Published in final edited form as:

J Neurol. 2013 July ; 260(7): 1748–1751. doi:10.1007/s00415-013-6858-6.

Obstructive sleep apnea in idiopathic intracranial hypertension: comparison with matched population data

Matthew J. Thurtell^{1,6,7,8,9}, Lynn Marie Trotti², Edward O. Bixler¹⁰, David B. Rye², Donald L. Bliwise², Nancy J. Newman^{1,2,3}, Valérie Biousse^{1,2}, and Beau B. Bruce^{1,2,4,5}

¹Department of Ophthalmology, Emory University, Atlanta, GA, USA

²Department of Neurology, Emory University, Atlanta, GA, USA

³Department of Neurological Surgery, Emory University, Atlanta, GA, USA

⁴Department of Rollins School of Public Health, Emory University, Atlanta, GA, USA

⁵Department of Laney Graduate School, Emory University, Atlanta, GA, USA

⁶Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa City, IA, USA

⁷Department of Neurology, University of Iowa, Iowa City, IA, USA

⁸Department of Neurology Service, Veterans Affairs Medical Center, Iowa City, IA, USA

⁹Center for the Prevention and Treatment of Visual Loss, Veterans Affairs Medical Center, Iowa City, IA, USA

¹⁰Department of Psychiatry, Pennsylvania State University College of Medicine, Hershey, PA, USA

Abstract

Patients with idiopathic intracranial hypertension (IIH) frequently have coexisting obstructive sleep apnea (OSA). We aimed to determine if the prevalence and severity of OSA is greater in patients with IIH than would be expected given their other risk factors for OSA. We included 24 patients (20 women, 4 men) with newly-diagnosed IIH who had undergone overnight polysomnography. We calculated the expected apnea-hypopnea index (AHI) for each patient, based on their age, sex, race, body mass index (BMI), and menopausal status, using a model derived from 1741 randomly-sampled members of the general population who had undergone overnight polysomnography. We compared the AHI values obtained from polysomnography with those predicted by the model using a paired t-test. Our study had 80% power to detect a 10 unit change in mean AHI at $\alpha=0.05$. Eight patients (33.3%; 6 women, 2 men) had OSA by polysomnography. AHIs from polysomnography were not significantly different from those predicted by the model (mean difference 3.5, 95% CI: $-3.0-9.9$, $p=0.28$). We conclude that the prevalence and severity of OSA in IIH patients is no greater than would be expected for their age, sex, race, BMI, and menopausal status. It remains unclear if the presence or treatment of OSA influences the clinical course of IIH.

Corresponding Author: Matthew J. Thurtell, M.B.B.S., F.R.A.C.P. Department of Ophthalmology & Visual Sciences University of Iowa 200 Hawkins Drive PFP Iowa City, IA 52242 mj.thurtell@gmail.com Tel: 319-356-1951 Fax: 319-353-7996.

Conflict of Interest: Dr. Thurtell reports no conflicts of interest. Dr. Trotti reports no conflicts of interest. Dr. Bixler reports no conflicts of interest. Dr. Rye reports no conflicts of interest. Dr. Bliwise reports no conflicts of interest. Dr. Newman reports no conflicts of interest. Dr. Biousse reports no conflicts of interest. Dr. Bruce reports no conflicts of interest.

Keywords

Idiopathic intracranial hypertension; Papilledema; Obstructive sleep apnea; Intracranial pressure

Introduction

Idiopathic intracranial hypertension (IIH; also known as pseudotumor cerebri) is a syndrome of increased intracranial pressure (ICP) of unknown etiology that most commonly occurs in obese women of childbearing age [1]. It is a diagnosis of exclusion, defined by the modified Dandy criteria: 1) signs and symptoms of increased ICP; 2) no localizing signs, except for sixth nerve palsy; 3) normal neuroimaging; 4) cerebrospinal fluid (CSF) opening pressure of >25 cmH₂O, with normal CSF constituents; and 5) no alternate explanation for the increased ICP [1]. Obstructive sleep apnea (OSA) is a common condition in which there are intermittent partial and complete limitations in airflow (i.e., hypopneas and apneas), with associated hypoxia and sympathetic arousals, during sleep [2]. It is associated with obesity, age, male sex, and post-menopausal status in women [2–5]. OSA is common in patients with IIH [6–8]. Because OSA is known to cause intermittent increases in ICP, it has been postulated to play a role in the pathogenesis of IIH in patients who have coexisting OSA [9–12]. However, because prior studies have lacked an IIH-free control group, it remains unclear if the prevalence and severity of OSA is greater in IIH patients than would be expected given their other risk factors for OSA, especially obesity. We aimed to compare the severity of OSA based on AHI determined by polysomnography in a group of IIH patients with their predicted severity of OSA had they been members of the general population with the same demographic features.

