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Evaluation of Risk Factors in Patients with Primary Open Angle Glaucoma and Ocular Hypertension

Primer Açık Açılı Glokomlu ve Oküler Hipertansiyonlu Hastalarda Risk Faktörlerinin Değerlendirilmesi

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Özet

Amaç: Primer açık açılı glokomlu (PAAG) olguları ve Oküler Hipertansiyonlu (OHT) olguları yaş, cinsiyet, göz içi basıncı (GİB), santral kornea kalınlığı (SKK), sferik ekivalan değeri, sigara içiciliği, aile hikayesi ve ek sistemik hastalık mevcudiyeti açısından karşılaştırmak ve bu verilerin birbiriyle olan ilişkisini değerlendirmek.

Gereç ve Yöntemler: 40 PAAG'li ve 40 OHT'li olgu, hasta grubu ve glokomu olmayan 40 olgu kontrol grubu olarak kabul edildi. Yaş, cinsiyet, GİB, SKK, sferik ekivalan değeri, soygeçmişte glokom hikayesi, ebeveynler arası akraba evliliği hikayesi, sigara kullanımı ve ilave sistemik hastalıklar kaydedildi.

Bulgular: Cinsiyet dağılımı ve yaş ortalaması açısından gruplar arasında anlamlı fark görülmedi. PAAG ve OHT gruplarında GİB kontrol grupları agöre anlamlı olarak yüksek iken PAAG ve OHT grupları arasındaki fark ise anlamlı değildi. OHT grubunda ortalama SKK değeri, PAAG ve kontrol gruplarına göre anlamlı olarak daha yüksekti. GİB ile SKK arasında istatistiksel analizde anlamlı korelasyon tespit edilmedi. Sferik ekivalan ortalama değerleri yönünden gruplar arasında anlamlı bir fark saptanmadı. Hipertansiyon, diyabetes mellitus, koroner arter hastalığı insidansı yönünden gruplar arasında farklılık yoktu. PAAG ve OHT gruplarında pozitif aile hikayesi oranı, kontrol grubuna göre anlamlı yüksekti. Gruplar arasında akraba evliliği hikayesi yönünden anlamlı fark tespit edilmedi. Sigara kullanım öyküsü açısından gruplar arasında anlamlı fark izlenmedi.

Sonuç: PAAG ve OHT gruplarında yüksek GİB en önemli risk faktörüdür. PAAG ve OHT gruplarında anlamlı derecede ailesel glokom öyküsüne rastlanması genetik faktörlerin önemli bir risk faktörü olabileceğini göstermektedir.

Anahtar Kelimeler: Kornea kalınlığı, miyopi, oküler hipertansiyon, primer açık açılı glokom, sigara

Abstract

Objective: The purpose of our study was to compare the age, gender, intraocular pressure (IOP), central corneal thickness (CCT), spherical equivalent values, smoking, family history of glaucoma, and additional systemic diseases in patients with primary open-angle glaucoma (POAG) and patients with ocular hypertension (OHT); and to evaluate the relationships of these factors with each other.

Materials and Methods: 40 patients with POAG, 40 patients with OHT, and 40 individuals as a control group were included in the study. Age, gender, IOP, CCT, spherical equivalent values, family history of glaucoma, history of consanguineous marriage, smoking, and systemic diseases of each subject were recorded.

Results: There was no significant difference in gender and average age between the groups. IOP values were higher in the POAG and OHT groups than in the control group. There was no significant difference in IOP values between POAG and OHT groups. CCT was higher in the OHT group than in the other groups. There was no significant correlation between IOP and CCT values. There was no significant difference in mean spherical equivalent values. The incidence of hypertension, coronary heart disease, and diabetes mellitus was similar in all groups. Family history of glaucoma is increased in the POAG and OHT group compared with the control group. There was no significant difference in the history of consanguineous marriage, alcohol usage, and smoking status among all groups.

