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Effects of Obstructive Sleep Apnea Syndrome on the Eye

Obstrüktif Uyku Apne Sendromunun Göz Üzerindeki Etkileri

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ABSTRACT

Background: The purpose of this study is to investigate the eye pathologies, primarily glaucoma and Floppy Eyelid syndrome (FES), of patients with Obstructive Sleep Apnea syndrome (OSAS).

Materials and Methods: One hundred sixty two patients with OSAS, who were diagnosed through polysomnography (PSG), were consulted to the ophthalmology clinic. The patients were classified on the Apnea-hypopnea index (AHI). It was accepted that AHI⩽5 was normal, 5⩽ AHI <15 was mild OSAS, 15⩽ AHI <30 was moderate OSAS, and AHI ⩾30 was severe OSAS.

Results: The mean age of the patients was 48.9±10.6 years. Statistically, there was a significant correlation between age and body mass index for the groups. It was observed that moderate and severe OSAS groups had FES more frequently for both eyes. There was no increase in intraocular pressure (IOP) and no presence of optic disc edema, which might cause glaucoma, in any of our patients. We could not find a correlation between AHI and peripapillary retinal nerve fiber layer, IOP and C/D ratio and there was no significant difference among the study groups.

Conclusion: For the moderate and severe groups, the frequency of FES was significantly correlated for both eyes of patients. The etiological studies have shown relatively more frequent OSAS among the patients with non-arteritis ischemic optic neuropathy (NAION) and glaucoma in the literature. Therefore, we believe patients with OSAS need to be examined for glaucoma and NAION for a long term. Moreover, it would be helpful to refer pulmonology clinics for PSG for patients who has FES, glaucoma and NAION with an unknown etiology.

Keywords: OSAS, FES, PSG, AHI, glaucoma

ÖZ

Amaç: Bu çalışmanın amacı, Obstrüktif Uyku Apne sendromu (OUAS) hastalarının başta glokom ve Floppy Göz Kapağı sendromu (FES) olmak üzere göz patolojilerinin araştırılmasıdır.

Gereç ve Yöntemler: Polisomnografi (PSG) ile tanı alan 162 OUAS hastası oftalmoloji kliniğine konsülte edildi. Hastalar Apne-hipopne indeksine (AHİ) göre sınıflandırıldı. AHİ⩽ 5 normal, 5⩽ AHİ<15 hafif OUAS, 15⩽ AHİ<30 orta OUAS ve AHİ ⩾30 şiddetli OUAS olarak kabul edildi.

Bulgular: Hastaların ortalama yaşı 48,9±10,6 yıldı. İstatistiksel olarak, yaş ve vücut kitle indeksi gruplar arasında anlamlı idi. Orta ve ağır OUAS gruplarında her iki gözde daha sık FES olduğu görüldü. Hastalarımızın hiçbirinde göz içi basıncında (GİB) artış ya da glokoma neden olabilecek optik disk ödemi görülmedi. AHİ ile peripapiller retina sinir lifi tabakası, GİB ve C/D oranı arasında bir ilişki ve çalışma grupları arasında anlamlı bir fark bulamadık.

Sonuç: Orta ve şiddetli grup için, FES sıklığı, hastaların her iki gözü için önemli ölçüde ilişkiliydi. Etiyolojik çalışmalar literatürde non-arteritis iskemik optik nöropati (NAION) ve glokomlu hastalarda nispeten daha sık OUAS olduğunu göstermiştir. Bu nedenle,

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ÖZ

OUAS hastalarının glokom ve NAION açısından uzun süreli muayene edilmesi gerektiğine inanıyoruz. Ayrıca etiyolojisi bilinmeyen FES, glokom ve NAION hastalarında PSG için pulmonoloji kliniklerine yönlendirilmesi faydalı olacaktır.

