ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 03 | March - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ANTI-HYPERTENSIVES AND ITS EFFECT ON OCULAR PERFUSION PRESSURE

Ophthalomology

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ABSTRACT

Aim: To compare ocular perfusion pressure (OPP) in primary hypertensive patients on treatment and normotensive subjects. **Materials and methods:** This is a cross-sectional, observational hospital-based study, which included 55 patients with primary hypertension on treatment (group A) and 55 normotensives (group B). All patients underwent comprehensive ophthalmic evaluation. An average of three recordings of intraocular pressure (IOP) and blood pressure (BP) taken 1 hour apart was used to calculate systolic (SOPP), diastolic (DOPP) and mean OPP (MOPP) which was compared between the two groups. Statistical analysis was performed by SPSS (Version, 17) software. P value of ≤0.05 was considered as statistically significant. **Results:** The SOPP, DOPP and MOPP was significantly higher in group A. There was no association between the group of antihypertensive medications and IOP or OPP. **Conclusion:** Well controlled primary hypertensives tended to have higher OPP compared to normotensives possibly suggesting its protective effect against glaucoma.

KEYWORDS

Ocular Perfusion Pressure, Systemic Hypertension, Open Angle Glaucoma.

INTRODUCTION

Ocular perfusion pressure (OPP) is the pressure available to drive blood through the intraocular vasculature, with the degree of perfusion being influenced by resistance to flow, which is a function of vessel caliber or the vessel tone [3]. It is measured as the 2/3 of mean arterial blood pressure-Intraocular pressure (2/3 MABP-IOP) where, mean arterial blood pressure is diastolic BP+1/3(systolic BP-diastolic BP). Factor 2/3 accounts for drop in blood pressure between the brachial and ophthalmic artery when the subject is seated [3].

Systolic OPP is defined as difference between systolic BP and IOP (SBP-IOP) whereas diastolic OPP is derived by subtracting diastolic BP and IOP (DBP-IOP).

A reliable direct measure of OPP using suction cup method, contact lens dynamometer is desirable but due to limitations of need of a well trained examiner to produce reproducible results and it being tiresome procedure indirect measurements of BP and IOP to determine OPP values is followed till date [3].

A bimodal relationship exists between BP and risk of glaucoma indicating that patients with either high or low BP have a higher risk of developing POAG [5].

Hypotensive patients suffer from low OPP at optic nerve head and hypertensive patients develop atherosclerotic changes over time thus leading to increased vascular resistance and compromised vascular autoregulation as well as impaired nutrient exchange in capillary bed at optic nerve head [6].

In hypertensive patients, glaucomatous damage occurs due to ischemia of optic nerve head or retinal ganglion cells because of reduced perfusion pressure due to structural changes in arterioles such as vascular remodelling and hypertrophy reducing vasodilatation, also there are findings that suggest an alteration in endothelin-1 levels in hypertensive subjects leading to dysfunction processes in endothelial regulation which further reduces the ocular blood flow in patients with glaucoma [5].

Therefore, OPP decreases in both hypotension and hypertension resulting in ischemic damage to retinal ganglion cells.

Increased IOP was associated with increased BP such that an increase of 10mmHg in systolic BP caused IOP to raise by about 0.2mmHg and diastolic BP raise by 10mmHg lead to about 0.4mmHg increase in IOP[9]

The vascular hypothesis of open angle glaucoma states that low BP relative to low IOP leads to low OPP impairing perfusion of optic nerve head contributing to glaucomatous damage [14].

Subjects with SOPP > 130mmHg had a higher risk of developing POAG than those with SOPP between 111 and 120mmHg. Subjects with DOPP ≤ 50mmHg have a 2.2 times greater risk of developing POAG than those with DOPP between 61 and 70mmHg. Subjects with MOPP ≤ 40mmHg have 2 times greater risk of developing POAG than those with MOPP between 41 and 50mmHg [5].

Subjects with a diastolic OPP lower than 50mmHg have a four times greater risk of developing OAG than those with a DOPP of 80mmHg [3]. Relative risk for development of glaucoma was 2.0 for SOPP, 2.1 for DOPP and was 2.6 for MOPP [11].

In individuals with normal BP and autoregulation, rise in IOP would be required for ONH blood flow to get compromised, whereas in case of arterial hypotension, or other vascular risk factors a normal IOP too may interfere with ONH blood flow. This mechanism is important in pathogenesis of glaucomatous optic neuropathy particularly in normotensive glaucoma.

