Co-existence of obstructive sleep apnea and primary open angle glaucoma

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KEYWORDS
Obstructive sleep apnea; Primary open angle glaucoma; Polysomnography

Abstract
Introduction: Obstructive sleep apnea (OSA) is a condition characterized by repetitive collapse of upper airway during sleep. The associated hypoxemia characteristic of OSA may lead to sporadic perfusion abnormalities of the optic nerve and subsequent glaucomatous optic neuropathy.

Objectives: To assess the possible co-existence of OSA and primary open angle glaucoma (POAG) and to find out to what extent this may differ by the site of primary referral.

Methods: Two groups of patients were involved; group 1: sixteen patients with a confirmed diagnosis of OSA recruited from the Chest Department, Faculty of Medicine, Cairo University, with no history suggestive of ophthalmological complaints, and group 2: fifteen patients with POAG referred from the glaucoma clinic. All patients were subjected to: full history taking, Epworth Sleepiness Scale, anthropometric measures, polysomnography (PSG), and ophthalmological examination.

Results: Forty percent of patients presented from the glaucoma outpatient clinic had OSA as proved by PSG; 50% had mild OSA and 50% had moderate OSA, compared to patients with OSA who were primarily presented at the chest department and evaluated for POAG [6.25%, p-value = 0.037]. The intraocular pressure among group 2 patients did not significantly differ between patients with and without OSA for the right and left eyes [p-value = 0.78] and [p-value = 0.96], respectively.

Conclusion: The study supports the co-existence of OSA and POAG and highlights the great need for physician awareness. Accurate assessment is needed taking into consideration the serious effects of untreated OSA on the optic nerve.

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Introduction

The earliest association of sleep apnea syndrome (SAS) and glaucoma was suggested by Walsh and Montplaisir [1]. Their investigation was initiated by the observation of a patient with a family history of glaucoma who also had family members with sleep disturbances. Since that report, association between SAS and glaucoma has been proposed and challenged [2].

Under normal circumstances, auto-regulatory mechanisms exist in the optic nerve head vasculature that can maintain normal perfusion pressure, even with moderate intraocular pressure elevation. In glaucoma, insufficient auto-regulation of optic nerve blood flow may lead to optic nerve ischemia [3]. The repetitive airway collapse and associated hypoxemia characteristic of obstructive sleep apnea (OSA) may lead to sporadic perfusion abnormalities of the optic nerve and subsequent glaucomatous optic neuropathy. A definitive association between the two disorders would represent a meaningful finding and help to risk stratify individuals for glaucoma diagnosis [4].

Aim of the work

To assess the possible co-existence of obstructive sleep apnea (OSA) and primary open angle glaucoma (POAG) and to find out to what extent this may differ by the site of primary referral.

Patients and method

The present study was carried out at the Chest Department, Faculty of Medicine, Cairo University in collaboration with the Ophthalmology Department, between December 2013 and May 2014. The study involved two groups of patients;

Group 1: sixteen patients with confirmed diagnosis of OSA recruited from the Chest Department. They had no history suggestive of ophthalmological complaints for whom full ophthalmological assessment was done to detect signs of POAG.

Group 2: fifteen patients with POAG referred from the glaucoma clinic. Polysomnography study was done for assessment of the presence of OSA. This group was subdivided according to results of polysomnography into:

- Group 2A: patients with OSA.
- Group 2B: patients without OSA.

All patients of the study population were subjected to;

1. Medical history including; age, sex, and presence of co-morbidity (diabetes mellitus, hypertension, and ischemic heart disease).
2. History suggestive of sleep disturbance disorder including; loud snoring, witnessed apneas during sleep, nocturia, nocturnal choking, insomnia with frequent awakenings, morning headache, excessive day time sleepiness, and difficulty in concentration.
3. Calculation of body mass index (BMI = weight/height², kg/m²).
4. Evaluation of excessive day time sleepiness using the Epworth Sleepiness Scale [5].
5. Polysomnography (PSG).
6. Ophthalmological examination.