Anahtar Kelimeler: OUAS, YES, PSG, AHİ, glokom

Introduction

Sleep is essential for healthy life and it occurs in almost one third of life. Basically, it can be described as unconscious status which can be taken up by stimuli like sound, light or touching (1). Physiology of sleep has been revealed partially after the 20th century through the use of electroencephalogram (EEG). Respiratory effects of sleep were shown for the first time by Gastaut in 1965 by using polysomnography (PSG) (2) which is accepted as "gold standard" for the diagnosis of Sleep Apnea syndrome (3).

Obstructive sleep apnea is a syndrome (OSAS) characterized by episodic obstruction of upper respiratory tract (total obstructions cause apnea; partial obstructions cause hypopnea) and a decrease in the levels of O_2 saturation during sleep (3). Risk factors for the syndrome have not been revealed completely except certain risk factors such as age (over 65 years), obesity, male gender (4,5), and familial history of OSAS (6). However, mechanisms of this syndrome have not been elucidated yet due to complicated anatomic, muscular, neuromuscular, neural factors and other involving factors.

OSAS leads to many complications in the cardiovascular and neuropsychiatric systems and also in many other systems in the body. The eye is one of the organs that is affected by this syndrome. Forty percent of patients diagnosed with moderate and severe OSAS have significantly higher eye symptoms when compared to the control group (7).

In this study, we evaluated the eye signs and vision of patients who underwent all-night PSG with a pre-diagnosis of OSAS. Thus, we aimed to get an idea about referring patients with OSAS to eye clinics for routine eye examination and non-routine eye examinations.

Material and Methods

Approval of this study was received from the Ethics Committee of Recep Tayyip Erdoğan University Faculty of Medicine in March, 2013 (2013/54). The study was performed on 324 eyes of 162 patients who did not have any diagnosis for ophthalmologic disorders and were hospitalized for PSG survey in Department of Pulmonology. Patients who underwent all-night PSG in the sleep laboratory of Recep Tayyip Erdoğan University with a pre-diagnosis of sleep apnea between April 2013 and November 2013 were included in the study. Written informed consent was obtained from all patients who met the study criteria, and the patients were referred to the ophthalmology clinic on the morning of the test. Patients under the age of 18 years, who had any known eye disease, history of head injury or cranial operation, previously known chronic renal failure, and a diagnosis of Diabetes Mellitus and who stated that they did not want to participate in the study, were excluded from the study. Demographic characteristics such as age, gender and body mass index (BMI), duration of complaints, Epworth sleepiness scale score, PSG results (AHI, oxygen desaturation index, minimum and mean oxygen saturations) and all eye examination findings were recorded.

PSG

PSG (Grass Technologies Comet, EEG/PSG with as40 Amplifier System, 2008, Ohio/USA) examinations have been proceeded with 4 EEG channels as C3/A2, C4/A2, O1/A2, O2/A1; 2 electrooculography channels as ROC/A1, LOC/A1; 3 electromyography channels as one submandibular, two tibial; electrocardiography; an air-flow sensor (nasal-oral thermistor); thoracic and abdominal piezoelectric belts, and pulse-oximeter. Every 30 seconds of measurements have been accepted as one "epoch unit". Patients have been measured for at least 6 hours. Sleepiness score, based on American Academy of Sleep Medicine 2007, was done according to R&K (Rechtschaffen A. & Kales A.) standard scoring system (8). Patients were classified into four groups based on the Apnea-hypopnea index (AHI). It was accepted that AHI⩽5 was normal, 5⩽ AHI <15 was mild OSAS, 15⩽ AHI <30 was moderate OSAS, and AHI ⩾30 was severe OSAS.

