

## Original research article

## A clinical investigation to evaluate the association of glaucoma with systemic hypertension and its effect on visual morbidity: a prospective study

Dr. Akanchha Kumari<sup>1</sup>, Dr. Bikash Kumar Pandey<sup>2</sup>

<sup>1</sup>Senior Resident, Department of Ophthalmology, AIIMS, Patna, Bihar, India

<sup>2</sup>Senior resident, Department of Ophthalmology, Jawahar Lal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

Corresponding Author: Dr. Bikash Kumar Pandey

### Abstract

**Aim:** the aim of the present study 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, AIIMS, Patna, Bihar, India, for 15 months. It was performed on 100 patients between the age groups of 30 to 65 years which included newly diagnosed hypertensives 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 to ICO Glaucoma Guidelines.

**Results:** Among the 100 hypertension patients involved in the study, 56 patients (56%) were found to have glaucoma. 59 patients (59%) were female and 41 patients (41%) were male. Age group affected was 14% between 30-40 years, 25% between 50 to 60 years and 61% between 60 and 70 years, the mean age being 58.7 years. The increased incidence of OHT among hypertensives was statistically significant with a p value of 0.01. Decreased IOP was highest among patients taking CCB in 24 patients (50%), followed by beta blockers in 2 patients (28.57%), ACE inhibitors 11 patients (37.93%), ARB 5 patients (41.67%) and diuretics in 1 patient (25%). The range of IOP in the treated population was between 10-16mmHg and this difference in those on hypertension medications was statistically significant with p value = 0.02.

**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.

### Introduction

Glaucoma is a group of ocular disorders characterized by optic neuropathy and visual field loss. This may or may not be accompanied by a rise in intraocular pressure (IOP). It is a chronic progressive disease and eventually leads to irreversible form of blindness. In India, glaucoma is estimated to affect over 11 million people<sup>1</sup> and is the third most common cause of blindness after cataract and corneal blindness.<sup>2</sup> Vascular risk factors such as systemic hypertension, atherosclerosis, and vasospasm have been recognized as potential factors that are capable of increasing the risk of primary open-angle glaucoma (POAG) and normal tension glaucoma (NTG).<sup>3,4</sup> It has been hypothesized that low blood pressure (BP) relative to

IOP leads to low ocular perfusion pressure (OPP) of the optic nerve leading to glaucomatous disc changes and visual field loss.<sup>3,5</sup> Chronically elevated BP leads to arteriosclerotic changes and changes in the size of the precapillary arterioles which gives rise to increased resistance to blood flow and hence reduced perfusion.<sup>6</sup> In the Blue Mountain Eye Study and the Egna-Neumarkt study, the association has been found between POAG and systemic hypertension.<sup>7,8</sup> In contrast, studies performed by Deb et al. and Vijaya et al. have reported no significant association between the two.<sup>9-11</sup> Recent literature suggests that the measurement of OPP is a highly relevant parameter in open-angle glaucoma patients.<sup>12</sup> Fluctuations in the OPP is a known contributing factor in the development of glaucomatous disc changes in the subgroup of POAG, as known as NTG.<sup>13</sup> It has also been observed that individuals on antihypertensive medications were 2–3 times more likely to be affected by glaucoma. This may be attributed to the bedtime dosage of antihypertensive drugs which cause a drop in nocturnal BP, eventually leading to a reduction in OPP.<sup>9</sup> A study performed by Pache and Flammer reported a nocturnal dip in BP as an important risk factor for POAG.<sup>14</sup> The Thessaloniki eye study noted that lowering of BP from antihypertensive treatment was associated with glaucomatous changes.<sup>15</sup>

### Material and Methods

This was a prospective study conducted in the Department of Ophthalmology, AIIMS, Patna, Bihar, India, for 15 months, after taking the approval of the protocol review committee and institutional ethics committee.

### Methodology

It was performed on 100 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 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 to 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 biomicroscopy 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.

#### Statistical analysis

The collected data were analysed using IBM SPSS statistics software 20 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were 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 100 hypertension patients involved in the study, 56 patients (56%) were found to have glaucoma. 59 patients (59%) were female and 41 patients (41%) were male. Age group affected was 14% between 30-40 years, 25% between 50 to 60 years and 61% between 60 and 70 years, the mean age being 58.7 years.

Hypertensive patients diagnosed with having glaucoma had a mean duration of 4.51 years. Among the 39 newly diagnosed patients 24 patients had glaucoma and 15 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 6 patients (13.95%), ocular hypertension (OHT) in 36 patients (83.72%) and normal tension glaucoma (NTG) in 1 patients 2.33%. 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 14% and neuroretinal thinning in 10%. Visual field analysis showed nasal step with isolated scotomas in the Bjerrum's area as the commonest change in 6% patients. Corneal thickness in patients diagnosed with ocular hypertension was on an average 0.742. +/-0.02mm. Thicker cornea was noted in 30%. Thinner cornea was noted in 2% of patients.

The oral hypotensive medication taken by patients were categorized into 5 groups as calcium channel blockers (CCB), diuretics, angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARB) and beta blockers. Total number of patients taking oral hypertensives was 70. In the group on medications the range of IOP was between 14- 26mmHg.

Decreased IOP was highest among patients taking CCB in 24 patients (50%), followed by beta blockers in 2 patients (28.57%), ACE inhibitors 11 patients (37.93%), ARB 5 patients (41.67%) and diuretics in 1 patient (25%). The range of IOP in the treated population was between 10-16mmHg and this difference in those on hypertension medications was statistically significant with p value = 0.02.

