

Prevalence of Open Angle Glaucoma in Patients with Obstructive Sleep Apnea

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ABSTRACT

Background: obstructive sleep apnea seems to have multi-organ harmful effects. Its association with glaucoma was previously reported. However, the debate exists around prevalence of glaucoma and the pathophysiology explains its association with obstructive sleep apnea is not fully known.

Objective: the present study was designed to estimate the incidence of normal tension glaucoma among patients with obstructive sleep apnea.

Patients and Methods: sixty patients with obstructive sleep apnea and another age and sex matched 60 controls were included. Five patients in the study group refused to complete the study and only 55 patients constitute the study group. All participants underwent polysomnographic and ophthalmologic (measurement of intraocular pressure and fundus examination) studies. Data was collected, documented and statistically analyzed.

Results: both study and control groups were comparable regarding patients' demographic and associated chronic medical disease. The prevalence of normal tension glaucoma in patients with obstructive sleep apnea was 27.3% and it was 3.3% in control subjects. Cup disk ratio and oxygen desaturation index were significantly increased, while oxygen saturation significantly decreased in patients with obstructive sleep apnea. In addition, obstructive sleep apnea index (measure of severity) was proportionately correlated with intraocular pressure, oxygen desaturation index, cup to disk ratio and negatively correlated with oxygen saturation.

Conclusion: open angle glaucoma significantly increased in obstructive sleep apnea and significantly associated with disease severity.

Keywords: obstructive sleep apnea; polysomnography; normal tension glaucoma; open angle glaucoma.

INTRODUCTION

The short episodes of partial or complete airway collapse during sleep were defined as obstructive sleep apnea-hypopnea syndrome. When episodes occur five or more times during an hour, there is pathological state of breathing. Obstructive sleep apnea (OSA) usually presented with snoring and excessive day-time sleeping and diagnosed by polysomnographic (PSG) apnea-hypopnea index (AHI), which is a measure of disease severity^(1,2).

Numerous diseases of the eye encountered frequently in association with OSA. These may include floppy-eyelid syndrome and optic nerve disorders (papilledema, glaucoma, ischemic neuropathy)^(3,4,5). Normal-tension glaucoma (NTG) is defined as optic neuropathy with a glaucomatous optic nerve head, progressive thinning of retinal nerve fiber layer, specific visual field defects, open angle of anterior chamber and normal intraocular pressure (IOP < 21 mmHg)⁽⁶⁾. Known risk factors for NTG include abnormalities in ocular blood (abnormal flow and coagulation), hypotension, ischemic disorders of blood vessels and autoimmunity⁽⁷⁾. However, the pathogenesis is not fully understood. It is most likely that NTG is a complex syndrome consisting of a variety of pathological pathways such as: lower tolerance of normal IOP, perfusion deficit and vascular dysregulation, trans-laminar pressure gradient and impaired cerebrospinal fluid circulation⁽⁸⁾.

OBJECTIVE OF THE STUDY:

The present study was designed to evaluate the prevalence of normal tension glaucoma among patients with obstructive sleep apnea.

PATIENTS AND METHODS

The present study is a case-control study. The study included 60 patients with confirmed diagnosis of obstructive sleep apnea. Another age and sex matched 60 subjects without OSA were included as a comparative (control) group. All patients and controls were selected from Otorhinolaryngology departments in Al-Azhar University hospitals (Cairo and New Damietta) during the period from October 2016 to January 2019. Both patients and control groups were picked up by the Otolaryngology authors. The diagnosis of consecutive patients was confirmed by polysomnography as having OSA and the subjects proved by the polysomnogram that they don't have OSA were enrolled on this current study as patients and control groups respectively. In addition, subjects in control group were matched with patients in the study group regarding their demographics and comorbid medical conditions.

Inclusion criteria:

Patients who underwent an overnight polysomnography with their results at hand and confirmed diagnosis of OSA (study group). In addition, patients who completed an ophthalmologic examination were included.

Exclusion criteria:

Patients with OSA who already have a confirmed diagnosis of glaucoma or who under treatment for glaucoma were excluded from the study. Five patients were excluded due to refusal of participation. Thus, the final 55 patients were included in the study group).