Epworth Sleepiness Scale (ESS)

ESS is the most commonly used questionnaire for subjective assessment of daytime sleepiness [5]. All patients were asked how likely they doze off or fall asleep in the following situations:

- Sitting and reading.
- Watching television.
- Sitting inactive in a public place.
- As a car passenger for an hour without break.
- Lying down to rest in the afternoon.
- Sitting and talking to someone.
- Sitting quietly after lunch without alcohol.
- In a car, while stopping for a few minutes in traffic.

The following scale was then used to choose the most appropriate number for each situation:

- 0 = would never doze.
- 1 = slight chance of dozing.
- 2 = moderate chance of dozing.
- 3 = high chance of dozing.

Interpretations of ESS:

- (a) Supernormal (if ESS 0–5).
- (b) Normal (if ESS 5–10).
- (c) Sleepy (if ESS 10–15).
- (d) Very sleepy (if ESS 15–20).
- (e) Dangerously sleepy (if ESS > 20).

Polysomnography (PSG)

PSG is the objective method for assessment of sleep disordered breathing. Before the study, patients were advised to avoid tea and coffee intake or any other drugs that may have influence on the quality of sleep as sedative, hypnotics, tranquilizers, etc.

Each patient presented to the sleep laboratory unit at the Chest Department, Cairo University hospital, one hour before his/her usual bed time to get familiar and adapt to the environment. Full explanation of the nature and the aim of polysomnography were performed. The duration of PSG was about seven continuous hours. Patients were connected to SOMNO screen TM plus (cardio-respiratory screening) which is a computer-based high technology PSG. It included:

- Pulse oximeter applied to the index finger to detect arterial oxygen saturation (SaO₂) in terms of; number of desaturation, minimal nocturnal SaO₂ (%), baseline saturation (%), average saturation (%), number of desaturations < 90%, number of desaturations < 80%, saturation time < 90%, and average desaturation (%).
- A microphone was applied on the neck beside the larynx to detect snoring.
Thermal sensors and the nasal pressure transducer to detect oronasal air flow.

- Single lead ECG to monitor heart rhythm.
- Detection of chest and abdominal movements using two separate belts.
- Leg movements were recorded via anterior tibialis electromyogram.

The following data were recorded:

- **Total sleep time**: It is the total duration of light sleep (stages N1 and N2), deep sleep (stage N3), and rapid eye movement (REM) sleep.
- **Sleep efficiency**: It is the total sleep time divided by the total recording time (i.e., the time in bed).
- **Sleep stage latency**: The latency to any sleep stage is the duration from sleep onset to the initiation of that sleep stage.

**Apnea**: defined by,
- a. Reduction in airflow greater than 90% of baseline, recorded by oronasal thermistor or nasal pressure cannula.
- b. Duration \( \geq 10 \) s.
- c. Reduction in airflow at least 90% of the event.

An apnea was further classified as obstructive, central or mixed based on the assessment of respiratory effort during the event [6].

**Hypopnea**: defined by,
- a. Reduction in airflow \( \geq 50\% \) from baseline, recorded by nasal pressure cannula or alternatively by oronasal thermistor.
- b. Duration \( \geq 10 \) s.
- c. Reduction in airflow at least 90% of the event.
- d. Reduction in saturation \( \geq 4\% \) from baseline prior to the event.

A desaturation is scored when the following two parameters are met; minimum drop required is 4% (the minimum decrease in oxygen level to score a desaturation), minimum duration required is 10 s [6].

**Apnea hypopnea index (AHI)**: refers to the number of apneas and hypopneas per hour of sleep

**Respiratory Disturbance Index (RDI)**: The number of apneas, hypopneas and RERAs per hour of sleep

**Snoring index**: the number of snoring events per hour of sleep.

The severity of sleep-related obstructive breathing events will be rated as follows: mild: 5–15 events/h; moderate: 15–30 events/h; and severe >30 events/h [7].