Eye Examination

After signing consent form, patients were referred to department of ophthalmology. Visual acuity was examined via Snellen Chart and autorefractometer. Ocular tension [intraocular pressure, (IOP)] was measured by the Goldman Applanation Tonometer. Central cornea thickness (CCT) was calculated by a corneal pachymeter (NIDEK; noncontact tonometer NT-2000, 2008 Japan). Anterior and posterior chambers were examined by biomicroscope. Dilated-fundus examinations were performed after pupils were enlarged with 1% tropicamide. Optic nerve and retinal nerve fiber layer (RNFL) thickness was examined with optical coherence tomography (OCT); (Carl Zeiss Meditec, Dublin, CA, USA). Findings were evaluated with laboratory results.

Statistical Analysis

Data were recorded into SPSS 16.0 for Windows (IBM Corp., Armonk, New York, ABD). Descriptive statistics were used for demographic data, BMI, AHI, minimum and mean O_2 saturation and eye findings. Median values were given for continuous variables; categorical variables were shown in percentage (%). Chi-square tests were used for categorical comparison to define a relationship between independent variables. ANOVA with post-hoc Tukey HSD test was used for comparison among the groups. P-values lower than 0.05 were accepted as significant.

Results

Forty-three of patients were female (27%), and 119 were male (73%). According to the PSG results, the AHI was below 5 in 23 patients. On the other hand, 33, 19 and 87 patients were observed in the mild, moderate and severe OSAS group, respectively. The mean patient age of the entire cohort was 48.9±10.6 (minimum: 25-maximum: 73) years. The mean age was 42±8 years (29-54 years) for the AHI normal patient group, 46.1±9.5 years (27-62 years) for the mild OSAS group, 49.5±9 years (31-65 years) for the moderate OSAS group, and 50.4±11 years (25-73 years) for the severe OSAS group. There was a statistically significant difference among the groups in terms of age (p=0.011). However, this significance was observed only between the normal patient group and the patient group with severe OSAS. The mean BMI was 33.6±6.4 kg/m^2 in the entire group. The mean BMI was 29.3±6.8 kg/m^2 in the normal patient group, 31.8±5.4 kg/m^2 in the mild OSAS group, 33.7±4.8 kg/m^2 in the moderate OSAS group, and 35.2±6.4 kg/m^2 in the severe OSAS group (p=0.001). BMI values were significant among the groups and this significance originated from the patient group with severe OSAS.

The average score in ESS was 7.2±4.1 and there was a significant difference among the groups (p<0.001). The average AHI was 31.7±23.9 (minimum: 1.3, maximum: 137), the average O_2 desaturation index was 20±22.2, the lowest O_2 saturation (minO_2 hr) was 80.3±8.1%, and the average O_2 saturation (mean/average O_2 hr) was 92.3±2.7%. When the relationship between OSAS severity and O_2 desaturation index, minO_2 and meanO_2 values was examined, it was seen that there was a statistically significant difference among the groups (p<0.001). This significance was also due to the severe OSAS patient group. All demographic characteristics and PSG results of the study population are summarized in Table 1.

In the study, when compared to the AHI normal group and mild OSAS group, right eye floppy eyelid and left eye Floppy Eyelid syndrome (FES) were found to be significantly higher in the moderate and severe OSAS group (p=0.016 vs. p=0.024, respectively). Statistically, there was no significant difference among the groups in terms of IOP, RNFL, CCT and C/D ratio. 62 patients had blepharitis. Although there was no significant difference in blepharitis among the groups, the highest rate (46%) was seen in the severe OSAS group.

There was no significant difference in papillary conjunctivitis among the groups; however, conjunctivitis was observed more frequently in the moderate (47%) and severe (43%) OSAS groups. Adjusted visual acuities were found to be normal but there was no significant difference in refraction values among the groups.

None of our patients had glaucoma in IOP measurements and ophthalmic examination. There was no OSAS patient developing optic disc edema, central serous chorioretinopathy and filamentous keratitis. The eye examination findings of the entire study population according to the OSAS severity are summarized in Table 2.

Discussion

In this prospective study, we aimed to determine the frequency of eye-related pathologies in patients who underwent all-night PSG with a pre-diagnosis of sleep apnea. Data of totally 163 patients, including 43 women and 120 men, were evaluated in the study.

