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Influence of Diastolic Blood Pressure on Glaucoma Progression in Glaucoma Patients with Systemic Hypertension

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ABSTRACT

The aim of this study is to determine relationship between glaucoma progression and diastolic blood pressure. It was conducted on 64 glaucoma patients at the Department of Ophthalmology of Clinical Hospital Centre Zagreb in three years period. The patients were on anti glaucoma therapy and had mean intraocular pressure values under 20 mmHg. At the same time they were on antihypertensive drug therapy. Patients were classified according Glaucoma Staging System based on the perimetric indices mean deviation (MD) and Pattern Standard Deviation into stage 2–4 (moderate glaucoma) at baseline. Rate of visual field progression was calculated in db/year for MD in the last three visits. Patients were divided in 3 groups according to progression – stabile, moderate and progressive. There was no statistically significant difference between 3 groups in terms of intraocular pressure values at baseline and in follow up period. After reviewing their blood pressure, the progressive group showed a significantly lower diastolic blood pressure compared to both stable group and the group with moderate progression. There was no statistical difference between the group with moderate progression and the stable group in terms of diastolic blood pressure. Results suggest that greater risk of glaucoma progression is connected with lower diastolic blood pressure. Diastolic pressure values could be important as one of the risk factors for progression in glaucoma patients with controlled intraocular pressure values.

Key words: *glaucoma progression, diastolic blood pressure, glaucoma, hypertension, perimetry*

Introduction

Intraocular pressure (IOP) is the most important risk factor for open angle glaucoma (OAG) onset and progression and currently the only risk factor amenable to modification by the ophthalmologists. However, there are limitations to treating IOP including the fact that many glaucoma patients do not have a statically elevated pressure, many patients with elevated IOP never develop glaucoma and many patients continue to progress despite good control of IOP[1]. Although open angle glaucoma has an unknown etiology, glaucomatous optic neuropathy could be also an ischemic optic neuropathy. In fact, the »vascular hypothesis« is based on the premise that abnormal ocular perfusion pressure plays a major role in the pathogenesis of glaucoma. Ocular perfusion pressure (OPP) is defined as the difference between the arterial blood pressure and the intraocular pressure (IOP), which is considered a substitute for the venous pressure. IOP-independent mechanisms contribute to disease onset and progression and the link between blood pressure and intraocular pressure is of particular interest, especially in cases of low tension glaucoma[2]. Evidence from large-scale studies such as the Barbados Eye Study[3], Baltimore Eye Study[4] and the Singapore Malay Eye Study[5], suggests that blood pressure plays a role in OAG progression. Rotterdam Eye Study[6] demonstrated an increased risk of OAG for patients with elevated blood pressure treated with calcium channel blockers specifically after 6.5 years of follow-up. This finding is interesting because calcium channel blockers reduce blood pressure but not IOP, while systemic beta-blockers affect perfusion pressure to a lesser degree because they cause both a reduction in blood pressure and IOP. The evidence linking hypotension and glaucoma is more consistent and the majority of studies suggest that hypotension, particularly nocturnal hypotension should be considered an important risk factor for the development and progression of glaucoma, particularly with regard to nor-

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mal tension glaucoma. Many studies have found nocturnal blood pressure levels to be significantly lower in both normal tension glaucoma patients and progressive glaucoma patients, suggesting a possible causative link[7,8]. Furthermore, a large number of studies[9,10] have found associations between large nocturnal dips in blood pressure (>20%) and the progression of glaucoma.

Some large-scale studies have found an increased risk of OAG with diastolic perfusion pressure (DPP) lower than 55 mmHg[11,12].

Purpose of our study was to determine relation between glaucoma progression and the level of diastolic blood pressure in open angle glaucoma patients with medically treated systemic hypertension.

Material and Methods

64 glaucoma patients with systemic hypertension at the Department of Ophthalmology University Hospital Centre Zagreb met inclusion criteria for this study. All patients had moderate glaucoma stage 2–4 accordingly to Glaucoma Staging System (GSS)[13] with mean intraocular pressure values under 20 mmHg obtained with one or two anti glaucoma drugs. At the same time they were on antihypertensive drug therapy. There were 62.17% male and 54.17% female, mean age 65.32 for men and 62.45 for women. There was no statistical difference in sex and age distribution. Follow up period was 3 years. Patients were observed every 6 months and visual fields were performed once or twice a year. Intraocular pressure, central corneal thickness, blood pressure measurement (right arm sitting) were performed at each visit. Diastolic perfusion pressure (DPP) was calculated by equation for DPP (DPP=DBP–IOP)[14]. Standard automated perimetry (SAP) Haag-Streit Octopus 900/G2 glaucoma program was used. Glaucomatous progression was defined on the basis of visual field change determined with SAP. The Glaucoma Staging System (GSS)[13] was used for visual field defect classification at baseline. All included patients were classified according Glaucoma Staging System based on the perimetric indices mean deviation (MD) and Pattern Standard Deviation (PSD) into stage 2–4 (moderate glaucoma). The representative point of the examination is placed in a chart in accordance with the values of these indices. The chart shows defined areas for the different stages of disease (Stage 0 – Stage 5). It also separates generalized, localized and mixed defects. Rate of visual field progression was calculated in db/year after 3 years of follow up. Patients with progression up to 0.2 db/year were considered stable, 0.2–0.4 moderate and rate of progression more than 0.4 db/year was considered rapid.