Materials and methods

Ethics Approval and Patient Consents

The study was approved by the Emory University Institutional Review Board. Only de-identified data were shared with non-Emory researchers. Since the data were collected and analyzed retrospectively, patients were not required to give written informed consent.

Patients

Between March 2008 and June 2010, IIH patients seen in the Neuro-Ophthalmology clinic at Emory University were referred for overnight polysomnography, to screen for OSA, as part of their routine evaluation. Polysomnography could not be obtained in all patients (e.g., in those who declined or did not have medical insurance). We included patients with a new diagnosis of IIH, satisfying modified Dandy criteria [1], in whom polysomnography had been obtained in the Sleep Disorders Center at Emory University. Included patients had a lumbar puncture and neuroimaging as part of their initial work-up. We excluded patients who were pregnant or aged less than 16 years. Demographic and anthropomorphic data (age, sex, race, body mass index [BMI], and menopausal status) were recorded at the initial evaluation.

Polysomnography

All patients had overnight laboratory-based video polysomnography in the Sleep Disorders Center at Emory University, including EEG, electro-oculography, surface mentalis and anterior tibialis EMG, EKG, respiratory airflow (measured by thermistor) and effort (measured by piezoelectric sensors), and oxyhemoglobin saturation. The presence of apneas and hypopneas was determined using the same criteria used for scoring the population data [3, 4]. An apnea was defined as a cessation of breathing >10 seconds and a hypopnea was

defined as a decrease in airflow of approximately 50% or more with an associated oxygen desaturation of 4% or more. The oxygen desaturation index (ODI) was calculated as the average number of oxygen desaturations of 4% or more per hour of sleep. The apneahypopnea index (AHI) was calculated as the average number of apneas and hypopneas per hour of sleep. OSA was considered present when the AHI was ≥ 5 ; the severity of OSA was graded as mild if the AHI was 5 to <15 , moderate if the AHI was 15 to <30 , and severe if the AHI was ≥ 30 [13].

Population Model

Using overnight polysomnography data from 1741 randomly-sampled members of the general population [3, 4], one of the authors (EOB) developed a multivariable linear regression model for predicting AHI on the basis of age, sex, race, BMI, and menopausal status. Based on this model, we were able to compare the AHIs of our ITH patients with the mean AHIs of a large number of population-based controls “matched” to our patients by age, sex, race, BMI, and menopausal status.

Data analysis

Univariate analyses were used to summarize the demographic data (age, race, sex, and BMI), AHIs from polysomnography, and AHIs predicted by the population-based model. AHIs from polysomnography were compared to those predicted by the population-based model using a paired t-test. Our study had 80% power to detect a 10 unit change in mean AHI at $\alpha=0.05$.

Results

Patient demographics

Twenty-four ITH patients were included; 20 were female (83%), 13 were white (54%), and 11 were black (46%). Ages ranged from 16–54 years (median, 32 years; mean $\pm$ SD, 32 ± 10 years). BMI ranged from 27.3–45.9 kg/m² (median, 39.5 kg/m²; mean $\pm$ SD, 38.1 ± 5.3 kg/m²). Two (10%) of the female patients were post-menopausal. No patient was receiving hormone-replacement therapy.

Thirty-one ITH patients were not included in the study, because they either did not obtain polysomnography as requested or the study was performed at another institution and unavailable for detailed rescoring using the same criteria as for the population data. There was no difference in age (mean, 31 years, $p=0.52$), sex (28 women [90%], $p=0.44$), race (16 black [52%], $p=0.67$), or BMI (mean, 38.5 kg/m², $p=0.81$) between the patients who were included in the study and those who were not.

