Original Research Article

Study of Prevalence of Obstructive Sleep Apnoea Syndrome in Patients With Primary Open-Angle Glaucoma in A Tertiary Care Hospital of West Bengal

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Abstract

Purpose

This study was conducted to investigate the prevalence of obstructive sleep apnea (OSA) in diagnosed patients of POAG. We also investigated whether there is an association between severity of OSA and the incidence of glaucoma. **Method**: Forty-two consecutive primary open-angle glaucoma patients (24 females and 18 males) who attended the out-patient clinic of the Department of Ophthalmology between July 2016 and February 2018 were included in this study. All patients underwent polysomnographic examination. **Results**:The prevalence of obstructive sleep apnoea syndrome was 33.3% in patients with primary open-angle glaucoma; the severity of the condition was mild in 14.3% and moderate in 19.0% of the subjects. The age (P=0.047) and neck circumference (P=0.024) in patients with obstructive sleep apnoea syndrome were significantly greater than those without the syndrome. Triceps skinfold thickness in glaucomatous obstructive sleep apnoea syndrome patients reached near significance versus those without the syndrome (P=0.078). Snoring was observed in all glaucoma cases with obstructive sleep apnoea syndrome. The intra-ocular pressure of patients with primary open-angle glaucoma with obstructive sleep apnoea syndrome was significantly lower than those without obstructive sleep apnoea syndrome (P=0.006 and P=0.035 for the right and left eyes, respectively). Significant difference in the cup/disc ratio and visual acuity was observed, except visual field defect, between primary open-angle glaucoma patients with and without obstructive sleep apnoea syndrome.**Conclusion:** Our study showed that there is a significant prevalence of obstructive sleep apnoea syndrome in patients with primary open-angle glaucoma**.**

Keywords: Obstructive Sleep Apnea (OSA); Primary Open Angle Glaucoma (POAG); Polysomnography (sleep study); Neck Circumference; Triceps Skinfold Thickness; Snoring; Intra-Ocular Pressure; Cup/Disc Ratio; Visual Acuity.

Introduction

Sleep apnea characterized by brief interruptions of breathing during sleep, and sleep apnea syndrome is defined as episodes of apnea and hypopnea during sleep accompanied by symptoms of functional impairment after sleep[1]. Obstructive sleep apnea (OSA) is a type of sleep apnea that results from complete or partial collapse of the pharyngeal airway during sleep, and is characterized by brief interruptions of breathing. OSA increases the risk for cardiovascular morbidity and mortality, and can also cause hypertension and increased insulin resistance. OSA has also been associated with daytime sleepiness. Sleep-disordered diseases are associated with a number of eye disorders including floppy eyelid syndrome, optic neuropathy, keratoconus, retinal vascular tortuosity and congestion, retinal bleeding, non-arteritic anterior ischaemic optic

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neuropathy and papilloedema secondary to increased intracranial pressure, normal tension glaucoma, and primary open-angle glaucoma (POAG)[2-4]. Sleep disordered breathing may impair autoregulation of optic nerve perfusion due to the direct effect of hypoxia. Glaucoma is a multifactorial and specific optic neuropathy often characterised by increased intra-ocular pressure (IOP) that results in typical and progressive visual field loss[5]. The prevalence of glaucoma in the general population is between 1% and 2%[6]. While the aetiology of POAG still remains unclear, several risk factors have been associated with the condition. It was known that OSAS effects the oxygenation, neurohumoral factors, and vascular haemodynamics [2,4]. It has been suggested that OSAS aggravates or even causes glaucoma by impaired optic nerve head blood flow and tissue atrophy, infarction due to vascular dysregulation or by direct damage to the optic nerve secondary to prolonged hypoxia[2-6]. The association between glaucoma and OSAS has been reported in many studies. Most of them focused on the prevalence of glaucoma in OSAS patients and indicated it as a risk factor. Some of these articles have been observational case reports or case series[2,7]. The objective of this study was to investigate the prevalence of OSAS in patients with primary open-angle glaucoma.

