ISSN: 0975-1556

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2021; 13(3); 396-403
Original Research Article

An Investigation to Assess the Clinical Relationship Between Glaucoma and systemic Hypertension as well as its Impact on Visual Morbidity

Shreya[1], Binod Kumar Sharma[2], Priyanka[3], Srishti Sharma[4]

[1]Senior Resident, Department of Ophthalmology, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India
[2]Consultant Physician & Cardiologist, Sharma Healthcare Clinic, Begusarai, Bihar, India
[3]Senior Resident, Department of Physiology, DMCH, Laheriasarai, Darbhanga, Bihar, India
[4]General Medical Officer, Binodur, Begusarai, Bihar, India

Received: 01-07-2021 / Revised: 04-08-2021 / Accepted: 23-08-2021
Corresponding author: Dr. Binod Kumar Sharma
Conflict of interest: Nil

Abstract

Aim: The aim of present study is to evaluate the clinical correlation of glaucoma with systemic hypertension and its effect on visual morbidity. **Methods:** This was a prospective study conducted in the Department of Ophthalmology, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India, for 10 months. It was performed on 120 patients between the age group of 30 to 65 years which included newly diagnosed hypertensive and previously diagnosed hypertensive receiving treatment and on follow up now. Patients are classified as hypertensive based on elevated BP readings of >120/80 mm Hg on two separate occasions according to current American Heart Association. The oral hypotensive medication taken by patients were categorized into 5 groups as calcium channel blockers (CCB), diuretics, angiotensin converting enzyme inhibitors (ACE), angiotensin receptor blockers and beta blockers. Glaucoma was defined as progressive optic neuropathy associated with visual field loss in which IOP is a modifiable factor according ICO Glaucoma Guidelines. **Results:** Among the 120 hypertension patients involved in the study, 50 patients (41.33%) were found to have glaucoma. 70 patients (58.33%) were female, and 50 patients (41.67%) were male. Age group affected was 15.83% between 30-40 years, 31.67% between 40 to 50 years and 52.50% above 50 years, the mean age being 56.2 years. Decreased IOP was highest among patients taking CCB in 25 patients (46.30%), followed by beta blockers in 4 patients (40%), ACE inhibitors 13 patients (38.24%), ARB 7 patients (43.75%) and diuretics in 1 patient (16.67%). The range of IOP in the treated population was between 10-16 mmHg and this difference in those on hypertension medications was statistically significant with p-value = 0. 01. **Conclusion:** Hypertension can cause both reduction and elevation in IOP. Treatment of hypertension does lower the IOP and prevent further progression of glaucoma and prevent any visual loss.

Keywords: Hypertension, Glaucoma, IOP

Introduction

An abnormally high blood pressure (BP) is a major cause of morbidity and mortality in the Western countries[1] including South Africa[2] and is one of the most common clinical conditions requiring long term medical care.[3] Hypertension is characterized by a persistent systolic BP of more than 140 mmHg and a diastolic BP of more than 90 mmHg.[4] Increased BP can result in symptoms such as dizziness, headache as well as more serious complications such as coronary artery disease, heart failure or even death.[5]

Hypertension is also associated with ocular complications such as optic neuropathy and hypertensive retinopathy which is one of the leading causes of blindness in developing countries.[6] Similarly, an abnormally increased intraocular pressure (IOP), which is known to be a glaucoma risk factor[7,8] causes permanent damage to the optic nerve leading to vision impairment[3]. Glaucoma affects more than 66 million people worldwide and as a result at least 6.8 million individuals have bilateral blindness[3]. Therefore, both high BP and IOP should be given adequate attention by primary eye-care practitioners including optometrists. This suggests the need for optometrists and other eye-care practitioners to routinely measure BP and IOP on their patients.

