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Effects of Use of a Continuous Positive Airway Pressure Device on Glaucoma

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to investigate the prevalence of glaucoma in obstructive sleep apnea syndrome (OSAS) and to determine the efficacy of the equipment used in the treatment of this disease.

Material/Methods: In this cross-sectional study, 38 patients with OSAS used the continuous positive airway pressure (CPAP) device (Group 1) and 32 patients with OSAS refused CPAP device (Group 2). Thirty-six patients did not have OSAS (Group 3).

Results: Patient age, gender, height, weight, and neck circumference did not differ among groups ($p>0.05$); and the apnea-hypopnea index (AHI) and respiratory disturbance index (RDI) values did not differ between Groups 1 and 2 ($p>0.05$). Vision and pachymetric values did not differ among groups ($p>0.05$). The IOP was significantly higher in Group 2 than in Group 1 ($p<0.05$) but did not differ between Groups 1 and 3 ($p>0.05$). The fundus C/D ratio was significantly higher ($p<0.05$) in Group 2 than in the other groups but did not differ between Groups 1 and 3 ($p>0.05$). In Group 1, 2, and 3, 5.2%, 12.5%, and 0%, respectively, of patients had glaucoma.

Conclusions: OSAS should be considered a significant risk factor for glaucoma. Eye tests may help to identify individuals with undiagnosed OSAS, and such testing of patients with diagnosed OSAS may allow early detection of glaucoma and referral of such patients for CPAP therapy to prevent development of complications.

MeSH Keywords: Continuous Positive Airway Pressure • Glaucoma, Open-Angle • Intraocular Pressure • Sleep Apnea Syndromes

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Background

Obstructive sleep apnea syndrome (OSAS) is a condition characterized by recurrent partial or complete upper airway obstruction during sleep [1]. OSAS is associated with repeated respiratory tract blockade and reduced air inhalation. Recurrent airway interference during sleep triggers hypoxia, hypercapnia, and intrathoracic pressure changes that affect autonomic, hemodynamic, humoral, and neuroendocrine regulation [2]. Whole-night polysomnography (PSG) is the criterion standard for OSAS diagnosis. Commonly, continuous positive airway pressure (CPAP) is used during the night to prevent upper airway collapse [1]. The hypoxemia associated with OSAS is associated with increased incidences of various neural conditions, including cerebrovascular accidents, reduced mental ability, depressive disorders, headache, peripheral neuropathy, and non-arteritic ischemic optic neuropathy [1,3,4].

Glaucoma is an optic neuropathy associated with damage to the head of the optic nerve, triggering characteristic changes in the shape of the nerve, combined with visual difficulties [5]. Glaucoma is not a single disease, but rather a group of ocular disorders of various etiologies. Most glaucoma patients exhibit increased intraocular pressure (IOP) that can directly damage the optic nerve (open-angle glaucoma=OAG) [6]. However, some glaucoma patients exhibit normal or reduced IOP (normal-tension glaucoma=NTG), depending on whether they have other systemic conditions such as diabetes mellitus, heart disease, and obesity [7]. Several researchers have shown an association between OSAS and NTG and/or OAG [8–11]. However, other studies have found no such relationships [12–14].

Thus, we aimed to investigate the association of OSAS and glaucoma and the effects of CPAP device use on glaucoma.

Material and Methods

This study was performed in the Otolaryngology and Ophthalmology Departments of Corlu State Hospital from September to November 2013. Ethics Committee approval was obtained from the Bakirkoy Training and Research Hospital (2013) and informed written consent was obtained from all participants. We studied 70 consecutive patients formally diagnosed with OSAS and 36 healthy patients; all patient records were completed by the Sleep Laboratory Center.

Polysomnography: The apnea-hypopnea index (AHI) and the respiratory disturbance index (RDI) were recorded. Patients with severe OSAS (AHI value over 30) constituted the study patients (Groups 1 and 2) and healthy subjects who underwent PSG but did not have OSAS (AHI values less than 5) formed a control group (Group 3).

Ophthalmological examination: All subjects underwent a full ocular evaluation, including the Snellen visual acuity test, measurement of apparent refraction, slit-light biomicroscopy of anterior eye segments, IOP measurement, gonioscopy and binocular examination of the optic disc. Visual testing used the 24-2 Humphrey visual field analyzer (Humphrey Instrument Corporation).