Ethical consideration:

All eligible subjects signed consent for participation in the study after full explanation of the study protocol. In addition, the study protocol was approved by the local ethics and research committee. Patient's congeniality and their right to withdraw at any time were guaranteed.

Polysomnography:

Polysomnography was done at multiple sleep labs according to the availability and the patients' preference. The polysomnographic analysis was carried out in an automatic manner, but results were scored manually. The scoring of respiratory findings was done in standard criteria as described by Iber *et al.*⁽⁹⁾. A total number of apneas and/or hypopneas in one hour were defined as apnea hypopnea index. In addition, oxygen desaturation index was used as an index of nocturnal hypoxemia. It is defined as the number of episodes of oxygen saturation falling by more than 4% during one hour of sleep.

Ophthalmologic examination:

Ophthalmologic examination was carried out by an ophthalmologist. It included measurement of intraocular pressure and fundus examination, to search for manifestations of glaucomatous optic disc changes. The diagnosis of normal tension glaucoma was done according to criteria defined by Primary Open Angle Glaucoma Preferred Practice Pattern's definition and diagnostic recommendations, described by American Academy of Ophthalmology⁽¹⁰⁾. The ophthalmologist was totally blind to results of the polysomnogram (degree of sleep apnea). The following criteria must be fulfilled to confirm the diagnosis of NTG: IOP < 21 mmHg, CD ratio over 0.5 or the difference between two eyes >0.2, glaucomatous field defects (scotomata) which cannot be explained by neurologic or fundus lesion and the iridocorneal angle is open.

Statistical analysis of data:

For numerical data, mean and standard deviations were calculated and unpaired student (t) test was used for comparison. On the other side, categorical variables were expressed as frequency and percent distribution, and group comparison was carried out by Chi square (χ^2) or Mann-Whitney test. Spearman's correlation coefficient was calculated and p value <0.05

was considered significant. All statistical analyses were carried out by statistical package for social science (SPSS) version 18 (SPSS Inc., Chicago, USA).

RESULTS

The present study included 120 subjects, 60 presented with obstructive sleep apnea (study group) (five patients refused to complete the study and thus only 55 patients were included in the final analysis) and 60 without obstructive sleep apnea (control group). Both groups were comparable as regard to patient gender (males represented 50.9% and 48.3% of study and control groups respectively, $P=0.78$). In addition, patient age ranged from 39 to 66 years; and there was no significant difference between OSA and control groups as regard to age; 57.96 ± 4.99 vs 56.65 ± 4.72 years respectively, $P=0.15$. Also, both groups were comparable as regard to patients' weight, height and BMI; $P=0.16$, 0.21 , and 0.93 respectively. Further, there was no significant differences between both groups as regard to hypertension, was reported in 45.2% of all subjects, while diabetes, reported in 46.1% and ischemic heart disease (IHD) was reported in 17.4% and there was no significant difference between both groups; $P=0.24$, 0.80 , and 0.78 respectively (table 1).

In the present study, intraocular pressure (IOP) ranged from 14 to 20 mmHg; and there was no significant difference between OSA and control groups (17.09 ± 1.33 vs 16.63 ± 1.31 respectively). Regarding to cup to disk (CD) ratio; ranged from 0.2 to 0.8 and there was statistically significant increase in OSA when compared to control group (0.32 ± 0.18 vs 0.22 ± 0.06 respectively, $P< 0.001$). Similarly, the development of normal tension glaucoma was significantly ($P< 0.001$) more prevalent in patients with OSA (27.3%) when compared to control group (3.3%). The visual field defect was in the form of nasal step, arcuate scotoma, paracentral scotoma and Bjerrum scotoma in 2, 5, 3 and 5 patients in OSA group and in 0, 1, 0, 1 in control groups respectively with statistically significant difference ($P< 0.009$) (table 2).

The apnea hypopnea index (AHI) ranged from 0 to 40 with statistically significant increase in OSA when compared to control group (17.80 ± 9.26 vs 1.98 ± 1.15 respectively, $P< 0.001$). The AHI grades in OSA group were mild in 28 patients (50.9%), moderate in 20 patients (36.4%) and severe in 7 patients (12.7%). In addition, oxygen desaturation index (ODI) ranged from 2 to 52 with significant increase in OSA group (17.02 ± 12.24) when compared to control group (2.71 ± 1.64), $P< 0.001$). On the other side, mean oxygen saturation was significantly decreased in OSA group when compared to control group (92.60 ± 4.70 vs 94.73 ± 1.90 respectively, $P< 0.001$) (table 2).

