ORIGINAL ARTICLE

Effect of sleep related breathing disorders on ocular function

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Abstract
Introduction: Sleep disorders are common and obstructive sleep apnea hypopnea syndrome (OSAHS) is the commonest. OSAHS is not commonly diagnosed by the ophthalmologist, but it has many systemic and ocular complications.
Aim of the work: The aim of this study was to detect the effect of sleep related breathing disorders on ocular function.
Patients and methods: Thirty patients with OSAHS were enrolled after obtaining informed consents. Patients were subjected to full history taking, Epworth sleepiness scale, anthropometric data, Mallampati score, clinical apnea score, sleep study and complete ocular examination.
Results: 4 patients had mild OSAHS (13.33%), 12 patients had moderate OSAHS (40%) and 14 patients had severe OSAHS (46.67%) two of them had sleep hypoventilation. 4 patients were free from any ocular manifestations. In 26 patients one or more of the following ocular findings were found: floppy eyelid syndrome (FES) was detected in 3 (10%) patients, glaucoma was diagnosed in 5 (16.67%) patients, senile cataract was found in 3 (10%) patients, nonarteritic anterior ischemic optic neuropathy (NAION) was detected in 4 (13.33%) patients, papilledema was diagnosed in 3 (10%) patients and 18 (60%) patients had dry eye manifestations.

In conclusion: The increased prevalence of ocular symptoms and signs in patients with OSAHS indicates a need to increase awareness and establish close collaboration with the sleep physicians with clear pathways for review of OSAHS patients by the ophthalmic services. We should study the effect of treatment of OSAHS on the ocular manifestations.

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[AHI] ≥ 5/h), whereas the remaining 10% of patients who have OHS have an AHI less than 5/h. OSAHS is a potentially serious sleep disorder characterized by recurrent episodes of breathing cessation during sleep secondary to upper airway collapse. Complete apnea or partial hypopnea episodes can last from 10 s or more and may occur up to hundreds of times nightly. It is often accompanied with swings in heart rate, a decrease in oxygen saturation, and brief electroencephalogram arousals. Sleep apnea is a disorder not commonly diagnosed by the ophthalmologist, but it has many systemic and ocular complications [1].

Floppy eyelid syndrome (FES), first described in 1981 by Culbertson and Ostler, is characterized by elastic upper eyelids that are easily everted with minimal lateral traction, associated with a papillary conjunctivitis of the upper palpebral conjunctiva. A weak tarsal plate allows the lid to fold upon itself with ease [2]. Obesity may be a confounding factor in the association of FES and OSAHS as many patients with OSAHS suffer from obesity [3].

Both normal tension and primary open-angle glaucoma have been associated with sleep apnea. Theories of mechanism include: (1) impaired optic nerve head blood flow secondary to episodes of apnea, (2) optic nerve vascular dysregulation secondary to arteriosclerosis and variations in arterial blood pressure, and (3) episodes of hypoxia. As ocular blood flow has been suggested as a mechanism in glaucoma [4].

Non-Arteritic Ischemic Optic Neuropathy (NAION), an ischemic event may be secondary to impaired optic nerve head blood flow autoregulation from apnea. Optic nerve vascular dysregulation may also be a result of variations in arterial blood pressure seen in OSA, which may be due to an imbalance between nitric oxide and endothelin. Additionally, direct damage by periods of hypoxia likely plays a role [5,6].

Bucci and Krohel first reported a case of papilledema in a patient with OSAHS in 1988, who had surgical treatment correcting his OSAHS which resolved his papilledema [7]. Since, then, numerous cases have been reported of patients found to have papilledema and idiopathic intracranial hypertension. Many of these patients, however, have had normal opening pressures on lumbar puncture. Correction of their OSAHS with continuous positive airway pressure (CPAP) treatment had resolved the papilledema [8].

Patients with sleep apnea have increased levels of circulating epinephrine and norepinephrine. With elevated levels of catecholamines, OSAHS has been hypothesized to be a direct risk factor for central serous chorioretinopathy (CSCR) [9].

Retinal vein occlusions may be associated with OSAHS as they may be secondary to a slow-down of blood flow circulation secondary to hypoxemia and elevated nocturnal intracranial pressure. Strictly acting on the retinal microcirculation, OSAHS may directly have a causal effect on retinal vein occlusions [10].