Methods

A prospective case series that included 60 consecutive adult primary open-angle glaucoma patients who attended the out-patient clinic of a tertiary care eye centre of west bengal between July 2016 and February 2018. Informed consent was obtained from the study participants. Individuals with diabetes mellitus (n=8), thyroid function disorders (n=4), hyperlipidaemia (n=4), and who refused to participate in the study (n=2) were excluded from study. Therefore all 42 patients were subjected to routine examination. All patients underwent routine eye examination, including best corrected visual acuity, manifest refraction, slit-lamp examination of the anterior eye segment, IOP measurement, gonioscopy, and binocular examination of the optic disc. Patients were considered to have primary open-angle glaucoma if they had untreated IOP of ≥21 mm Hg, an open anterior chamber angle, glaucomatous visual field defects or glaucomatous cupping of the optic disk. Data collection prior to the sleep test, all primary open-angle glaucoma patients completed a questionnaire about sleep disturbance. Data from the questionnaire were used to evaluate basic OSAS symptoms such as snoring (presence of snoring for at least five nights per week), witnessed apnoea (spouse or relatives of patients with OSAS, identifying noisy and irregular snoring, and arrested respiration through the mouth and nose), and daytime sleepiness. The Epworth Sleepiness Scale was used to objectively evaluate excessive daytime sleepiness. If the score obtained on this scale was above 10, excessive daytime sleepiness was considered present[8]. All primary open-angle glaucoma patients received an otorhinolaryngeal examination. Data were analysed using the Statistical Package for the Social Sciences (Windows version 10.0; SPSS Inc, Chicago [IL], US). Mann Whitney U test was used for comparing quantitative data. Chi squared test or Fisher's exact test was used to compare categorical data.

Results

Of the 42 primary open-angle glaucoma patients, 24 were female and 18 were male. Demographic and clinical features of the patients are summarised in Table 1. Snoring was the most prevalent (81.0%) major symptom of OSAS; snoring was habitual in 42.9% of the patients. Daytime sleepiness and witnessed apnoea were found in 23.8% and 14.3% of the patients, respectively. While no major symptom was present in 52.4% of POAG patients, three major symptoms were concomitantly present in one (4.8%) POAG patient (Table 2). Polysomnographic study showed that OSAS was present in 33.3% (n=14) of the POAG patients (apnoea-hypopnoea index [AHI] ≥5/hour). The severity of OSAS was mild (AHI of 5-15/hour) in 14.3% (n=3) and moderate (AHI of 16-30/hour) in 19.0% (n=4) of the patients and severe AHI more than 30 /hour) mean in 50 % (n=7) . Age (P=0.047) and neck circumference (P=0.024) were significantly higher in primary open-angle glaucoma patients with OSAS versus those without OSAS; triceps skinfold thickness was also higher in OSAS patients, but it did not reach statistical significance (P=0.078). No significant difference was observed between primary open-angle glaucoma patients with and without OSAS with regard to body mass index and the duration of one or more major OSAS symptom (Table 3). Primary open-angle glaucoma patients with and without OSAS did not differ significantly in terms of smoking, hypertension, cup/disc ratio, and visual acuity. Male patients are more prone to develop OSAS. Intra-ocular pressure in POAG patients with OSAS was significantly lower than that in patients without OSAS (P=0.006 and P=0.035 for the right and left eyes, respectively). Apnoea-hypopnoea index was significantly higher (P<0.001) and the

desaturation on PSG was significantly lower (P=0.043) in POAG patients with OSAS than those without OSAS. Visual field defects were significantly more common in POAG patients with OSAS (P=0.038) (Table 4).Obstructive sleep apnoea syndrome was not observed in primary open-angle glaucoma patients with no snoring (including simple snoring). As the degree of snoring increased, OSAS prevalence reached almost statistical significance. The symptoms of habitual snoring (P<0.001) and witnessed apnoea (P=0.026) were significantly more frequent in POAG patients with OSAS versus those without OSAS (Table 5).

