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Original Research Article

Comparative Assessment of the Vascular Perspective Between Normal Tension Glaucoma and Primary Open-Angle Glaucoma Patients

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Conflict of interest: Nil

Abstract

Aim: Comparative study between normal tension glaucoma and primary open-angle glaucoma.

Materials and methods: Total 100 patients attended the eye OPD in 12 months having primary open angle glaucoma patient and normal tension glaucoma was recruited in the research. Group A: Patient with or without primary hypertension having primary open angle glaucoma. Group B: Patient with or without primary hypertension having normotensive glaucoma Group C: Patient age-matched controls without hypertension.

Results: A total number of study populations were 100 patients. The average age of the study population was 55.38 ±8.92 years and ranging from 40 to 77 years. There was strong correlation between MAP (mean arterial pressure) and MOPP (mean ocular perfusion pressure) amongst NTG group. There was strong correlation between MAP (mean arterial pressure) and MOPP amongst NTG with hypertension group. In POAG with hypertensive group with medication, the correlation between MAP (mean arterial pressure) and MOPP (mean ocular perfusion pressure) was strong, while MOPP was inversely correlated with IOP showing strong association. The MAP was weakly correlated with IOP. In POAG with hypertensive group without medication, MAP (mean arterial pressure) was also strongly correlated with MOPP, while MOPP was inversely correlated with IOP showing strong association and MAP showed inverse correlation with IOP showing strong correlation. In NTG with hypertensive group with medication, MAP was strongly correlated with MOPP.

Conclusion: This study demonstrates that in all groups a moderately strong correlation existed between MAP and MOPP and IOP and MOPP were inversely correlated.

Keywords: IOP, MOPP, MAP, Glaucoma.

Introduction

Glaucoma is a chronic progressive optic neuropathy with characteristic optic nerve head changes and visual field defects for which increased IOP is an important risk factor. Although factors other than IOP are involved in glaucoma, IOP is important because it is the only risk factor which can be pharma co modulated to date. Cartwright and Anderson in their study on patients with NTG with asymmetric IOP showed that glaucomatous damage was greater in the eye with higher IOP [1]. Visual field loss of patients whose IOP is lowered pharmacologically is usually slowed [2]. Most glaucoma patients appear to have abnormal sensitivity to IOP that may be offset if IOP is lowered to mid normal or low normal range and perhaps 90% or more may benefit from sufficiently low IOP. Measurement of accurate IOP is important not only for classification but for clinical management of glaucoma patients. It is important therefore to ensure that IOP readings are taken using highly accurate method. Goldman Applanation Tonometry (GAT) has been considered to be the gold standard for measurement of IOP. Ehlers et al have shown that central corneal thickness affects the accuracy of applanation tonometry. Reduced corneal thickness of 0.45mm causes an underestimation of IOP by up to 4.7mmHg, whereas an increased CCT of 0.59mm could cause an overestimation of 5.2mmHg. [3] Therefore in individuals with thick cornea, IOP measurement by GAT may show falsely high readings and for thin cornea low readings. Central Corneal Thickness (CCT) is an important factor to be evaluated when assessing target IOP levels for the management of glaucoma and also during follow up. Shih CY et al concluded that central corneal thickness has significant effect on the clinical management of patients with glaucoma and glaucoma suspects [4]. The vascular hypothesis of OAG states that a low blood pressure (BP) relative to IOP can lead to low mean ocular perfusion pressure (MOPP), thus impairing perfusion of the ONH with resultant glaucomatous cupping and visual field loss [5,8]. Assessment of the diurnal fluctuations in IOP and MOPP is, therefore, clinically relevant in glaucoma patients [6]. The term normal tension glaucoma refers to typical glaucomatous optic disc cupping and visual field loss in eyes that have normal IOP, open angles, and the absence of any contributing ocular or specific systemic disorders. This entity is often called ‘low-tension glaucoma,’ which is a misnomer because the IOP is usually at the upper end of the normal range and rarely low systemic hypertension as such may directly damage the small vessels of the optic disc and increase the risk of glaucoma.

Materials and methods:

The present comparative study was conducted in the department of Ophthalmology, Anugrah Narayan Magadh Medical College Hospital (ANMMCH), Gaya, Bihar, India for 12 months.

A total number of 100 patients attended in eye OPD in one year having primary open angle glaucoma patient including normal tension glaucoma.

Group A: Patient with or without primary hypertension having primary open angle glaucoma.

Group B: Patient with or without primary hypertension having normotensive glaucoma.

