DISTRIBUTION OF OCULAR PERFUSION PRESSURE IN HYPERTENSIVE PATIENTS AND ITS RELATIONSHIP IN DEVELOPMENT OF OPEN ANGLE GLAUCOMA

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ABSTRACT

AIM

To study the distribution of ocular perfusion pressure in hypertensive patients and its relationship in development of open-angle glaucoma.

DESIGN

Cross-sectional observational study.

MATERIALS AND METHODS

A total of 200 subjects who were above 40 years of age diagnosed with essential hypertension by a physician were selected irrespective of their treatment status. Intraocular pressure was measured with Goldman applanation tonometry. Systolic and diastolic blood pressure were recorded with sphygmomanometer. Optic disc evaluation was done using +90D lens. Mean Ocular Perfusion Pressure (MOPP) was calculated using the standardised formula: [Mean Ocular Perfusion Pressure (MOPP) = 2/3 (Mean Arterial Pressure)- IOP] where Mean Arterial Pressure (MAP) = diastolic BP (DBP) + 1/3 systolic BP-diastolic BP (SBP-DBP). The difference between systolic and diastolic blood pressure is identified as the pulse pressure.

ANALYSIS

The association between MOPP and open angle glaucoma was analysed using Odds ratio in which the risk was higher in lowest quartile (Q1) [OR-1.9200] than in higher quartile (Q4) [OR-1.00].

CONCLUSION

Subjects with low ocular perfusion pressure due to increased IOP (or) decreased BP are more likely to develop open angle glaucoma providing further evidence in vascular pathogenesis.

KEYWORDS

Mean Ocular Perfusion Pressure, Open Angle Glaucoma, Hypertensives.

HOW TO CITE THIS ARTICLE: Raajaseharan T, Rajasekaran M. Distribution of ocular perfusion pressure in hypertensive patients and its relationship in development of open angle glaucoma. J. Evid. Based Med. Healthc. 2016; 3(69), 3748-3751. DOI: 10.18410/jebmh/2016/802

INTRODUCTION: Glaucoma is defined as a multifactorial optic neuropathy in which there is a characteristic acquired loss of retinal ganglion cells and atrophy of optic nerve.[1] Elevated intraocular pressure is already a known major risk factor for occurrence of the disease and its progression, hence decreasing IOP is the major criteria in treatment to halt the progression of the disease.[2] However, only 33% of patients with open-angle glucoma have documented elevations in IOP.[2] Many studies indicate that reduction of ocular blood flow plays a major role in the pathogenesis of open-angle glaucoma while it is thought to be secondary to vascular dysregulation in susceptible patients.[3,4] Hence, the term Ocular Perfusion Pressure was introduced.

Mean ocular perfusion pressure is the net pressure gradient causing the blood to flow to the eye. It's the difference in pressure between the arterial and venous parts of vascular bed throughout the eye including optic nerve head. The potential consequences of abnormal low levels of OPP include optic nerve head and retinal ischaemia as well as reperfusion injury leading to development of open angle glaucoma and it's progression.[1] Hence, OPP changes occur when there is a change in either in BP/IOP or both. When blood pressure decreases or IOP raises, ocular perfusion pressure becomes low. This is maintained by the presence of autoregulation mechanism. Autoregulation impairment means the eye is less able to cope up with the continuos episodes of low ocular perfusion pressure and with overtime produces a cumulative effect producing progressive retinal ganglion cell loss inturn causing nerve fibre defect ultimately progressing to field defect.[5] Hence, OPP is termed recently as 'Risk Factor' (or) 'Progression Factor' in the development of open angle glaucoma.

