

## A STUDY ON VARIATION OF INTRAOCULAR PRESSURE AND OCULAR PERFUSION PRESSURE OVER A 24-HOUR PERIOD

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### ABSTRACT

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#### BACKGROUND

Glaucoma is the second leading cause of blindness globally. Intraocular pressure and vascular risk factors have been proposed to be important risk factors in the development of glaucoma.

The aim of this study is to describe the variation of ocular perfusion pressure and intraocular pressure in normal subjects, glaucoma suspects, which include Ocular Hypertension (OHT) suspects and Normotensive Glaucoma (NTG) suspects and established primary open-angle glaucoma patients over a period of 24 hours.

#### MATERIALS AND METHODS

A cross-sectional study was conducted for 24 hours at the glaucoma services of a tertiary eye care hospital at Chennai. Totally, 30 eyes (right eye) of 30 patients were included and they were categorised into four groups- Group A (normal)- Subjects with normal IOP, fields and normal optic nerve head and RNFL on fundus examination; 12 eyes were included. Group B (ocular hypertension suspects)- Subjects with normal fields and normal optic nerve head on fundus examination, but with elevated IOP; 8 eyes were included. Group C (normotensive glaucoma NTG suspects)- Subjects with normal IOP and fields, but with optic nerve head changes like increased cup disc ratio, focal notching, focal NRR thinning or RNFL wedge defects; 8 eyes were included. Group D (primary open-angle glaucoma)- Subjects with increased IOP, typical glaucomatous field defects and optic nerve head and RNFL changes suggestive of glaucoma; 7 eyes were included. A thorough baseline investigation including applanation tonometry with central corneal thickness correction, gonioscopy and fields by automated perimeter (Octopus 301 perimeter) were done. Intraocular pressure and blood pressure were recorded at 12 p.m., 6 p.m., 12 a.m. and 6 a.m. The systolic, diastolic and mean ocular perfusion pressures were calculated.

#### RESULTS

Four parameters viz. intraocular pressure, systolic perfusion pressure, diastolic perfusion pressure and mean perfusion pressure were analysed over a period of 24 hours. The intraocular pressure fluctuation over 24-hour period in Group A was minimal with a standard deviation of 1.15. In group B, the mean intraocular pressure was lowest during 12 a.m. and the fluctuations were more with standard deviation of 1.63. Maximum fluctuations in IOP were found in Group C with standard deviation of 4.76. Systolic, diastolic and mean ocular perfusion pressures were lowest in POAG group with a dip at 12 a.m. In POAG group, diastolic perfusion pressures were as low as 35 mm Hg.

#### CONCLUSION

This study has demonstrated that the mean and diastolic ocular perfusion pressure is significantly lower in primary open-angle glaucoma group and NTG suspects when compared to other groups. This study also shows that large diurnal fluctuation of IOP is an important risk factor in open-angle and normotensive glaucomas.

#### KEYWORDS

Ocular Perfusion Pressure, Intraocular Pressure Variation, Glaucoma.

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#### BACKGROUND

Glaucoma is a chronic progressive optic neuropathy characterised by progressive loss of retinal ganglion cells. Various pathogenic mechanisms leading to glaucomatous optic neuropathy have been identified. Two main theories are mechanical and vascular.<sup>1</sup> The vascular theory of glaucomatous neuropathy states that abnormal perfusion of optic nerve head leads to ganglion cell loss. Ocular perfusion pressure is the difference between the arterial BP and the Intraocular Pressure (IOP), which is considered a substitute

for the venous pressure. Circadian variation of the mean ocular perfusion pressure is related to disease severity in normal-tension glaucoma.<sup>2</sup>

**Aims and Objectives**

1. To study the variation of intraocular pressure in normal subjects, glaucoma suspects, which include Ocular Hypertension (OHT) suspects and Normotensive Glaucoma (NTG) suspects and primary open-angle glaucoma patients over a period of 24 hours.
2. To study the variation of systolic and diastolic ocular perfusion pressure in the above-mentioned groups for a period of 24 hours.

**MATERIALS AND METHODS**

A cross-sectional study was conducted for 24 hours at the glaucoma services of a tertiary eye care hospital at Chennai.

**Inclusion Criteria**

- Subjects more than 45 years of age.
- Best corrected visual acuity of more of equal than 6/18 by Snellen’s chart.
- Open angles in gonioscopy (more than or equal to Shaffer’s grade 3) were included.

