Original Article
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Medical Journal of the Islamic Republic of Iran (MJIRI)
Iran University of Medical Sciences

Obstructive sleep apnea syndrome and non-arteritic anterior ischemic optic neuropathy: a case control study

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Received: 25 January 2015 Accepted: 16 September 2015 Published: 22 November 2015

Abstract

Background: Sleep apnea is temporary cessation or absence of breathing during sleep. Significant increase in blood pressure is clinically seen in apneic episodes. The aim of this study was to examine sleep apnea syndrome as a risk factor for non- arthritic anterior ischemic optic neuropathy (NAION) in a case control study.

Methods: Nineteen NAION patients (9 men and 10 women) and 31 age and sex matched control participants (18 men and 13 women) were evaluated for obstructive sleep apnea syndrome (OSAS). Full night polysomnography was performed and proportion of OSAS was compared between the NAION patients and the control group. Other risk factors for NAION such as hypertension, diabetes, hyperlipidemia, ischemic heart disease and tobacco consumption were also evaluated. Chi square test and independent samples t-test were used for statistical analysis.

Results: OF the 19 NAION patients, 18 (95%) had OSAS, and of the control group 13 (41.9%) had OSAS. The frequency of OSAS was significantly higher among NAION patients compared to the controls ($p< 0.001$). The Mean Respiratory Disturbance Index (RDI) was 37.65/h SD= 37.61/h in NAION patients and it was 15.05/h SD= 11.97/h ($p= 0.018$) in controls. The frequency of diabetes and hypertension was significantly higher in the NAION patients than in controls.

Conclusion: based on the results of this study, it seems that there is an association between NAION and OSAS.

Keywords: Non-Arteritic Anterior Ischemic Optic Neuropathy, Obstructive Sleep Apnea Syndrome, Polysomnography, Respiratory Disturbance Index.

Cite this article as: Ghaleh Bandi MF, Naserbakht M, Tabasi A, Marghaiezadeh A, Riazee Esfahani M, Golzarian Z. Obstructive sleep apnea syndrome and non-arteritic anterior is-chemic optic neuropathy: a case control study. *Med J Islam Repub Iran* 2015 (22 November). Vol. 29:300.

Introduction

Non-arthritic Anterior Ischemic Optic Neuropathy (NAION) is a disease characterized by sudden, painless visual loss that may progress over hours to days. Visual acuity is almost always decreased and visual field examination reveals altitudinal field defects. The inferior (visual) field, is involved more than the superior(visual) field, particularly in nasal quadrant (1). This condition is due to retrolaminar optic nerve infarction because of obstruction or decreased perfusion through short posterior ciliary arteries (2). NAION typically occurs among patients over 50 years of age (3). The annual incidence rate of the disease is estimated to be 2.3 -10.3 cases per 100000 persons in all ages (4). The prevalence rate

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of the disease is 0.54 per 1000000 persons in all ages (5). The exact cause of NAION is not known; however, some of systemic conditions accompanied with NAION consist of systemic hypertension (1,4,6,7), ischemic heart disease (1,4,6-9) hypercholesterolemia (1,6), stroke (1), smoking (1,4,7), nocturnal hypotension (1,4,8-10) and atherosclerosis (1).

Sleep apnea is temporary cessation or absence of breathing during sleep. Significant increase in blood pressure is clinically seen in apneic episodes. The maximal elevations occur after the resumption of ventilation. If apneic spells occur continually during sleep, it may lead to severe decrease in blood O2 saturation. At this time, elevation in blood pressure is very severe and it may rise to 200 mmHg in systolic blood pressure and 120 mmHg in diastolic blood pressure. Despite the strong effect of hypercapnia in vasodilatation of cerebral vessels, cerebral blood flow during sleep decreases in apneic patients more than other people. Several mechanisms which may explain the association of OSA and NAION include: a) Impaired optic nerve head blood flow auto regulation secondary to repeated apneas (11); b) Optic nerve vascular dysregulation secondary to OSA-induced arterial blood flow variations; c) Arterial hypertension and arteriosclerosis; this dysregulation may be due to the imbalance between nitric oxide and endothelia; d) Platelet activation may cause micro infarcts in the optic nerve (12); e) Direct optic nerve damage can occur as a consequence of repetitive or prolonged hypoxia or increased intracranial pressure during the repetitive apnea (13).

Considering the mentioned points, it can be presumed that sleep apnea syndrome can act as a risk factor for NAION particularly because most affected patients with NAION notice their visual loss first after they wake up (10). This prospective case control study was designed to evaluate the association between abstractive sleep apnea syndrome and NAION, but the methodology we used was slightly different from that of the previous studies. Moreover, we matched age, which was an important confounding factor in previous studies, in the two groups in this study.