Group C: Patient age-matched controls without hypertension

Methodology

Single measurement of blood pressure was done for all the subjects in the right arm in sitting position using a mercury sphygmomanometer (auscultatory technique using the first, and fifth phases of the Korotkoff sounds as per the American Heart Association Blood

pressure measurement recommendations) [10]. IOP was measured in both the eyes using a applanation tonometry while dilated fundus examination performed using a +90 D lens for all the subjects. Mean arterial pressure (MAP) calculated as DBP + 1/3 (SBP–DBP). MOPP calculated using a standardized formula (MOPP = 2/3 × MAP– IOP).11,12 Study Tools used were applanation tonometry, Gonioscope, Noncontact tonometer for measurement of Central corneal thickness, Humphrey field analyser, Optical coherence tomography, Ultrasound Tachymeter and Direct ophthalmoscope, Indirect ophthalmoscope+90D for fundoscopic examination.

Inclusion Criteria:

Patients diagnosed to have essential hypertension, either self-reported hypertension or newly diagnosed cases (defined as ≥140 mm Hg systolic BP [SBP] and/or ≥90 mm Hg diastolic BP [DBP]), age above 40 years with primary open angle glaucoma and normal tension glaucoma and age above 40 years without hypertension having primary open angle glaucoma and normal tension glaucoma were included in this study.

Exclusion Criteria:

Patients with hypertension due to secondary causes, age <40 years with or without primary open angle glaucoma, normal tension glaucoma and secondary glaucoma were excluded in this study.

Statistical Analysis:

Data was collected and entered in Microsoft Excel then into statistical database SPSS (statistical package for social sciences, version 25.0, windows compatible).

Results:

The average age of the study population was 55.38 ±8.92 years and ranging from 40 to 77 years. The study was male preponderant. Maximum number of patients was from 41-50 years (49%) age groups. Maximum number of patients was primary open angle glaucoma (51%). SBP, DBP, MAP, IOP and VCDR were found to be statistically significant with different study group. (Table no: 1) SBP, DBP, MAP, IOP and VCDR were found to be statistically significant with different study subgroup (hypertensive vs non-hypertensive). (Table 2) There was strong correlation between MAP and MOPP amongst NTG group. (Table3) There was strong correlation between MAP and MOPP amongst NTG with hypertension group. (Table 4) In POAG with hypertensive group with medication, the correlation between MAP and MOPP was strong, while MOPP was inversely correlated with IOP showing strong association. The MAP was weakly correlated with IOP. In POAG with hypertensive group without medication, MAP was also strongly correlated with MOPP, while MOPP was inversely correlated with IOP showing strong association and MAP showed inverse correlation with IOP showing strong correlation. (Table 5) In NTG with hypertensive group with medication, MAP was strongly correlated with MOPP. While MOPP was inversely correlated with IOP showing strong association. In NTG with hypertensive group without medication, the result was same as NTG with hypertension with medication group. (Table 6).

Table 1: Relationship between different study group and study parameters

GROUP	SBP	DBP	MAP	IOP	MOPP	VCDR
POAG	145.19 ± 15.06	91.35 ± 9.03	108.49 ± 14.48	31.79 ± 7.20	52.67 ± 11.52	0.71 ± 0.11
NTG	131.00 ± 12.75	85.84 ± 5.81	100.89 ± 7.84	19.47 ± 1.82	55.28 ± 5.28	0.69 ± 0.07
NORMAL	126.16 ± 5.04	81.90 ± 3.39	96.66 ± 3.45	14.10 ± 1.65	56.04 ± 2.45	0.31 ± 0.06
p-value	<0.001	<0.001	<0.001	<0.001	0.481	<0.001

Table 2: Relationship between different study group (hypertensive vs non-hypertensive) and study parameters

Subgroup	SBP	DBP	MAP	IOP	MOPP	VCDR
POAG with hypertension	158.03 ± 5.96	98.52 ± 3.94	118.35 ± 4.41	26.00 ± 2.90	62.57 ± 4.43	1`0.69 ± 0.09
POAG without hypertension	131.07 ± 7.36	83.47 ± 5.91	97.63 ± 13.94	38.17 ± 4.65	41.78 ± 5.41	0.83 ± 0.13
NTG with hypertension	151.50 ± 3.39	95.00 ± 1.46	113.83 ± 1.64	19.75 ± 1.00	63.72 ± 1.55	0.81 ± 0.06
NTG without hypertension	123.87 ± 3.90	82.65 ± 2.20	96.39 ± 1.50	19.37 ± 2.03	52.35 ± 1.68	0.76 ± 0.06
Normal	126.16 ± 5.04	81.90 ± 3.39	96.66 ± 3.45	14.10 ± 1.65	56.04 ± 2.45	0.40 ± 0.06
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 3: According to different study group Spearman's Rank Correlation (ρ) in different study parameters