Conclusion: High IOP was the most important risk factor in POAG and OHT groups. A significant familial history of glaucoma in POAG and OHT groups suggests that genetic factors may be an important risk factor.

Keywords: Corneal thickness, myopia, ocular hypertension, primary open angle glaucoma, smoking

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INTRODUCTION

Glaucoma is an optic neuropathy distinguished by the excavation and thinning of the optic disc's neural and connective tissue components, independent of intraocular pressure (IOP). This condition is accompanied by specific visual field defects (1).

Primary open-angle glaucoma (POAG) is the most common type of glaucoma. It affects about 1% of people over the age of 40. POAG is a chronic, bilateral optic neuropathy with an open anterior chamber angle and IOP higher than 21 mmHg, with acquired optic nerve fiber loss and visual field defects (2).

Ocular Hypertension (OHT) is characterized by an IOP higher than 21 mmHg and an open iridocorneal angle despite the absence of glaucoma-specific optic nerve head changes or visual field losses. If OHT is not treated or monitored regularly, it carries the risk of POAG. The incidence of developing POAG in individuals with OHT is approximately 10% (3). Glaucoma has a multifactorial etiology. Factors such as IOP, age, gender, race, genetics, central corneal thickness (CCT), refractive errors, systemic diseases, smoking, and alcohol use are considered risk factors for POAG and OHT (2,3).

Optic nerve head perfusion abnormalities, increased vascular resistance or systemic hypotension can cause glaucomatous damage despite normal IOP (4). IOP tends to increase with age. Age-related structural changes in the optic nerve head make the eye more susceptible to glaucoma (2,5). The higher prevalence of glaucoma in the family history of individuals diagnosed with POAG or OHT suggests a potentially significant role of genetic factors in etiology. The risk is also three times higher in people with a first-degree relative with POAG (6-11). Structural changes that occur along with axial elongation in myopic eyes make these eyes more vulnerable to the development of POAG (12,13). Systemic diseases with vascular involvement such as diabetes mellitus and arterial hypertension increase the risk of glaucoma by pathologic changes in the optic nerve head (14-19). The toxic metabolites and free radicals arising from cigarette and alcohol consumption lead to increased oxidative stress, affecting various parts of the eye (20,21).

Glaucomatous damage can be avoided as much as possible if the modifiable risk factors are well known. Our study aimed to determine ocular, systemic, genetic, and environmental factors to recognize individuals at high risk of developing POAG and OHT, and to perform better follow-up of patients with glaucoma.

MATERIALS AND METHODS

Subject

A total of 40 patients diagnosed and monitored for POAG and 40 patients with OHT were included in the

study. Additionally, 40 individuals without glaucoma were included as a control group based on examination and test results. The examination findings were retrospectively recorded from their medical records.

Inclusion criteria for the POAG group were IOP>21 mmHg on repeated measurements without antiglaucomatous treatment, glaucomatous retinal nerve fiber layer (RNFL) defects and no other cause of damage, glaucomatous visual field defects, anterior chamber angle grade 3 and 4 according to the Schaffer classification system on gonioscopy.

Inclusion criteria for the OHT group were IOP>21 mmHg, normal optic disc and RNFL normal visual field, anterior chamber angle grade 3 and 4 according to the Schaffer classification system on gonioscopy. Inclusion criteria for the control group were IOP <21 mmHg, corrected visual acuity of 10/10, no ocular disease, normal optic disc, RNFL, and no visual field defect.