**Exclusion Criteria**

- Subjects less than 45 years of age.
- Best corrected visual acuity of by less than 6/18 by Snellen’s chart.
- Narrow or closed angles in gonioscopy.
- Other causes of optic neuropathy like trauma, toxic optic neuropathy.
- Secondary glaucomas like posttraumatic glaucoma, neovascular glaucoma.

Totally, 35 eyes (right eye) of 35 participants were included. Subjects underwent the following baseline investigations.

- Anterior segment examination by slit-lamp examination and fundus examination with +90 D lens.
- Intraocular pressure measurement by Goldman applanation tonometer and central corneal thickness measurement by contact ultrasound pachymeter. Correction of 0.7 mmHg was given for eye with CCT above or less than 520 μ (if CCT <520 μ, corrected IOP = actual IOP + 0.7 mm \* (520-CCT) Hg; if CCT >520 μ, corrected IOP = Actual IOP - 0.7 mm \* (CCT-520) Hg.
- Gonioscopy by Goldman single mirror lens.
- Visual fields by automated perimetry (Octopus 301).

**They were classified into the following four groups-**

1. Group A (normal)- Subjects with normal IOP, fields and normal optic nerve head and RNFL on fundus examination. 12 eyes were included.
2. Group B (ocular hypertension suspects)- Subjects with normal fields and normal optic nerve head on fundus

examination, but with elevated IOP. 8 eyes were included.

3. Group C (normotensive glaucoma suspects)- Subjects with normal IOP and fields, but with optic nerve head changes like increased cup disc ratio, focal notching, focal NRR thinning or RNFL wedge defects. 8 eyes were included.
4. Group D (primary open-angle glaucoma)- Subjects with increased IOP, typical glaucomatous field defects and Optic nerve head and RNFL changes suggestive of glaucoma. 7 eyes were included.

The intraocular pressure and blood pressure were recorded at 12 a.m., 6 a.m., 12 p.m. and 6 p.m. Intraocular pressure was recorded by Goldmann applanation tonometry. Blood pressure was recorded from left arm with the patient in sitting posture. Blood pressure recording was done after the patient was comfortably seated for 5 minutes. The systolic and diastolic ocular perfusion pressures were calculated as follows.

Systolic Ocular Perfusion Pressure (SOPP) = systolic blood pressure - intraocular pressure.

Diastolic Ocular Perfusion Pressure (DOPP) = diastolic blood pressure - intraocular pressure.

Mean arterial pressure = diastolic BP + 1/3 (systolic BP-diastolic BP).

Mean Ocular Perfusion Pressure (MOPP) = mean arterial pressure - intraocular pressure.

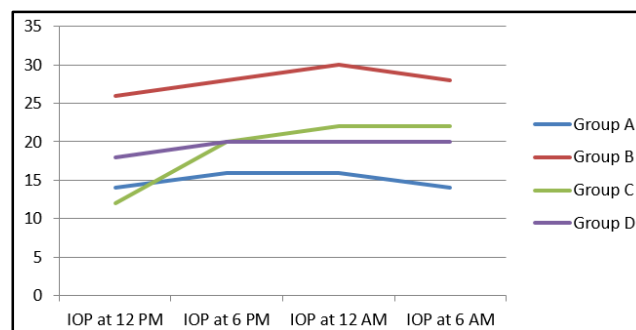
**RESULTS**

Of the 35 participants who were included, 17 were males and 18 were females. 14 of them were known hypertensive patients on antihypertensive medications. They continued their antihypertensive medications during the 24-hour period.

The mean intraocular pressure in mmHg of the four groups at 12 p.m., 6 p.m., 12 a.m. and 6 a.m. are as follows.

Groups	IOP at 12 p.m.	IOP at 6 p.m.	IOP at 12 a.m.	IOP at 6 a.m.
Group A	14	16	16	14
Group B	26	28	30	28
Group C	12	20	22	22
Group D	18	20	20	20

