

The Interplay of Anti-Hypertensive Medications, Ocular Perfusion Pressure and Glaucoma Progression

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Abstract

Background: Study Design: Analytical Observational study. **Purpose:** To evaluate the effect of Anti-hypertensives on Systolic perfusion pressure (SPP), Diastolic perfusion pressure (DPP), Ocular perfusion pressure (OPP) and their association with progression of Primary Open Angle Glaucoma (POAG). **Materials And Methods:** Based on ICD-10, patients on Anti-hypertensives were divided into Early (n=15), Moderate (n=15) and Advanced (n=15) glaucoma and their SPP, DPP, OPP were assessed. Anova test was used to see the statistical significance among groups. P value <0.05 was considered significant. **Results:** DPP, SPP and OPP were significantly lower in Advanced stages of glaucoma when compared to Early and Moderate stages. **Conclusion:** Anti-hypertensives lowering the Perfusion pressures will have a detrimental effect on already compromised optic nerve head in Glaucoma patients. High SBP leads to decrease in vessel diameter whereas patients with low DPP will have low OPP. Bed time Anti-hypertensives exaggerate the Nocturnal dipping of BP further aggravating the disease process. Hence it is better to avoid night dosage in patients with very low OPPs.

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Introduction

Glaucoma is a chronic progressive optic neuropathy characterised by retinal ganglion cell death and associated visual field loss.¹ Systemic hypertension has been related to increased Intraocular pressure (IOP) and higher risk of Glaucoma.² Among vascular factors associated with glaucoma, blood pressure (BP) is the most studied, because it is related to microvascular blood flow and IOP, the two main elements that determine the ocular perfusion pressure (OPP).³ Recently, a bimodal relationship was described between BP and the risk of glaucoma, indicating that patients with either high or low BP have a higher risk of developing or progression of glaucoma.^{4,5} The OPP could be reduced during the decrease or elevation of BP, and this may result in ischemic injury of the retinal ganglion cells in the absence of adequate mechanism of autoregulation.⁶ In patients with systemic hypertension and glaucoma, vascular dysfunction does not allow the activation of ocular blood flow regulation mechanisms, increasing susceptibility to POAG.^{7,8} Several markers can be used to assess the risk of

glaucoma, one of which is OCULAR PERFUSION PRESSURE, a potential marker of Optic nerve head (ONH) perfusion and the major culprit in causing glaucoma.

Aim and objectives

To evaluate the relationship between Anti-hypertensive medications and Progression of Glaucoma.

To assess the effect of Anti-hypertensive medication at bedtime on Systolic perfusion pressure (SPP), Diastolic perfusion pressure (DPP) and Ocular perfusion pressure (OPP) and their association with progression of Glaucoma.

Materials and Methods

Study type: Analytical Observational Study

Study duration: 6 months

Sampling method: Convenience sampling

Setting: Department of ophthalmology, Tertiary care centre, Andhra Pradesh

Sample size: 45 Glaucoma patients who were on Anti-hypertensive medications were divided into three groups based on ICD-10 guidelines. 15 cases of Early, Moderate and Advanced glaucoma. The study was done in accordance with the ethical committee guidelines and all the patients were informed about the purpose of study

All the patients who were a known case of Primary open angle glaucoma and on treatment with anti glaucoma medications, having Systemic hypertension and using Antihypertensive medications at bedtime for at least 1 year were included in this study

Patients who were known hypertensives but not on bedtime anti-hypertensive medication, Patients with Ocular hypertension (OHT), Patients on irregular anti glaucoma therapy, Patients who underwent Surgical intervention for glaucoma, Secondary glaucomas, Secondary causes for high IOP, Non glaucomatous optic neuropathies, Secondary hypertension were excluded from this study