Table (1):Comparison between OSA and control groups as regard to patient demographics and associated chronic medical disease

Variables		OSA group (n=55)	Control group (n=60)	Total (n=115)	χ^2 t-test*	P-value
Sex (n,%)	Male	28(50.9%)	29(48.3%)	7(49.6%)	0.07	0.78
	Female	27(49.1%)	31(51.7%)	8(50.4%)		
Age (year): Range:		57.96±4.99 39-66	56.65±4.72 45-65	7.27±4.87 39-66	1.44*	0.15
Weigh (kg, M± SD) Range:		109.05±5.77; 91-120	107.66±4.77 89-115	108.33±5.29 89-120	1.39*	0.16
Height (m, M± SD)) Range:		1.651±0.043 1.58-1.74	1.642±0.035 1.55-1.70	1.646±0.039 1.55-1.74	1.24*	0.21
BMI (kg/m ²) Range:		39.98±1.58 35.86-42.58	39.95±2.15 35.65-47.87	39.96±1.89 35.65-47.87	0.07*	0.93
Hypertension		28(50.9%)	24(40.0%)	2(45.2%)	1.37	0.24
Diabetes mellitus		26(47.3%)	27(45.0%)	3(46.1%)	0.06	0.80
Ischemic heart disease		9(16.4%)	11(18.3%)	10(17.4%)	0.08	0.78

Table (2):Comparison between OSA and control groups as regard to results of ophthalmologic and polysomnographic examination

Variables		OSA group (n=55)	Control group (n=60)	Total (n=115)	χ^2 t-test*	P-value
IOP Range:		17.09±1.33 15-20	16.63±1.31 14-20	16.85±1.31 14-20	1.87*	0.06
CD ratio Range:		0.32±0.18 0.2-0.80	0.22±0.06 0.2 -0.5	0.27±0.14 0.20-0.80	3.81*	<0.001**
Glaucoma		15(27.3%)	2(3.3%)	17(14.8%)	13.05	<0.001**
Field defect	Nasal step	2(3.6%)	0(0.0%)	2(1.7%)	13.44	0.009**
	Arcuate scotoma	5(9.1%)	1 (1.7%)	6(5.2%)		
	Paracentral scotoma	3(5.6%)	0(0.0%)	3(2.6%)		
	Bjerrum scotoma	5(9.1%)	1 (1.7%)	6(5.2%)		
AHI Range:		17.80±9.26 8-40	1.98±1.15 0.0- 4.0	9.54±10.21 0 -40	13.11*	<0.001**
AHI Grade	Mild	28(50.9%)	---	---	---	---
	Moderate	20(36.4%)	---	---	---	---
	Severe	7(12.7%)	---	---	---	---
ODI Range:		17.02±12.24 6-52	2.71±1.64 2-11	9.56±11.13 2-52	8.96*	<0.001**
O ₂ So ₂ Range:		92.60±4.70 80-99	94.73±1.90 88-98	93.71±3.67 80-99	3.23*	0.002**

CD: cup to disk, ODI: oxygen desaturation index, AHI: apnea hypopnea index , **: Statistically significant difference

Table (3): Correlation between AHI and other variables

Variables	AHI*	
	r	p
Age	-0.11	0.26
Weight	0.08	0.41
Height	-0.03	0.72
BMI	0.11	0.25
IOP	0.42	0.001**
ODI	0.91	0.001**
CD ratio	0.76	0.001**
O ₂ saturation	-0.72	0.001**

*AHI: apnea hypopnea index.

** : Statistically significant difference

In the present work, AHI was proportional and significantly correlated with each of IOP, ODI, CD ratio and inversely correlated with oxygen saturation. However, there was no significant correlation with patient age, weight, height and BMI (table 3).