The criteria for OAG diagnosis were: IOP over 21 mmHg, anterior positioning of the chamber, glaucomatous visual area defects, glaucomatous cupping within the optic disk, and the absence of a fundus or neurological lesion (apart from glaucomatous cupping) that explained the visual defect. The criteria for NTG diagnosis were: optic nerve changes including reduction of the thickness of the retinal fibre layer, the presence of characteristic visual defects, an open anterior chamber on gonioscopy, and an IOP below 21 mmHg.

The following patients were excluded: those who had undergone prior ocular surgery, had experienced ocular trauma, had anterior or posterior segment disease and/or cataracts, had secondary glaucoma, had used steroids over the long term, and/or had cerebrovascular disease and/or diabetes.

Statistical analysis

Data were analyzed using SPSS version 22.0 for Windows (SPSS Inc., Chicago, IL, USA). ANOVA (with the Tukey test) and the Kruskal-Wallis and Mann-Whitney tests were to compare quantitative data between groups. The distributions of all variables were assessed using the Kolmogorov-Smirnov test. A p value <0.05 was considered to indicate statistical significance.

Results

Thirty-eight patients with OSAS used the CPAP device (Group 1) and 32 patients with OSAS but without use of this device (Group 2). Thirty-six patients did not have OSAS (Group 3). Our 3 group was not statistically significantly different ($p>0.05$) in terms of age, sex, length, weight, body mass index (BMI), or neck diameter (Table 1); nor did the AHI or RDI values differ between groups 1 and 2 ($p>0.05$) (Table 1). Vision and pachymetric values did not differ among groups ($p>0.05$) (Table 2). The IOP was significantly higher in Group 2 than Group 1 ($p<0.05$) but was similar in Groups 1 and 3 ($p>0.05$) (Table 2, Figure 1). The fundus C/D ratio was significantly higher ($p<0.05$) in Group 2 than the other groups, but was similar in Groups 1 and 3 ($p>0.05$) (Table 2, Figure 2). Glaucoma prevalence in Groups 1, 2, and 3 was 5.2%, 12.5%, and 0%, respectively.

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Table 1. Clinical characteristics and baseline measures in OSAS and control groups.

		CPAP Group		Without CPAP Group		Without OSAS Group		p
		Mean ±s.d.	Med	Mean ±s.d.	Med	Mean ±s.d.	Med	
Age		49.1±10.2	49.0	53.4±11.6	53.5	46.8±12.0	48.0	0.054
Gender	Male	31 81.6%		25 78.1%		21 58.3%		0.057
	Female	7 18.4%		7 21.9%		15 41.7%		
Length		173.0±6.6	173.0	173.6±7.4	173.5	170.5±7.6	169.5	0.158
Weight		103.8±19.4	105.0	105.5±19.4	103.0	100.0±20.8	97.5	0.507
BMI		34.7±5.9	35.4	34.9±5.7	35.9	34.2±5.4	35.5	0.863
Neck diameter		44.9±3.2	46.0	44.5±3.4	46.0	43.4±3.7	42.5	0.143
AHI		62.9±27.0	56.0	55.6±27.3	52.0			0.169
RDI		63.8±26.0	57.0	57.7±27.5	53.5			0.260

ANOVA / Mann-whitney u test /Chi-square test. * P-value: statistical significance of the difference between three groups. The data is given as mean ± standard deviation.

Table 2. Oculerparameters in OSAS and control groups.

	CPAP Group		Without CPAP Group		Without OSAS Group		p
	Mean ±s.d.	Med	Mean ±s.d.	Med	Mean ±s.d.	Med	
Vision	0.9±0.2	1.0	1.0±0.2	1.0	1.0±0.0	1.0	0.793
Average IOP	15.1±3.5*	14.0	16.7±3.1	17.0	14.1±2.4*	14.0	**0.000**
Fundus c/d ratio	0.4±0.1*	0.3	0.4±0.2	0.5	0.3±0.1*	0.3	**0.000**
Pachymetry	558.2±33.6	563	560.5±30.6	560	560.5±30.2	560	0.951

Kruskal-wallis / Mann-whitney u test / *Difference with group without CPAP p<0.05 * P-value: statistical significance of the difference between three groups. The data is given as mean ± standard deviation.