Detailed examination forms that were thoroughly completed during the application and follow-up of all cases within the scope of the study included the following parameters: age, gender, IOP, CCT, spherical equivalent values, family history of glaucoma, history of consanguinity in parents, smoking and alcohol usage, presence of systemic diseases (diabetes mellitus, hypertension, hyperlipidemia, thyroid disorders, migraine, coronary artery disease, neurodegenerative diseases such as Alzheimer's and Parkinson's, hematological disorders). Spherical equivalent values obtained after visual acuity examination, intraocular pressure values measured by different people with Goldmann Applanation Tonometer, angle classification according to Shaffer classification system with Zeiss gonioscopy lens, CCT values last measured and recorded with Pentacam® (Oculus, Germany), RNFL analysis with Spectral Domain OCT[®] (Heidelberg Engineering Spectralis, Germany) and 30-2 visual field threshold test values obtained with Humphrey® Automatic Perimeter (Humprey Field analyzer 750i, Humprey-Zeiss, USA) were recorded.

Statistical Analysis

Statistical evaluation was performed using the SPSS[®] (Statistical Package for Social Sciences, Worldwide Headquarters SPSS Inc.) software package for Windows[®]. One-way analysis of variance (ANOVA) test was employed for intergroup comparisons. A significance level of P<0.05 was considered statistically significant. In cases of important differences, Tukey and Tamhane's T2 tests were applied to determine which groups the differences originated. The Chi-squared test was used for categorical comparisons between groups.

The study was approved by the Ethics Committee (Date: 20/06/2014, Protocol No: 2014/680) and all procedures were applied to the Declaration of Helsinki.

RESULTS

No significant differences were observed among the groups regarding gender distribution and age averages (p=0.238 and p=0.51, respectively) (Table 1).

The mean IOP value for both eyes was statistically significantly higher in the POAG and OHT groups compared to the control group (p=0.000). However, the difference in mean IOP between the POAG and OHT groups was not statistically significant (p=0.52 and p=0.62, respectively) (Table 1). When the relationship between age and IOP was evaluated in the POAG and OHT groups using Pearson correlation analysis, no significant correlation was observed (p=0.755 and p=0.347, respectively).

No significant difference was found in terms of mean IOP values between genders (p=0.66).

In the OHT group, the mean CCT values were higher in both eyes compared to the POAG and control groups (on the right, p=0.001 and p=0.008, respectively; on the left, p=0.013 and p=0.006, respectively). There was no significant difference between the POAG and control groups (on the right, p=0.955; on the left, p=0.987) (Table 1). The relationship between IOP and CCT was evaluated using Pearson correlation analysis, but no significant correlation was found (p=0.663 and p=0.534, respectively).

There was no significant difference detected among the three groups in terms of mean spherical equivalent values (on the right eye p=0.686; on the left eye p=0.640) (Table 1). Statistically significant differences were not observed among the groups in terms of diabetes mellitus, hypertension, hyperlipidemia, and coronary artery disease (respectively, p=0.417, p=0.058, p=0.79, p=0.236) (Table 2). Within all groups, there was 1 individual (2.5%) with hypothyroidism in the control group and 1 individual (2.5%) with a history of cerebrovascular disease in the OHT group (Table 2). No statistically significant difference was observed among the groups in terms of smoking and alcohol usage (p=0.492 and p=0,899 respectively) (Table 2). The positive family history rate was statistically higher in both the POAG and OHT groups compared to the control group (p=0.000). However, the difference between the POAG and OHT groups was not statistically significant (p=0.953) (Table 2). There was no statistically significant difference among the groups in terms of a history of first-degree consanguinity (p=0.899) (Table 2). There was no history of migraine, neurodegenerative disease and hematologic disease.

DISCUSSION

Between the ages of 20 and 40, the IOP follows a bell-shaped curve, and as age advances, this curve shifts towards higher IOP values. This phenomenon indicates a positive independent correlation between age and IOP (5). With age, the connective tissue of the optic nerve head becomes stiffer and the axons of the retinal ganglion cells become more sensitive to changes in intraocular pressure due to impaired perfusion. The incidence of POAG is 0.5% in the age range of 40-49 and 11% in individuals aged 80 and above (22). Similarly, the prevalence of OHT is around 4-7% in the population aged 40 and above, this rate increases with age (23,24).