Data are presented as mean ± standard deviation. The comparison of stable and progressive group was done using Student's t test. A probability lower than $p<0.05$ was considered statistically significant.

Results

Analyzing the visual field findings in 64 glaucoma patients in 3 year of follow up period, we classified 23 (35.93%) patients with progression: 11 (17.18%) patients in progressive group with progression more than 0.4 db/year and 12 (18.75%) patients in moderate progression group within 0.4 db/year of progression. 41 (64.06%) patients did not have marked progression in visual field (0.2 db/year or less) (Figure 1). There was no statistically significant difference between 3 groups in age. In terms of gender, in the progression group there were predominantly women – 7 (63.64%) and 4 (36.36%) men. In the moderate progression group gender ratio was 1:1, and in the stable group we found higher percentage of men (62.17%). There was no statistically significant difference between 3 groups in terms of mean intraocular pressure values at baseline and in follow up period (Table 1).

After reviewing their blood pressure, the progressive group showed a significantly lower diastolic blood pressure compared to both stable group and the group with moderate progression. Mean diastolic blood pressure in progressive group was low – 65.62±4.32 in comparison with mean diastolic pressure in the stable group – 84.54±5.99 and this difference was statistically significant. There was no statistically significant difference between the group with moderate progression and the stable group in terms of diastolic blood pressure. Congruently,

TABLE 1
DEMOGRAPHIC CHARACTERISTICS, IOP, CCT, DBP, DPP

	Stable (N=41)	Moderate (N=12)	Progressive (N=11)	Significance level
% male	62.17	54.17	36.36	
Mean IOP at baseline	16.88±3.13	16.33±4.00	16.91±2.89	p=0.74
	17.43±2.17	16.29±3.46	16.47±3.15	p=0.72
Mean IOP in 3 years	552.79±37.53	542.59±43.11	540.12±36.52	p=0.33
Mean CCT	84.54±5.99	72.87±6,57	65.62±4.32	p<0.01
Mean DBP	65.63±5.43	54.72±6.87	47.33±5.87	p<0.01
Mean DPP	65.43±12.03	59.35±14.23	61.58±10.47	p=0.87

IOP – intraocular pressure, DBP – diastolic blood pressure, CCT – central corneal thickness, DPP – diastolic perfusion pressure

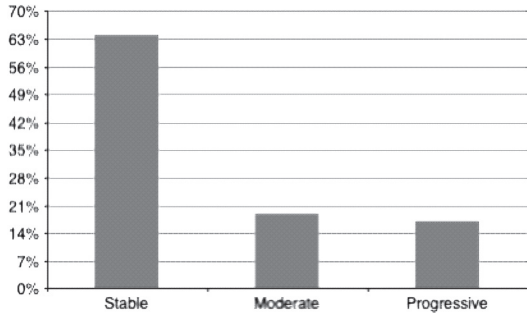

Fig. 1. Percentage of visual field progression in 64 glaucoma patients in 3 years follow up period: stable (64.06%), moderate progression (18.75%) and progressive (17.18%).

mean diastolic perfusion pressure was statistically significantly lower in progressive group compared with stable group (Table 1).

Discussion

Although high blood pressure has been shown to be associated with OAG[14], low ocular perfusion pressure and low systolic blood pressure are also known risk factor for OAG. There are many evidences from studies that nocturnal hypotension plays a role in the development and progression of glaucoma[15–18]. This bimodal distribution of risk factors (both high and low blood pressure demonstrates some of the challenges in studying the relationship of glaucoma and blood pressure[19,20].

Findings from our study support the results of the Barbados Eye Study[3] that diastolic perfusion pressure under 55 mmHg more than doubled the risk of OAG. Observations that decreased blood flow is found in OAG but not in patients with ocular hypertension and matched IOP indicates a reduction in choroidal and short posterior ciliary artery circulation in primary open angle glaucoma[19]. This is in line with the findings of this study, because increased IOP with raised diastolic blood pressure could potentially result in adequate diastolic perfusion pressure as in stable group of our patients. Congruently, many studies have found that lower diastolic perfusion pressure essentially equates to a higher risk for OAG: Baltimore Eye Study[4], Egna-Neumarket Study[14], Barbados Eye Study[3] and the Rotterdam Eye Study[6].