CPAP administered through a nasal or face mask has remained the mainstay of treatment in OSAHS since its advent in the 1980s. Non-specific behavioral measures such as weight loss, avoiding smoking, alcohol, and sedatives can impact on symptoms’ control, but are inadequate for moderate to severe disease. Effect of these treatment measures on the ocular manifestations is less well documented, as most literature documents ocular changes at the time of diagnosis of the sleep disorder [1,5]. Isolated case reports in the literature have suggested reversal of symptoms of FES accompanied with significant weight loss [11] and initiation of CPAP [12]. More recently, effects of CPAP on intraocular pressure and performance in visual field (VF) testing have been reported [13,14]. In addition, leaking from the masks used with CPAP can cause ocular irritation and even induce conjunctivitis [15,16].

**Aim of the work**

The aim of this study was to detect the effect of sleep related breathing disorders on ocular function.

**Subjects and methods**

**Study population and subjects**

Thirty patients with documented obstructive sleep apnea hypopnea syndrome, admitted to the chest department, Alexandria main university hospital were enrolled after obtaining informed consents.

**Study measurements**

All patients were subjected to the following:

1. Full history taking including age, sex, smoking index and history of other diseases.
2. Epworth sleepiness scale [17].
3. Anthropometric data including: Body mass index (BMI), neck circumference (NC), and waist/hip ratio. BMI derived from the weight and height using the formula (Quetelet’s index = weight (kg)/height (m)²).
4. Thorough clinical examination including: Mallampati score, general examination and local chest examination to exclude other chest diseases and exacerbation.
5. Clinical apnea score [18].
6. Sleep study: all patients were subjected to overnight polysomnogram using somoscreen plus RC combi 39 including the following channels:
   - Flow (Cannula &/or Thermistor).
   - Snore (Cannula &/or Mic).
   - Thoracic Effort (RIP Option).
   - Abdominal Effort (RIP Option).
   - Oxygen saturation (Spo2).
   - Plethysmogram.
   - Pulse Rate.
   - Electrocardiogram (ECG).
   - Obstruction.
   - CPAP/BiPAP Pressure.
   - Periodic leg movement (PLM).
   - Electroencephalogram (EEG) (Fig. 1).

Apneas and hypopneas were scored using criteria established by the American Academy of Sleep Medicine (2012) [19]. Score a respiratory event in adults as an apnea if both of the following were met:

a. There is a drop in the peak signal excursion by ≥90% of pre-event baseline using an oronasal thermal sensor.

b. The duration of the ≥90% drop in sensor signal is ≥10 s.

In 2012 the American Academy of Sleep Medicine (AASM) Sleep Apnea Definitions Task Force reviewed the rules for
scoring respiratory events in 2007 and gave new definition for hypopnea.

Score a respiratory event as a hypopnea if all of the following were met:

- The peak signal excursions drop by $\geq 30\%$ of pre-event baseline using nasal pressure.
- The duration of the $\geq 30\%$ drop in signal excursions is $\geq 10\ s$.
- There is $\geq 3\%$ oxygen desaturation from pre-event baseline or the event is associated with an arousal.

The following parameters were calculated:

- Apnea hypopnea index (AHI): AHI is the total number of apnea and/or hypopnea per hour of sleep.
- Baseline $O_2$ saturation: it is the oxygen saturation at the start of the study.
- Mean $O_2$ saturation: it is the mean value of oxygen saturation during the total sleep time.
- Minimal $O_2$ saturation: it is the lowest oxygen saturation recorded during the total sleep time.
- Oxygen desaturation index (ODI): it is the total number of desaturations by at least 3% from the previous tracing per hour of sleep and it is calculated by dividing the total number of desaturations by at least 3% from the previous tracing over the total sleep time (hrs).
- $T90\%$: it is the percentage of sleep time with oxygen saturation below 90%.
- Hypoventilation: We examined the overnight oximetric tracing to assess if there was hypoventilation. Hypoventilation was considered when there was a sustained decrease of $SpO_2$ as detected by the oximeter (sagging of the oximetric tracing). Oximeter is a reliable tool to detect hypoventilation whenever the patient is on room air and not receiving any supplemental oxygen.

After the sleep study all patients were subjected to CPAP as a therapy to be titrated by a follow up study.

