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A Study On Bedtime Antihypertensive Medications And Their Influence On Glaucoma Progression

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ABSTRACT

Background: To analyze the affect of antihypertensive medications like calcium channel blockers (CCB) and Angiotensin receptor blockers (ARB) at bedtime on Ocular perfusion pressure (OPP) and severity of Primary open-angle glaucoma (POAG). **Material and methods:** A case-control study of 60 glaucoma patients were included over 6 months. There were 40 glaucoma patients on antihypertensive drugs (20 on calcium channel blockers and 20 on angiotensin receptor blockers) and 20 without hypertension (Controls) in each of the three groups. **Results:** The two groups of antihypertensive drugs were calcium channel blockers (CCB) and angiotensin receptor blockers (ARB). When compared to controls, the use of calcium channel blockers (CCB) and angiotensin receptor blockers (ARB) was found to increase the progression of OAG slightly (CI 49.25 – 55.67, CI 44.34 – 57.20, and CI 51.19 – 60.35, respectively); this was discovered because the P-value in ocular perfusion pressure (0.0074) is statistically significant. **Conclusions:** Antihypertensive drugs lower blood pressure, which in turn lowers perfusion pressure. This will negatively impact glaucoma patients with already weakened optic nerve head.

Keywords: Antihypertensive medication, Glaucoma, Intra-ocular pressure, Ocular perfusion pressure.

I. INTRODUCTION

Glaucoma is a persistent, progressive optic neuropathy, characterized by the death of retinal ganglion cells and the ensuing irreversible loss of visual field [1]. Elevated intraocular pressure (IOP) and glaucoma are risk factors for high blood pressure, which is treated with systemic antihypertensive medication [2]. As blood pressure (BP) is correlated with both microvascular blood flow and intraocular pressure (IOP), the two major factors that establish ocular perfusion pressure, it is the most researched vascular factor associated with glaucoma [3]. The risk of glaucoma and blood pressure has recently been found to exhibit a bimodal

relationship, implying that those with high or low blood pressure are more likely to develop or worsen glaucoma [4] [5]. Tissue ischemia-reperfusion injury could result from ocular blood vessel autoregulation being compromised, which would leave tissues vulnerable to changes in OPP [6]. When ocular blood flow regulating systems are prevented from activating in patients with systemic hypertension and glaucoma, vascular dysfunction increases the risk of POAG [7] [8]. OCULAR PERFUSION PRESSURE is one of the markers that can be used to determine the risk of glaucoma. It is the primary cause of glaucoma and a possible indicator of the perfusion of the optic nerve head (ONH).

II. MATERIALS AND METHODS

A case-control study was conducted for a period of 6 months, i.e., from September 2023 to February 2024, on the glaucoma patients who were on anti-glaucoma medication. The study was conducted at the department of ophthalmology, in a tertiary hospital. The institutional research ethics committee reviewed the study [ASRAM/BHR 193/2023], and before data collection, each participant gave their informed consent.

A total of 60 glaucoma patients meeting the inclusion and exclusion criteria were divided into three groups of 40 glaucoma patients who were on antihypertensive medications (Calcium Channel Blockers – 20 patients and Angiotensin Receptor Blockers – 20 patients) and 20 glaucoma patients with no hypertension (Controls). All the patients with POAG who were being treated with antiglaucoma medications, who had systemic hypertension, and who were using antihypertensive medications (CCBs and ARBs) for at least 1 year at bedtime were included in this study.

This study excluded individuals with known hypertension who were not taking antihypertensive drugs at night, as well as those who took anti-glaucoma drugs irregularly and had undergone glaucoma surgery as well as secondary glaucoma.