Gender is not considered a risk factor for glaucoma. There is no difference in the prevalence of glaucoma between men and women of the same age (25). Accordingly, no significant difference was observed between and within groups in terms of gender distribution in our study.

Table 1. Distribution of the groups in terms of age, gender, IOP, CCT and spherical equivalent values						
		POAG (n=40) (mean±SD)	OHT (n=40) (mean±SD)	Control (n=40) (mean±SD)		
Age		57.70±10.71	52.17±12.44	51.30±14.27		
Gender	Female	17 (%42.5)	18 (%47.5)	24 (%60.0)		
	male	23 (%57.5)	22 (%52.5)	16 (%40.0)		
IOP (mmHg)	right eye	27.15±4.27	25.36±1.68	14.51±3.04		
	left eye	27.00±4.38	25.20±1.86	14.32±2.80		
CCT (µm)	right eye	544.12±34.00	567.95±16.83	547.70±34.80		
	left eye	547.22±38.55	567.40±19.31	549.52±29.69		
Sph. Equivalent (D)	right eye	-0.27±1.80	-0.34±1.07	-0.10±0.81		
	left eye	-0.24±1.31	-0.34±1.11	-0.10±0.85		

family history							
	POAG (n=40)	OHT (n=40)	Control (n=40)	p value			
Diabetes Mellitus	10 (%25)	6 (%15)	6 (%15)	0.417			
Systemic Hypertension	18 (%45)	9 (%22.5)	10 (%25)	0.058			
Hyperlipidemia	5 (%12.5)	3 (% 7.5)	0	0.79			
Coronary Artery Disease	3 (%7.5)	2 (%5)	0	0.236			
Cerebrovascular Disease	0	1 (%2.5)	0	-			
Thyroid Disease	0	0	1 (%2.5)	-			
Smoking	8 (%20)	9 (%22.5)	5 (%12.5)	0.492			
Alcohol use	3 (%7.5)	3 (%7.5)	4 (%10)	0.899			
Family history	12 (%30)	14 (%35)	2 (%5)	0.000			
Consanguineous marriage	4 (%10)	3 (%7.5)	3 (%7.5)	0.899			

Table 2. Distribution and statistical comparison of the cases in terms of systemic diseases, harmful habits and family history

According to studies, high IOP is the most important risk factor for glaucoma. The rate of visual field loss is slower in glaucoma patients whose IOP is under control (26). The probability of glaucoma was found to be 10% when IOP was 23 mmHg and 50% when IOP was 27 mmHg (27). In the results of the Ocular Hypertension Treatment Study Group, during a 5-year follow-up of OHT cases with IOP of 24 mmHg and above, it was observed that POAG developed in 4.4% of those using antiglaucoma medication and 9% of those not using medication. The difference between the treated group and controls increased over time (16). In our study, we observed that the IOP was significantly higher in both the POAG and OHT groups compared to the control group.

Various studies using ultrasound pachymetry, contact specular microscopic pachymetry, optical coherence tomography, and scheimpflug corneal tomography devices have shown that patients with OHT have thicker CCT values compared to normal populations and individuals with glaucoma (28-30). In our study, we also found that CCT was statistically significantly higher in the OHT group compared to the other two groups. In addition, Gordon et al. (16) observed that the risk of glaucoma development was three times higher in eyes with 555 μ m or thinner CCT compared to eyes with 588 μ m or thicker CCT in patients with OHT.

In myopic eyes, the sclera becomes thinner due to increased axial length. This makes the optic disc more sensitive to IOP changes. Particularly in myopia more than 6 diopters, the prevalence of glaucoma is higher (12,13). In the Blue Mountain Eye Study, POAG was found to be associated with myopia, while a borderline association was defined with OHT (31). The mean spherical values of refractive error in eyes with POAG and OHT tend to be more myopic compared to normal individuals (32). However, no significant difference was found when the mean spherical equivalent values were compared with the control group in our study.