A study conducted by Amit K Deb et al [7] showed that subjects on antihypertensive medications had two to three fold increased risk of having glaucoma whose cause may be attributed to bedtime dosing of antihypertensive medication which causes a drop in nocturnal BP and thus reducing OPP or may also be due to severity and chronicity of hypertension which disrupts the autoregulatory mechanisms of blood flow in ONH.

A study by Langman et al [16] found that anti-hypertensive medications like β-blockers have a beneficial effect on the progression to glaucoma, though not statistically significant while that of angiotensin-converting enzyme (ACE) inhibitors or calcium channel blockers had a statistically significant increase in the risk of progression to glaucoma [1]. Thiazide diuretic had increased risk of glaucoma [2]. These changes with antihypertensive medications may be due to their bedtime dosage causing a drop in nocturnal BP, eventually leading to reduction in OPP. Therefore, blood pressure has to be evaluated in all patients of glaucoma especially in normotensive glaucoma, POAG patients with documented progression of glaucoma and in those with co-existing systemic microvascular disease.

A study conducted by Anna Horwitz et al [15] found that all drugs except vasodilators have a protective effect against glaucoma, particularly

anti-adrenergic drugs (α-blockers) have greatest protective effect. It also showed that treatment with anti-hypertensive medication postpones the onset of glaucoma and leads to a reduction in trend of glaucoma by 43%.

Since OPP is one of the risk factors for development and progression of open angle glaucoma and as it is affected by systemic blood pressure fluctuation and thus on anti-hypertensive medication, this study is planned to compare the OPP in hypertensive subjects on treatment with normotensive subjects and evaluate the association between OPP and anti-hypertensive medications.

MATERIALS AND METHODS

After obtaining institutional ethical committee approval this study was conducted at Bapuji eye hospital, Karnataka, India.

It was a cross-sectional observational study comprising a total of 110 subjects, among which 55 subjects (group A) were primary hypertensives on treatment and the remaining 55 subjects (group B) were normotensives.

1. Patient demographics were noted.
2. Hypertensive subjects were asked about details of antihy pertensive medications, dosing and duration. Patients with secondary causes for hypertension (endocrine causes, renal causes, steroid use), diabetes mellitus, thyroid disease, cardiovascular disease, unwilling to participate were excluded from study.
3. IOP and BP were recorded as below,

- An average of three readings of IOP measured 1 hour apart in both eyes using Goldmann applanation tonometer was recorded.
- An average of three readings of BP measured 1 hour apart by auscultatory technique taken with mercury sphygmomanometer in sitting position was recorded.

4. Detailed ophthalmic examination including slit lamp examination and posterior segment examination was done.
5. Following parameters were calculated as,

- Mean arterial blood pressure (MABP) = diastolic BP + 1/3(SBP-DBP).
- Systolic ocular perfusion pressure (SOPP)= Systolic BP-IOP.
- Diastolic ocular perfusion pressure (DOPP)= Diastolic BP-IOP.
- Mean ocular perfusion pressure (MOPP) = (2/3 MABP) -IOP.

SPSS (Version, 17) software was used for data analysis. Results are presented as Mean ± SD and range values for continuous measurements and frequencies as number and percentages. Unpaired t test was used to compare the means between two groups. One way ANOVA was used for simultaneous multiple group comparisons. Categorical data was analysed by Chi-square test. A P value of ≤0.05 was considered as statistically significant.

RESULTS

A total of 110 individuals participated in this study among which group A included 55 subjects who were primary hypertensives on treatment and group B included 55 subjects who were normotensives.

Results of the study are as shown below,

Table 1: BASELINE DEMOGRAPHICS OF PARTICIPANTS IN TWO GROUPS.

		Group A	Group B	Group A vs Group B
No. of cases		55	55	
Age (years)	Mean ± SD	53.9 ± 8.0	47.7 ± 5.4	t = 4.72, P < 0.05, S
	Range	40 - 73 years	40- 60 years	
Sex	Male	31(56.4%)	27(49.1%)	X^2 = 0.58, P = 0.45, NS
	Female	24(43.6%)	28(50.9)	

Mean age in group A was 53.9 years and that in group B was 47.7 years. Group A constituted of 56% males and 44% of females whereas group B had 27 49% of males and 51% of females.