GROUP				MAP	IOP	MOPP
POAG	Spearman's rho	MAP	Correlation Coefficient		-0.824	0.92
			p Value		<0.001	<0.001
		IOP	Correlation Coefficient	-0.824		-0.90
			p Value	<0.001		<0.001
		MOPP	Correlation Coefficient	0.925	-0.901	
			p Value	<0.001	<0.001	
NTG	Spearman's rho	MAP	Correlation Coefficient		0.009	0.88
			p Value		0.947	<0.001
		IOP	Correlation Coefficient	0.009		-0.37
			p Value	0.947		0.002
		MOPP	Correlation Coefficient	0.986	-0.479	
			p Value	<0.001	0.002	
NORMAL	Spearman's rho	MAP	Correlation Coefficient		0.095	0.85
			p Value		0.612	<0.001
		IOP	Correlation	0.095		-0.39

			Coefficient			
			p Value	0.612		0.002
		MOPP	Correlation Coefficient	0.958	-0.491	
			p Value	<0.001	0.002	

Table 4: According to different study sub-groups Spearman's Rank Correlation (ρ) in different study parameters

Subgroup				MAP	IOP	MOPP
POAG with hypertension	Spearman's rho	MAP	Correlation Coefficient		0.004	0.856
			p Value		0.873	<0.001
		IOP	Correlation Coefficient	0.005		-0.718
			p Value	0.873		<0.001
		MOPP	Correlation Coefficient	0.856	-0.718	
			p Value	<0.001	<0.001	
POAG without hypertension	Spearman's rho	MAP	Correlation Coefficient		-0.206	0.767
			p Value		0.144	<0.001
		IOP	Correlation Coefficient	-0.206		-0.844
			p Value	0.144		<0.001
		MOPP	Correlation Coefficient	0.767	-0.844	
			p Value	<0.001	<0.001	
NTG with hypertension	Spearman's rho	MAP	Correlation Coefficient		-0.677	0.862
			p Value		0.019	<0.001
		IOP	Correlation Coefficient	-0.677		-0.860
			p Value	0.019		0.001
		MOPP	Correlation Coefficient	0.862	-0.860	
			p Value	<0.001	0.001	
NTG without hypertension	Spearman's rho	**MAP**	**Correlation Coefficient**		0.057	0.819
			p Value		0.805	<0.001
		IOP	**Correlation Coefficient**	0.057		-0.706
			p Value	0.805		<0.001
		MOPP	**Correlation Coefficient**	0.819	-0.706	
			p Value	<0.001	<0.001	
Normal	Spearman's rho	**MAP**	**Correlation Coefficient**		0.085	0.958
			p Value		0.612	<0.001
		IOP	**Correlation Coefficient**	0.095		-0.491
			p Value	0.612		0.002
		MOPP	**Correlation Coefficient**	0.958	-0.491	
			p Value	<0.001	0.002	

Table 5: Spearman's correlation coefficient (ρ) between POAG with hypertension with medication and POAG with Hypertension without medication

GROUP					MAP	IOP	MOPP
POAG	With medication	Spearman's rho	MAP	Correlation Coefficient	1.000	-0.175	0.908
				p Value		0.337	<0.001
			IOP	Correlation Coefficient		1.000	-0.782
				p Value			<0.001
			MOPP	Correlation Coefficient			1.000
				p Value			
	Without medication	Spearman's rho	MAP	Correlation Coefficient	1.000	0.191	0.796
				p Value		0.279	<0.001
			IOP	Correlation Coefficient		1.000	-0.651
				p Value			0.001
			MOPP	Correlation Coefficient		-0.551	1.000
				p Value		0.001	

Table 6: Spearman's correlation coefficient (ρ) between NTG with hypertension with medication and NTG with Hypertension without medication

GROUP					MAP	IOP	MOPP
NTG	With medication	Spearman's rho	MAP	Correlation Coefficient	1.000	-0.677	0.862
				p Value		0.134	<0.001
			IOP	Correlation Coefficient		1.000	-0.860
				p Value			0.029
			MOPP	Correlation Coefficient			1.000
				p Value			
	Without medication	Spearman's rho	MAP	Correlation Coefficient	1.000	-0.677	0.862
				p Value		0.144	<0.001
			IOP	Correlation Coefficient		1.000	-0.860
				p Value			0.03
			MOPP	Correlation Coefficient			1.000
				p Value			

