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Glaucoma in Patients with Parkinson's Disease

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Abstract

Objective: To determine if patients with Parkinson's disease (PD) have an increased risk of glaucoma.

Materials and methods: The cross-sectional case-control study. One hundred consecutive patients (196 eyes) with idiopathic PD and a control group consisting of 100 healthy matched for age and sex patients (196 eyes) underwent a complete ophthalmological examination of both eyes, including assessment of slit lamp examination of the eye anterior segment and fundus, intraocular pressure and evaluation of the peripapillary retinal nerve fiber layer (RNFL) thickness. Participants were also evaluated in terms of perfusion pressures in the eyes.

Results: The frequency of glaucoma was higher in eyes of PD patients in comparison to controls (16.33% vs. 6.63%; p=0.004) and intraocular pressure was significantly lower (16.88 ± 3.18 vs. 17.76 ± 3.21 mm Hg; p=0.009). Systolic and diastolic blood pressure, as well as calculated perfusion pressures did not differ significantly between PD and control group with exception of higher diastolic perfusion pressure in PD patients' eyes. The retinal fiber layer thickness did not significantly differ between investigated no-glaucoma groups, but revealed significant reduction in superior and inferior quadrant in glaucoma PD patients.

Conclusion: PD patients have increased risk of glaucoma.

Keywords: Parkinson's disease; Glaucoma; Intraocular pressure; Ocular perfusion pressure; Optical coherence tomography; Retinal nerve fiber layer

Introduction

According the World Health Organization, glaucoma is the first cause of irreversible blindness worldwide. It is a group of eye diseases which result in damage to the retinal ganglion cells (which axons form the optic nerve) and lead to the disturbance of signal transmission from the retina to the visual cortex [1]. Glaucoma is usually associated with increased intraocular pressure (>21 mm Hg). However, in predisposed persons even normal values of intraocular pressure may lead to the damage of the optic nerve (normal tension glaucoma). There are few studies that suggested increased glaucoma morbidity in Parkinson's disease (PD) patients and one of possible explanation is excessive oxidative stress which is present in PD and glaucoma. Neurodegeneration in PD lead to systemic dopamine depletion. Dopamine is also present in the eye in the subtype of amacrine cells A18 in the inner plexiform layer of the retina [2], while dopaminergic receptors are spread across the whole retina. Although their number is relatively small, due to widespread and long axons they may influence directly through the synapses on a variety of subtypes amacrine cells and bipolar cells [3]. Dopamine released in the inner plexiform layer has the ability to diffuse distance equal to the thickness of the entire retina. Thus, the amacrine cells A18 may indirectly affect the functions of all the other cells of the retina, including ganglion cells [2]. In the eye, dopamine has various functions, including part in the cyclic regulation of intraocular pressure with the aid of dopaminergic receptors located on the ciliary body epithelium [4] and anti-apoptotic role [5]. The results of post-mortem tests showed lower levels of dopamine in the retinas of patients with PD who did not used exogenous dopamine for at least five days before death compared to age-matched controls, what confirm that in course of PD there is a reduction of dopamine concentration in the retina, probably as a result of amacrine cells' A18 dysfunction [6,7]. The problem of ocular diseases associated with PD is not well known. The aim of this study was to determine if patients with PD have an increased risk of sight-threatening glaucoma because good vision has a great role in everyday life and rehabilitation of these patients.

Material and Methods

One hundred (56 Male/44 Female) patients (196 eyes) aged 68.5 ± 10.2 years with idiopathic PD and a control group of 100 healthy age- and sex- matched patients (196 eyes) with mean age of 68.6 ± 9.8 years (p=0.95) were enrolled to the study. Mean duration of PD was 5.6 ± 4.8 years and advancement equal 1.8 ± 0.7 according to modified Hoehn and Yahr scale. All participants with any systemic diseases and medications known to influence the organ of vision or previous ocular surgery other than uneventful phacoemulsification were excluded from the study. Patients with diagnosed idiopathic PD were referred on ophthalmological examination from the neurological outpatient clinics. PD patients were examined in the morning without taking any anti-parkinsonian drugs. The diagnosis of glaucoma was based on the presence of at least one of the following criteria: a characteristic repeatable pattern of glaucomatous visual field loss and a cup-to-disk ratio of 0.8 or greater with an optic nerve head appearance consistent with glaucoma. To determine whether PD patients have an increased risk of glaucoma due to elevated intraocular pressure or decreased perfusion pressure only eyes without glaucoma were recruited to comparison due