Patients were assessed for best correct visual acuity (BCVA), Slit lamp examination of Anterior segment, IOP by Goldmann Applanation tonometer (GAT), Visual field assessment by Humphrey Visual Field Analyser (HFA), Gonioscopy for both the eyes using ZEISS 4-mirror Indirect Contact gonioscopy lens, Dilated Fundus Examination, Supine position Blood Pressure was recorded after a 5minute period of rest. MEAN OCULAR PERFUSION PRESSURE was CALCULATED USING FORMULA: $MOPP = 2/3 \times [MAP - IOP]$ where $MAP = DBP + 1/3 [SBP - DBP]$

$SPP = SBP - IOP$

$DPP = DBP - IOP$

Statistical Analysis

Descriptive analysis of the collected data was done using MICROSOFT EXCEL DATA SHEET and SPSS SOFTWARE Trail version 20

Significance was assessed using ANOVA: Single factor test. In the above statistical tool the probability value “p” < 0.05 was considered statistically significant.

Results

The mean intraocular pressure in patients with Early Glaucoma was 15.2 +/- 2.36 and in patients with Moderate glaucoma 16.9 +/- 3.19 and in Advanced glaucoma it was 15.3 +/- 4.11. The P value was 0.289 which shows no statistically significant difference in the intraocular pressure among those three groups.

Table 1

INTRAOCULAR PRESSURE	MEAN ± STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)	P VALUE
EARLY GLAUCOMA	15.2 ± 2.36 (13.89 - 16.51)	0.289
MODERATE GLAUCOMA	16.9 ± 3.19 (15.14 – 18.66)	
ADVANCED GLAUCOMA	15.3 ± 4.11 (13.02 – 17.58)	

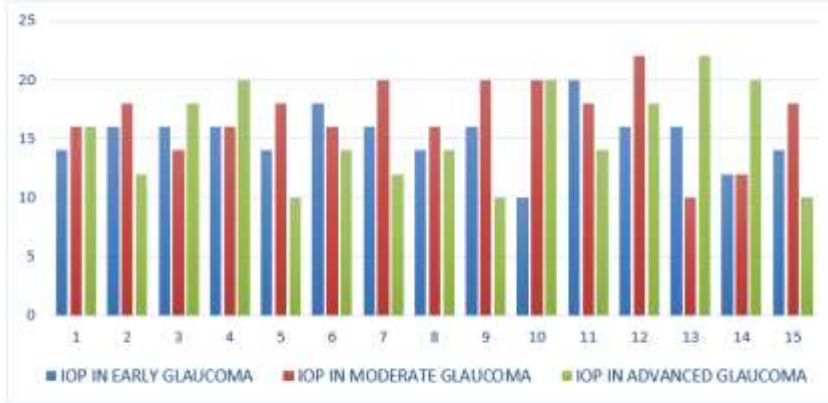


Figure 1: INTRAOCULAR PRESSURE (mmhg)

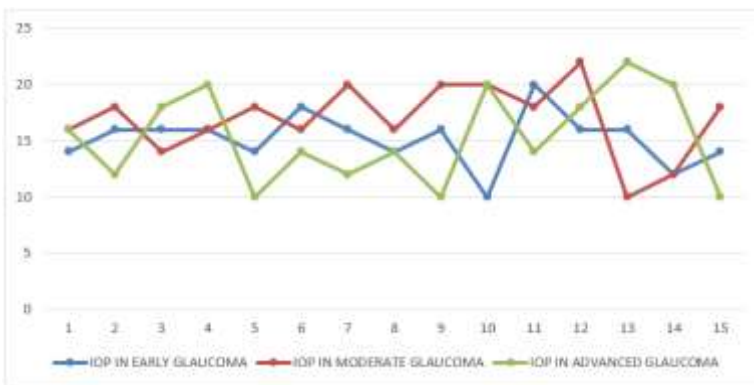


Figure 2: INTRAOCULAR PRESSURE (mmhg)

The mean ocular perfusion pressure (OPP) in Patients with Early Glaucoma was 60.50 +/- 1.42mmhg and in patients with Moderate Glaucoma was 58.58 +/- 1.83 mmhg and in patients with Advanced glaucoma was 50.82 +/- 1.74. The P value was 0.0004 which shows statistically significant difference in Ocular perfusion pressure among those 3 groups.