Discussion:

In present study, highest MAP found in POAG with hypertension group (i.e., 118.35) and lowest MAP found in NTG without hypertension (i.e., 96.39). Highest SBP was found in POAG with hypertension (i.e., 158.03mm Hg) and lowest in NTG without hypertension (i.e., 123mm Hg), highest DBP found in POAG with Hypertension group (i.e., 98.52 mm Hg) and lowest in normal group (81.90 mm hg). IOP was found highest in POAG without hypertension (i.e., 38.17) and lowest in normal group (i.e., 14.10). Highest MOPP was in NTG with hypertension (i.e., 63.72) and lowest in POAG without hypertension (41.78). VCDR found highest in POAG without hypertension (i.e., 0.83) and lowest in normal group (0.31). Several studies had been done to establish the relation between these criteria in various glaucomatous groups.

Association between systemic hypertension and POAG had been evaluated in various population-based studies that yield contradictory results. Population-based studies have consistently found an association between high blood pressure and IOP. In general, each 10

mmHg rise in systolic blood pressure is associated with only a small increase in IOP (approximately 0.28 mmHg). As these studies covered populations with different ethnic backgrounds including Caucasians (Egna Neumarkt Study, Rotterdam Study, Beaver Dam Study) [7,9], Africans (Barbados Eye Study) [8] and Asians (Tanjong Pagar Study) [9] it is likely that they are widely applicable. Indeed, some epidemiological studies (Table 1) like Rotterdam eye study [11], Blue Mountain Eye study, Egna Neumarkt Glaucoma Study [10] suggest that systemic hypertension causes increased risk of primary open angle glaucoma while Thessaloniki Eye Study [10], Early Manifest Glaucoma Trial [11] and the Barbados Eye Study[13] suggest that systemic hypertension have reduced risk factor for primary open angle glaucoma. Baltimore eye survey [12] suggest that age-dependent risk for younger and increased risk for older patients. In the Egna Neumarkt study [10], the association was found between primary POAG and systemic hypertension. A positive correlation was also found between systemic BP and IOP.

In our study we found that all indices of hypertension (viz. SBP, DBP and MAP) between the groups who had POAG, NTG or normal groups.

On performing a Spearman's correlation in all groups, we found a moderately strong correlation between MAP and MOPP (i.e., 0.776), whereas the correlation between MAP and IOP had weak positive value (i.e., 0.453). IOP and MOPP were inversely correlated, and the value was weak -0.457. On further subgroup analysis strong negative correlation between MAP and IOP in POAG group ($\rho = -0.824$) but it was very weak in NTG ($\rho = 0.009$) and normal patient ($\rho = 0.085$).

When we study their correlation of MAP vs. MOPP the strongest correlation found in POAG groups ($\rho = 0.825$) it was found in NTG ($\rho = 0.986$) as well as in normal ($\rho = 0.958$) patients.

When we come to correlation of IOP with MOPP we found that there is strong inverse correlation in POAG groups ($\rho = -0.801$) the inverse correlation was seen in NTG and normal patient too, but it was weak (-0.479 and -0.491 respectively). When we study the correlation between the values after discriminating on the basis of hypertension in POAG patient being presence or absence we found that ρ for MAP vs. IOP with hypertension was very weak (0.004) and POAG without hypertension it was inverse correlation but weak (-0.206). Spearman's rho for MAP vs. MOPP in POAG group with or without hypertension was in positive correlation (0.856 and 0.767 respectively) showing slightly stronger in POAG with hypertension group. In IOP vs. MOPP found that ρ value was in inverse correlation in POAG with or without hypertension (-0.718 and -0.844 respectively) slightly stronger in POAG without hypertension group [13,15].

In the NTG group when we bring hypertension in the picture, we found that ρ for MAP vs. IOP in hypertensive patient inverse strong correlation (-0.677) and without hypertension was very weak (0.057). Spearman's rho for MAP vs. MOPP in NTG with hypertensive group (0.862) and without hypertensive group (0.819) found to be in strong correlation. In IOP vs. MOPP found that ρ value in hypertensive (-0.860) and without hypertension (-0.706) which is marginally higher in hypertensive group.

Conclusion:

This study demonstrates that in all groups a moderately strong correlation existed between MAP and MOPP and IOP and MOPP were inversely correlated. On subgroup analysis strong negative correlation between MAP and IOP in

POAG patients was noted but it was very weak in NTG and controls. The correlation of IOP with MOPP in POAG patients was strong and inverse while it was too weak in NTG and controls.

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