Table 1:**General characteristics of patients**

Characteristic	No. (%) or mean ± SD (range
Gender	
Female	24 (57.1)
Male	18 (42.9)
Age (years)	56.0 ± 10.1 (38.0-79.0)
Body mass index (kg/m²)	27.8 ± 5.5 (17.3-40.1)
Neck diameter (cm)	37.9 ± 3.4 (31.0-44.0)
Triceps skinfold thickness (mm)	14.0 ± 2.9 (10.0-20.0)
Haematocrit (%)	41.3 ± 3.2 (33.8-45.9)
OSAS symptom duration (months)	5.2 ± 6.0 (0-20.0)
Smoking	11 (52.4

Abbreviations:OSAS= obstructive sleep apnoea syndrome; SD=standard deviation

Table 2:**Frequency of obstructive sleep apnoea syndrome (OSAS) symptoms in patients with primary open-angle glaucoma**

OSAS symptom	No. (%) of patients (n=21)
Snoring	34 (81.0)
Snoring severity Not present Mild Moderate Severe	 8 (19.0) 24 (57.1) 0 10 (23.8)
Habitual snoring*	18 (42.9)
Witnessed apnoea*	6 (14.3)
Daytime sleepiness*	10(23.8)
Major symptom Not present 1 Major symptom 2 Major symptoms 3 Major symptoms	 22(52.4) 8 (19.0) 10(23.8) 2 (4.8)

*major symptoms

Table 3:**The comparison of the features of primary open-angle glaucoma patients with and without obstructive sleep apnoea syndrome (OSAS)**

Characteristic	Mean ± standard deviation		P value
	With OSAS	Without OSAS	
Age (years)	63.2 ± 11.5	53.6 ± 7.8	0.047
Body mass index (kg/m²)	27.9 ± 7.4	27.7 ± 6.6	0.970
Neck circumference (cm	40.4 ± 2.8	36.6 ± 3.0	0.024
Triceps skinfold thickness (mm	15.4 ± 1.5	13.2 ± 3.2	0.078
Haematocrit (%)	42.7 ± 2.1	40.6 ± 3.1	0.117
Symptom duration (years)	6.7 ± 7.0	4.5 ± 5.5	0.473

Table 4: The comparison of clinical and ophthalmological features of primary openangle glaucoma patients with and without obstructive sleep apnoea syndrome (OSAS

Clinical and ophthalmological feature	No or Mean ± SD		P value
	With OSAS	Without OSAS	
Gender			
• female (n=24)	04 (55.6%)	20(44.4%)	
• Male(n=18)	10 (44.4%)	8 (83.3%)	0.159
SMOKING			
• Yes (n=22)	10 (45.5%)	12 (54.5%)	
• No (n=20)	4 (20.0%)	16 (80.0%)	0.361
Hypertension			
• Yes (n=14)	2 (14.3%)	12 (85.7%)	
• No (n=28)	12 (42.9%)	16(57.1%)	0.337
IOP (mm Hg)			
• Right (n=22)			
• Left (n=20))	14.0 ± 2.5	18.5 ± 3.9	0.006
	14.7 ± 2.6	17.8 ± 2.8	0.035
Cup/disc ratio			
• Right (n=22)	0.4 ± 0.2	0.4 ± 0.2	0.968
• Left (n=20)	0.4 ± 0.1	0.4 ± 0.2	0.817
Visual acuity			
• Right (n=14)	0.7 ± 0.2	0.8 ± 0.2	0.608
• Left (n=28)	0.7 ± 0.1	0.9 ± 0.1	0.223
Visual field defect			
Not present (n=28)	10(35.7%)	18(64.3%)	
• Unilateral(N=4)	14 (100.0%)	0	
• Bilateral (n=10)	0	10 (100.0%)	0.038
AHI	13.8 ± 6.8	2.7 ± 1.6	<0.001
Lowest desaturation in PSG (%	81.3 ± 7.4	85.6 ± 11.1	0.043

Table 5: Frequency of obstructive sleep apnoea syndrome (OSAS) symptoms in patients with primary open-angle glaucoma

