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RESEARCH ARTICLE

EFFECT OF OCULAR PERFUSION PRESSURE TO ISOMETRIC HANDGRIP TEST IN PATIENTS WITH PRIMARY OPEN ANGLE GLAUCOMA (POAG): A TEST FOR AUTONOMIC ACTIVITY

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ABSTRACT

Background Glaucoma is diagnosed by presence of "classical triad"- characteristic feature of visual field defects, morphological changes in optic disc (cupping) and raised intraocular pressure (IOP). Several studies related to blood pressure and ocular perfusion pressure (OPP) implicated vascular risk factors in the pathogenesis of glaucoma yet abnormal autoregulation in glaucoma is not fully clear. The most common method of evaluating autoregulatory function is through provocation like isometric head up tilt testing, which put the vascular system under stress and evoke an autoregulatory response maintaining normal ocular perfusion, a failure to this is indicative of disturbed auto regulation. Materials and methods The study subjects of age between 45-65 years of either sex comprised of 20 patients with Primary open angle glaucoma (IOP >21mmhg) (group II) and 20 age and sex matched healthy controls (group I). Blood Pressure and Mean OPP was recorded at rest and immediately after relaese, then after 5minutes. MOPP was calculated as MOPP=2/3MAP – IOP. Results Mean basal MAP in group II was significantly higher (104.73 ±1.45) (p=0.001) as compared to group I. The findings showed highly significant low values of basal MOPP (p<0.000) in group II (POAG) compared to control group. During handgrip test the value of MAP was significantly higher and MOPP was significantly low (P<0.000) in group II. The significant high value of MAP (p<0.000) and low MOPP in group II during recovery period indicated delayed recovery due to sympatho-vagal imbalance. Conclusion Basal values of MAP and MOPP and changes observed during isometric exercise (stress test) and during recovery period indicated ocular vascular alterations and abnormal autoregulatory mechanism in POAG patients as compared to healthy controls.

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INTRODUCTION

Traditionally the management of glaucoma has focussed on the therapeutic reduction of intraocular pressure (IOP) to a certain target level with the aim of limiting the progression of Optic nerve head (ONH) damage. Disturbed vascular function has long been recognised with regard to glaucomatous optic neuropathy (GON), with authors as early as 1925 proposing an alternative vascular theory of glaucoma development along with the aetiological involvement of microcirculatory disturbances and vascular dysregulation. The role of both ocular and systemic vascular factors in the development of GON has been subsequently explored by numerous researchers; however understanding of the complex interactions between these factors implicated in the aetiology of the disease is still incomplete (Leske, 2007; Kumarswamy *et al*., 2006; Schmidl *et al*., 2011). Ocular perfusion pressure (OPP) refers to the force exerted by flowing of the blood through the intraocular vessels and is defined as the difference between the arterial and venous pressure. As a direct measure of arterial and venous pressure, experimentation has revealed that, due to the drop in BP between the heart and the OA, retinal arterial pressure can be estimated as 2/3 of the mean arterial pressure (MAP) and venous pressure can be taken to be approximately equal to the level of IOP, OPP can be calculated as ; MOPP = 2/3MAP – IOP, where MAP = Diastolic BP+ 1/3 Pulse pressure and Pulse pressure = systoloic BP – diastolic BP. The relationship between blood flow and OPP in the eye is complex and as the equation above demonstrates both a lowering of MAP and an increase in IOP could potentially reduce OPP.

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The most common method of evaluating autoregulatory function is through assessing the response of the ocular and systemic vasculature to provocation. This provocation can take the form of posture changes, artificial lowering of IOP, cold provocation, hand grip testing, induced hypoxia and hypercapnia. Such provocations put the vascular system under stress and should evoke an autoregulatory response which allows maintenance of normal ocular perfusion, a failure to observe this autoregulatory response is indicative of disturbed autoregulation. Although the exact mechanisms underlying autoregulation are still unclear, however metabolic, myogenic, neurogenic and humoral factors are all known to trigger autoregulatory responses in the ocular circulation, as are endothelial derived vasoactive agents. Autoregulation is a complex process involving the ANS (neurogenic control), systemic BP (myogenic control), circulating hormones (humoral control) and the endothelium. Abnormalities such as endothelial dysfunction, vasospastic syndrome and ANS dysfunctions have been implicated to play a role in the development of autoregulatory abnormalities in glaucoma (Kiel and Shepherd, 1992; Flammer *et al*., 2001; Flammer and Mozaffarieh, 2008; Heijl *et al*., 2002; Anderson, 1999; Polska *et al*., 2007).

