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A Comparative Study of Colour Doppler Imaging of Ophthalmic Artery in Primary Open Angle Glaucoma and the Age Matched Healthy Volunteers

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Abstract
The research was conducted to study the various haemodynamic parameters (peak systolic velocity, end diastolic velocity, pulsatility index & resistivity index) using Colour Doppler Imaging in Ophthalmic artery in untreated patients of primary open angle glaucoma and the age matched healthy volunteers and the effect of anti-glaucoma treatment on these parameters on subsequent follow-ups. Neither the patients nor the control subjects were using any systemic medication which can affect these parameters. Baseline differences between groups were assessed by Student's t-test. Differences between groups (pre and post treatment) were determined using one-way ANOVA analysis. P ≤0.05 was considered the level of significance. All the glaucoma subjects showed some abnormalities of the ophthalmic artery blood flow parameters. Blood flow velocities were significantly (p<0.0001) decreased and resistivity index were significantly (p<0.0001) increased in glaucoma patients as compared to the control group. While the pulsatility index was significantly (p<0.0001) increased in the POAG group when compared to the normals. (p<0.003).
Anti glaucoma treatment caused normalization of hemodynamic parameters after treatment. Blood flow velocities (PSV, EDV) were increased from their baseline values and resistance to the blood flow in the ophthalmic artery was decreased after treatment as compared to the baseline. Pulsatility index was also normalized after the treatment in the POAG & and all the results were statistically significant. (p<0.0001).

Introduction

Glaucoma, a chronic, progressive optic neuropathy, is the second leading cause of blindness worldwide and affects approximately 60 million people, with only half of them being aware of the fact, and an even smaller percentage receiving adequate treatment.[1] About 5.8% of the blindness in India is caused by glaucoma. It is estimated that there will be 79.6 million cases of glaucoma worldwide by 2020. Of these, 74% will have open angle glaucoma. Normal tension glaucoma (NTG) is a subset of primary open angle glaucoma (POAG) accounting for up to 35% (nearly one-third) of the POAG patients.[2]

The mechanism of impairment of visual function in glaucoma is still unclear. It has been said that an elevated intraocular pressure (IOP), [3,4] alone caused the optic nerve damage. Therefore, the mainstay of current therapies has been to decrease the main modifiable risk factor - intraocular pressure (IOP). However, despite significant decrease in IOP, there are a significant number of patients that show signs of disease progression. The search for other risk factors has led to the

identification of a number of vascular alterations in patients with glaucoma, especially the ones with an otherwise normal IOP.

Foremost among the proposed risk factors is ischemia, contributing to the loss of optic nerve axons, a concept recognized for more than 100 years. [5 6 7]

Ocular hemodynamics in young, healthy individuals is autoregulated to maintain constant blood flow to sensitive ocular tissues despite fluctuating blood pressure and IOP. It is thought that defective autoregulation of ocular blood flow results in ischemic damage in glaucoma patients.[8,9,10] Studies have established fluctuation of mean ocular perfusion pressure as the most consistent risk factor for clinical severity in glaucoma patients. Both anatomic (retinal nerve fiber layer thickness) and functional (visual field) outcome variables were significantly worse in patients with greater fluctuation of perfusion pressure. Also many vascular diseases have been attributed to glaucoma including diabetes, hypertension, and migraine.

However, it is difficult to study the ocular circulatory dynamics in human eyes owing to the limitation of the evaluation methods. New technologies for ocular blood flow evaluation have been introduced in clinical practice. Colour Doppler imaging (CDI) is a recent advance in diagnostic imaging for the study of vascular disorders. CDI has its strategic place and is particularly useful because of its low invasiveness and the great reproducibility and reliability of its results. CDI enables us to evaluate blood flow at specific locations by simultaneous B-mode imaging. The technique has been developed to investigate orbital arterial blood supply in the eye and orbit by identifying waveforms from specific sites. CDI has been widely used in glaucoma to study pathogenetic aspects of the disease and the vascular effects of its treatment.

Ophthalmic artery is the main source of blood supply to the optic nerve, and possible abnormalities of its blood flow may represent a significant vascular risk factor for the development of glaucomatous optic neuropathy.