2.1 STUDY PROCEDURE

The evaluations comprised a visual acuity test utilizing Snellen's test and LogMAR scores and an anterior segment examination using a slit-lamp. Intra Ocular Pressure (IOP) was measured using the Goldmann Applanation Tonometer (GAT), Visual field assessment was done by using the Humphrey Visual Field Analyser (HFA) and Gonioscopy for both eyes using a ZEISS 4-mirror Indirect Contact gonioscopy lens. After that Dilated Fundus Examination was done on all the patients. In the Supine position, Blood Pressure was recorded after 5 minutes of rest. By this Mean Ocular Perfusion Pressure [MOPP] was calculated using the formula: MOPP = 2/3 × [MAP-IOP]

Mean Arteriolar Pressure (MAP) = DBP+1/3 [SBP-DBP]

III. STATISTICAL ANALYSIS

Data analysis was conducted using Microsoft Excel. Numerical data are presented using the mean and standard deviation. For normally distributed data, intergroup comparisons were performed using ANOVA, while an independent samples t-test was used to compare calcium channel blockers and ARBs within the group. The p-value was deemed statistically significant if it was less than 0.05.

IV. RESULTS

The study included 60 glaucoma patients in total, 40 glaucoma patients using antihypertensive medications (CCBs-20 and ARBs-20), and 20 glaucoma patients who were controls over hypertension.

INTRAOCULAR PRESSURE

INTRAOCULAR PRESSURE	MEAN + STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)	P VALUE
CCBs	15.5 + 2.81 (12.69 – 18.31)	0.725
ARBs	15.6 + 3.64 (11.96 – 19.24)	
CONTROLS	16.2 + 2.33 (13.87 – 18.53)	

The mean intraocular pressure for patients taking CCBs was 15.5 ± 2.81 mmHg [CI: 12.69 – 18.31]. The mean intraocular pressure for patients taking ARBs was 15.6 mmHg [CI: 11.96 – 19.24]. The mean intraocular pressure for the control group was 16.2 mmHg [CI: 13.87 – 18.53]. The p-value of 0.725 indicates that there is no statistically significant difference in intraocular pressure between the CCB group, ARBs, and the control group.

SYSTOLIC BLOOD PRESSURE

SYSTOLIC BLOOD PRESSURE	MEAN + STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)	P VALUE
CCBs	124.8 + 12.62 (112.18 – 137.42)	0.157
ARBs	120.3 + 12.98 (107.32 – 133.28)	
CONTROLS	128.2 + 12.87 (115.33 – 141.07)	

The mean systolic blood pressure for patients taking CCBs was 124.8 mmHg [CI: 112.18 – 137.42]. The mean systolic blood pressure for patients taking ARBs was 120.3 mmHg [CI: 107.32 – 133.28]. The mean systolic blood pressure for the control group was 128.2 mmHg [CI: 115.33 – 141.07]. The p-value of 0.157 indicates that there is no statistically significant difference in systolic blood pressure between the CCB group, ARBs, and the control group.

DIASTOLIC BLOOD PRESSURE

DIASTOLIC BLOOD PRESSURE	MEAN + STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)	P VALUE
CCBs	78.9 + 5.44 (73.46 – 84.34)	0.000192
ARBs	77.5 + 6.48 (71.02 – 83.98)	
CONTROLS	85.7 + 6.62 (79.08 – 92.32)	

The mean diastolic blood pressure for patients taking CCBs was 78.9 mmHg [CI: 73.46 – 84.34]. The mean diastolic blood pressure for patients taking ARBs was 77.5 mmHg [CI: 71.02 – 83.98]. The mean diastolic blood pressure for the control group was 85.7 mmHg [CI: 79.08 – 92.32]. The p-value of 0.000192 indicates that there is a statistically significant difference in diastolic blood pressure between the CCBs group, ARBs, and the control group.

OCCULAR PERFUSION PRESSURE

OCULAR PERFUSION PRESSURE	MEAN + STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)	P VALUE
CCBs	52.46 + 3.21 (49.25 – 55.67)	0.0074
ARBs	50.77 + 6.43 (44.34 – 57.20)	
CONTROLS	55.77 + 4.58 (51.19 – 60.35)	

The mean ocular perfusion pressure for patients taking CCBs was 52.46 mmHg [CI: 49.25 – 55.67]. The mean ocular perfusion pressure for patients taking ARBs was 50.77 mmHg [CI: 44.34 – 57.20]. The mean ocular perfusion pressure for the control group was 55.77 mmHg [CI: 51.19 – 60.35]. The p-value of 0.0074 indicates that there is a statistically significant difference in ocular perfusion pressure between the CCB group, ARBs, and the control group.