Methods

We designed and conducted a case-control study. This study was a prospective age and sex matched case control study performed over 53 months (February 2007-Agust 2011). The NAION group consisted of 19 patients who referred to the Neuroophthalmology Clinic of Farabi hospital in Tehran University of Medical Sciences, Tehran, Iran. A neurologist and an ophthalmologist confirmed the diagnosis. The inclusion criteria were as follows: Sudden painless visual loss, optic disk swelling accompanied with flame shape hemorrhages followed by optic disk pallor in ophthalmoscopy exam, and relative afferent papillary defect and visual field defects consistent with optic neuropathy. To exclude such diseases as optic neuritis and temporal arteritis, patients younger than 45 years of age underwent more investigations including magnetic resonance imaging, and those patients who had erythrocyte sedimentation rate> 40 mm/h underwent a biopsy to rule out temporal arteritis. Patients who had temporal arteritis or other vasculitis were excluded.

The control group was selected from those patients who came to a psychiatry clinic. All persons in the control group were within the age range of the case group, no evidence of NAION was found in them. Moreover, none of them had a history of psychiatric disease. Their illness put them in the category of mild anxiety and mood disorders, and they were not taking psychiatric drugs continuously.

For each NAION patient at least one age and sex matched control was selected. Written informed consent was obtained from all cases and controls. Both case and control groups were studied by a sleep specialist. To assess the symptoms, a questionnaire and Epworth Sleepiness Scale were used for each individual. All participants

were investigated for sleep apnea syndrome by full night standard polysomnography. Polysomnography was performed while the patient was breathing the room air. Electrophysiological sleep parameters included Central, occipital EEG, right and left EOG and submental EMG; periodic limb movements were monitored by anterior tibialis EMG, airflow, respiratory effort, arterial pulse oximetry and ECG. Raw data were manually scored in 30 second epochs for sleep stages using the Rechtschaffen & Kales standard criteria (14) Apnea is defined as a decrease in the airflow to 0-20% of normal that lasts for a period of 10 seconds or longer and hypopnea is a decrease in airflow of 10 seconds or more and is scored when the decrease of airflow with desaturation of 3% or decrease of airflow at least 50% or decrease of airflow is accompanied with EEG arousal. Respiratory Disturbance Index (RDI) was computed as the total of all respiratory events divided by the total sleep time in hours. An expert sleep specialist analyzed all of polysomnography data of all participants in the study manually. Diagnosis and grading of sleep apnea syndrome were based on RDI; and the RDI<5 was regarded as normal, RDI of 5-20 was defined as a mild disease, RDI of 20-40 was considered as moderate disease and RDI> 40 as severe disease.

In addition, other risk factors such as hypertension, diabetes mellitus, ischemic heart disease, and hyperlipidemia and tobacco consumption were investigated in both groups.

Statistical Analysis

The prevalence of qualitative variables in case and control groups were compared using chi square test, and continuous variables were described by mean (SD), and means were compared by independent samples t-test. Backward stepwise logistic regression (with the presence or absence of NAION as the dependent variable) was employed to identify variables that were independently associated with NAION. A two sided $p< 0.05$ was considered statistically significant.

Results

The NAION and control groups consisted of 19 and 31 participants, respectively (9 men and 10 women in NAION group and 18 men and 13 women in the control group). The prevalence of diabetes, hypertension, hyperlipidemia and IHD in the NAION group was more than the control group, but a significant relationship was found for diabetes ($p< 0.001$) and hypertension ($p= 0.001$). Only one participant in the NAION group had a history of cerebrovas-

Table 1. Demographic Characteristics and Clinical Characteristics among NAION cases and controls

	Cases (N=19)	Controls (N=31)	p
Body Mass Index (Mean±SD)	27.8±3.5	27.5±5.2	0.81
Diabetes (n (%))	9(45%)	1(3.2%)	<0.001
Hypertension (n (%))	13(68.4%)	6(19.6%)	0.001
Hyperlipidemia (n (%))	3(15%)	0(9.4%)	0.02
Tobacco Consumption (n (%))	3(20%)	10(20.8%)	0.143
Ischemic Heart Disease (n(%))	4(21.1%)	2(6.5%)	0.12

Table 2. Polysomnographic and Symptoms Data

	Case	Control	p
Epworth Sleepiness Score	8.8 SD=4.2	7.2 SD=3.9	0.186
Snoring	8(42.1%)	10(32.3%)	0.55
RDI	39.15 SD=38.01	9.03 SD=10.6	0.003
OSAS	18(95%)	13(41.9%)	<0.001
Mild	6(33.3%)	7(53.8%)	0.162
Moderate	5(27.8%)	5(38.5%)	
Severe	7(38.9%)	1(7%)	
Hypoxemia	13(68.4%)	8(32.3%)	<0.001
Mean O2 Saturation	91.1 SD=2.75	92.6 SD=2.5	0.055
Lowest O2 Desaturation	76.8 SD=10.86	84.9 SD=8.4	0.005

Table 3. Logistic Regression on Non-Arthritic Anterior Ischemic Optic Neuropathy

Variable	B	OR	SE	p
OSAS	3.335	28.070	1.409	.018
DM	2.839	17.103	1.276	.026
HTN	1.951	7.032	.875	.026

Note: The overall model attained Cox & Snell $R^2 = 0.47$

cular attack (CVA) (Table 1).