Table 2

OCULAR PERFUSION PRESSURE	MEAN ± STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)
EARLY GLAUCOMA	60.50 ± 1.42 (57.45 – 63.55)
MODERATE GLAUCOMA	58.58 ± 1.83 (54.66 – 62.5)
ADVANCED GLAUCOMA	50.82 ± 1.74 (47.09 – 54.55)

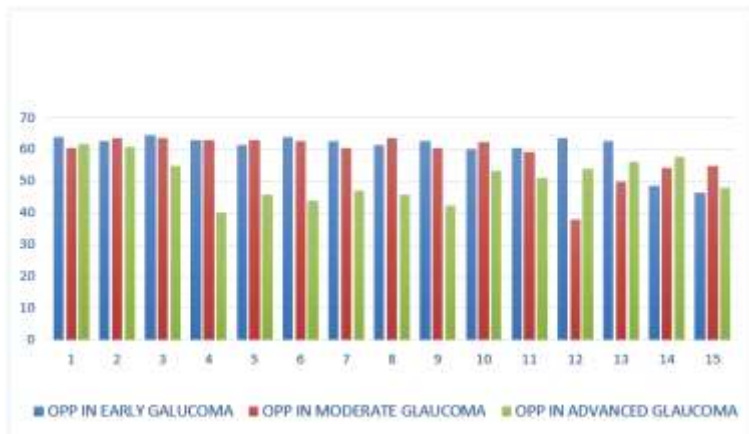


Figure 3: OCULAR PERFUSION PRESSURE(mmhg)

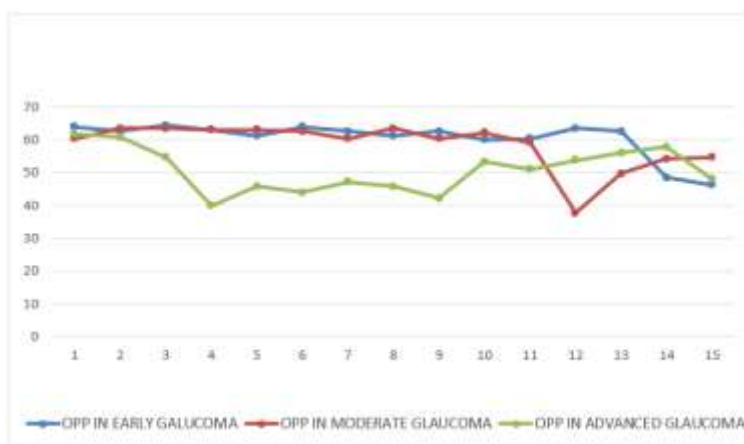


Figure 4: OCULAR PERFUSION PRESSURE (mmhg)

The Diastolic Perfusion pressure (DPP) was 74.27 +/- 1.83 mmhg in patients with Early Glaucoma and it was 67.87 +/- 2.10 mmhg in patients with Moderate glaucoma and it was 58.67 +/- 1.70 mmhg in patients with Advanced glaucoma and the P value was 0.000003 which shows statistically significant difference in Diastolic perfusion pressure among the groups.

Table 3

DIASTOLIC PERFUSION PRESSURE	MEAN ± STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)
EARLY GLAUCOMA	74.27 ± 1.83 (70.35 – 78.19)
MODERATE GLAUCOMA	67.87 ± 2.10 (63.37 – 72.37)
ADVANCED GLAUCOMA	58.67 ± 1.70 (55.03 – 62.31)