Table 2: Comparison of BP, IOP and OPP between two groups

Variable	Group A	Group B	Group A vs Group B	
	Mean±SD	Mean±SD	T	P
MABP	101.2±4.7	91.3±6.9	8.80	< 0.001, HS
Avg IOP (mmHg) (RE)	14.5±2.7	13.7±2.0	1.78	0.08, NS
Avg IOP (mmHg) (LE)	14.5±2.8	14.0±1.9	1.00	0.32, NS
SOPP(RE)	116.2±8.7	103.9±7.2	8.04	< 0.001, HS
SOPP(LE)	116.2±8.4	103.6±7.2	8.48	< 0.001, HS
DOPP(RE)	71.9±5.2	64.6±6.9	6.28	< 0.001, HS
DOPP(LE)	71.9±5.3	64.3±6.9	6.60	< 0.001, HS
MOPP(RE)	53.0±3.9	47.2±4.0	7.69	< 0.001, HS
MOPP(LE)	52.9±3.8	46.9±3.9	8.39	< 0.001, HS
Unpaired t test		(Values are Mean ± SD)		
P < 0.001, High sig.				

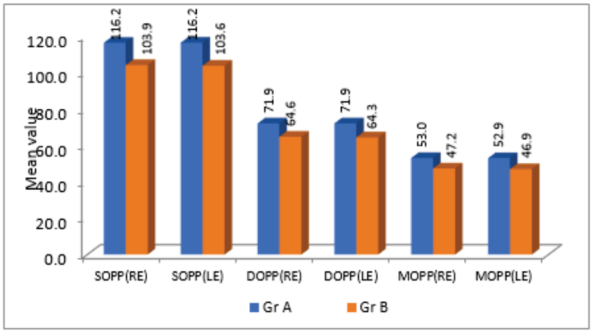

Fig 1: Graphical representation of comparison of OPP between two groups.

Mean arterial BP in group A was 101.2mmHg and that in group B was 91.3mmHg.

Average IOP in group A was 14.5mmHg and that in group B was ranging from 13.7 to 14mmHg.

Statistical analysis of comparison of IOP between both the groups showed non-significant (p=0.08, p=0.32) results as calculated by unpaired t test.

SOPP, DOPP and MOPP in group A were 116.2±8.7mmHg, 71.9±5.2mmHg, 53±3.9mmHg respectively. Similarly in group B SOPP. DOPP and MOPP were 103±7.2mmHg, 64±6.9mmHg, 47±4mmHg respectively.

Comparison of OPP parameters among two groups statistically by unpaired t test showed, highly significant results.

Table 3: Treatment wise changes in BP and IOP

Rx group		No. of patients	MABP	Avg IOP (mmHg) (RE)	Avg IOP (mmHg) (LE)
1	ARB	16 (29.1%)	100.9±3.9	15.5±2.7	15.4±2.6
2	ARB + Diuretic	12 (21.8%)	101.5±4.9	14.3±2.9	14.7±2.7
3	β blocker	12 (21.8%)	100.6±5.2	13.3±1.6	13.2±2.0
4	Calcium channel blocker	12 (21.8%)	101.8±5.1	14.9±2.8	15.1±3.3
5	Calcium channel blocker + β blocker	3 (5.5%)	101.3±7.1	12.7±4.2	11.3±1.2
ANOVA, F			0.11	1.59	2.40
P value			0.98, NS	0.19, NS	0.06, NS
One way ANOVA			(Values are Mean ± SD)		
P > 0.05, NS					

Out of 55 primary hypertensive subjects in group A,
29% (16) were treated with angiotensin receptor blocker (ARB) group of drugs, 22% (12) were on combination therapy of ARB+ diuretic group, 22% (12) were on β blockers, 22% (12) were on calcium channel blockers and 6% (3) were on combination therapy of calcium channel blockers and β blockers.

Mean arterial BP among all above mentioned group of antihypertensive drugs ranged from 100.6mmHg to 101.8mmHg. Statistical analysis by ANOVA test showed non-significant (p=0.98) results.

Average IOP in those subjects on,

ARBs was 15.5mmHg, ARB + diuretic combination drugs was 14mmHg, β blockers was 13mmHg, calcium channel blockers was 15mmHg, calcium channel blockers + β blockers was 11.3 to 12.7mmHg. Statistical analysis by one way ANOVA test showed non-significant (p=0.19, p=0.06) results.

Table 4: Treatment wise changes in OPP parameters.