**Table 1. The Mean IOP in mmHg in Different Groups Over 24 Hours**



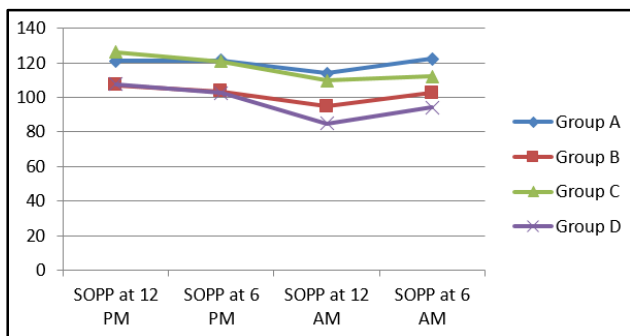
**Graph 1. Showing IOP Fluctuations Over 24-Hours Period in Various Groups**

This graph shows that the intraocular pressure fluctuation over 24-hour period in group A was minimal with a standard deviation of 1.15. In group B, the mean intraocular pressure was highest during 12 a.m. and the fluctuations were more with standard deviation of 1.63. Maximum fluctuations in IOP were found in Group C with standard deviation of 4.76.

Groups	SOPP at 12 p.m.	SOPP at 6 p.m.	SOPP at 12 a.m.	SOPP at 6 a.m.
Group A	121.17	121.5	113.83	122.17
Group B	107	103.5	94.75	102.5
Group C	126.28	120.85	109.71	112
Group D	107.5	102.5	85	94

**Table 2. Showing Mean Systolic Ocular Perfusion Pressures (SOPP) in Different Groups Over 24-Hours Period**

The mean systolic ocular perfusion pressure in all the four groups were lowest during 12 a.m. period. Among the groups, group A showed a minimum fluctuation in systolic ocular perfusion pressure over 24-hours period with standard deviation of 3.8. In group B, the systolic ocular perfusion pressures were lower than normal subjects and showed a higher fluctuation with standard deviation of 5.1. In group C, fluctuation of systolic ocular perfusion pressures were higher than group B with a standard deviation of 7.7. Group D showed highest fluctuation of systolic ocular perfusion pressure with a standard deviation value of 9.8.



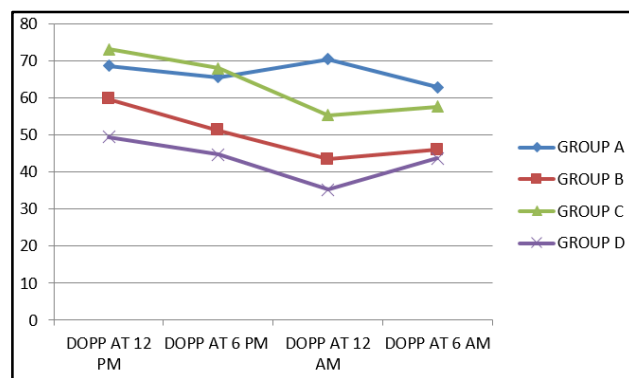
**Graph 2. Showing the Mean Systolic Ocular Perfusion Pressures in Different Groups Over 24-Hours Period**

Systolic ocular perfusion values were lower in primary open-angle glaucoma and in both glaucoma suspect groups (group B and C) when compared to the normal subjects. The lowest value was found in primary open-angle glaucoma group (Group D) at 12 a.m.

Groups	DOPP at 12 p.m.	DOPP at 6 p.m.	DOPP at 12 a.m.	DOPP at 6 a.m.
Group A	68.67	65.67	70.5	63
Group B	59.75	51.25	43.5	46
Group C	73.14	68	55.42	57.71
Group D	49.5	44.75	35.25	43.75

**Table 3. Showing Mean Diastolic Ocular Perfusion Pressure (DOPP) of Different Groups Over 24-Hour Period**

The mean diastolic perfusion pressure in group A showed minimum fluctuation with a standard deviation value of 3.30. In group A, unlike the systolic ocular perfusion pressure, the diastolic ocular perfusion pressure values were lowest at 6 a.m. In other groups, the mean diastolic ocular perfusion pressure values were lowest during 12 a.m. Group C showed a maximum fluctuation of diastolic ocular perfusion pressure with a standard deviation of 8.4. In group D, though the fluctuations were lower than group B and C, the diastolic perfusion pressures were as low as 30 at 12 a.m. (mean 35.25).