DISCUSSION

The present study revealed that OSA was associated with a 27.3% prevalence of normal tension glaucoma, which is significantly higher when compared to patients without OSA matched for age, sex and BMI. These results are comparable to those reported by **Bendel et al.**⁽¹¹⁾ in 2008 who studied one hundred patients with moderate to severe OSA to estimate the prevalence of glaucoma, and they diagnosed glaucoma in 27%. Also, **Waller et al.**⁽¹²⁾ carried out a study on 100 OSA patients, and reported glaucoma prevalence of 27%.

Furthermore, **Friedlander et al.**⁽¹³⁾ reported a prevalence rate of 21.0% of primary open angle glaucoma among patients with OSA. However, the reported incidence in the present study is lower than that reported by **Gharraf et al.**⁽¹⁴⁾ who demonstrated that normal tension glaucoma was encountered in 35% (14 out of 40 patients) and in 6.7% of obese patients without OSA with statistically significant difference between the two groups. On the other side, **Mojon et al.**⁽¹⁵⁾ reported a prevalence of 7.2% in patients with OSA. In addition, **Mohamed and Massoud**⁽¹⁶⁾ reported a prevalence rate of 16.67% of glaucoma among OSA patients.

In the present work, both patients with OSA and control subjects were matched for age, sex, weight, height, BMI and comorbid conditions. These results contradict those reported by **Aptel et al.**⁽¹⁷⁾ who reported that patients with OSA were older in age, had higher weight, BMI and usually males. The possible explanation for this contradiction could be attributed to the difference in study design, inclusion criteria and sample size. The present work is a case-control, while that of **Aptel's et al.** study is a cross sectional.

In our study, there was no significant difference between patients with OSA and those without OSA as regard to IOP. These results are comparable to those reported by **Shalaby et al.**⁽¹⁸⁾ who reported that, the IOP of patients with primary open angle glaucoma (POAG) with and without OSA showed no significant difference.

In the present study, there was significant increase of CD ratio in patients with OSA when compared to controls. In addition, CD ratio was significantly correlated with AHI. These results are comparable to those reported by **Gharraf et al.**⁽¹⁴⁾ and **Kargi et al.**⁽¹⁹⁾ who reported that the thickness of retinal nerve fiber layer (RNFL) was significantly reduced in

patients with OSA compared to control subjects, and this decrease is significantly correlated with OSA severity. These effects were attributed to decreased ocular perfusion related to hypoxia and vasospasm of OSA, and reported that, RNFL may precede clinical detection of glaucoma, representing an opportunity for early detection glaucoma.

RNFL thinning in OSA could be attributed to two mechanisms; the first included the following sequence: the sleep in OSA is associated with a decrease in the ventilatory drive due to hypoxia and hypercapnia. Hypoxemia is associated with production of high levels of vasoconstrictor endothelin. In addition, in OSA, the nitric oxide production (vasodilator) is markedly impaired⁽²⁰⁾.

The second mechanism is that the nocturnal vascular changes caused by OSA may be the cause of RNFL thinning. Hypoxia indirectly elevates intracranial pressure during sleep and reduced cerebral perfusion pressure may disturb blood supply of the optic nerve in patients with OSA. Vascular disturbances may cause diffuse loss or localized defects of the RNFL before the clinical manifestations of glaucoma⁽²¹⁾.

In our study, the visual field changes was deep and close to fixation point in 10 of the 17 (58.8%) patients with field changes and it was comparable to **Capriole et al.**⁽²²⁾ study that found visual field defects in NTG to be significantly deeper and closer to fixation than in other types of glaucoma.

In the present work, there was positive, significant correlation between OSA severity (measured by AHI) and glaucomatous changes; the results, which comparable to those reported by **Aptel et al.**⁽¹⁷⁾. In addition, they reported increased prevalence of glaucoma with increased severity of OSA.

The present study confirmed the association between OSA and development of glaucoma. This association could be explained by one of two theories, mechanical or vascular. The mechanical one postulated that, optic nerve changes are due to raise in IOP due to disturbance of sleep architecture and an increase in sympathetic tone. The vascular theory proposes that repeated and prolonged hypoxia due to upper airway collapse may decrease the oxygen supply to the optic nerve with subsequent development of optic neuropathy⁽⁴⁾.

CONCLUSION

Results of the present work revealed that, there is an increased prevalence of normal tension glaucoma in obstructive sleep apnea and it's significantly associated with disease severity.

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