Rx group		SOPP (RE)	SOPP (LE)	DOPP (RE)	DOPP (LE)	MOPP (RE)	MOPP (LE)
1	ARB	115.1±5.0	115.3±5.0	70.5±4.9	70.6±5.0	51.7±3.2	51.9±3.2
2	ARB + Diuretic	116.4±7.8	116.0±7.4	72.6±5.5	72.2±5.6	53.4±3.8	53.0±3.6
3	β blocker	114.8±11.1	115.0±10.9	73.5±5.6	73.7±5.6	53.7±4.2	53.9±4.1
4	Calcium channel blocker	117.8±10.5	117.6±9.8	71.4±5.1	71.3±5.1	52.9±4.1	52.8±3.8
5	Calcium channel blocker + β blocker	120.7±13.3	122.0±12.2	72.7±6.1	74.0±5.3	54.9±6.6	56.2±5.2
ANOVA, F		0.41	0.54	0.65	0.73	0.71	1.10
P value		0.80, NS	0.71, NS	0.63, NS	0.57, NS	0.59, NS	0.37, NS

OPP parameters such as SOPP, DOPP and MOPP among various group of anti-hypertensive drugs is,
SOPP in those patients on,
ARBs was 115mmHg, ARB + diuretic was 116mmHg, β blockers was 115mmHg, calcium channel blockers was 118mmHg, calcium channel blockers + β blockers was 120.7 to 122mmHg.
DOPP in those patients on,
ARBs was 71mmHg, ARB + diuretic was 72mmHg, β blockers was 74mmHg, calcium channel blockers was 71mmHg, calcium channel blockers + β blockers was 72.7 to 74mmHg.
MOPP in those patients on,
ARBs was 52mmHg, ARB + diuretic was 53mmHg, β blockers was 54mmHg, calcium channel blockers was 53mmHg, calcium channel blockers + β blockers was 54.9 to 56.2mmHg.
Statistical analysis of SOPP, DOPP and MOPP in subjects on various anti-hypertensive group of drugs showed non-significant (p>0.05) results as evaluated by ANOVA test.

DISCUSSION

In our study including 55 controlled hypertensive and 55 normotensive subjects, we found that SOPP, DOPP and MOPP in controlled hypertensive group is statistically higher than normotensive group as indicated by p<0.001 (table 2) reported from an unpaired t test indicating that OPP in eyes of controlled hypertensive subjects is stable and thus showing its importance in glaucomatous damage. On studying about correlation between different group of anti-hypertensives and its effect on IOP, OPP no statistical significance was noted which might be attributed to small sample size of 55 subjects. In a study conducted by Anna Horwitz et al [15], antihypertensive medication is shown to reduce the rate at which risk of glaucoma develops over time. Thus, this study shows preventive effect of antihypertensive medication against development of glaucoma.

Thus, our study corroborates the study conducted by Anna Horwitz et al. In the Baltimore eye survey high IOP was found in patients with systemic hypertension and was a risk factor for development of POAG. Evidence from literature and clinical trials suggests that OPP can also be linked to open angle glaucoma. OPP which is difference between IOP and BP is low in hypertensive patients. Lower ocular perfusion pressure was found to be an independent risk factor for open angle glaucoma [4]. Ocular perfusion pressure changes were more likely to be made in patients with hypertension than normotensive patients.

In a study conducted by Gore et al [13], mean OPP, systolic OPP and diastolic OPP were found to be lower in patients of POAG as compared to control group thus providing evidence that low perfusion pressure is an important vascular factor associated with high prevalence of OAG.

In a study conducted by Khandelwal et al [4], mean OPP was higher in hypertensive group as compared to normotensive subjects and mean OPP was significantly low in patients taking antihypertensive drugs as compared to those not on antihypertensive treatment.

Various factors listed below might have limited our findings,

1. We could not measure 24hour BP and IOP to account for nocturnal changes in IOP and BP. As we know by literature that nocturnal hypotension causes drop in OPP leading to ONH damage it becomes an important assessment.
2. BP measurements recorded in clinic could be confounded by white coat hypertension, masked hypertension.
3. We restricted our definition of treatment to patients taking antihypertensive medications and did not include lifestyle modifications alone.
4. We did not follow our patients to screen for development of glaucomatous changes.

Thus, further a longitudinal study to follow up and also inclusion of diurnal recordings of IOP and BP, influence of types of antihypertensive drug in ocular blood flow is needed to corroborate findings.

CONCLUSION

The findings of our cross-sectional observational study suggest that a significant association exists between OPP parameters in controlled hypertensive subjects vs normotensive subjects with OPP being higher in the former than the latter, showing the effect of hypertension control on OPP and thus on optic nerve head.

Further, a longitudinal study constituting large sample size, with diurnal recording of IOP and BP should be considered to corroborate findings of our study.

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