In hand grip test heart rate and blood pressure increase partly due to central motor command and partly by mechanical changes in response to contraction of the muscles that activate small fibres in the afferent limb of the reflex arch. The normal response is rise in diastolic pressure more than 15mmHg and rise in heart rate by 30%. BP rises due to sympathetic activity and HR rises due to decreased parasympathetic activity. The isometric hand-grip test increases heart rate, arterial pressure, and sympathetic nerve activity. The protective role of the sympathetic nervous system in the vasoconstriction of the choroidal circulation in response to arterial hypertension has been studied in animals and humans. The previous data, together with other investigations, indicate that the maintenance of constant choroidal blood flow during sympathetic stimulation in humans is achieved through an increase in ocular vascular resistance **(**Riva, 1997; Hayreh, 1990; Rechtman and Harris, 2008**)**.

METHODS

The present study was conducted with an aim to see the effect of sympatho-vagal if any on mean ocular perfusion pressure at rest and during isometric exercise (stress). The study subjects of age between 45-65 years of either sex comprised of two groups:

Group I- Twenty age and sex matched healthy controls.
Groups II- Twenty patients with POAG.

Inclusion Criteria for group II (POAG) are:

- Intraocular pressure >21 mm Hg without treatment.
- Optic disc changes suggestive of glaucomatous damage including one or more of these signs: neuroretinal rim notching ,optic disc excavation, vertical or horizontal cup to disk (C/D) ratio >0.5 or C/D asymmetry between 2 eyes greater than 0.2,and peripapillary splinter hemorrhages.
- Visual field outside normal limits on Humphery automated perimetry on three perimetry readings.
- All angles (360^0) open on gonioscopy.
- Pupil diameter ≥ 3mm without mydriatic or miotic drugs.

Exclusion Criteria

- Patients with secondary causes of glaucoma, hazy media, optic neuritis, any disease involving the macula, retina, or visual pathway, high myopia (>6Dioptre), previous intraocular surgery and on drugs known to cause optic neuropathy.
- Patients with diabetes mellitus and hypertension.

The study was in accordance with the code of ethics, approval been taken from institutional ethical committee. A written consent was taken and the whole procedure was explained in detail to each subject in his/her own language.Each subject had undergone a complete opthalmological examination in glaucoma clinic, IOP measurement withGoldmannapplanation tonometer. Blood Pressure was measured from the upper left arm using sphygmomanometer in recumbent position. and MOPP was calculated as MOPP=2/3MAP – IOP.The patient was asked to lie in supine position holding the handgrip dynamometer in the dominant hand and take a full grip on it. Maximal voluntary contraction (MVC) was noted. The subject was asked to maintain a tension of 30% of MVC for 2 minutes. HRV and BP were measured immediately after the release of handgrip and then after 5minutes (recovery period). MOPP during the sustained hand grip and recovery was calculated. The data obtained was statisticallyanalysed by using SPSS(version 17). Basal MOPP of group I (healthy controls) was compared with group II (POAG) by unpaired student t test. Two-tailed significance value was set at .05.

RESULTS

The mean basal IOP was significantly higher (26.3±1.75) ($p<0.000$) in group II.Mean basal MAP in group II was significantly higher (104.73 ±1.45) ($p=0.001$) as compared to group I. The Tables also showed highly significant low values of basal MOPP ($p<0.000$) in group II (POAG) compared to control group. (Table 1, Figure 2).

Table 1. Basal IOP, MAP and MOPP in group I and II

Parameter	Group I mean±SD	Group II mean±SD	P-val
IOP (mmHg)	15.45±1.96	26.3±1.75	<0.000
MAP (mmHg)	91.85±2.03	104.73±1.45	0.001
MOPP (mmHg)	45.96±1.89	43.52±2.71	<0.000

The value of MAP was significantly higher and MOPP was significantly low ($P<0.000$) in group II (POAG) in handgrip exercise. (Table 2, Figure 3) The significant high value of MAP ($p<0.000$) in group II during recovery period indicated delayed recovery due to sympatho-vagal imbalance i.e more withdrawal of parasympathetic and relatively greater sympathetic activity. (Table 3, Figure 4)

Table 2. MAP and MOPP of group I, & II during handgrip testing

Parameter	Group I mean±SD	Group II mean±SD	P-val
MAP(mmHg)	101.53±3.59	108.13±6.05	<0.001
MOPP(mmHg)	52.23±3.59	45.78±4.9	<0.000

*p<.05 significant
* * p<0.001 high significant
* * *p<0.000 very high significant