Studies have confirmed that measurements of the hemodynamic variables of this vessel are reproducible and reliable data than the SPCAs and other vessels. [11,12]

Therefore a study was carried out on Colour Doppler imaging in healthy and glaucomatous subjects. In this study, we compared the hemodynamic parameters of glaucomatous subjects with those of age matched healthy volunteers. We also studied the effect of antiglaucoma treatment on these hemodynamic variables on subsequent follow ups.

Materials and Method

In this prospective study fifty subjects were included (32 males and 18 females), the distribution of these subjects was as follows:

GROUPS	NO.OF SUBJECTS
GROUP A (POAG)	24 cases
GROUP B (CONTROL)	26 cases

the hemodynamic parameters of the Ophthalmic artery using Colour Doppler Imaging were determined. The parameters used for study were quantitative peak systolic velocity (PSV), end diastolic velocity (EDV), pulsatility index (PI) and the resistivity index (RI). Average age of the patients was 51.9± 10.4 years.

Patients were instructed to avoid caffeine intake, smoking, and exercise for 3 hours prior to the study visit. All CDI measurements were performed by a single observer The eye with greater glaucomatous damage was chosen in glaucoma patients, and in healthy individuals, the eye was randomly selected.

The basic parameters which we considered in our study were-

- PEAK SYSTOLIC VELOCITY (PSV) - defined as the highest velocity of blood flow during the systolic phase of the cardiac cycle.
- END DIASTOLIC VELOCITY (EDV) - defined as the velocity of blood flow at the

end of the diastolic phase of the cardiac cycle.

- GOSLING'S PULSATILITY INDEX- (PI)

PI= PSV- EDV/ MFV

where MFV= Mean blood flow velocity.