**Table 1: Hypertension duration and glaucoma association**

| HTN Duration | N  | Mean | STD Deviation | P Value |
|--------------|----|------|---------------|---------|
| Glaucoma Yes | 43 | 4.51 | 4.498         | 0.711   |
| No           | 57 | 7.11 | 4.875         |         |

**Table 2: Hypertension medication and IOP reduction**

| Medication     |       | Glaucoma |        | Total |
|----------------|-------|----------|--------|-------|
|                |       | No       | Yes    |       |
| CCB            | Count | 24       | 24     | 48    |
|                | %     | 50%      | 50%    | 100%  |
| Diuretics      | Count | 3        | 1      | 4     |
|                | %     | 75%      | 25%    | 100%  |
| ACE inhibitors | Count | 18       | 11     | 29    |
|                | %     | 62.07%   | 37.93% | 100%  |
| ARB            | Count | 7        | 5      | 12    |
|                | %     | 58.33%   | 41.67% | 100%  |
| Beta blockers  | Count | 5        | 2      | 7     |
|                | %     | 71.43%   | 28.57% | 100%  |
| Total          | Count | 57       | 43     | 100   |
|                | %     | 57%      | 43%    | 100%  |

Increased BP and IOP may have adverse effects 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. Intraocular pressure is affected by raised systemic blood pressure. The overlapping pathogenesis in both hypertension and glaucoma has been found to be due to an increased blood pressure especially systolic which increases ciliary artery perfusion pressure.<sup>16</sup> This in turn leads to an increased filtration of aqueous fluid through the ciliary body thus causing elevation in IOP.<sup>17</sup> Raised blood pressure also affects the episcleral venous pressure which regulates the aqueous flow across trabecular meshwork through Schlemms canal.<sup>18</sup> 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.<sup>19</sup>

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.<sup>20</sup> Klein et al. stated that beta blocker drugs had a protective effect for glaucoma and hypertension.<sup>21</sup> 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 antihypertensive drugs was not associated with any increased risk of open angle glaucoma but that ocular perfusion pressure has a significant

effect on IOP.<sup>22</sup> From our cohort of patients we found that oral anti hypertensive drugs does have beneficial effect in the control of IOP.

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 antihypertensive 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.<sup>23</sup> 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.<sup>24</sup> Another important facet 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.<sup>25</sup> 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.<sup>26</sup> Treatment of hypertension does lower the IOP and prevent further progression of glaucoma and prevent any visual loss.<sup>27</sup> 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. George R, Ve RS, Vijaya L. Glaucoma in India: Estimated burden of disease. *J Glaucoma* 2010;19:391-7.
2. Rekhi GS, Kulshreshtha OP. Common causes of blindness: A pilot survey in Jaipur, Rajasthan. *Indian J Ophthalmol* 1991;39:108-11.
3. Omoti AE, Enock ME, Okeigbemen VW, Akpe BA, Fuh UC. Vascular risk factors for open angle glaucoma in African eyes. *Middle East Afr J Ophthalmol* 2009;16:146-50.
4. Ali El Afrit M, Trojet S, Mazlout H, Hamdouni M, Korchene N, Kraiem A. Vascular profile of patients with normal tension glaucoma. *Tunis Med* 2008;86:355-7.
5. Caprioli J, Coleman AL; Blood Flow in Glaucoma Discussion. Blood pressure, perfusion pressure, and glaucoma. *Am J Ophthalmol* 2010;149:704-12.

6. Memarzadeh F, Ying-Lai M, Chung J, Azen SP, Varma R; Los Angeles Latino Eye Study Group. Blood pressure, perfusion pressure, and open-angle glaucoma: The Los Angeles Latino eye study. *Invest Ophthalmol Vis Sci* 2010;51:2872-7.
7. Mitchell P, Lee AJ, Rochtchina E, Wang JJ. Open-angle glaucoma and systemic hypertension: The blue mountains eye study. *J Glaucoma* 2004;13:319-26.
8. Bonomi L, Marchini G, Marraffa M, Bernardi P, Morbio R, Varotto A. Vascular risk factors for primary open angle glaucoma: The Egna-Neumarkt study. *Ophthalmology* 2000;107:1287-93.
9. Deb AK, Kaliaperumal S, Rao VA, Sengupta S. Relationship between systemic hypertension, perfusion pressure and glaucoma: A comparative study in an adult Indian population. *Indian J Ophthalmol* 2014;62:917-22.
10. Vijaya L, George R, Baskaran M, Arvind H, Raju P, Ramesh SV, et al. Prevalence of primary open-angle glaucoma in an urban South Indian population and comparison with a rural population. The Chennai glaucoma study. *Ophthalmology* 2008;115:648-540.
11. Vijaya L, George R, Paul PG, Baskaran M, Arvind H, Raju P, et al. Prevalence of open-angle glaucoma in a rural South Indian population. *Invest Ophthalmol Vis Sci* 2005;46:4461-7.
12. Quaranta L, Katsanos A, Russo A, Riva I. 24-hour intraocular pressure and ocular perfusion pressure in glaucoma. *Surv Ophthalmol* 2013;58:26-41.
13. Choi J, Jeong J, Cho HS, Kook MS. Effect of nocturnal blood pressure reduction on circadian fluctuation of mean ocular perfusion pressure: A risk factor for normal tension glaucoma. *Invest Ophthalmol Vis Sci* 2006;47:831-6.
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. Bill A. The role of ciliary blood flow and ultrafiltration in aqueous humor formation. *Exp Eye Res.* 1973;16(4):287-98.
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, Krasiński 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.

**Received: 02-09-2020 || Revised: 07-10-2020 || Accepted: 27-10-2020**