Financial or Other, Competing Interest: None.
Submission 15-07-2016, Peer Review 25-07-2016,
Acceptance 16-08-2016, Published 29-08-2016.
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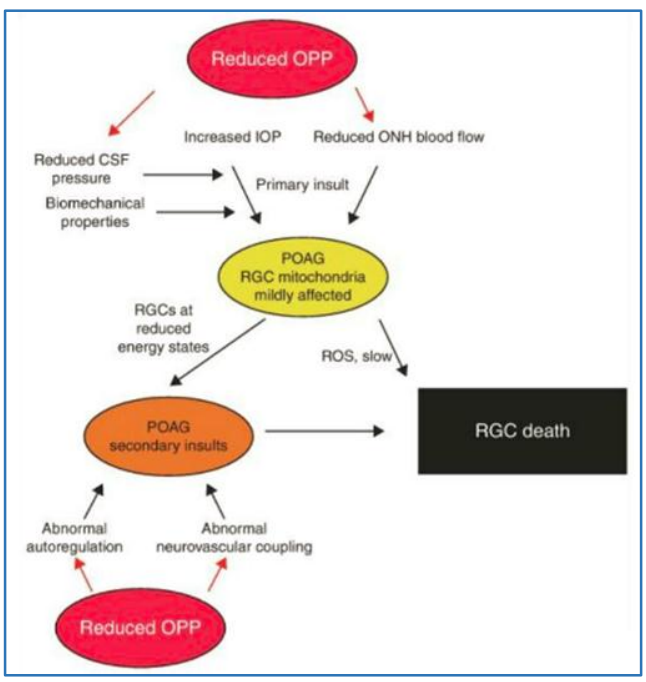
DOI: 10.18410/jebmh/2016/802

The pathogenesis of glaucomatous damage due to decreased ocular perfusion pressure maybe due to:

a. Optic nerve head ischaemia, which reduce nutrients to retinal ganglion cell axons.
b. Once primary insult has occurred at the level of optic nerve head, retinal ganglion cells appear to function at reduced energy levels with affected mitochondria.
c. Oxidative stress associated with extensive production of reactive oxygen species, free radicals, hydrogen peroxide.[6]



MATERIALS AND METHODS: The study was carried out at Department of Ophthalmology in a tertiary healthcare center. Ethical clearance was obtained from Institutional Ethical Committee. Informed consent was obtained from all subjects. Enrolled subjects were above 40 years of age. Participants were recruited from a convenient sample of 200 patients who were diagnosed with essential hypertension by a physician and selected irrespective of their treatment status (on treatment, not on treatment, or irregular treatment). Patients with hypertension due to secondary causes (Endocrine/Kidney disease/Steroid induced) were excluded. 3 measurements of BP were recorded 5 minutes apart with sphygmomanometer and average recording taken. IOP was recorded with applanation tonometer. Optic disc evaluation was done usng +90D lens. MOPP was calculated using standardised formula.

Mean Ocular Perfusion Pressure [MOPP] = 2/3*MAP (mean arterial pressure)-IOP. Where MAP=DBP (diastolic blood pressure) + 1/3 [SBP (systolic blood pressure) - DBP (Diastolic blood pressure)]. Basically, difference between systolic and diastolic blood pressure is the pulse pressure and MOPP is difference between arterial blood flow and venous blood flow. All subjects with high IOP (>21 mmHg) or CD ratio >=0.5 (or) assymetry of >0.2 were evaluated for fields examination.

Glaucomatous patients were diagnosed by the appearance of glaucomatous cupping and characteristics field defects with (or) without increase in IOP.

STATISTICAL ANALYSIS:
Total Patients = 200.

	Mean Ocular Perfusion Pressure	**Total No. of Cases at Risk (n)**	**Positive Patients (n1)**
Q1	<50 mmHg	28	3
Q2	50-55 mmHg	64	4
Q3	56-60 mmHg	74	4
Q4	>60 mmHg	34	2
Total		**200**	**13**

MOPP (mmHg)

	Q4	**Q3**	**Q2**	**Q1**
All Persons n Cases at Risk	34/200	74/200	64/200	28/200
MOPP (Values)	>60	56-60	50-55	<50
N1 cases (Positive)	2	4	4	3
Odd's Risk Ratio	1.00 (Reference)	0.9143	1.0667	1.9200

Univariate regression models were used to determine the association between the covariants and risk of glaucoma. Statistical analysis was carried out using Odds ratio. In our study, we used 200 patients who were hypertensives and their MOPP was calculated. Using logistic regression, the association between MOPP and glaucoma was analysed. The relationship being evaluated as outcome status by Odds ratio.

