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Prevalence of glaucoma in patients with obstructive sleep apnea

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Abstract

Introduction: Determining prevalence of glaucoma in patients with obstructive sleep apnea syndrome (OSAS) could be meaningful from public health point of view in Indian scenario, given that only few studies are reported so far.

Aim: To study the prevalence of glaucoma in patients with OSAS.

Materials and Methods: This was a prospective, observational study carried out between June 2014 and June 2016 in a tertiary care hospital. The study enrolled patients who were diagnosed with OSAS by the overnight polysomnography, depending upon inclusion and exclusion criteria. The included patients underwent complete ophthalmological evaluation including visual acuity, intra-ocular pressure, slit lamp examination with biomicroscopy, gonioscopy, indirect ophthalmoscopy, automated perimetry and optical coherence tomography.

Results: A total of 34 patients diagnosed with OSAS (28 male; mean age 53.94±14.34 year) were included in the study. Among 34 patients, 16 patients had severe, 13 had moderate and 5 had mild OSAS, respectively. Of the 34 patients included in the study, 10 patients had glaucoma (n=5 primary open angle glaucoma and n= 5 preperimetric glaucoma) with prevalence of 29.4%. There is no correlation between severity of OSAS and mean deviation (r= -0.062; p=0.73), pattern standard deviation (r= -0.024; p=0.89) and retinal nerve fibre layer thickness (r= 0.057; p=0.751). Duration of OSAS negatively correlated with RNFL thickness (r= -0.736; p<0.001).

Conclusions: Our study demonstrated high prevalence of glaucoma in patients diagnosed with OSAS in Indian scenario. However, further large scale studies are required.

Keywords: Obstructive sleep apnea syndrome, Glaucoma, Ophthalmic disorders, Optical coherence tomography, Prevalence.

Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent complete or partial upper airway obstruction during sleep which may last up to 2 minutes, leading to negative intrathoracic pressure, hypoxia and hypercapnea. The consequence of these changes triggers arousal from sleep due to increase in ventilator drive. Repetitive sleep disruption during night causes excessive daytime sleepiness, chronic fatigue and decreased cognitive abilities. OSAS has been identified as risk factor in cardiovascular, cerebrovascular, behavioral, cognitive, metabolic and endocrinological disorders.[(1)] Moreover, several studies also documented association between OSAS with some ophthalmological disorders, namely floppy eyelid syndrome, keratoconus, papilledema, optic neuropath, filamentary or infectious keratitis and papillary conjunctivitis.[(2-8)]

Glaucoma is a progressive optic neuropathy described as a distinctive pattern of optic nerve head and visual field defects.[(1)] It is the second leading cause of irreversible blindness (14% of all blindness) worldwide and it is estimated that 79.6 million people will be affected by the disease in the year 2020.[(9)] However, the disease remains asymptomatic until well advanced. In 1982, Walsh and Montplaisir first reported the association between OSAS and glaucoma.[(10)] Recently, several studies also reported a link between glaucomatous changes in patients with OSAS.[(11-14)] However, there is scarcity of data related to prevalence of glaucoma in patients with OSAS in Indian scenario. Hence, this study was designed to investigate prevalence of glaucoma in patients diagnosed with OSAS. Current optical coherence technology (OCT) technology, simple-to-use, and cost-effective tool with the use of spectral domain, allows direct visualization and measurement of various parameters with improved accuracy. Hence, we also performed OCT to determine change in RNFL thickness in patients with OSAS.

Methodology

This prospective, observational study recruited patients who were diagnosed with OSAS by the sleep unit of the neurology department of Amrita Institute of medical sciences between June 2014 and June 2016. All the patients diagnosed with OSAS (by sleep unit) by overnight polysomnography. The patients were excluded from the study if they had one of the following: 1) history of uveitis, family history of glaucoma, pre-existing anterior segment and retinal disorders, chronic steroid use, heavy smoking and alcohol abuse; 2) co-existing neurological diseases that might affect visual field; 3) secondary glaucoma; or 4) severely ill patients who were unable to perform automated perimetry.

Polysomnography was constituted by two EEG channels, two EOG channels, one EMG channel recording from the submental muscle, one nasal current channel, one thoracic motion channel, one abdominal motion channel, one oximeter channel, a microphone,

two leg movement channels from the right and left anterior tibialis muscles, and video recordings made during night time. Patients were diagnosed with OSAS based on apnea-hypopnea index (AHI) (AHI<5 was considered normal; AHI between 5 and 15 was considered as "mild OSAS"; AHI between 16 and 30 as "moderate OSAS" and AHI over 30 was regarded as "severe OSAS").