Polysomnography results

Polysomnography-derived AHI ranged from 0–63.3 (median, 3.3; 9.4 ± 15.8 , mean $\pm$ SD). Note that central apneas (apneas without associated respiratory effort) were rarely observed. ODI ranged from 0–58.9 (median, 3.1; 8.8 ± 14.6 , mean $\pm$ SD). Eight patients (33.3%), six women (30%) and 2 men (50%), had OSA by polysomnography; 4 (16.7%) had mild OSA, 1 (4.2%) had moderate OSA, and 3 (12.5%) had severe OSA. AHIs from polysomnography were not significantly different from those predicted by the model (mean difference 3.5, 95% CI: -3.0 to 9.9 , $p=0.28$). Limiting the analysis to the four men in the study, the AHIs from polysomnography were not significantly different from those predicted by the population-based model (mean difference 0.53, 95% CI: -15.6 to 16.7 , $p=0.92$).

Discussion

OSA is known to be associated with headache and increased intracranial pressure [9]. Increases in intracranial pressure are thought to occur during apneic episodes because hypercapnia, hypoxia, and cerebral vasodilation bring about an increase in intracranial blood volume [9, 10]. It has been postulated that the increases in intracranial pressure may result in compression of the cerebral venous sinuses, giving rise to transverse venous sinus stenoses that lead to sustained increases in intracranial pressure and, consequently, IIH [12]. Indeed, OSA is said to be associated with IIH, but this presumption is largely based on the findings of non-consecutive case series [6, 7]. These series suggest that up to 60% of IIH patients have OSA [8]. However, since these series have lacked a control group, it remains unclear if OSA is an independent risk factor for IIH or, rather, a consequence of the high prevalence of other risk factors for OSA, especially obesity, in IIH patients [8]. A recent, retrospective analysis of billing records reported an increased hazard of IIH in patients with OSA who were not receiving continuous positive airway pressure (CPAP) therapy, but no increased hazard in those who were receiving CPAP therapy, suggesting that patients with untreated OSA are at increased risk of developing IIH [14]. However, because this study was only able to control for obesity through billing codes, rather than the patient's actual BMI (as in our study), residual confounding is likely to be present.

We obtained polysomnography in 24 newly diagnosed IIH patients and compared our findings with the predictions of a model derived from polysomnography data obtained from more than 1500 members of the general population, matched for age, sex, race, BMI, and menopausal status. Although our study was retrospective and included a relatively small number of patients, it was adequately powered to detect a clinically meaningful difference (10 unit change) in AHI; we found no difference between the values predicted by the model and those obtained in the patients. Our findings suggest that OSA occurs in IIH patients due to the presence of other risk factors for OSA, in particular obesity.

Our findings do not suggest that OSA is a risk factor for IIH, in itself, and concur with another study that found no papilledema among 35 OSA patients [15]. Several studies have suggested that there is a high prevalence of OSA in men with IIH [7, 16]. While it appears that our men had a higher than expected prevalence of sleep apnea (50%), there was no difference in their measured and predicted AHIs, based on their age, sex, race, and BMI. Nevertheless, given the small number of men included in our study, further investigation into whether or not OSA is a risk factor for IIH in men is needed. Polysomnography should still be considered in IIH patients who are at high risk for OSA [8], because it is associated with increased cardiovascular morbidity and mortality [17]. It remains unclear if the presence or treatment of OSA influences the severity or natural history of IIH [12]. Larger, prospective, and controlled studies are required to further evaluate the relationship between OSA and IIH, and the effect of OSA treatment on the clinical course of IIH.

Acknowledgments

Funding: NIH/NEI core grant P30-EY06360 (Department of Ophthalmology); Research to Prevent Blindness Lew R. Wasserman Merit Award (NJN); Department of Ophthalmology grant (MJT, BBB) from Research to Prevent Blindness Inc, New York, NY. In addition, Dr. Bruce receives research support from the NIH/NEI (K23-EY019341).

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