Eighteen (95%) of 19 patients with NAION had OSAS. According to RDI, 7 (35%) patients had mild disease, 5 (25%) moderate and 7 (35%) had severe disease. In the control group, among the 31 participants, 13 (41.9%) had OSAS, 7 (53.8%) had mild disease, 5 (38.5%) had moderate disease and only 1 (7%) had severe OSAS. There was a significant difference in the mean RDI between cases and controls (p=0.018 with 95%CI 4.303-40.902), and the prevalence of OSAS was significantly higher in NAION patients than in controls (p< 0.001) (Table 2).

All significant correlates of NAION were entered into a Backward Stepwise (Wald) logistic regression to predict NAION, OSAS, diabetic mellitus, hyperlipidemia, and hypertension, and they were all found to be significant predictors of NAION (Table 3). Overall, the model accounted for 47% of the variance in NAION.

Discussion

Only few studies evaluated the association between OSAS and NAION. Majon et al. compared the prevalence of OSAS in 17 NAION patients with 17 age and sex matched controls and found that 71% of NAION cases had OSAS diagnosed by overnight polysomnography compared to 24% prevalence of OSAS in controls (Pvalue:0.005) (10). Palombi et al. compared the prevalence of OSAS in 27 NAION patients with the prevalence of OSAS in the general population (15). They found 89% prevalence of OSAS in NAION group, and the risk ratio for a NAION patient to have OSAS was 4.9 compared to the general population. Stein and colleagues after adjusting for confounding variables, found that patients diagnosed with sleep apnea who were not treated with continuous positive airway pressure (CPAP) had a 16% increase in the hazard of developing NAION when compared to controls without sleep apnea (16).

Another case control study performed by Li et al. evaluated the association between OSAS and NAION (17); 73 NAION cases were compared with 73 age and sex matched controls using the Sleep Apnea scale of the Sleep Disorders Questioner (SA-SDQ). The results of their study revealed that the prevalence of OSAS in NAION patients and controls was 30.1% and 17.8%, respectively; and they also found that NAION patients were 2.62 times (95% CI 1.03 to 6.60) more likely to have OSAS than controls (16,18). These four studies found an association between OSAS and NAION, but Behbehani et al. reported 3 cases of OSAS that developed NAION despite of being treated with CPAP (19). In our study, the prevalence of OSAS was significantly higher among NAION patients than controls (p< 0.001), and the prevalence of OSAS in NAION patients was higher than what was reported in previous studies such as in Majon et al. Palombi et al. and Li et al. studies (95% versus 71%, 89% and 30.1%). However, the prevalence of OSAS in controls was obviously higher than other studies such as Majon et al. and Li et al. studies (35.8% versus 18% and 17.8%). In our study, 7 (36.8%) of NAION patients had severe form of OSAS and only 1 (7.1%) control participant had severe OSAS. Clinically, it seems that there is an association between NAION and severity of OSAS, but such an association is weak statistically (Chi square test p= 0.052) and perhaps this is due to the small sample size. In our study, the prevalence of diabetes, hypertension and ischemic heart disease was significantly higher in NAION patients than in controls. Therefore, it

seems logical to treat OSAS efficiently to prevent its complications and also evaluate patients with NAION for OSAS. As de Groot indicated in his review, several risk factors have been suggested for NAION including old age, systemic hypertension, hypercholesterolemia, diabetes mellitus, small cup-to disk ratio and sleep apnea. sleep apnea was found to be 1.5 to 2-fold more frequent than the rate of the other identified risk factors typically associated with NAION (hypertension, diabetes) (20). In this study, logistic regression analysis revealed that diabetes mellitus, hypertension and sleep apnea were significantly associated with NAION. In addition, sleep apnea was found to be 1.5 to 4-fold more frequent than the rate of the other identified predictive factors (hypertension, diabetes) associated with NAION. It is noteworthy to mention that the results of this study along with the results of other studies can help analyze the relationship between NAION and OSA.

Conclusion

The frequency of OSAS in patients with NAION in our study was very high (95%), suggesting that OSAS should be screened in all of NAION patients and NAION should be screened in all of OSAS patients (if age> 50).

Acknowledgments

This research was supported by Department and Research Center of ENT and Head & Neck Surgery Iran University of Medical Sciences.. We would like to express our appreciation to the “Noor Sleep Center” and “Neuroophthalmology Clinic of Farabi Hospital” for their participation in the implementation of this study.

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