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to known prolonged pressure lowering effect of antiglaucoma drops (85 PD patients (164 eyes) aged 67.4 ± 10.3 years and 85 controls (164 eyes) aged 67.6 ± 10.0 years, p=0.91). After 5 min of rest systolic and diastolic blood pressure (SBP and DBP) was measured on the left arm of each patient. Mean arterial pressure (MAP)=DBP+(1/3)(SBP–DBP), mean perfusion pressure (MPP)=Mean Arterial Pressure – Intraocular Pressure (IOP), Ocular Perfusion Pressure (OPP)=(2/3 mean arterial pressure) - IOP, systolic perfusion pressure (SPP)=SBP-IOP and diastolic perfusion pressure (DPP)=DBP - IOP, was calculated. Subsequently, all participants underwent a complete ophthalmological examination of both eyes, including assessment of intraocular pressure (PASCAL Dynamic Contour Tonometer), anterior segment and fundus examination (biomicroscopy, 90D Volk lens) and measurements of the retinal nerve fiber layer (RNFL) thickness near the entry of the optic nerve with Optical Coherence Tomography (OCT) scans (fast algorithms, time domain Stratus OCT, Carl Zeiss Meditec). The static perimetry were performed when there was a need to confirm glaucoma (24-4 test, Humphrey Visual Field Analyser). All subjects participating in this study gave their informed written consent. The project was approved by Ethics Committee of the Pomeranian Medical University. The results were compared using Mann-Whitney U test for quantitative and rank variables, or using Fisher's exact test for qualitative variables. A p-value <0.05 was considered significant. Quantitative data are presented as mean ± standard deviation (SD). Qualitative data are presented as percentages of eyes/patients and number of eyes/patients.

Results

Glaucoma was found in 16.33% (32/196) eyes of patients with PD and 6.63% (13/196) eyes of controls (p=0.004). All these patients were found to have primary open-angle glaucoma. However, intraocular pressure in the eyes of PD patients without glaucoma was significantly lower when compared to control cases (16.88 ± 3.18 vs. 17.76 ± 3.21 mm Hg; p=0.009). Systolic and diastolic blood pressure, as well as calculated perfusion pressures did not differ significantly between PD and control group with exception of higher DPP in PD patients' eyes (Table 1).

The difference of peripapillary RNFL thickness in all four quadrants (Temporal, Superior, Nasal, Inferior) were not significant between no-glaucoma participants from PD and control group. However, the analysis of peripapillary RNFL thickness between glaucoma and no-glaucoma PD patients revealed significant reduction in superior and inferior quadrants (Table 2), which is consistent with the place of the first glaucoma changes on the optic nerve head.

Discussion

The results of our study suggest that PD patients may have an increased risk of glaucoma. We reported primary open-angle glaucoma in 16.33% eyes of PD patients in comparison to 6.63% eyes of controls. Currently, there is only one study pointing on an increased rate of glaucoma in patients with PD (23.7%), mostly normal tension glaucoma [8]. An increased risk of glaucoma in course of PD may be a result of decreased level of reduced glutathione (GSH), one of the prominent antioxidants found in the eye [9,10]. GSH protects ocular tissue from damage caused by oxidative stress, which is implicated in the pathogenesis of primary open angle glaucoma, especially with normal IOP [11]. One latest study analyzed risk of PD development in glaucoma and no-galucoma patients [12]. The Authors concluded that primarily open angle glaucoma is not a predictor of PD. Although, the process of neurodegeneration in glaucoma and PD may be similar (excessive oxidative stress), we believe that glaucoma in PD patients

	PD	Controls	p
IOP	16.87 ± 3.18	17.76 ± 3.21	0.01
SBP	128.32 ± 18.47	130.65 ± 18.7	ns
DBP	80.73 ± 10.65	79.23 ± 9.40	ns
MAP	96.59 ± 11.64	96.37 ± 11.42	ns
SPP	111.44 ± 18.77	112.88 ±18.92	ns
DPP	63.85 ± 11.52	61.47 ± 10.03	0.02
OPP	47.51 ± 8.64	46.48 ± 8.28	ns
MPP	79.71 ± 12.34	78.61 ± 11.88	ns

IOP: Intraocular Pressure; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; DPP: Diastolic Perfusion Pressure; SPP: Systolic Perfusion Pressure; OPP: Ocular Perfusion Pressure; MPP: Mean Perfusion Pressure; ns: not significant (p>0.05)

Table 1: Comparison of intraocular pressure, systolic and diastolic blood pressure and perfusion pressures in the eyes of no-glaucoma PD patients and controls. The data are presented as mean ± standard deviation.