Several cross-sectional studies of Western populations have shown a positive relationship between systemic BP and IOP.[3,9,10] McLeod *et al*.[11] found that change in IOP was positively correlated with change in systolic BP. Similarly, Leshe and Podgor[12] found a significant positive correlation between IOP and BP. In people aged between 43-86 years, living in Beaver Dam, Wisconsin (USA), a longitudinal study[13] of systemic BP, IOP and history of use of some BP medications revealed that intraocular pressures were significantly correlated with systolic and diastolic blood pressures at both baseline and follow up. Although McLeod *et al*.[11] found no consistent relationship between IOP and BP initially in their study, when an autoregressive model was used to examine the relationship between change in BP and IOP after one or two years, a change in IOP was positively correlated to change in systolic BP. The results indicated that changes in IOP over time are associated with changes in systolic BP. It has also been observed that individuals on anti-hypertensive medications were 2–3 times more likely to be affected by glaucoma. This may be attributed to the bedtime dosage of anti-hypertensive drugs which cause a drop in nocturnal BP, eventually leading to a reduction in OPP. A study performed by Pache and Flammer reported a nocturnal dip in BP as an important risk factor for POAG.[14] The Thessaloniki eye study noted that lowering of BP from antihypertensive treatment was associated with glaucomatous changes.[15]

Material and Methods

This was a prospective study conducted in the Department of Ophthalmology, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India, for 10 months, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

After taking informed consent detailed history was taken from the patient or the relatives if the patient was not in good condition. The technique, risks, benefits, results and associated complications of the procedure were discussed with all patients.

It was performed on 120 patients between the age groups of 30 to 65 years which included newly diagnosed hypertensives and previously diagnosed hypertensives receiving treatment and on follow up now. Patients with other systemic diseases or vascular pathologies were excluded from the study. Those with hypertension but less than 30 years of age were not enrolled into the study as both glaucoma and

hypertension could be due to congenital causes in young individuals. All patients had a minimum follow up of 6 months and the need for regular review visits was explained to them. During the first visit and each follow up opinions regarding the progress of hypertension was obtained from the departments of cardiology, internal medicine and neurology.

Patients are classified as hypertensive based on elevated BP readings of >120/80 mm Hg on two separate occasions according to current American Heart Association. Blood pressure measurements were made over 3 visits and the average of last two measurements was used for analysis. Recording was done with manual sphygmomanometer. The oral hypotensive medication taken by patients were categorized into 5 groups as calcium channel blockers (CCB), diuretics, angiotensin converting enzyme inhibitors (ACE), angiotensin receptor blockers and beta blockers.

Glaucoma was defined as progressive optic neuropathy associated with visual field loss in which IOP is a modifiable factor according ICO Glaucoma Guidelines.

A detailed history of age, sex, duration of hypertension, history of other co morbidities and treatment were collected. The participants then underwent a detailed ophthalmological evaluation including visual acuity, anterior segment evaluation using slit-lamp bio-microscopy and fundus evaluation using a + 90 D lens/ indirect ophthalmoscope. IOP measurement was done by applanation tonometry with Goldman Applanation Tonometer. Fluorescein was instilled in each eye and the tonometer was set at 10mmHg. Mires were viewed through the prism and measurements were read from the rotating dial. The same procedure was repeated in the other eye. Phasing technique of repeating recordings was done and the average IOP was used in the study. Gonioscopy was performed and the visual field of patients was analysed using Humphrey visual field analyser.

Analysis

The collected data were analysed using IBM SPSS statistics software 21 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean & S.D. were used for continuous variables. To find if significant difference existed between the bivariate samples in independent groups the unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used. In both the above statistical tools the probability value 0.05 was considered as a significant level.

Results

Among the 120 hypertension patients involved in the study, 50 patients (41.33%) were found to have glaucoma. 70 patients (58.33%) were female and 50 patients (41.67%) were male. Age group affected was 15.83% between 30-40 years, 31.67% between 40 to 50 years and 52.50% above 50 years, the mean age being 56.2 years.

Hypertensive patients diagnosed with having glaucoma had a mean duration of 5.02 years. Among the 50 newly diagnosed patients 30 patients had glaucoma and 17 patients did not have glaucoma. They had been on oral hypertension medications for a duration ranging from 1 month to 6 months.

Type of glaucoma associated with systemic hypertension was primary open angle glaucoma (POAG) in 8 patients (16%), ocular hypertension (OHT) in 41 patients (82%) and normal tension glaucoma (NTG) in 1 patient (2%).The increased incidence of OHT among hypertensives was statistically significant with a p-value of 0.01. We did not see any association with angle closure glaucoma or secondary open angle in any of our patients.

In those with OHT, predominant fundus changes were seen as increased cup disc ratio in 16% and neuroretinal thinning in 12%. Visual field analysis showed nasal

step with isolated scotomas in the Bjerrum's area as the commonest change in 7% patients. Corneal thickness in patients diagnosed with ocular hypertension was on an average 0.759. +/-0.02mm. Thicker cornea was noted in 32% whereas thinner cornea was noted in 2% of patients.