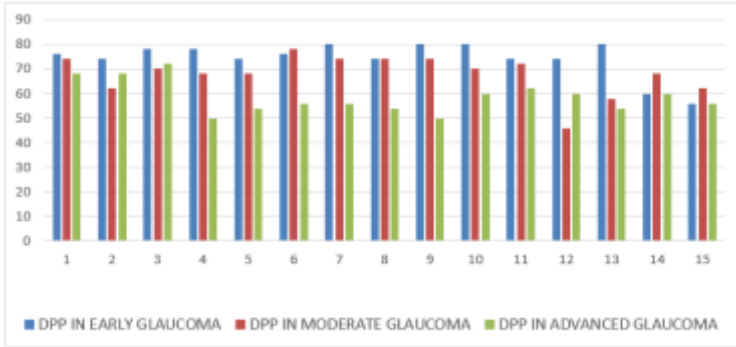


Figure 5: DIASTOLIC PERFUSION PRESSURE (mmhg)

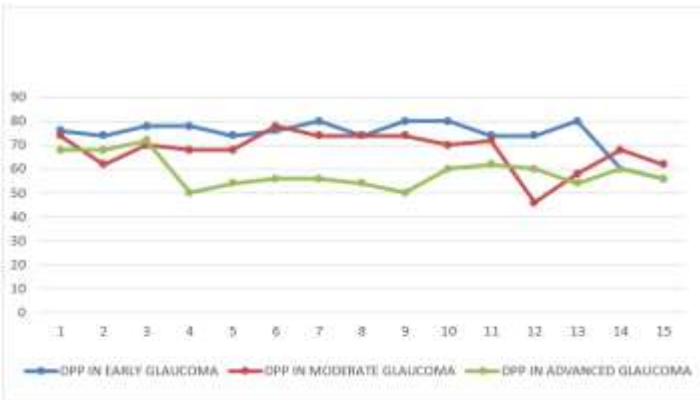


Figure 6: DIASTOLIC PERFUSION PRESSURE(mmhg)

The mean systolic perfusion pressure in patients with Early Glaucoma was 123.73 +/- 3.38 mmhg and in patients with Moderate Glaucoma was 127.87 +/- 5.32 mmhg and in patients with Advanced Glaucoma was 111.33 +/- 5.55 mmhg and the P value was 0.05 which shows statistically significant difference in Systolic perfusion pressure among the groups

Table 4

SYSTOLIC PERFUSION PRESSURE	MEAN ± STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)
EARLY GLAUCOMA	123.73 ± 3.38 (116.48 – 135.14)
MODERATE GLAUCOMA	127.87 ± 5.32 (116.46 – 139.28)
ADVANCED GLAUCOMA	111.33 ± 5.55 (99.43 – 123.23)

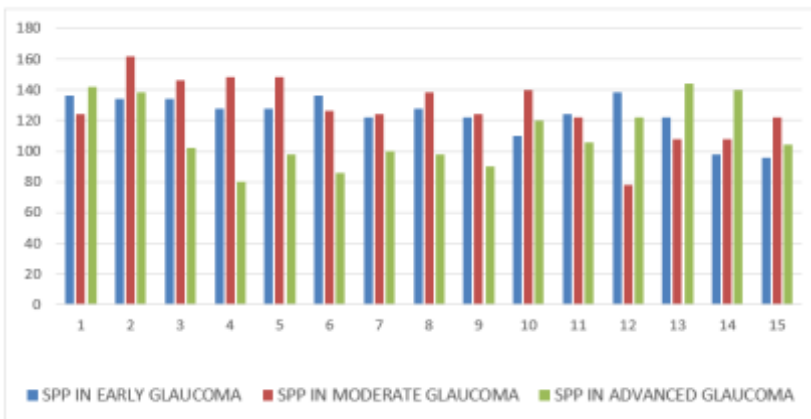


Figure 6: SYSTOLIC PERFUSION PRESSURE (mmhg)