The Barbados Eye Study[3] showed that diastolic perfusion pressure may be an important factor for classifying a patient as progressing with 2.6 times higher relative risk, compared to all other factors examined (age 1.1 times; family history 2.4 times; higher IOP 1.1 times; systolic blood pressure 0.8 times; and CCTs 1.4 times).

An association between the degree of nerve fiber layer loss (using optical coherence tomography) and the time of day that hypertensive medication was administered (in the evening as opposed earlier in the day)[21] was shown in glaucoma patients in 24-hour blood pressure profiles. This effect was suggested to potentially arise from greater nocturnal dips in blood pressure when medications were taken later in the day.

Lower diastolic pressure is found in open angle glaucoma patients predominantly in the study with 24 healthy individuals and 29 open angle glaucoma patients who underwent intraocular pressure and blood pressure measurements every 2 h, starting at 08:00 until 06:00 of the next morning[21]. This is in agreement with finding from our study where mean diastolic blood pressure was shown to be an important risk factor for OAG progression. Mean diastolic blood pressure value in the group of progressive glaucoma patients was 65.62±4.32 mmHg, which was statistically significantly lower in comparison with diastolic blood pressure values in glaucoma patients without progression. The notion that reduced diastolic perfusion pressure potentially impairs ocular blood blow in the absence of auto regulation has been suggested in some studies[22,23].

As lower diastolic blood pressure can decrease ocular perfusion, there are likely clinical ophthalmic complications associated with medical intervention for hypertension. Although lowering of blood pressure is justified in terms of reducing cardiovascular risk, extra consideration should be extended to patients on glaucoma therapy or with ocular hypertension to ensure that perfusion pressures are not reduced to the point of creating ischemia to the optic nerve. Consistently, aggressive treatment of hypertension has been shown in some cases to cause serious damage to both the heart and brain[24,25].

Although controversial, it is of interest to note, that arterial hypertension actually appears to be a protective factor in glaucoma in some epidemiological studies[26,27]. There is necessity for close collaboration between glaucomatologists and primary care physicians regarding the patient's diastolic blood pressure values in the overall management of glaucomatous optic neuropathy.

Conclusion

Patients with progressive glaucoma at "normal" IOP remind us of the fact that other glaucoma risk factors besides intraocular pressure could be important. If non-IOP related factors such as low blood pressure are contributing to progression in these patients, we may be exposing our patients to undue risk with further intraocular pressure lowering which may require aggressive intervention such as surgery. If ocular perfusion pressure is one of the final common pathways linking low blood pressure to glaucoma risk, then lowering IOP, which also improves ocular perfusion pressure, would still be expected to reduce the risk from low blood pressure. Aggressive treatment of arterial hypertension should be avoided because it can lead to low diastolic blood pressure and consequently low perfusion pressure. Additional research is needed in both of these areas to provide new treatment strategies for clinicians.

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UTJECAJ DIJASTOLIČKOG KRVNOG TLAKA NA PROGRESIJU GLAUKOMA KOD PACIJENATA S GLAUKOMOM I SUSTAVNOM HIPERTENZIJOM

SAŽETAK

Cilj ove studije je utvrditi povezanost između progresije glaukoma i dijastoličkog krvnog tlaka. Studija je provedena na 64 pacijenata s glaukomom pri Klinici za očne bolesti KBC Zagreb u trogodišnjem periodu. Pacijenti su bili na antiglaukomskoj terapiji i imali su srednje vrijednosti očnogi tlaka ispod 20 mmHg. Istovremeno su bili i na antihipertenzivnoj medikamentoznoj terapiji. Pacijenti su u početku klasificirani prema Glaucoma Staging System, koji se zasniva na srednjoj devijaciji perimetrijskih indeksa (MD) i Obrascu standardne devijacije, u stadij 2–4 (umjereni glaukom). Stupanj progresije vidnog polja je izračunat u db/godina za MD u posljednja tri posjeta. Pacijenti su podijeljeni u tri skupine – stabilni, umjereni i progresivni. Nije nađena statistički značajna razlika između tri skupine u odnosu na očni tlak u početku i periodu praćenja. Nakon analiziranja njihovog krvnog tlaka, progresivna skupina pokazala je značajno niži dijastolički krvni tlak u odnosu na stabilnu i skupinu s umjerenom progresijom. Nije bilo statističke rzlike između skupine s umjerenom progresijom i stabilne skupine u odnosu na dijstolički krvni tlak. Rezultati upućuju na to da je veći rizik od progresije glaukoma povezan s nižim dijastoličkim krvnim tlakom. Vrijednosti dijastoličkog krnog tlaka mogle bi biti značajne kao jedan od čimbenika rizika za progresiju kod pacijenata s glaukomom i kontroliranim vrijednostima očnog tlaka.