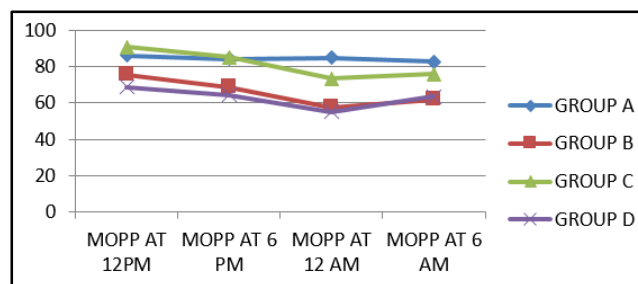


**Graph 3. Showing the Mean Diastolic Ocular Perfusion Pressures in Different Groups Over 24-Hours Period**

Groups	MOPP at 12 p.m.	MOPP at 6 p.m.	MOPP at 12 a.m.	MOPP at 6 a.m.
Group A	86.16	84.27	84.94	82.7
Group B	75.56	68.83	57.73	62
Group C	90.85	85.16	73.52	75.8
Group D	68.66	64.33	55.08	63.33

**Table 4. Average Mean Ocular Perfusion Pressure (MOPP) in Different Groups at Different Times Over 24 Hours**

This table shows that there is minimum fluctuation in mean ocular perfusion pressure in group A with a standard deviation of 1.44. Like systolic and diastolic ocular perfusion pressure, the mean ocular perfusion pressure values were also lowest in group D at 12 a.m. Group C showed maximum fluctuation of mean ocular perfusion pressure with a standard deviation value of 8.1.



**Graph 4. Showing the Mean Ocular Perfusion Pressures in Different Groups Over 24-Hours Period**

## DISCUSSION

In our study, four parameters viz. intraocular pressure, systolic perfusion pressure, diastolic perfusion pressure and mean perfusion pressure were analysed over a period of 24 hours. Intraocular Pressure (IOP) is known to vary throughout the 24-hour period of a day in healthy individuals and patients with glaucoma.<sup>3</sup> The intraocular pressure fluctuation over 24-hour period in group A (normal) was minimal with a standard deviation of 1.15 and peak at 12 a.m. IOP fluctuation in POAG group was more than the normal individuals. In OHT suspect group, the mean intraocular pressure was highest during 12 a.m. and the fluctuations were more with standard deviation of 1.63. A study done by Grippo et al<sup>4</sup> had similar results in which both OHTN and glaucoma groups demonstrated higher diurnal mean IOPs as well as greater diurnal IOP variation compared to healthy controls. A study by Young Rok Lee et al<sup>5</sup> showed that the nocturnal elevation of IOP occurs in a large proportion of NTG patients. Similar findings were noted in our study in NTG suspect group with maximum IOP fluctuation and peak IOP at 12 a.m. Our study suggests that large IOP fluctuations could be a risk factor for glaucoma similar to other studies.<sup>6</sup>

Several studies have suggested that loss of autoregulation in ocular blood flow maybe present in primary open-angle glaucoma.<sup>7,8,9</sup> If ocular autoregulation is defective, the calculated Mean Ocular Perfusion Pressure (MOPP) maybe low. It has also been suggested that relative diurnal or circadian change in MOPP may be a risk factor for POAG.<sup>10,11</sup> Leske et al studying the relationship between blood pressure and glaucoma reported increased prevalence of glaucoma when the diastolic perfusion pressure fell below 55 mmHg.<sup>12</sup> Similar results were obtained in our study with POAG group having diastolic perfusion pressures as low as 35 mmHg. In our study, systolic, diastolic and mean ocular perfusion pressures were lowest in POAG group with a dip at 12 a.m. Fuchsjager-Mayrl et al reported that the haemodynamics of ocular parameters are lower in patients with OAG in comparison with normal patients.<sup>13</sup> Tokunaga et al<sup>14</sup> demonstrated the association between nocturnal dip in blood pressure and progression of POAG.

This study could have some limitations. Intraocular pressure and blood pressure measurements were far from physiologic conditions as they required awakening patients during the sleep period. This could have potentially disturbed sleep organisation and introduced stress-related artefacts. Since intraocular pressure and blood pressure measurements were performed in sitting position, dynamic changes related to daily-life physical activities were ignored. This could be overcome by ambulatory blood pressure and intraocular pressure monitoring over 24 hours using contact lens.

## CONCLUSION

Our study has demonstrated that the fluctuation of intraocular is more in patients with primary open-angle glaucoma and normotensive glaucoma suspects when compared to normal individuals. Our study has also

demonstrated that the ocular perfusion pressure is significantly lower and shows a nocturnal dip in primary open-angle glaucoma group when compared to other groups. Our study supports the vascular theory in the pathogenesis of glaucoma.

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