The oral hypotensive medication taken by patients were categorized into 5 groups as calcium channelblockers (CCB), diuretics, angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARB) and beta blockers. Total number of patients taking oral hypertensives was 75. In the group on medications the range of IOP was between 14-26mmHg.

Decreased IOP was highest among patients taking CCB in 25 patients (46.30%), followed by beta blockers in 4 patients (40%), ACE inhibitors 13 patients (38.24%), ARB 7 patients (43.75%) and diuretics in 1 patient (16.67%). The range of IOP in the treated population was between 10-16 mmHg and this difference in those on hypertension medications was statistically significant with p-value = 0. 01.

Table 1: Demographic Profile

Gender	**Number of patients**	**Percentage**
Male	70	58.33
Female	50	41.67
Age in years		
30-40	19	15.83
40-50	38	31.67
Above 50	63	52.50

Table 2: Hypertension duration and glaucoma association

Glaucoma	N	Mean Duration	STD Deviation	P Value
Yes	50	5.02	5.22	0.591
No	70	8.03	5.74	

Table 3: Hypertension medication and IOP reduction

Medication	**Glaucoma**		Total
	No	Yes	
CCB	29	25	54
	53.70%	46.30%	100%
Diuretics	5	1	6
	83.33%	16.67%	100%
ACE inhibitors Count	21	13	34
	61.76%	38.24%	100%
ARB	9	7	16
	56.25%	43.75%	100%
Beta blockers	6	4	10
	60%	40%	100%
Total	70	50	120
	58.83%	41.33%	100%

Discussion

Increased BP and IOP may have adverse effect if left unattended. This suggests the need for patients to be always examined for any BP or IOP changes whenever they visit primary eye-care professionals. This study

was therefore carried out to investigate possible relationships between systemic BP and IOP in a young indian adult population.

We have found that change in IOP is directly and significantly associated with changes in systemic blood pressures. This would suggest that treatment of blood pressure might have an effect on risk of developing glaucoma, as IOP is probably the most important risk factor for glaucoma in general populations. We have previously shown that those with higher IOP at baseline were more likely to have larger cup:disc ratio 5 years later. While our findings do not directly indicate a beneficial effect of reduced blood pressure on the risk of glaucoma, they are compatible with that possibility.[16]

This in turn leads to an increased filtration of aqueous fluid through the ciliary body thus causing elevation in IOP.[17] Raised blood pressure also affects the episcleral venous pressure which regulates the aqueous flow across trabecular mesh work through Schlemms canal.[18] However, we found in our patients that an increased diastolic BP more frequently caused raised IOP.

It has been reported following various studies that for every 1mm increase in perfusion pressure there will be an increase of 1mm in IOP. There is an alteration in sodium transport in the distal nephrons and ciliary epithelium, leading to increased excursion of sodium into the renal filtrate and aqueous humour respectively. This is mediated by corticosteroid hormone (cortisol and aldosterone) and glucocorticoid and mineralocorticoid receptors.[19]

In this study, the type of glaucoma associated with systemic hypertension was primary open angle glaucoma (POAG) in 8 patients (16%), ocular hypertension (OHT) in 41 patients (82%) and normal tension glaucoma (NTG) in 1 patient 2%. The increased incidence of OHT among hypertensives was statistically significant with a p-value of 0.01. In our study, OHT was the commonest type of glaucoma and was associated with structural and functional changes in the optic nerve head and visual fields. It has already been established in literature that a thinner or thicker cornea can give IOP readings which may be higher or lower than the actual value. A correction to the recorded IOP is always has to be done based on the pachymetry readings before treatment for glaucoma is started.

Reduced IOP readings were associated more in patients taking CCB, ACE inhibitors and ARB drugs. This is in concurrence with Langman et al. who stated that IP association showed increased odds ratio in hypertensive patients taking CCB, ACE inhibitors and ARB drugs.[20] Klein et al. stated that beta blocker drugs had a protective effect for glaucoma and hypertension.[21] In our study we noted that those on calcium channel blockers had least involvement of the ONH but those on beta blockers had lowest recordings of IOP. This variation of effects on glaucoma has not been reported in previous studies to the best of our knowledge. Leske et al. found that anti-hypertensive drugs were not associated with any increased risk of open angle glaucoma, but that ocular perfusion pressure has a significant effect on IOP.[22] From our cohort of patients we found that oral anti hypertensive drugs does have beneficial effect in the control of IOP.