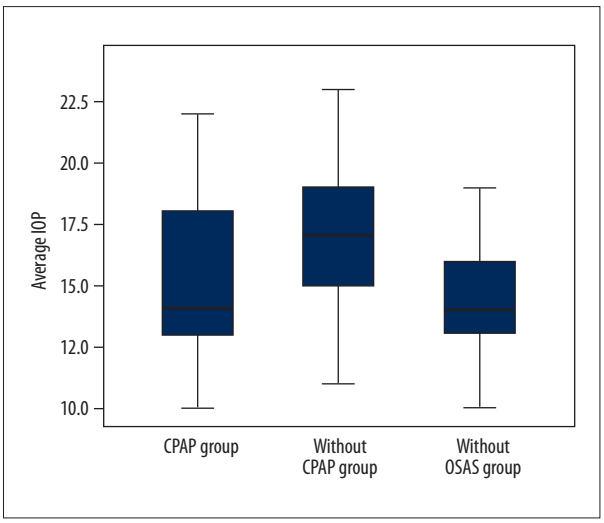

Figure 1. Comparison of CPAP group, without CPAP group and without OSAS group based on IOP.

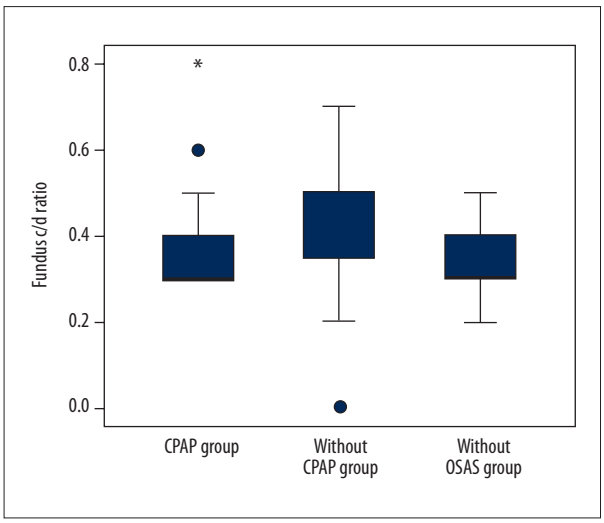

Figure 2. Comparison of CPAP group, without CPAP group and without OSAS group based on Fundus c/d ratio.

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Discussion

The 2 principal theories on glaucoma pathogenesis are the mechanical and vascular theories. The mechanical theory suggests that abnormally high IOP eventually directly destroys the optic nerve [5]. The vascular hypothesis suggests that the blood supply is inadequate to support the optic nerve *per se*. Glaucoma is categorized into several types, of which NTG [4,9,10,15,16] and OAG [10,15,16] are principally linked to OSAS. OAG is the most common form of glaucoma, although its etiology is not well understood. However, many risk factors have been described, including within families, certain ethnic backgrounds, myopia, a thin cornea, and age over 40 years [6]. In the literature there are some articles hypothesizing that glaucoma is a disorder with a series of characteristic pathological alterations of collagen in its content, distribution, ultrastructure, and metabolism. Abnormality of collagen in the outflow pathway tissues results in elevation of IOP [17].

Onen et al. [11] reported an incidence of sleep-disordered breathing (OSAS was part of the spectrum) of 47.6% in 212 OAG patients. In Mojon et al. [7], OSAS was present in 50% of patients younger than 45 years and 63% of older patients with NTG. The same authors evaluated 69 patients with OSAS and found that the prevalence of glaucoma was 7.2%, considerably greater than the 2% of a healthy balanced population [15].

Chen et al. [18] conducted a population-based retrospective cohort study on 2528 patients with OSAS and 10 112 without (the comparison cohort). They found both pharyngeal and nasal surgery for OSAS effectively reduced the risk of glaucoma. In terms of OSAS management, our results are supported by those results.