All patients enrolled in the study underwent a comprehensive ophthalmological examination including best-correct visual acuity, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy with a three-mirror contact lens and fundoscopy. Central corneal thickness (CCT) was measured by taking the average of 5 consecutive ultrasound pachymetry measurements. Automated visual field (VF) examination was performed with Swedish Interactive Threshold Algorithm (SITA) standard 30-2 Humphrey automated perimetry (Carl Zeiss Meditec Inc., Dublin, California, USA). A reliable visual field was defined as one with <20% fixation loss and <33% false positive or false negative errors. The procedure was repeated twice and only reproducible and reliable fields were included in the study. Mean deviation (MD) and pattern standard deviation (PSD) were recorded for each patient. OCT was performed using spectral domain OCT (Carl Zeiss Meditec Inc., Dublin, California, USA; HD-OCT Model 400) following dilation of pupils (with 1% tropicamide and 10%phenylephrine). Three images were obtained with each image consisting of 256 A-scans along with a 3.4mm diameter circular ring around the optic disc. Peripapillary retinal nerve fibre layer (RNFL) was automatically calculated by Fast RNFL algorithm.

Following criteria were adopted for diagnosis of primary open angle glaucoma: 1) glaucomatous optic disc changes which was defined as optic nerve cupping (cup-disc ratio (c/d) >0.5 or cup-disk asymmetry >0.2), neuroretinal rim thinning, partial or complete focal disc notching, and rim hemorrhages; 2) corresponding visual field defects (such as localized defects, paracentral scotoma, Bjerrum scotoma, nasal step, temporal sector defect, and diffuse defect which cannot be explained by any neurologic or fundus lesion) OR corresponding glaucomatous visual field defects (3 or more significant ($p<0.05$) nonedge contiguous point with at least 1 at the $p<0.01$ level on the same side of horizontal meridian in the pattern deviation plot and graded outside normal limits in the glaucoma hemifield test); 3) Open iridocorneal angle on gonioscopy. The patients was considered to have pre-perimetric glaucoma if 1) glaucomatous disc changes as defined above; 2) normal visual fields and 3) open angles on gonioscopy.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics version 20 (SPSS Inc., Chicago, IL, USA). Quantitative data was given as mean±SD. ANOVA test or Chi-square was used to compare data among three groups. The correlation between AHI and ophthalmological variables as well as RNFL thickness and duration of OSA was analysed by Spearman correlation analysis. A p-value below 0.05 was accepted as statistically significant.

Results

A total of 36 patients were diagnosed with OSAS during study period. However, as one patient had proliferative diabetic retinopathy in both eyes and 1 patient had macular hole in one eye, they were excluded. Hence, this study finally included 34 patients (28 males; 6 females) with OSAS. Age of the patients ranges from 16 years to 74 years (mean 53.94±14.34 year). Average oxygen saturation and BMI was 72.81±14.81 and 31.19±5.14 kg/m^2, respectively. Comorbidities were diabetes mellitus (13), hypertension (16) and coronary artery disease (6). Among included patients with OSAS, 5 had mild OSAS, 13 had moderate OSAS and 16 had severe OSAS.

Of the 34 patients included in the study, 5 patients (n=2 moderate OSAS; n=3 severe OSAS) had primary open angle glaucoma (14.7%) and 5 patients (n=1 mild OSAS; n=3 moderate OSAS; n=1 severe OSAS) had preperimetric glaucoma (14.7%). Hence, the overall prevalence of glaucoma was 29.4%.

Pearson correlation was performed to determine correlation AHI and various ophthalmic parameter. There is statistically significant negative correlation between RNFL thickness and duration of OSAS ($r= -0.736$; $p<0.001$). However, AHI did not statistically significantly correlate with MD ($r= -0.062$; $p=0.73$) and PSD ($r= -0.024$; $p=0.89$) and RNFL thickness ($r= 0.057$; $p=0.751$).

Discussion

Recent research revealed OSAS as a risk factor for glaucoma. Both mechanical and vascular factors are postulated to be involved in the pathogenesis of glaucoma.[1] In vascular theory, it is hypothesized that insufficient blood supply due to repetitive upper airway collapse lead to repetitive and prolonged episodes of hypoxia and hypercapnia which directly damage to optic nerve. Moreover, arousal from sleep activates sympathetic tone. As a consequence of sympathetic activation, there will be cascade of reactions which eventually damage optic nerve.[1,15] Mechanical theory considers that OSAS changes normal sleep architecture and activates sympathetic tone that may increase intraocular pressure. Raised intraocular pressure lead to axon damage at optic nerve and ultimately cause glaucoma.[1,15]

Several studies demonstrated high prevalence of glaucoma in patients with OSAS (Table 3). Moreover, long-term retrospective study also reported a statistically significant increase in the incidence of

glaucoma in patients with OSAS compared to patients without OSAS. It should be noted that patients with glaucoma can loss 40% retinal ganglion cell axons before manifestation of visual defect.[16] As the treatment of OSAS has been found to stabilize glaucoma, ophthalmic evaluation of all patients diagnosed with OSAS is endorsed. However, to the best of our knowledge, none of the previous study has investigated prevalence of glaucoma in patients with OSAS in Indian scenario. Hence, we designed this study to determine prevalence of glaucoma in patients with OSAS in Indian scenario.