7. Full ophthalmological assessment through:
   - Ophthalmic history taking (patients suffering from any previous ocular problems were excluded from the study).
   - Uncorrected visual acuity (UCVA) measurement.
   - Manifest refraction (MR).
   - Best corrected visual acuity (BCVA) measurement.
   - Slit lamp biomicroscopic examination of the anterior segment of the eye and the ocular surface.
   - Dilated fundus examination for assessment of the condition of the retina and the optic nerve head.
   - Intraocular pressure measurement by applanation tonometry.
   - The following investigations were performed when needed:
     - Fluorescein angiography.
     - Visual field assessment.
     - Optical coherence tomography.

**Statistical analysis**

Statistical analysis was performed with Sigma Stat 2.0 (Systat Software Inc., Point Richmond, Calif) and SPSS 14 (SPSS, Chicago, Ill) for Windows.
Results

This study was carried on 30 patients subjected to the sleep study; 19 males (63.33%) and 11 females (36.67%). The age ranged from 36 to 75 years with a mean ± SD value of 54.6 ± 9.3 years, 18 patients (60%) were current or former smokers and the pack year index had a mean ± SD value of 36.1 ± 20.32; 20 patients (66.67%) were diabetic and 15 patients (50%) had history of hypertension. Epworth sleepiness scale (ESS) showed that 24 patients out of 30 (80%) had hypersomnolence with an ESS of 10/24 or more.

The BMI of the patients ranged from 26.34 to 55.53 kg/m² with a mean ± SD value of 33.25 ± 6.71 kg/m², 22 of them (73.33%) were obese with BMI ≥ 30 kg/m² and 8 of them (26.67%) were overweight with BMI ≥ 25–29.9 kg/m². The neck circumference (NC) ranged from 36 to 43 cm with a mean ± SD value of 38.1 ± 2.87 cm. The waist/hip ratio ranged from 0.89 to 1.12 with a mean ± SD value of 1 ± 0.05.

The Mallampati score ranged from 1 to 4 with a mean ± SD value of 2.7 ± 0.87. The clinical apnea score ranged from 0 to 5 with a mean ± SD value of 1.53 ± 1.22.

Table (1) showed the polysomnographic respiratory data of the studied patients, 4 patients had mild OSAHS (13.33%), 12 patients had moderate OSAHS (40%) and 14 patients had severe OSAHS (46.67%) two of them had sleep hypoventilation.

Table (2) showed the ocular findings of the studied patients; 4 patients were free from any ocular manifestations (patients with mild OSAHS). In 26 patients (patients with moderate and severe OSAHS) one or more of the following findings were found: floppy eyelid syndrome (FES) was detected in 3 (10%) patients, glaucoma was diagnosed in 5 (16.67%) patients, senile cataract was found in 3 (10%) patients, nonarteritic anterior ischemic optic neuropathy (NAION) was detected in 4 (13.33%) patients, papilledema was diagnosed in 3 (10%) patients and 18 (60%) patients had dry eye manifestations [in the form of conjunctival hyperaemia, lid parallel conjunctival folds and conjunctivo-chalasis (redundant conjunctival)] (Figs. 2–5).

Table 1  Data of the sleep study.

<table>
<thead>
<tr>
<th>The sleep parameters</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea/hypopnea index</td>
<td>65 ± 29.75/h</td>
</tr>
<tr>
<td>Basal oxygen saturation</td>
<td>91.73 ± 4.90%</td>
</tr>
<tr>
<td>Mean oxygen saturation</td>
<td>83.95 ± 7.59%</td>
</tr>
<tr>
<td>Minimal oxygen saturation</td>
<td>61.62 ± 18.74%</td>
</tr>
<tr>
<td>Oxygen desaturation index (ODI)</td>
<td>49.78 ± 22.32/h</td>
</tr>
<tr>
<td>T90%</td>
<td>3.46 ± 1.21% of the total sleep time</td>
</tr>
</tbody>
</table>

Table 2  Data of the ocular findings.

<table>
<thead>
<tr>
<th>The ocular findings</th>
<th>Number and percentage of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Floppy eyelid syndrome (FES)</td>
<td>(n = 3) 10%</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>(n = 5) 16.67%</td>
</tr>
<tr>
<td>Senile cataract</td>
<td>(n = 3) 10%</td>
</tr>
<tr>
<td>Non-arteritic ischemic optic neuropathy (NAION)</td>
<td>(n = 4) 13.33%</td>
</tr>
<tr>
<td>Papilledema</td>
<td>(n = 3) 10%</td>
</tr>
<tr>
<td>Dry eye manifestations [in the form of conjunctival hyperaemia, lid parallel conjunctival folds and conjunctivo-chalasis (redundant conjunctival)]</td>
<td>(n = 18) 60%</td>
</tr>
<tr>
<td>Free from any ocular manifestations</td>
<td>(n = 4) 13.33%</td>
</tr>
</tbody>
</table>
Effect of sleep related breathing disorders on ocular function