Observations

Colour Doppler Measurements in the two Groups

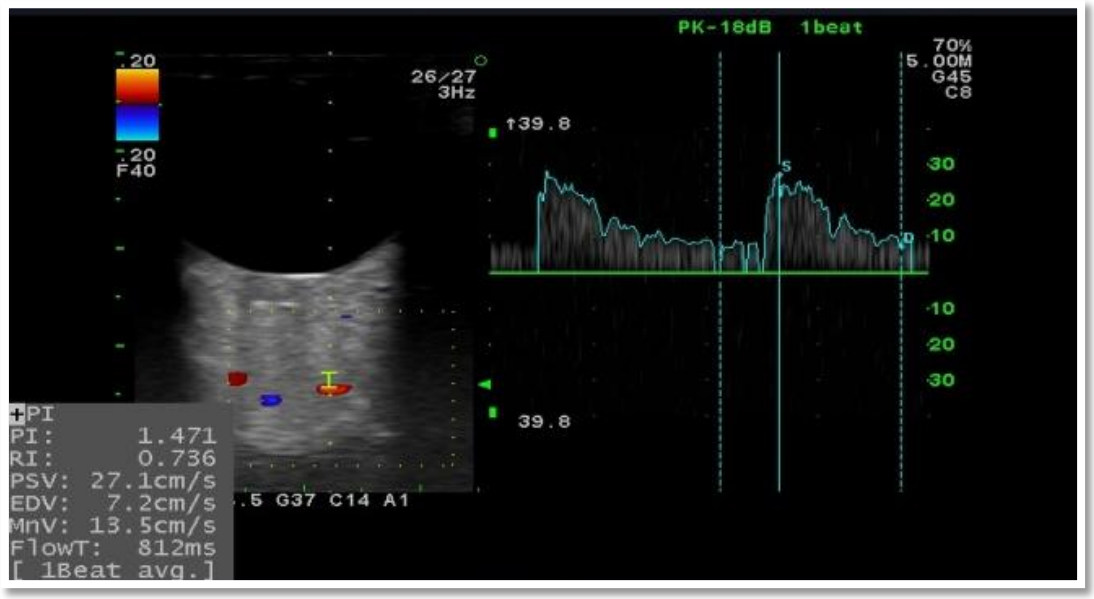

Fig.1- Colour Doppler photograph of an age matched healthy volunteer

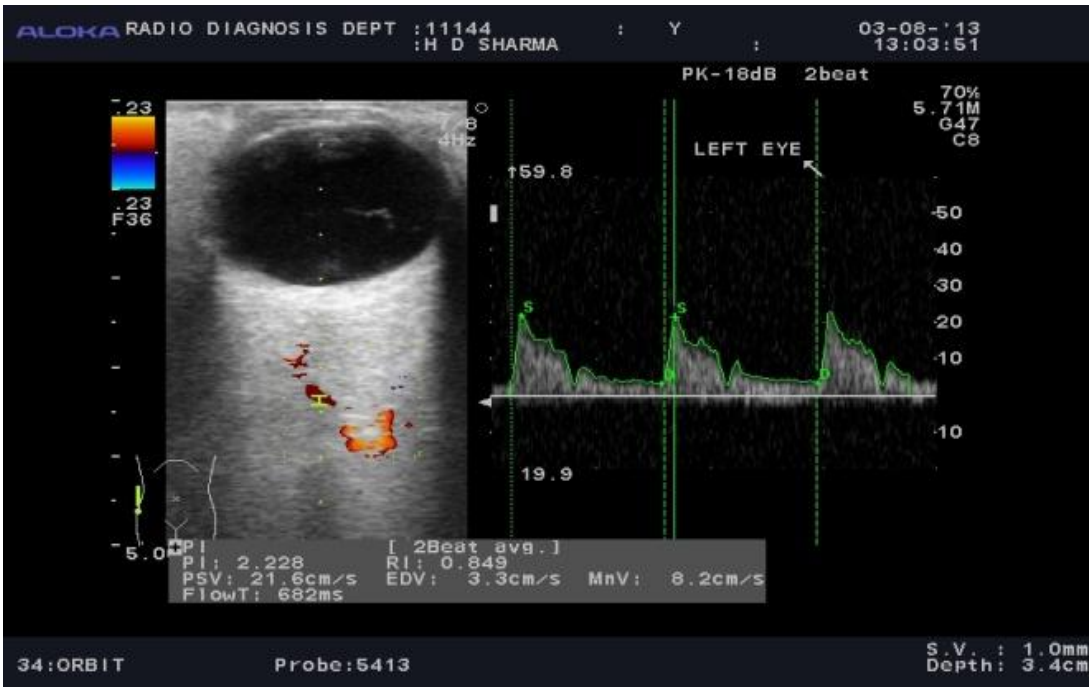

Fig.2- Colour Doppler photograph of a case of primary open angle glaucoma

Table 1. Baseline hemodynamic parameters among the two groups: (Values are expressed in terms of Mean ± SD)

GROUP	IOP (mm Hg)	PSV (cm/sec)	EDV (cm/sec)	PI	RI
GROUP A (POAG)	29.8±5.0	18.2±3.80	3.71±1.40	2.80±0.42	0.93±0.12
GROUP B (CONTROL)	16.6±1.7	35.4±3.04	8.08±0.69	1.80±0.17	0.77±0.03

Table 2. Hemodynamic parameters in POAG group (baseline and on subsequent follow ups): (Values are expressed in terms of Mean ± SD)

GROUP	IOP (mm Hg)	PSV (cm/s)	EDV (cm/s)	PI	RI
A. PRE TREATMENT	29.8±5.0	18.2±3.8	3.7±1.4	2.80±0.40	0.93±0.10
B. POST TREATMENT					
1month	25.3±4.4	22.0±3.5	5.4±1.2	2.31±.34	0.85±0.10
2 months	21.6±3.3	26.4±5.1	6.1±1.5	1.99±0.40	0.82±0.11
4 months	18.1±1.9	29.8±7.0	7.0±2.3	1.96±0.36	0.78±0.11

Table 1 shows the baseline peak systolic velocity among the two groups. In present study, it was observed that the peak systolic velocity was significantly ($p<0.0001$) decreased in glaucoma patients as compared to the control.

the baseline end diastolic velocity was decreased in glaucomatous subjects as compared to the age matched healthy volunteers, the baseline pulsatility index was increased in the POAG group ($p<0.0001$) as compared to the control group ,the baseline resistivity index was significantly ($p<0.0001$) increased in the glaucomatous subjects as compared to healthy controls . In present study, it was observed that the blood flow velocities were reduced in glaucomatous subjects and resistivity indices were increased as compared to the control group.