In our study, majority of the patients with OSAS were male (28/34) which reflected fact that OSAS is more prevalent in male gender. Overall prevalence of glaucoma in our study was 29.4% which is higher than other reported studies. The unexpectedly higher prevalence of glaucoma in our study may be attributed by variation in diagnostic criteria of glaucoma. We adopted criteria which diagnosed 5 glaucoma suspects (based upon optic nerve changes only) as patients with glaucoma (preperimetric glaucoma). The study design can be considered as another potential cause of higher prevalence of glaucoma in our study as ophthalmic examinations were conducted with the knowledge that all the patients had OSAS. The results of our study also revealed RNFL thickness decreased as duration of OSAS increased. There is no correlation of severity of OSAS with MD, PSD and RNFL thickness. However, interpretation of results needs consideration of smaller sample size.

We acknowledge limitations of the study. First, the study enrolled limited sample of patients. Second, the study did not include control subjects without OSAS. Third, the study did not examine effect of treatment for OSAS on RNFL thickness i.e. Whether treatment prevents decrease in RNFL thickness. Despite of these limitations, the study provides valuable information. In conclusion, the results of our study demonstrated high prevalence of glaucoma in patients diagnosed with OSAS in Indian scenario. Hence, we recommend that all the patients diagnosed with OSAS should be examined for glaucoma. However, further large scale studies are required to confirm the findings of study.

Table 1: Demographic and baseline clinical characteristics of the patients according to severity of obstructive sleep apnea syndrome

Parameters	Mild OSAS n=5	Moderate OSAS n=13	Severe OSAS n=16	p-value
Age, years (mean±SD)	60 ± 13.8	54 ± 15.1	51± 14.1	0.529
Male, n (%)	4 (14.3%)	10 (35.7%)	14 (50.0%)	0.760
BMI, kg/m^2 (mean±SD)	28.4 ± 1.9	30.9 ± 6.4	32.3 ± 4.6	0.344
IOP, mmHg (mean±SD)	16.3 ± 2.3	17.3 ± 2.8	17.1 ± 3.0	0.789
CCT, micron (mean±SD)	556.6 ± 28.6	526.8 ± 30.2	538.6 ± 24.8	0.128
Rim area, (mean±SD) mmsq	1.18 ± 0.22	1.13 ± 0.25	1.15 ± 0.39	0.948
Disc area, (mean±SD) mmsq	2.28 ± 0.44	2.24 ± 0.49	2.12 ± 0.31	0.639
VCDR, (mean±SD)	0.56 ± 0.15	0.62 ± 0.15	0.57 ± 0.18	0.690
MD, (mean±SD)	-2.08 ± 0.90	-2.69 ± 1.42	-5.33 ± 5.73	0.149
PSD, (mean±SD)	2.39 ± 0.54	3.22 ± 1.80	4.14 ± 3.84	0.456
RNFL, microns (mean±SD)	68.12±7.62	68.69±7.83	66.64±10.13	0.825

BMI- body mass index; CCT- corrected corneal thickness; IOP-intraocular pressure; MD-mean deviation; PSD-pattern standard deviation; RNLF –retinal nerve fiber layer; VCDR – vertical cup disc ratio

Table 2: Baseline characteristics of glaucoma and non-glaucoma groups

Parameters	Glaucoma right eye	Glaucoma left eye	Non-glaucoma right eye	Non-glaucoma left eye
IOP, (mean±SD) in mmHg	19.5 ±3.72	20.1 ±2.69	15.58±1.74	16.25 ±2.03
CCT, (mean±SD)	541.20 ±27.7	541.30±28.7	533.88 ±30.0	535.17±28.1
VCDR, (mean±SD)	0.82 ±0.08	0.82±0.07	0.50±0.09	0.82±0.07
RNFL, microns (mean±SD)	72 ±12.21	73.5 ±9.02	88.96 ±7.9206	89.71±7.47
MD, (mean±SD)	-7.77 ±8.81	-5.59 ±6.22	-2.85 ±1.27	-2.71±0.97
PSD, (mean±SD)	6.83±4.68	5.71±4.75	2.40±1.39	2.58 ±0.60

CCT- corrected corneal thickness; IOP-intraocular pressure; MD-mean deviation; PSD-pattern standard deviation; RNLF –retinal nerve fiber layer; VCDR – vertical cup disc ratio

Table 3: Prevalence of glaucoma in patients with obstructive sleep apnea syndrome in published studies

Name of author (Publication year)	Patients with OSAS	Study design	Type of glaucoma	Incidence/ Prevalence of glaucoma
Mojon et al. (1999) (6)	n=69	Cross-sectional	POAG	7.2%
Geyer et al. (2003) (17)	N=228	Cross-sectional	POAG	2%
Sergi et al. (2007) (14)	n=51	Cross-sectional	NTG	5.9%
Bendel et al. (2008) (18)	n=100	Case-series	NTG	27%
Karakucuk et al. (2008) (19)	n=31	Cross-sectional	POAG and NTG	12.9%
Kadyan et al. (2010) (20)	n=89	Cross-sectional	POAG	3.4%
Lin et al. (2011) (13)	n=209	Cross-sectional	NTG	5.7%
Hashim et al. (2014) (11)	n=39	Longitudinal	POAG and NTG	20.51%

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