Discussion

OSAHS is associated with a number of serious systemic diseases and also several eye disorders including floppy eyelid syndrome, optic neuropathy, glaucoma, anterior ischemic optic neuropathy and papilledema secondary to raised intracranial pressure. Treatment of OSAHS may help floppy eyelid syndrome, stop progression of associated glaucoma, and reduce intracranial pressure in patients with associated papilledema. The diagnosis of OSAHS can only be made with formal sleep studies, but asking a small number of appropriate questions will help screen those patients who should be referred to sleep studies [5].

In this study, all patients with mild OSAHS were free from any ocular manifestations and ocular manifestations existed in patients with moderate and severe OSAHS. Floppy eyelid syndrome (FES) was detected in 3 (10%) patients with OSAHS. FFS is one of the ocular disorders that have been associated with OSAHS. It is characterized by rubbery, redundant upper eyelid tissue and papillary conjunctivitis, and is seen most commonly in obese middle-aged men. The affected eyelid may correspond to the side on which the patient prefers to sleep. The etiology is uncertain, but current theories include an upregulation of elastin-degrading matrix metalloproteinases possibly caused by direct eyelid trauma, ischemia–reperfusion injury due to pressure placed on the eyelid, or low arterial oxygen tension during sleep; again obesity is a risk factor for both FES and OSAHS. When FES is severe, the eyelid may spontaneously evert during sleep and rub on the patient’s pillow, causing an acute exacerbation of mechanically induced conjunctivitis. The prevalence of OSAHS in patients with FES has been reported to be as high as 90 percent; only 2–5 percent of patients with OSAHS may have FES. Thus, it is impractical to screen all patients with OSAHS for FES. However, all patients with FES who do not have an established diagnosis of OSAHS should have a thorough sleep history taken and, when appropriate, should be referred to sleep evaluation including polysomnography. Patients with FES and OSAHS who are already being treated with CPAP need to have their masks properly fitted to avoid additional eye injury due to misdirected air further drying out the eyes [20].

The range of reported rates of FES prevalence (2.3–32%) in different series of OSAHS patients includes Karger et al. [21], 1/44, 2.3%; Roberts et al. [22], 1/46, 2.2%; McNab [23], 3/20, 15%; and in 1999 Mojon et al. [24], found 14/44 (32%) patients with OSAHS had FES. All, but one of the studies (i.e. Robert et al. [22]), were conducted at the time of initial referral to OSAHS before initiation of CPAP.

In the current study, glaucoma was diagnosed in 5 (16.67%) patients; the link between glaucoma and OSAHS is controversial. There was a high prevalence of both primary open-angle glaucoma and normal-tension glaucoma among patients with OSAH. Several studies have identified OSAHS in patients with glaucomatous optic disc cupping and associated visual field defects who do not respond to medical or surgical intraocular pressure lowering treatments, but whose visual fields stabilize when treated with CPAP [4,5]. One Chinese study showed that patients with OSAHS were four times more likely to have glaucomatous optic disc changes and visual field defects than age-matched controls [25].

Another study by Mojon et al. [4] reported the prevalence of glaucoma among 69 patients with obstructive sleep apnea to be 7.2%. Waller et al. [26] criticized the design of many studies looking for a relationship between glaucoma and obstructive sleep apnea. Their criticisms included flawed from reliance on reported symptoms, lack of properly matched controls, etc. In Waller et al’s study of 100 patients with obstructive sleep apnea, they found the prevalence of glaucoma to be 27%. Based on Mojon and Waller’s reports, the most cautious approach would be to have all obstructive sleep apnea patients screened for glaucoma, and OSAHS should be considered as a possibility in all patients with primary open angle or normal tension glaucoma.

In the present study, nonarteritic anterior ischemic optic neuropathy (NAION) was detected in 4 (13.33%) patients. The prevalence of obstructive sleep apnea among those with NAION has been reported at 71–89%. The prevalence of NAION among those with OSA has not been studied. The possible causal relationship between OSAHS and NAION is very similar to their list of possible mechanisms relating glaucoma and obstructive sleep apnea [5].