**Ophthalmological examination**

All patients underwent basic examination (Fig. 1), including:

- The best corrected visual acuity ± pinhole assisted visual acuity using Snellen chart (Snellen chart projector CCP-3100).
- Refraction using the auto-refractometer (Canon Auto Ref R-30, Japan).
- Intraocular pressure (IOP) measurement using Goldmann tonometer.
- Full anterior segment examination using the slit-lamp;
  - Nidek SL-450 slit-lamp (Aichi, Japan).
  - Huvitz slit-lamp Microscope HS-5000 (Huvitz Inc., Korea).
- Posterior segment examination by slit lamp bio-microscopy.

Suspected cases of glaucoma underwent gonioscopy and visual field testing using Humphrey perimeter. The diagnosis of POAG was based on the ISGEO (International Society of Geographical and Epidemiological Ophthalmology) definition of glaucoma [8]. The diagnosis was established by one of the following criterion:

- a. Vertical cup to disc ratio (VCDR) \( \geq 0.7 \) or VCDR asymmetry \( > 0.2 \) plus visual field defect compatible with glaucoma.
- b. VCDR \( \geq 0.8 \) plus none reliable visual field.
- c. In case of no view of optic disc: visual acuity \(< 3/60 \) plus IOP \( \geq 21 \) mmHg or visual acuity \(< 3/60 \) and evidence of previous filtering surgery.

**Statistical analysis**

Data were statistically described in terms of mean \( \pm \) standard deviation (SD), median and range, and number of cases and

![Figure 1](image-url)  (A) Slit lamp. (B) Volk Goldmann 3-mirror and 4-mirror lenses for gonioscopy. (C) IOP measurement using Goldmann tonometer.
percentages when the appropriate. Mann–Whitney test compared two independent groups and Chi-square/Fischer exact tests of proportion independence. *p*-value was significant at 0.05 level. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 20.0 for Microsoft Windows.

**Results**

The results are presented in Tables 1–5.

**Discussion**

The association between OSA and glaucoma was first reported in 1982 by Walsh and Montplaisir [1], who found a combination of OSA and glaucoma in five members of two generations of a family.

Later, Robert et al. [9] and McNab et al. [10] reported that some patients with sleep disorders screened for floppy eyelid syndrome were also being treated for glaucoma. Other authors also reported a significantly higher prevalence of sleep related breathing disorders in POAG patients compared to controls [11,2,12–13].

The main finding of the current study was that 40% of patients presented from glaucoma outpatient clinic had OSA as proved by PSG; 50% had mild OSA and 50% had moderate OSA, compared to patients with OSA who were primary presented at the chest department and evaluated for POAG [(6.25%), *p*-value = 0.037].

Our study further supported the co-existence of POAG and OSA and highlighted that it may differ according to the site of initial medical assessment and so warrants physician awareness.

In agreement of our finding, Balbay et al. [14] found the prevalence of OSA was 33.3% in glaucoma patients, 14.3% mild and 19% moderate, in a study conducted on 21 POAG patients attending the outpatient clinic of the department of Ophthalmology between July 2007 and February 2008. They also found the prevalence of OSA was significantly more common in glaucoma patients having the symptoms of habitual snoring, witnessed apneas than those of not, this contradicts our study in which there was no statistical significance regarding symptoms in glaucoma patients with OSA and glaucoma patients without OSA.

Another study by Mojon et al. [13] observed OSA in 7 of the 16 normal tension glaucoma patients (44%). However, their controls were all male subjects from a previously published study. Also, Abdal et al. [15] found OSA 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.