	RNFL Thickness			
	Temporal	Superior	NASAL	Inferior
No glaucoma controls	61.78	116.16	71.68	121.24
No glaucoma PD patients	63.05	119.40	77.15	123.93
Glaucoma PD patients	60.56	**98.32**	68.08	**98.36**
p-value	ns	**p<0.001**	ns	**p<0.001**

RNFL: Retinal Nerve Fiber Layer; ns: not significant (p>0.05)

Table 2: Mean values of peripapillary retinal nerve fiber layer (RNFL) thickness in PD patients and controls.

is a secondary process resulted from retinal dopamine depletion. When compared patients without glaucoma participated to present study, intraocular pressure turned out to be significantly lower in PD group and its mean value was within normal limits, what suggest that PD patients do not have the greatest risk factor of glaucomatous neuropathy development. Comparison of calculated perfusion pressures did not revealed significant differences between PD patients and controls, with exception of higher (better) DPP in the eyes of former. Ocular perfusion pressure, as the pressure at which blood enters the eye, may be a potential factor that contributes to glaucoma risk. That is why it is sensible to hypothesize that PD patients have increased risk of glaucoma due probable hypersensitivity of ganglion cells without dopaminergic anti-apoptotic protection from permanent oxidative stress. It cannot be excluded that even normal intraocular pressure is too high for these patients, similarly as occurs in normal tension glaucoma. It is widely known, that in such cases treatment with antiglaucoma drops markedly slow down the disease progression as a result of ganglion cells protection. That is why, it is important to consider implementing treatment with the first sign of glaucomatous neuropathy even if intraocular pressure is within normal limits. In present study, OCT examinations of peripapillary RNFL thickness did not revealed significant differences between PD patients and control cases without glaucoma. However, PD patients with glaucoma showed characteristic glaucomatous pattern of RNFL loss primarily in the inferior and superior quadrant. The results of previous OCT studies are inconclusive. Some studies revealed RNFL thinning in PD cases [13-16], while other does not support this [17-20]. The reason of result discrepancies may be qualification of PD patients with glaucoma to the analysis, which has proven influence on RNFL thickness. We believe that OCT has a significant role in the diagnosis and monitoring of glaucoma neuropathy, as PD patients may have difficulties in performance of static perimetry due to bradykinesia and tremor.

Good quality of vision has a great role in everyday life and

rehabilitation of PD patients. It plays an important role in the prevention of injuries caused by falls which are an important issue directly related to PD [21-26]. Lord and Dayhew [27] showed that people with impaired sight fall more often than people with normal vision capability. This is due to the fact that people with impaired vision may have trouble recognizing the dangers on the road, as well as making a correct response after stumbling [25]. Furthermore, they may less frequent exercise, which leads to muscle weakness and postural imbalances, as well as less go out, resulting in increased susceptibility to fractures due to vitamin D deficiency [25]. Proper control of motor function and posture requires the integration of sensory information from the organ of vision, the vestibular system and proprioreceptors. Individuals with PD have a reduced ability to correctly process and the use of feedback signals from proprioreceptors, which may be the result of the basal ganglia dysfunction in the brain, which are place of integration of sensory information from a variety of receptors, and produce a plan of the intended motion. These disorders are likely to be compensated by the sight [28,29]. Good visual function is also important in the rehabilitation of patients with PD. It seems that using specific dynamic visual stimulus, that generates so-called "optic flow", tends to compensate the deficit of feedback signals integration from the proprioreceptors and allows to maintain the correct pattern of movement [30,31]. The use of visual stimulation during exercise has also positive influence on the longer stability of the rehabilitation benefit [32]. The probable reason of this observation is fact that exercises improve only the musculoskeletal system, which after termination of the rehabilitation process is a short-term phenomenon [32]. Use of visual stimuli results in a permanent feedback which "bypass" damaged basal ganglia of the brain, what was illustrated by Positron Emission Tomography (PET) [33].

Conclusion

PD patients have increased risk of glaucoma which is the leading cause of irreversible blindness worldwide and good quality of vision has a great impact on the PD patients' quality of life and rehabilitation. That is why it is important do refer them for ophthalmological examination and in case of glaucoma neuropathy detection initiate the treatment, which has proven effectiveness in slowing down glaucoma progression even if intraocular pressure is within normal limits.

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