Symptom	No. (%) of patients		P value
	With OSAS	Without OSAS	
Snoring			
• Yes (n=34)	14 (41.2)	20 (58.8)	0.255
• Not present (n=8)	0	8 (100.0)	
Snoring severity			
• Not present (n=8)	0	8 (100)	
• Mild (n=24)	8(41.2)	16 (66.7)	0.165
• Moderate	0	0	
• Severe (n=10)	6 (60.0)	4 (40.4)	
Habitual snoring			
• Yes (n=18)	14(77.8)	4 (22.2	<0.001
• Not present (n=24)	0	24(100.0)	
Witnessed apnoea			

• Yes (n=6) • Not present (n=36)	6 (100.0) 8 (22.2)	0 28 (77.8)	0.026
Daytime sleepiness • Yes (n=10) • No (n=32)	 6 (60.0) 8 (25.0)	 4 (40.0) 24 (75.0)	 0.280
Major symptoms • No major symptom • 1 Major symptom (+) • 2 Major symptoms (+) • 3 Major symptoms (+)	 0 4 (50.0) 8 (80.0) 2 (100.0)	 22 (100.0) 4 (50.0) 2 (20.0) 0	 0.005
The presence of major symptoms • Yes (n=20) • Not present (n=22)	 14 (70.0) 0	 6 (30.0) 22(100.0)	 0.001

Discussion

This study revealed that the prevalence of OSAS and the associated symptoms were higher in POAG patients than that in the general population[1]. The prevalence of OSAS of at least mild severity was even higher compared with that in middle-aged adults (9% in women and 24% in men). Intra-ocular pressure in patients with OSAS were significantly lower than in those without OSAS. In this study a statistically significant but clinically insignificant difference between OSAS and non-OSAS patients regarding visual field defect. Earlier study revealed that there is a potential cardiovascular risk factors including systemic hypertension, atherosclerosis, vasospasm, and acute hypotension are associated with glaucoma[9]. Since glaucomatous optic neuropathy is multifactorial, treatment of OSAS—which is currently a known and modifiable risk factor—may help the control of IOP and management of glaucoma[10]. A recent study determined the prevalence of OSAS in POAG associated with snoring. Thirty-one snoring glaucomatous patients prospectively underwent PSG. Of these, 49% were diagnosed to have OSAS[11]. Mojon et al[2] performed overnight transcutaneous finger oximetry in 30 consecutive patients having POAG (mean age, 76.0 ± 7.9 years) and found that the oximetry disturbance index (ODI) was significantly higher (11%) in these patients compared with normal controls of the same age and sex distribution. They reported OSAS prevalence as 20% (n=6/30) in POAG patients according to ODI[2]. We found an OSAS prevalence of 33.3% in POAG patients according to AHI. Mojon et al[12] reported a 7.2% prevalence of NTG among 69 white patients with OSAS (mean age, 52.6 ± 9.7 years), and it was significantly higher than that expected in general white population (2%)[12].
Sergi et al[13] found a 59% prevalence of NTG in 51 OSAS patients (mean age, 64 ± 10 years). Contrary to the other studies, the prevalence of glaucoma in a study involving 228 patients with OSAS was reported to be the same as in the general population[14]. Age is a common risk factor of both OSAS and POAG; the latter itself is an ageing-associated disease. The incidence of OSAS in the general population has been shown to be the highest between 45 and 65 years of age[15].Thus, high mean age (56.0 years) in our study might have contributed to the observed high prevalence of OSAS. Snoring is known to be the most common symptom in OSAS[16]. A group of out-patients, including those with POAG and without POAG, was recruited for evaluation of sleep-disordered breathing symptoms such as snoring, excessive daytime sleepiness, and insomnia with the help of a questionnaire[6]. The authors reported high prevalence of sleep-disordered breathing in POAG patients. Compared with those without POAG, POAG patients showed a higher prevalence of snoring (47.6% vs 38.0%), snoring plus excessive daytime sleepiness (27.3% vs 17.3%), and snoring plus excessive daytime sleepiness plus insomnia (14.6% vs 7.8%).[9] The authors speculated that the large nocturnal fluctuations in blood pressure of OSAS patients may have interfered with normal ocular haemodynamics, making the eye vulnerable to glaucoma[6,9]. In the logistic regression model, snoring was significantly associated with glaucoma. However, that study was not a follow-up study of glaucomatous patients and snoring could not be