It was also found that all symptoms of sleep disordered breathing apart from difficulty in concentration were more common among patients of group 1 than group 2. This could explain why those patients sought medical advice primarily

<table>
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<th>Table 1</th>
<th>Clinical characteristics of the study population.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>Group 1 No. = 16</td>
</tr>
<tr>
<td>Age (mean ± SD) years</td>
<td>53.6 ± 10</td>
</tr>
<tr>
<td>Sex**</td>
<td>Males 3 (18.7%)</td>
</tr>
<tr>
<td></td>
<td>Females 13 (81.3%)</td>
</tr>
<tr>
<td>BMI (mean ± SD)</td>
<td>40.8 ± 8</td>
</tr>
<tr>
<td>Hypertension**</td>
<td>6 (37.5%)</td>
</tr>
<tr>
<td>Diabetes mellitus**</td>
<td>7 (43.7%)</td>
</tr>
<tr>
<td>IHD**</td>
<td>2 (12.5%)</td>
</tr>
</tbody>
</table>

Definition of abbreviations: SD = standard deviation, No. = number, BMI = body mass index, IHD = ischemic heart disease.

** Significant *p*-value less than 0.05. ND = not detected.

** Data were expressed as number and percentage.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Statistical analysis of symptoms of sleep disordered breathing among all patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>Group 1 No. = 16</td>
</tr>
<tr>
<td>Difficulty in concentration</td>
<td>9 (56.3%)</td>
</tr>
<tr>
<td>Snoring</td>
<td>13 (81.3%)</td>
</tr>
<tr>
<td>Excessive sleepiness</td>
<td>14 (87.5%)</td>
</tr>
<tr>
<td>Morning headache</td>
<td>11 (68.8%)</td>
</tr>
<tr>
<td>Nocturia</td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Witnessed apneas</td>
<td>11 (68.8%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>13 (81.3%)</td>
</tr>
<tr>
<td>ESS (median)**</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Data were expressed as number and percentage. ND: not detected.

** Significant *p*-value (between groups 2A and 2B) less than 0.05.

** ESS: Epworth Sleepiness Score.
due to their sleep related breathing disorders. It worth attention that there was no significant difference between symptoms of sleep disordered breathing and ESS among patients with OSA compared to patients without OSA among group 2 patients (Table 2). However there was a significant difference in RDI, AHI, number of desaturations and saturation time less than 90% between both groups (Table 3).

In our study, the intraocular pressure of patients with POAG with and without OSA showed no significant difference for the right eye and left eyes \([p\text{-value} = 0.78]\) and \([p\text{-value} = 0.96]\), respectively (Table 4). Contradictory to that, Balbay et al. [14] found that the intraocular pressure of patients with POAG who had OSA was significantly lower than those without OSA for the right and left eyes \([p\text{-value} = 0.006]\) and \([p\text{-value} = 0.035]\), respectively.

At the other side of the study, only one patient among cases diagnosed with OSA who were presented to the sleep lab at the chest department had POAG (6.25%). This percentage was lower than the finding of different studies (Table 5). Mojon et al. [16] reported the prevalence of glaucoma among 69 patients with obstructive sleep apnea to be 7.2%. Also, Tsang et al. [17] showed that patients with OSA were four times more likely to have glaucomatous optic disc changes and visual field defects than age-matched controls. Waller et al. [18] carried out a study on 100 patients with obstructive sleep apnea, and they found the prevalence of glaucoma to be 27%. Higher prevalence of glaucoma in patients with OSA was also found in a study carried out on 30 patients with OSA, and found that 16.67% of patients had glaucoma [19].

**Conclusion**

- Accurate assessment of sleep disorders should be carried out not only among patients seeking medical advice primarily for sleep disorders but also among patients seeking medical advice, particularly for glaucoma, at the glaucoma outpatient clinic.
In our study, although the prevalence of glaucoma in patients with OSA was lower than that found in different studies (may be due to small number of the study population); screening of all patients with OSA for the presence of glaucoma is advised considering the serious effects of OSA on the eye, particularly its effect on the optic nerve.

Further large studies are needed to assess the possible predictors of occurrence of POAG among patients with OSA.

Authors contribution

*Concept and study design: Alaa Eldine O. Shalaby, Mostafa I. Elshazly, and Yasmine M. El Sayed.
*Data collection and performance of PSG: Hoda M. Abdelhamid.
*Data analysis and interpretation were carried out by all of the authors.

*Drafted the manuscript: Samah Selim.
All authors revised and approved the manuscript.

References