure. A total of 252 patients of POAG were taken and 192 age‑matched controls. CDI was done to get the retroorbital flow velocities and RI was calculated. As in our study, in this study also, the RI values were higher in glaucoma patients as compared to nonglaucomatous patients. However, the values obtained were different. In our study, the mean RI in glaucoma cases was 0.795, whereas in their study, it was 0.85. The RI in our study for normal individuals was 0.735, whereas in this study, it was 0.84.

In 2012, Abegão Pinto et al. studied the correlation between arterial resistance and PI in glaucoma patients. Forty-nine cases of POAG, 62 cases of Normal Tension Glaucoma (NTG), and 48 healthy controls were taken. The RI in OA was found to be 0.81 in normal cases, 0.79 in NTG, and 0.79 in POAG. The PI values were 1.8, 1.9, and 1.8 for healthy, NTG, and POAG cases. In our study, however, the PI values were 1.365 for POAG cases and 1.265 for nonglaucoma patients.

A study done by Adeyinka et al. in the Tropical African Population in 2013 on 50 cases of newly diagnosed cases of POAG and 50 healthy adults revealed an increase in RI of patients with POAG (0.71 ± 0.05) as compared to normal adults (0.63 ± 0.03) in the OA.

In 2013, a meta-analysis was published by Meng et al. to analyze the diagnostic value of CDI of ocular blood flow in the retrobulbar vessels of the eyes with POAG. They included 23 studies in their analysis. Studies were included if they were randomized clinical controlled trials or observational studies and compared blood flow velocities including PSV, EDV, and RI in OA, CRA, and SPCA in POAG and normal eyes. The study concluded that CDI can be used as a potential diagnostic tool for POAG. A significant increase in RI in OA was observed with a mean deviation of 0.04 in all retrobulbar vessels. Our findings also corroborate the same.

In 2019, Tiwari et al. found the RI and PI values of normal individuals was 0.735, whereas in this study, it was 0.84.

It is to be emphasized that in our study, IOP was not the criteria to diagnose a case of POAG so a separate group was not accorded to cases of NTG. They were a part of Group 1 of our study. Furthermore, cases of POAG newly diagnosed as well as old cases on topical medications were included in our Group 1. The increase in the RI and PI values of POAG hints at a missing link in the treatment of POAG. They may well explain the deterioration of visual fields despite adequate IOP control. Ophthalmologists around the globe need to look into this and do further research over the ocular blood flow in glaucoma so that we can further enrich our knowledge of POAG and help improve the quality of life and treatment of our POAG patients.

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Conflicts of interest
There are no conflicts of interest.

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