Individuals with a family history of POAG in first-degree relatives have an approximately three times increased risk of developing POAG. The prevalence of a family history of glaucoma in POAG cases has been observed to be around 13% (6,33,34). Genome studies conducted in various populations have identified several gene loci associated with glaucoma (35). In our study, 30% of the POAG group, 35% of the OHT group and 5% of the control group had a family history of glaucoma. A significant increase in positive family history was found in the POAG and OHT groups compared to the control group, and this supports the role of genetic factors in glaucoma.

While some studies in the literature have indicated that diabetes might not be a significant risk factor for glaucoma, recent large-scale population studies have revealed a higher incidence of glaucoma among individuals with diabetes compared to those without diabetes (14-16). Diabetes and hyperglycemia cause loss of retinal ganglion cells by increasing oxidative stress and promoting cellular apoptosis through lipid glycation and impaired lipid metabolism (36). Excessive matrix metalloproteinase expression has been associated with structural changes in the optic nerve head of patients with diabetes (37). In our study, there was no statistically significant difference between the groups in terms of diabetes frequency.

Various studies have found an increased prevalence of POAG and OHT in systemic hypertensive individuals. Impaired autoregulation of the posterior ciliary blood circulation, direct microvascular damage, and hypotensive episodes, especially at night due to antihypertensive treatments, make the optic nerve more susceptible to glaucomatous damage with the effect of IOP, which tends to increase with age (17,18). No positive correlation has been observed between POAG and systemic hypertension unless the diastolic perfusion pressure falls below 50 mmHg (19). In this study, although there were more systemic hypertensive patients in the POAG group, the difference was not statistically significant when compared with the other two groups.

Whether smoking, an independent risk factor for atherosclerosis, is a risk factor for glaucoma is not clear. While some clinical trials suggest a link between smoking and glaucoma, large population-based studies have not demonstrated a significant association (20). In our study, there was no statistically significant difference among the three groups in terms of smoking.

Studies in individuals with hyperlipidemia have found that the risk of developing POAG is reduced. However, it is not clear whether this reduced risk is due to hyperlipidemia itself or the drugs used in the treatment of hyperlipidemia (38). However in a study with atorvastatin in patients with OHT, it was observed that IOP decreased (39) In our study, there were no hyperlipidemic cases in the control group, and the difference between the POAG and OHT groups was not statistically significant.

Although acute alcohol consumption has been shown to increase perfusion in the optic nerve head, it is not clear whether chronic alcohol usage is a risk factor for glaucoma (21). In our study, there was no significant difference between the three groups in terms of alcohol consumption.

There is no clear consensus on whether hypothyroidism is a risk factor for the development of glaucoma (40). In this study, statistical comparison could not be made because there was no patient with a history of hypothyroidism in POAG and OHT groups and only one case in the control group had a history of hypothyroidism.

The limitations of our study are that it is a retrospective study, does not have a large population, and lacks ethnic diversity since it was conducted in a single center.Because both POAG and OHT often progress without symptoms until vision loss becomes evident, understanding risk factors is crucial for early diagnosis. Regular eye examination, especially for individuals with one or more of these risk factors, is vital for early diagnosis and treatment. Public health initiatives and education campaigns can be developed to raise awareness and promote regular eye examinations and preventive measures in high-risk populations.

Devices that analyze capillary density in the optic nerve and macula regions can be used to better understand the relationship between glaucoma and factors that affect capillary structure, such as diabetes, thyroid disease, hyperlipidemia, smoking and alcohol. As genetic research reveals more about the gene loci associated with glaucoma, genetic risk screenings and gene therapies could become increasingly important for the management and treatment of glaucoma.

Ethical Approval: The study was approved by the Ethics Committee (Date: 20/06/2014, Protocol No: 2014/680) and all procedures were applied to the Declaration of Helsinki.

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