Obesity is a part of the metabolic syndrome and is a condition that is closely related to OSAS (9). For this reason, BMI should definitely be measured in patients with suspected OSAS. Obesity can cause OSAS directly by causing collapse in the upper airways. It also has an effect on the loss of respiratory muscle strength and an increase in inflammation through cytokines released from the adipose tissue (10). In our study population, the mean BMI was 33.6±6.4 kg/m^2, and the group with the highest BMI was the severe OSAS group.

FES is a condition characterized by easily rotating and drooping lids, papillary conjunctivitis, and corneal epithelial erosions (11). The prevalence of FES in the general population ranges from 2.3% to 3.8% (12). In a meta-analysis involving 6 studies with a total of 767 patients on the prevalence of FES in OSAS, it was shown that FES was statistically significantly more common in OSAS patients than in non-OSAS patients. The authors also stated that FES prevalence increased (odds ratio=2.56, 4.62, and 7.64 for mild, moderate, and severe OSAS, respectively) with disease severity, but there is a necessity for prospective cohort studies to determine whether FES is an independent risk factor for OSAS (13). In our study, in accordance with the literature, the incidence of FES according to OSAS severity differed among the groups.

On the other hand, when the IOP, RNFL, CCT and C/D ratios were evaluated, no statistically significant difference was found among the patient groups in our study population. In a study conducted in our country, Tapan et al. (14) evaluated the changes in the cornea and choroid layers of the eye in patients with OSAS of different severities and in the healthy control group by measuring

Table 1. General features of groups (n=162)

Groups/data	Normal (n=23)	Mild OSAS (n=33)	Moderate OSAS (n=19)	Severe OSAS (n=87)	p
Age (year)	42±8	46.1±9.5	49.5±9	50.4±11	0.011
BMI (kg/m^2)	29.3±6.8	31.8±5.4	33.7±4.8	35.2±6.4	0.001
Time of symptoms (year)	3.5	3.8	5.3	6.2	0.002
AHI (/hour)	3.8	8.3	17.3	48.1	<0.001
Epworth sleepiness scale	2	4	4	8	<0.001
Desaturation index	2	5	10	31	<0.001
Min O_2 saturation (%)	87	85	81	76	<0.001
Average of O_2 saturation (%)	94	93	92	91	<0001

OSAS: Obstructive Sleep Apnea syndrome, BMI: Body mass index, AHI: Apnea-hypopnea index

Table 2. Eye findings (n=162)

Groups/findings	Normal (n=23)	Mild OSAS (n=33)	Moderate OSAS (n=19)	Severe OSAS (n=87)	p
Number of patient (F/M)	4/19	11/22	6/13	20/67	0.560
Right eye IOP (mmHg) ± SD	15±3	15±3	15±2	15±3	0.910
Left eye IOP (mmHg) ± SD	15±3	16±2	16±2	16±2	0.300
Right eye RNFL (µm) ± SD	95±12	90±11	92±10	91±9	0.230
Left eye RNFL (µm) ± SD	93±11	90±13	93±10	91±11	0.670
Right eye CCT (µm) ± SD	547±43	548±39	553±28	540±66	0.760
Left eye CCT (µm) ± SD	549±48	548±39	552±52	550±32	0.970
Right eye C/D ratio	0.3±0.06	0.29±0.08	0.3±0.06	0.3±0.01	0.072
Left eye C/D ratio	0.31±0.08	0.3±0.09	0.3±0.06	0.3±0.09	0.976
Right eye (refraction) (decreased/normal)	6/17	11/22	6/13	36/51	0.723
Left eye (refraction) (decreased/normal)	6/17	13/21	5/13	35/52	0.821
Right eye ptosis (+/-)	0/23	0/33	0/19	0/87	-
Left eye ptosis (+/-)	0/23	0/33	0/19	1/86	0.855
Right/left eye floppy eyelid (+/-)	5/18	6/27	9/10	38/49	0.060
Right/left eye blepharitis (+/-)	4/19	12/21	6/13	40/47	0.270
Right/left eye filamentous keratitis (+/-)	0/23	0/33	0/19	0/87	-
Right eye papillary conjunctivitis (+/-)	6/17	10/23	9/10	37/50	0.455
Left eye papillary conjunctivitis (+/-)	6/17	10/23	9/10	38/49	0.450
Right/left eye optic disc edema (+/-)	0/23	0/33	0/19	0/87	-
Right/left eye optic neuropathy (+/-)	0/23	0/33	0/19	0/87	-
Right/left eye retinal vascular tortuosity (+/-)	1/22	1/32	1/18	2/85	0.780
Right/left eye central serous chorioretinopathy (+/-)	0/23	0/33	0/19	0/87	-