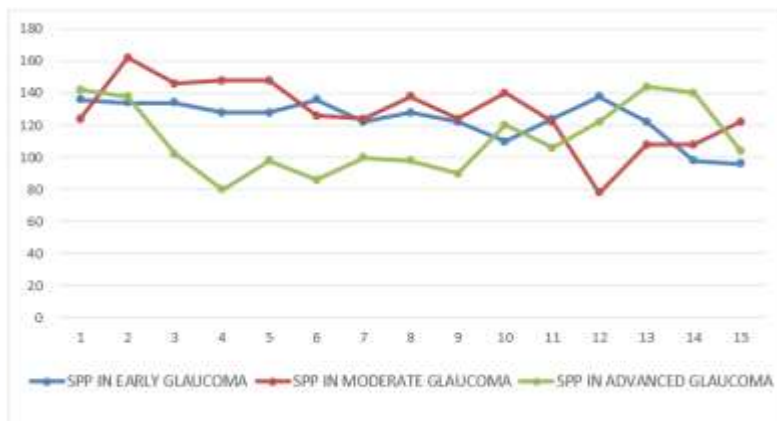


Figure 8: SYSTOLIC PERFUSION PRESSURE (mmhg)

Discussion:

This is a Multicentric study done in the Department of ophthalmology. This study ascertains that patients who are on rigorous antihypertensive treatment or due to nocturnal hypotension have low perfusion pressures and they are at increased risk for progression of glaucoma. Association between systemic hypertension and POAG has been evaluated by various population-based studies. Ocular Perfusion Pressure and the Risk of Open-Angle Glaucoma: Systematic Review and Meta-analysis by Ko eun Kim *et al.* concluded that Patients with POAG showed significantly lower OPP than controls.⁹ Correlation of open- angle glaucoma and ocular perfusion pressure in hypertensive individuals by Rekha Khandelwal *et al.* inferred that that hypertensive patients taking anti-HT treatment with POAG have lower mean OPP as compared to those without POAG.¹⁰ The Baltimore Eye Study showed a strong association between DPP < 50mmHg and the development of POAG.¹¹ The Singapore Malay Eye Study has reported that low DBP, low MOPP and low DOPP were independent risk factors for OAG.¹² Pache and Flammer reported hypotension and nocturnal drop in Blood pressure as an important risk factor for Open angle glaucoma.¹³ Egna-Neumarket Study has reported an increased risk of OAG with DPP <50 mmHg.¹⁴ Rotterdam Eye Study which was done to study prevalence of OAG in patients receiving antihypertensives and their study concluded that DPP < 50mmHg had increased risk of OAG.¹⁵ In Los Angeles Latino Study, there was an increased prevalence of OAG with lower MOPP, DOPP, SOPP.¹⁶ From these studies, it is understood that people on antihypertensive medications have an increased risk of developing and progression of glaucoma, which may be attributed to the bedtime dosing of anti-hypertensive medication or reduction in nocturnal BP.

Limitations of the study

The main limitation of this study is that blood pressure & IOP measurements were performed only once during daytime. Circadian influence on blood pressure and on IOP can be present and IOP peak, IOP fluctuations can be missed by a single reading.

Direct measurement of Ocular blood flow could result in different outcome as here we are calculating MOPP theoretically using a formula.

Conclusion

Lower OPP, Lower SPP and Lower DPP were associated with a higher risk of progression of glaucoma which was statistically proven. There was no statistically significant difference in IOP among three glaucoma groups suggesting that even with medically controlled IOP, there

was progression of glaucoma. The results from the present study implicated that PERFUSION PRESSURES play a potential role in the pathogenesis of glaucoma in subjects on antihypertensive drugs. Anti-hypertensives reduces the blood pressure, thus lowering the Perfusion pressures, will have a detrimental effect on already compromised optic nerve head in Glaucoma patients. Its not possible to increase ocular perfusion pressure as a part of glaucoma treatment. In exception, it maybe used to decrease rigorous antihypertensive treatment and to avoid the night dosage in patient with systemic hypertension to prevent nocturnal dipping of IOP and very low OPPs. Perfusion pressures can be potential clinical screening tools to identify those patients on overdosage with antihypertensive medications.

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