Table 2 shows the peak systolic velocities in POAG group (baseline and on subsequent follow ups). In present study, it was observed that after anti glaucoma treatment, IOP was reduced and subsequently peak systolic velocities were increased from their baseline values towards normalization and all the results were significant. ($p<0.0001$) also the end diastolic velocities were increased from their baseline values towards normalization and all the results were significant. ($p<0.0001$) it was also observed that after anti glaucoma treatment, IOP was reduced and subsequently the pulsatility indices were decreased from their baseline values towards normalization. And all the results were significant. ($p<0.0001$)

In present study, it was observed that after anti glaucoma treatment, IOP was reduced and subsequently the resistivity indices were decreased from their baseline values towards normalization. And all the results were significant. ($p<0.0001$)

The blood flow velocities were increased in glaucomatous subjects and resistivity indices were reduced from their baseline values towards normalization. Pulsatility indices were also normalized after treatment and all the results were significant. ($p<0.0001$)

Table. 3. Patients of POAG who showed fluctuation in their parameters
Among 24 patients of POAG

Number Of Patients (N)	8 (showed poorer response to treatment)					16 (showed better response to treatment)				
Average Age (Years)	≥60					<60				
	PARAMETERS					PARAMETERS				
GROUP	IOP (mmHg)	PSV (cm/s)	EDV (cm/s)	PI	RI	IOP (mmHg)	PSV (cm/s)	EDV (cm/s)	PI	RI
A. Pre Treatment	31± 7.0	18.9± 2.3	3.8± 0.7	2.61± 0.38	0.99± 0.18	29.3± 3.8	17.8± 4.4	3.7± 1.7	2.89± 0.42	0.89± 0.07
B. Post Treatment										
1 Month	24.7± 5.9	20.0 ± 2.3	4.5± 0.6	2.35± 0.35	0.93± 0.14	25.6± 3.5	23.0± 3.6	5.8± 1.2	2.29± 0.34	0.81± 0.04
2 Months	21.3± 4.4	20.3± 2.5	4.4 ± 0.5	2.41 ± 0.47	0.94± 0.13	21.8± 2.8	29.5± 2.7	7.0± 0.9	1.79± 0.05	0.77± 0.04
4 Months	18.3± 2.6	20.6± 2.3	4.2± 0.7	2.39± 0.31	0.91± 0.12	18± 1.6	34.4± 2.2	8.5± 1.1	1.74± 0.04	0.72± 0.03

The above table shows the hemodynamic parameters in POAG group (baseline and on subsequent follow ups). In present study, it was observed that after anti glaucoma treatment, IOP was reduced and subsequently the hemodynamic parameters were normalized in majority of patients (66%). However in a sizeable number of patients (nearly 33%), it was also observed that there was very little or no improvement and also there was fluctuation in the hemodynamic parameters of these patients during the follow ups despite an adequate IOP control. And also the effect of treatment in terms of normalization of hemodynamic parameters varied with the age. Younger subjects responded better to the treatment. ($p < 0.001$)

Conclusions

1) There is a deviation of hemodynamic parameters in glaucoma subjects as compared to age matched healthy volunteers.
2) There occurs a normalization of hemodynamic parameters with the treatment in majority of cases.
3) However, in a sizeable number of patients, normalization of hemodynamic parameters may not occur.
4) The effect of treatment in terms of normalization of hemodynamic parameters may vary with the age. Younger subjects responded better to the treatment.

Limitation of our study

Due to the short duration of follow up, glaucoma progression analysis could not be performed. Thus a correlation between hemodynamic parameters and progression of visual fields could not be established.

Recommendations

Further long term studies are needed to find out:

1) Diurnal variation of hemodynamic parameters.
2) The differential effect of various drugs on hemodynamic parameters.
3) The fluctuation in the hemodynamic parameters despite a well controlled IOP.
4) More advanced techniques for determination of hemodynamic parameters in small vessels like SPCA, and CRA and at the level of capillaries.

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