RESULT: In our study, MOPP was calculated for all the 200 hypertensive patients and patients were graded into 4 groups Q1 (<50), Q2 (50-55), Q3 (55-60), Q4 (>60).

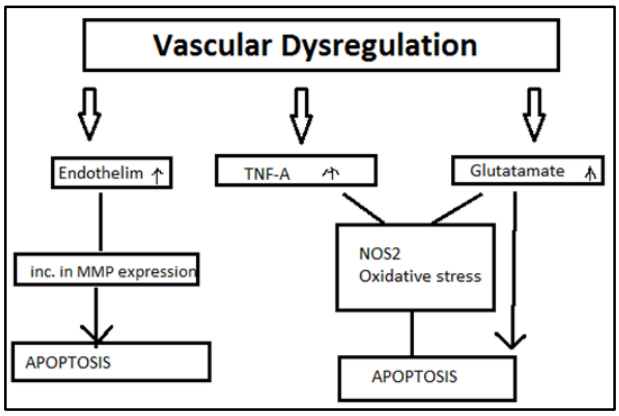
According to mean ocular perfusion pressure, the incidence of open angle glaucoma in each group were identified. Odds ratio was calculated in each group, which showed increased Odds ratio (1.9200) in Q1 group whose MOPP (<50 mmHg) compared to others. Q1 group comprised of the population, which had either increased IOP or decreased blood pressure. The people who were in Q1 group were mostly on antihypertensive treatment.

DISCUSSION: In our study, presence of systemic hypertension or elevation of IOP alone did not lead to increased likelihood of developing glaucoma. The frequency of occurrence of open angle glaucoma was found to be more in a smaller group, which had a lower perfusion pressure due to lower extremes of blood pressure (Averaging around <100/70).

Hence, from the analysis, we come to know that patients who are on rigorous antihypertensive treatment or due to nocturnal hypotension have low OPP are those who are at increased risk for development of glaucoma. A direct and clear relationship between BP and glaucomatous damage has however not been established clearly till now.[7] Association between systemic hypertension and POAG has been evaluated by various population-based studies that yield contradictory results. In Baltimore Eye Survey, cases who had OPP <30 mmHg, there was 6 fold higher risk of development of OAG.[8] In Egna-Neumarket Study, increased risk of OAG was associated with DBP <50 mmHg.[9] In proyecto VER study, 3-fold higher risk was observed among subjects with DBP <45 mmHg. In Barbados Eye Study, risk for long-term development of glaucoma was decreased DBP, decreased SBP, decreased MOPP (<40 mmHg).[10] In Early Manifest Glaucoma Trail, patients with lower systolic perfusion pressure at baseline progressed faster than their counterparts had->50% higher risk.[11] In Rotterdam Eye Study, which was done in patients only receiving antihypertensives to study prevalence of OAG. (RR-1.9), (DOPP <50 mmHg) had increased risk of OAG.[12] The Thessaloniki Eye Study, found increased disc cupping and decreased rim in those on antihypertensives making possible explanation that marked lowering of BP in susceptible individuals may lead to optic disc changes.[13] In Los Angeles Latino Study, lower MOPP, DOPP, SOPP had increased prevalence of OAG.[14]