Ocular Perfusion Pressure	MEAN + STANDARD DEVIATION (CONFIDENCE INTERVAL 95%)	P VALUE
CCBs	52.46 + 3.21 (49.25 – 55.67)	0.150
ARBs	50.77 + 6.43 (44.34 – 57.20)	

The mean ocular perfusion pressure for patients taking CCBs was 52.46 mmHg [CI: 49.25 – 55.67]. The mean ocular perfusion pressure for patients taking ARBs was 50.77 mmHg [CI: 44.34 – 57.20]. The p-value of 0.150 indicates that there is no statistically significant difference in ocular perfusion pressure between the CCB group and the ARB group.

V. DISCUSSION

The present study compared the risks of POAG among HTN patients receiving medications in order to examine the connection between systemic antihypertensive medication and POAG progression. The results demonstrated that the use of CCB and ARB was linked to poor OPP and higher chances of receiving a POAG diagnosis; however, the risks were unaffected by the duration of the drug usage.

According to the Barbados Eye Study, those with HTN who received treatment had a decreased chance of developing OAG [9]. Similar to the Singapore Malay Study [10], the nine-year incidence phase was unable to identify a meaningful correlation between antihypertensive medication and OAG [11]. On the other hand, the Rotterdam Eye Study demonstrated that only individuals undergoing antihypertensive medication were at higher risk of OAG due to decreased diastolic perfusion pressure [12]. In a similar vein, the Thessaloniki Eye Study found that individuals whose antihypertensive medication caused their DBP to drop below 90 mmHg had greater cupping and decreased rim area; however, those with similar DBP who did not get therapy did not show this association [13]. In addition, the kind of antihypertensive drug that is linked to a higher risk of OAG has not been conclusively determined by prior research. The Rotterdam Eye Study demonstrated that non-glaucomatous patients on CCB had a 1.8-fold greater chance of developing OAG [14]. Those using CCB also had noticeably higher odds of receiving an OAG diagnosis, according to a retrospective case-control study [15]. Additionally, a recent meta-analysis of ten research on the subject discovered that using CCB increased the risk of glaucoma [16]. However, substantial relationships between various types of antihypertensive drugs have been seen in another research. The same meta-analysis discovered that β-blockers were linked to a decreased risk of glaucoma [17]. Retrospective analysis of the Groningen Longitudinal Glaucoma Study cohort revealed that ARB slowed the course of glaucoma in elderly individuals and decreased the probability of uncertain conversion in those using ACEi or ARB [18]. According to the Jihei Sara Lee study, there is a minor increase in OAG risks associated with using CCB and ARB for the treatment of hypertension; however, these risks are largely minimized by antihypertensive medicines [19]. Mousa AR came to the conclusion that POAG may be more accurately predicted and its

efficacy could be guided by using OPP as an estimate of the real ocular blood flow, which takes into account both SBP and IOP [20]. The study we conducted discovered that HTN patients on CCB and ARB had a greater risk of POAG.

VI. LIMITATION

Circadian influences on blood pressure and IOP can exist, and an IOP peak or IOP swings can be overlooked by a single reading. Direct measurement of Ocular blood flow could result in different outcomes as we calculated MOPP theoretically using a formula here.

VII. CONCLUSION

The POAG patients who were using bedtime anti-hypertensive medication had lower OPP when compared to that of controls but there was no statistical significance between patients who were using CCBs and ARBs. Antihypertensive medication reduces the blood pressure, thus lowering the perfusion pressure, which will have a detrimental effect on the already compromised optic nerve head in glaucoma patients.

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