accepted as a prognostic factor of POAG[6]. Moreover, their study did not use objective measures such as overnight PSG for the diagnosis; instead, they only relied on self-reported symptoms[6,9]. In another study[17]., the prevalence of sleep-disordered breathing symptoms was higher in patients with NTG versus those without NTG (57% vs 3%). However, contrary to our study, they only offered PSG to patients with a positive sleep history[17]. In our study, the prevalence rates of snoring, habitual snoring, witnessed apnoea, excessive daytime sleepiness were 81.0%, 42.9%, 14.3%, and 23.8%, respectively. The concomitant presence of two or three major OSAS symptoms was observed in 23.8% and 4.8% of our POAG patients, respectively. Blumen Ohana et al[11] reported high prevalence of OSAS in patients with POAG and suggested that presence of snoring should be explored at interview. Conversely, patients who snore should be asked whether they have POAG, and if so, should undergo all-night sleep recording for the presence of OSAS[11].Mojon et al[3] also found that respiratory disturbance index (RDI) was positively correlated with IOP in 114 OSAS patients. Because of the observational nature of that study, they concluded only an association between glaucoma and OSAS rather than a direct causal relationship[3]. A study by Karakucuk et al[18] found that the prevalence of glaucoma in patients with OSAS was 12.9% (n=4/31); all these four patients with glaucoma were in the severe OSAS group. There was also a positive correlation between IOP and AHI, and they suggested that increased IOP values may reflect the severity of OSAS. In another cross-sectional study, there was no correlation between IOP and RDI[14]. In the present study, IOP level in patients with OSAS was significantly lower than that in those without OSAS. Intra-ocular pressure shows diurnal variation and patients with OSAS may have elevated IOP and perfusional disturbance of retinal nerve fibres during sleep. Therefore, these patients may have completely normal or low IOP during the daytime. On the other hand, most patients with OSAS were regularly under glaucoma medication which lowers the IOP to within normal limits. Sergi et al[20] did not find any difference in the cup/disk ratio between the study patients and the control group. They found a significant correlation between AHI and the cup/disk ratio but none between awake arterial blood gases and the ophthalmologic examination data[13]. They speculate that POAG could be a consequence of changes in vascular tone and of the increased platelet aggregability which frequently occur in OSAS patients. In contrast with their study, our study shows that the cup/disk ratio did not differ between POAG patients with and without OSAS. A study in Hong Kong[19] examined the computerised visual fields and optic discs of OSAS patients with normal IOP and compared these with non-OSAS population. Visual field indices were significantly lower and the incidence of suspicious glaucomatous disc changes was higher versus the control arm[19]. A variety of visual field defects in OSAS patients were also reported by Mojon et al in nine patients; the field defects stabilised in two of these after 18 months following continuous positive airway pressure (CPAP)[20]. Kremmer et al have also reported patients with NTG and progressive field loss despite IOP-lowering eye drops and surgery. Nevertheless, they stabilised field loss of patients after diagnosis of OSAS and treatment with CPAP[20]. Although there was statistically significant difference in the visual field defects of POAG patients with and without OSAS in our study, it was clinically insignificant. Only significant glaucomatous visual field defects were considered in our evaluation. Therefore, minor changes due to lenticular opacifications or other aetiology were not taken into account as major glaucomatous visual field changes. Hypoxaemia and haemodynamic changes resulting from intermittent apnoea and hypopnoea during sleep are believed to play a role in glaucomatous optic neuropathy[11]. Although there is no clear evidence for a cause-effect relationship in the present study, the high prevalence of OSAS in patients with POAG suggests a possible relationship.

Conclusion

Conclusuvely it was seen that the prevalence of OSAS was higher in POAG patients versus the general population. In clinical practice, OSAS is often not taken into diagnostic consideration in glaucoma patients. The high prevalence of OSAS in patients with POAG suggests the need to explore the long-term results of coincidence, relationship, and cross-interaction between these two common disorders. Further large-scale studies are required to explore the long-term results of these two common disorders, particularly in patients who have been treated with CPAP therapy. Adequate treatment of OSA, along with optimal ophthalmic care, may result in better control of glaucoma.

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