In 2002 Mojon et al. [27] proposed mechanisms for nonarteritic anterior ischemic optic neuropathy in patients with obstructive sleep apnea include the following: obstructive sleep apnea results in impaired vascular autoregulation of the optic nerve’s circulation; obstructive sleep apnea induces arteriosclerosis and arterial hypertension, which in turn induce optic nerve

![Figure 4 Conjunctival Hyperaemia.](image)

![Figure 5 Redundant Conjunctiva.](image)
vascular “dysregulation”: repetitive hypoxia directly damages the optic nerve; obstructive sleep apnea causes an imbalance between nitric oxide and endothelin (vasodilatory and vasoconstrictive factors). Palombi et al. [28] had noted an even higher prevalence in their study where 89% of patients with NAION had sleep apnea. It has been suggested that patients with NAION can be questioned about their sleep habits. One research group that did this elicited a history of OSAHS 2.5 times more often in patients with NAION than in controls [29].

In this study, papilledema was diagnosed in 3 (10%) patients. Papilledema also associated with OSAHS, is thought to be caused by nocturnal increase in intracranial pressure. Potential mechanisms include raised venous pressure due to forced inspiration against a closed airway or hypoxia-induced cerebral venous dilation. When neuroimaging is normal, a careful sleep history in a patient with papilledema is critical in order to determine whether OSAHS is a causative factor. In such patients, treatment of the OSAHS has been shown to improve, resolve or halt the progression of papilledema [5].

Sugita et al. [30] did 24-h monitoring of intracranial pressure in patients with obstructive sleep apnea. Sugita et al. found that intracranial pressure increases during sleep in association with apnea, and the longer the duration of the apnea, the greater the increase in ICP. Episodes of apnea would “precede and accompany” episodes of intracranial pressure increase. None of their patients had increased intracranial in the daytime. Sugita et al. hypothesized that the dull morning headaches that are common in those with obstructive sleep apnea may be attributable to cerebrospinal fluid pressure increase during sleep. Waller et al. [26] said that some patients with more severe obstructive sleep apnea have low blood oxygen levels and increased intracranial pressure even in the daytime.

Purvin et al. [31] studied four patients with obstructive sleep apnea and papilledema. Purvin et al. hypothesized that low blood oxygen and high CO₂ would cause cerebral vasodilation, which in turn would result in transient increase in intracranial pressure.

In the present study, 18 (60%) patients had dry eye manifestations in the form of chronic conjunctival hyperaemia, lid parallel conjunctival folds and conjunctivo-chalasis (redundant conjunctiva). A variety of common ocular surface problems have been associated with CPAP use which delivers air under pressure to the nose.

Leaks from the CPAP mask hitting the face and eyes are the main cause for dry eyes. Fixing these leaks can eliminate these dry eyes. When the patient starts to put the CPAP mask on, it is very important to let the mask loose on the face and then start the CPAP machine. In this way, the mask cushion will fill up with air. Then the patient can tighten the straps on the face. If the leaks could not stop, we should change the mask or use special goggles to protect the eyes from the air blowing in them.

Some patients with sleep apnea have problems with the tear ducts, sinuses and eyelids. The air that enters in the airways from the CPAP could also enter through these ducts to the eyes. If the air from the CPAP machine is also humidified, the liquid may accumulate under the skin around the eyes [24].

During the night, air may escape from around the mask and blow onto the eyes resulting in morning sensations of dry, irritated eyes and conjunctivitis, alternatively air may find its way up through the nasolacrimal duct, and cause similar problems. There are a series of valves that guard against retrograde flow up the duct, but in many people these valves are not totally effective in preventing retrograde flow [15]. Therefore the investigators try to find other methods of treatment of OSAHS and their findings establish proof-of-principle that targeted blockade of certain potassium channels at the hypoglossal motor pool is an effective strategy for reversing upper airway hypotonia and causing sustained reactivation of genioglossus throughout non rapid eye movement and rapid eye movement sleep. These findings identify an important new direction for translational approaches to the pharmacological treatment of obstructive sleep apnea [32].

**In conclusion**, the increased prevalence of ocular symptoms and signs in patients with OSAHS indicates a need to increase awareness and establish close collaboration with the sleep physicians with clear pathways for review of OSAHS patients by the ophthalmic services. We should study the effect of treatment of OSAHS with CPAP on the ocular manifestations.

**Conflict of interest**

The authors declare no conflict of interest.

**References**