In our study, the decreased IOP was highest among patients taking CCB in 25 patients (46.30%), followed by beta blockers in 4 patients (40%), ACE inhibitors 13 patients (38.24%), ARB 7 patients (43.75%) and diuretics in 1 patient (16.67%). The range of IOP in the treated population was between 10-16 mmHg and this difference in those on hypertension medications was statistically significant with p-value = 0. 01.

However, we feel that systemic beta blockers are another important factor that would have to be considered as they may mask an elevated IOP making a diagnosis of glaucoma difficult. IOP though only a risk

factor is important because it is the only treatable factor in glaucoma that can secondarily prevent progression of changes in the optic nerve head or visual field. Specifically, ACE inhibitors caused reduction in IOP only on long term use (greater than 1 year) although widely prescribed as anti-hypertensive agents. Calcium channel blockers and beta blockers in combination with CCB can increase ocular blood flow and thus play a neuro protective effect by reducing apoptosis of neurons.

Different anti-hypertensive medications are chosen based on associated heart failure or other systemic diseases and knowledge of the effect on IOP will be useful.[23] Beta blockers are not preferred in heart blocks or pulmonary obstructive disease and in such situations ACE inhibitors are used. CCB are usually second line agents.[24] Another important fact of treatment to be considered is that topical beta blockers in glaucoma management are not efficient in those on systemic beta blockers and hence treatment will have to be titrated accordingly.

There is an increased risk of glaucoma with both high and low BP. Drugs that can lower BP may sometimes increase the incidence of glaucoma due to specific effects on the optic nerve head. The exact cause of this complex relationship has not been understood but various influencing factors such as relationship between blood pressure and ocular perfusion pressure, dysfunctional autoregulation and peripheral vascular capacity have been suggested.[25] We found that the risk of glaucoma in hypertension is higher in women. Among all drugs used in the treatment of hypertension we concluded from our study that beta-blockers protect and calcium channel blockers and ACE inhibitors have a lesser effect on glaucoma. The limitation of the study was that the sample size and duration of study was less and a longer follow up could have provided more insight into disease progression. Hypertension and IOP have common biomechanical alteration in their pathogenesis.[26] Treatment of hypertension does lower the IOP and prevent further progression of glaucoma and prevent any visual loss.[27] A multidisciplinary approach which involves the ophthalmologist and treating physician will help in holistic monitoring the patient.

Conclusion

Hypertension can cause both reduction and elevation in IOP. Treatment of hypertension does lower the IOP and prevent further progression of glaucoma and prevent any visual loss.

References

1. Feeman WE. Prediction of the population at risk of atherothrombotic disease. Exp Clin Cardiol 2004 9 235-241.
2. Steyn K, Gaziano T, Bradshaw D, Laubscher R, Fourie J. Hypertension in South African adults: results from the demographic and health survey, 1998. J Hyper 2001 19 1717-1725.
3. Perlman JI, Delay CM, Sothern RB, Skolnick KA, Murray D, Jacobs RW, Shue JL, Kaplan E, Friedman NC, Nemchausky BA, Ryan MD, Kanabrocki EL. Relationships between 24h observations in intraocular pressure vs blood pressure, heart rate, nitric oxide and age in the medical chronobiology aging project. Clin Ter 2007 158 31-47.
4. Liang Y, Downs JC, Fortune B, Cull GA, Cioffi GA, Wang L. Impact of systemic blood pressure on the relationship between intraocular pressure and blood flow in the optic nerve head of non-human primates. Invest Ophthalmol Vis Sci 2009 50 2154-2160.
5. Khaw KT, Foster P. The eye - window to the soul or a mirror of systemic health? Or: What weight to give retinopathy as a risk factor for IHD. Heart 2009 95 348-349.
6. Gillow JT, Gibson JM, Dodson PM. Hypertension and diabetic retinopathy:

what's the story? Br J Ophthalmol 1999 83 1083–1087.
7. Luciano Bonomi MD, Giorgio Marchini MD, Michele Marraffa MD, Paolo Bernardi MD, Roberta Morbio MD, Aldo Varotto MD. Vascular risk factors for primary open angle glaucoma: The Egna-Neumarkt study. Br J Ophthalmol 2000 107 1287-1293.
8. Van Niekerk M, Van Rooyen FC, Joubert G, Hiemstra LA. The prevalence of the diagnosis of increased intra-ocular pressure in a general practice. SA Fam Pract 2006 48 16.
9. Mori K, Ando F, Nomura H, Sato Y, Shimokata H. Relationship between intraocular pressure and obesity in Japan. Int J Epidemiol 2000 29 661-666.
10. Lee JS, Lee SH, Oum BS, Chung JS, Cho BM, Hong JW. Relationship between intraocular pressure and systemic health parameters in a Korean population. Clin Exp Ophthalmol 2002 30 237-241.
11. McLeod SD, West SK, Quigley HA, Fozard JL. A longitudinal relationship between intra-ocular and blood pressures. Invest Ophthalmol Vis Sci 1990 31 2361-2366.
12. Kaiser HJ, Flammer J, Graf T, Stumpfig D. Systemic blood pressure in glaucoma patients. Graefe's Arch Clin Exp Ophthalmol 1993 231 677-680.
13. Klein BEK, Klein R, Knudtson MD. Intraocular pressure and systemic blood pressure: longitudinal perspective, the Beaver Dam Eye Study. Br J Ophthalmol 2005 89 284-287.
14. Pache M, Flammer J. A sick eye in a sick body? Systemic findings in patients with primary open-angle glaucoma. Surv Ophthalmol 2006;51:179-212.
15. Topouzis F, Coleman AL, Harris A, Jonescu-Cuypers C, Yu F, Mavroudis L, et al. Association of blood pressure status with the optic disk structure in non-glaucoma subjects: The Thessaloniki eye study. Am J Ophthalmol 2006;142:60-7.
16. Klein BE, Klein R, Jensen SC. Changes in the optic disc over a five-year interval. The Beaver Dam Eye Study. Curr Eye Res 1997;16:738–40.
17. Moraes CGD, Cioffi GA, Weinreb RN, Liebmann JM. New Recommendations for the Treatment of Systemic Hypertension and their Potential Implications for Glaucoma Management. J Glaucoma. 2018;27(7):567–71.
18. Melgarejo JD, Lee JH, Petitto M. Glaucomatous optic neuropathy associated with nocturnal dip in blood pressure: findings from the Maracaibo Aging Study. Ophthalmol. 2018;125:807–14.
19. Chen HY, Lai SW. Relation between intraocular pressure and systemic health parameters in Taiwan. South Med J. 2005;98(1):28–32.
20. Langman MJS. Systemic hypertension and glaucoma: mechanisms in common and co-occurrence. Br J Ophthalmol. 2005;89(8):960–3.
21. Klein BE, Klein R, Knudtson MD. Intraocular pressure and systemic blood pressure: longitudinal perspective: the Beaver Dam Eye Study. Br J Ophthalmol. 2005;89(3):284–291.
22. Leske MC. Ocular perfusion pressure and glaucoma: clinical trial and epidemiologic findings. Curr Opin Ophthalmol. 2009;20(2):73–8.
23. Levine RM, Yang A, Brahma V, Martone JF. Management of Blood Pressure in Patients with Glaucoma. Curr Cardiol Rep. 2017;19(11):109.
24. Krasinska B, Karolczak-Kulesza M, Krasi ´ nski Z, Pawlaczyk-Gabriel ´ K, łopatka P, Głuszek J, et al. Effects of the time of antihypertensive drugs administration on the stage of primary open-angle glaucoma in patients with arterial hypertension. Blood Press. 2012;21(4):240–8.
25. Schmidl D, Garhofer G, Schmetterer L. The complex interaction between ocular perfusion pressure and ocular blood flow – Relevance for glaucoma. Exp Eye Res. 2011;93(2):141–55.

26. Flammer J, Konieczka K, Bruno RM, Virdis A, Flammer AJ, Taddei S, et al. The eye and the heart. Eur Heart J. 2013;34(17):1270–8.

27. Horwitz A, Klemp M, Jeppesen J, Tsai JC, Torp-Pedersen C, Kolko M. Antihypertensive Medication Postpones the Onset of Glaucoma. Hypertens. 2017;69(2):202–10.