Table 3. MAP, MOPP of group I and II during handgrip recovery phase

Parameter	Group I mean±SD	Group II mean±SD	P-val
MAP(mmHg)	92.1±5.36	106.63±5.35	<0.000
MOPP(mmHg)	45.95±4.66	44.78±4.53	0.44

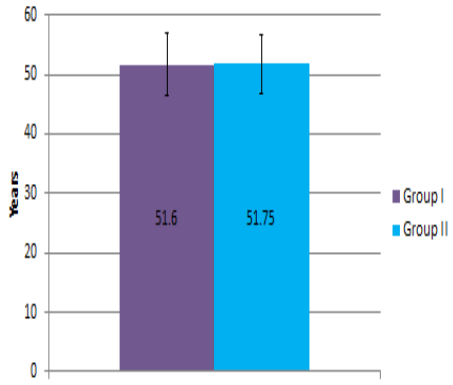

Figure 1. Comparison of mean age

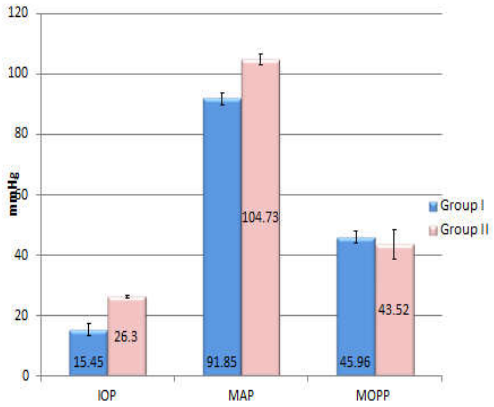

Figure 2. Comparison of basal values of IOP, MAP, MOPP

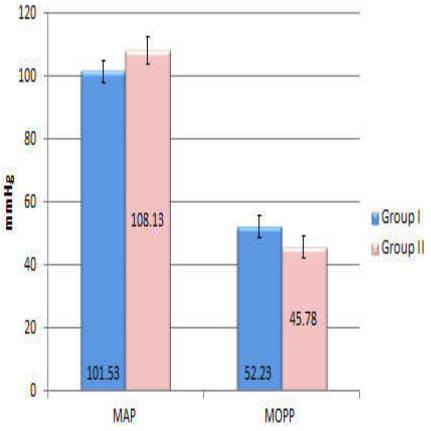

Figure 3. Comparison of MAP and MOPP on handgrip

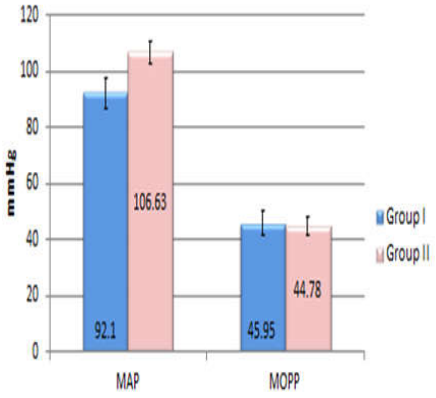

Figure 4. Comparison of MAP and MOPP during handgrip recovery phase

DISCUSSION

An overall increase in MAP and MOPP has been observed in both groups. However in group II MAP raised significantly (108.13 ± 6.05, p <0.000), where as the rise in MOPP was significantly less (p < 0.000) in comparison to group I. A study in patients with primary open-angle glaucoma with progressive damage despite normal or normalized IOP indicated that patients with a decrease of at least 10% in choroidal blood flow during the hand-grip test seem to have progression of visual field damage at lower levels of IOP, suggesting a higher sensitivity to IOP (Gugleta *et al*., 2003). As systemic BP is constanly regulated by ANS through modulation of cardiac output and total peripheral resistance, at the ocular level a close relationship exists BP, IOP and ocular perfusion pressure (Khurana and Setty, 1996). During recovery phase of Handgrip test in POAG patients MAP remained significantly higher and MOPP was insignificantly decreased in comparison to healthy controls, that indicated delayed recovery response.

Conclusion and future prospects

Reduced ocular perfusion pressure indicated autonomic dysfunction specially with overdrive of sympathetic activity, causing resistance in microvasculature. As glaucoma is multifactorial disorder of optic nerve, the resultant reduced blood supply in earlier stage may play role in pathophysiology of glaucoma due to ischaemia leading to ganglion cell death. Thus, noninvasive tools to assess autonomic activity must be incorporated as a part of investigation in clinical practice for early diagnosis of glaucoma cases.

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