Pepin et al. [19] claimed that OSAS patients experience a decline in night-time IOP, and that CPAP treatment restored the IOP to normal levels. IOP and blood pressure were measured every hour for 24 h in 18 newly diagnosed patients with OSAS, and again after 1 month of CPAP therapy. Prior to CPAP device use, 9 of the 18 patients (50%) exhibited no circadian changes in IOP. They found notable improvement in 24-h IOP profiles following commencement of CPAP therapy. The authors concluded that CPAP therapy may be useful in treating visual problems in OSAS patients. Use of CPAP decreases the level of sympathetic activity in OSAS patients, and reduces high blood pressure, heart rhythm, and plasma noradrenaline levels [20]. The renin-angiotensin-aldosterone system, the activity of which is enhanced in OSAS patients (and which may regulate IOP via the type 1 angiotensin receptor [20], is also stabilized by CPAP therapy, probably influencing the daytime decline in IOP. Our data are in line with those of Pepin et al. [19].

Kadyan et al. [21] found that the glaucoma prevalence in OSAS patients was similar to that in normal populations, and speculated that this might be because the vast majority of OSAS patients used CPAP therapy [3]. Our data support the idea that CPAP therapy prevents the development of glaucoma in OSAS patients.

Totals of 105 patients and 22 controls were examined via ocular coherence tomography (OCT) by Lin et al. [10], who found that the retinal nerve fiber thickness was less in patients with moderate to severe OSAS (AHIs >15) compared to those with mild OSAS (5< AHI <15) and controls. Tsang et al. [22] showed that Chinese patients with modest to severe OSAS had a 4-fold higher incidence of glaucomatous changes in the optic disc than matched controls (26% *vs.* 6.8%), and that those with severe OSAS (AHIs of up to 40) exhibited greater rates of changes than did those with moderate OSAS (AHIs of up to 20). Our data are compatible with and supported by results of Lin et al. [10] and Tsang et al. [22].

Mojon et al. studied NTG and OAG patients separately, and found high incidences of OSAS in both groups [7,8]. Although some studies have found high incidences of OSAS in NTG patients only [4,9], our results supported to those of Mojon et al.; OSAS was equally common in NTG and OAG patients. However, when it is considered that OAG is much more common, we concluded that the higher incidence of OSAS in NTG patients reflected a trend.

In a case study on NTG and OSAS patients, glaucoma progression ceased after 3.5 years of CPAP therapy; the authors attributed the effect directly to the therapy [23]. Our data support this conclusion.

Ophthalmic problems of patients with OSAS include not only glaucoma but also floppy eyelid syndrome, a non-arteritic anterior ischemic optic neuropathy [3,5]. We hope that improved awareness of the ocular challenges associated with OSAS will trigger more cross-referrals between sleep specialists and ophthalmic clinicians. In particular, in the coming years it may become routine for ophthalmic physicians to refer patients with such ocular conditions to sleep studies, particularly if a patient meets certain demographic criteria or complains of sleep difficulties. Likewise, sleep apnea professionals should advise all patients to undergo comprehensive ocular health evaluation with regular screening for glaucoma and floppy eyelid syndrome.

The IOP and C/D ratios was significantly higher in Group 2 than in Group 1 ($p<0.05$) but was similar in Groups 1 and 3. Glaucoma was most prevalent in Group 2 (4 patients versus 2 in Group 1); no Group 3 patients had glaucoma. The prevalence of glaucoma was 5.2% in Group 1, 12.5% in Group 2, and 0% in Group 3. Of all OSAS patients (Groups 1–2), the prevalence was 8.5%, very close to the 7.5% reported in Mojon et al. [8]. To the best of our knowledge, this is the first study to compare

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OSAS patient use of a CPAP device, glaucoma incidence, and relevant changes.

The present study had some limitations: the sample size was small, we calculated IOP only once instead of several times over 24 h, and we used OCT only for definitive glaucoma diagnosis (not all patients underwent OCT).

Conclusions

The glaucoma prevalence of OSAS patients is significantly higher than in the normal population, and use of a CPAP device has positive and healing effects on glaucoma. Further work is required to explain why different OSAS treatments may be associated with variable risks of glaucoma.

Conflict of interest

The authors declare no conflicts of interest.

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