SD: Standard deviation, RNFL: Retinal nerve fiber layer thickness, IOP: Intra ocular pressure, C/D ratio: Cup/Disc ratio, CCT: Central cornea thickness

with OCT. At the end of the study, the researchers found that there was no significant difference in corneal thickness between the patients with OSAS and healthy controls, and the choroidal thickness became thinner as the severity of OSAS increased (14). Blepharitis is a chronic inflammation of the rim of the eyelid. It is often caused by non-virulent staphylococcus and seborrheic dermatitis and it has been shown to be associated with sleep apnea (15,16). In our patient group, the rate of blepharitis was 38%, and the highest rate was seen in the severe OSAS group (46%).

Glaucoma was not detected in any of the patients in our study population according to IOP values and optic nerve head examination. In the literature, it has been reported that the prevalence of glaucoma in OSAS patients is 7.2%, and primary open-angle glaucoma, normotensive glaucoma and related RNFL thinning and visual field defects are more common in OSAS patients (17). However, studies evaluating RNFL thickness in OSAS patients present different results. Bayhan et al. (18) evaluated 92 OSAS patients, and they stated that the nasal and upper quadrant RNFL was thinner in the OSAS group. On the other hand, as in our study results, there are studies reporting that RNFL thickness is not different in patients with and without OSAS (19). While Yavaş et al. (20) reported that they observed increased frequency of OSAS in patients with central serous chorioretinopathy, Brodie et al. (21) showed in their study that there was no increased risk for central serous chorioretinopathy in OSAS patients. In our study, no patient had central serous chorioretinopathy.

Conclusion

It is almost inevitable to get affected for eyes which need high oxygen supply with well-vascularized structure in a disease which has neurovascular complications and hypoxia-hypercapnia episodes like OSAS. Statistically, only FES was found to be significantly high in patients with OSAS among the ophthalmologic disorders that were investigated in this study. The reason for that, as we believed, might be the lower average age compared to other studies and different AHI cut-off values. Further investigations are needed to elucidate the role of these variables. Nevertheless, the current literature information has shown that physicians who deal with OSAS patients should be aware of ophthalmologic complications of this syndrome. On the other hand, OSAS should be considered as an etiologic factor in patients with ophthalmologic disorders.

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Ethics

Ethics Committee Approval: Approval of this study was received from the Ethics Committee of Recep Tayyip Erdoğan University Faculty of Medicine in March, 2013 (2013/54).

Informed Consent: Written informed consent was obtained from all patients who met the study criteria, and the patients were referred to the ophthalmology clinic on the morning of the test.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.Y., M.K., H.Ç., Concept: A.Y., B.Ş., M.K., H.Ç., Ü.Ş., Design: A.Y., B.Ş., A.G., Ü.Ş., D.D., Data Collection or Processing: A.Y., M.K., H.Ç., Analysis or Interpretation: A.Y., B.Ş., A.G., H.Ç., D.D., Literature Search: A.Y., M.K., A.G., H.Ç., D.D., Writing: A.Y., B.Ş., Ü.Ş., D.D.

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