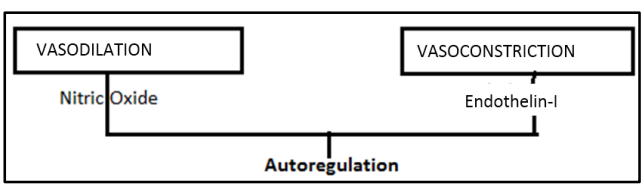
From these studies, it is understood that people on anti-hypertensive medications have an increased risk, which may be related to the bedtime dosing or reduction in nocturnal BP. The 2 principal theories, which explains the pathogenesis of glaucoma are the mechanical and the vascular theory. According to mechanical theory, increased IOP causes stretching of laminar beds and damage RGC'S. According to vascular theory, glaucoma develops as a consequence of insufficient blood flow, which maybe explained by following mechanism, which depends on vascular resistance. With vascular resistance, a positive association of glaucoma has been observed with migraine and peripheral vascular abnormalities that involve dysregulation of cerebral and peripheral vasculature respectively.(15,16)

The vascular resistance in ONH depends upon the state and calibre of blood vessels, which in turn is maintained by autoregulation.(17) A) Autoregulation is the ability of blood vessels to maintain a relatively constant blood flow, maintenance of pressure in capillaries, and nutrient supply whatever maybe the change in perfusion pressure and varied metabolic demand. Both optic nerve head and retina has autoregulation. An interrelation between choroid and retinal blood circulation is important for maintaining a healthy optic nerve. There is evidence that the retinal, ONH, choroidal blood flow show automatic regulatory capacity in response to OPP.(18,19,20)



The general idea is that the terminal arterioles regulates resistance to flow, i.e they dilate to increase blood flow when perfusion pressure falls and constricts to reduce the blood flow. Since, there is a cut-off limit that how far the vessels constrict or dilate, autoregulation operates only at critical levels, below which it becomes ineffective.

Also, the agents formed by vascular endothelium play an important role in autoregulation. The endothelial cells release various known endothelial vasoactive agents, which include prostanoids, nitric oxide, endothelins, angiotensins, oxygen free radicals, thrombaxane.(21,22)



Hence, all these factors contribute to a defective autoregulation. In supine position, during sleep, there is a short-term rise in IOP as a part of circadian rhythm and IOP is highest early in the morning and there is generally nocturnal hypotension.(23) Moreover, when patients are on systemic antihypertensives, which has a bedtime dose, the effect gets added with the recurrent spikes of IOP leading to defective ocular perfusion pressure and development of optic nerve head ischaemia in turn leading to damage of RGC'S, which in turn leads to ocurrence and progression of OAG.(24) Moreover, ocular blood flow is determined not only by ocular perfusion pressure, but also by blood vessel resistance, which in turn is related to blood viscosity and vessel diameter. Studies on specific antihypertensives for glaucoma patients is being carried out now. Glaucoma patients when usually refered to physicians preferably are given calcium channel blockers and beta-blockers are stopped for hypertensive management. The calcium channel blockers have vasodialatory effect by increasing the blood vessel diameter thereby increasing the blood flow eventhough it has BP lowering effect. Usually, they stop the night dosage of the drug and preferably prevent over medicating with antihypertensives in boderline hypertensive patients. This maintains the autoregulatory mechanism by maintaining not only constant blood flow (vascular reserve), but also preserves neuronal functions (functional reserve).

CONCLUSION: The main reason why the relation between ocular perfusion pressure and glaucoma is still not utilised in management lies in the difficulties to measure retinal and optic nerve head blood flow. Its not possible to increase ocular perfusion pressure as a part of glaucoma treatement. In exception, it maybe used to decrease rigorous antihypertensive treatment and to avoid the night dosage in patient with systemic hypertension to prevent very low OPPs. Hence, in our study, OPP measurement was done as a noninvasive, easy to obtain, inexpensive clinical data. It will be usefull in rural settings where more number of patients are seen regularly on a daily basis, it will be a cost efficient, easy to screen, and to obtain data, which can be used as a monitoring tool for patients who are on anti-hypertensive treatment.

It will be a clinical tool where serial recordings of MOPP of patients on nocturnal hypotension can be maintained and overmedication prevented accordingly to prevent the occurance and progression of glaucoma.

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