Sleep Medicine 45 (2018) 69–73

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Occurrence of nocturia is not mediated by nocturnal hypoxia length and severity in patients with sleep-disordered breathing

P. Finamore*, S. Scarlata, A. Laudisio, F. Galdi, M.E. Pipita, I. Chiarella, R. Giua, L. Cortese, C. Rivera, R. Antonelli Incalzi

Unit of Geriatrics, Campus Bio-Medico University, via Alvaro del Portillo 200, 00128 Rome, Italy

ARTICLE INFO

Article history:
Received 8 November 2017
Received in revised form
12 January 2018
Accepted 31 January 2018
Available online 7 February 2018

Keywords:
Nocturia
Polysomnography
Hypoxia
Oxygen desaturation index
Total sleep time with SpO_2<90%

ABSTRACT

Background: Nocturia is highly prevalent in subjects with respiratory sleep disturbances (ie obstructive sleep apnea). The aim of our study is to evaluate whether nocturia is associated with intermittent desaturations or hypoxia length and severity in people undergoing polysomnography.

Methods: We recruited 275 consecutive subjects attending the outpatient clinic for respiratory diseases at Campus Bio-Medico Teaching Hospital. Nocturia was defined as a self-reported voiding frequency ≥ two per night. The groups with and without nocturia were compared with parametric and non-parametric tests, as appropriated. Multivariable logistic regression analysis was used to assess the association of nocturia with patients' characteristics, including oxygen desaturation index (ODI), respiratory efforts (RE) and oxygen saturation below 90% (TST_{90}).

Results: Sixty-six (24%) subjects reported nocturia, the median ODI was 15 (8–31), the median RE was 22 (12–38) and the median TST_{90} was 4.7 (0.3–20.6). ODI and RE were significantly higher in subjects with nocturia as compared with controls. In the multivariable model, ODI was associated with an increased probability of nocturia (OR = 1.03; 95% CI = 1.01–1.06), and the higher the ODI score, the higher the probability to have nocturia (P for trend = 0.038). No significant association was found between TST_{90} and the occurrence of nocturia.

Conclusions: Intermittent desaturations and not hypoxia length and severity, expressed by TST_{90}, are associated with the occurrence of nocturia in subjects complaining sleep disturbances.

1. Introduction

Nocturia is a multifactorial condition affecting more than 30% of subjects over 60 years of age [1] and is usually assumed to be a correlate of benign prostatic hyperplasia in men and bladder incontinence in women. Nevertheless, nocturia is significantly more prevalent in patients with sleep-disordered breathing (SDB), mainly obstructive sleep apnea syndrome (OSAS), than in healthy controls [1], therefore nocturia should prompt a screening of SDB [2] if urological disorders, medical diseases (eg, diabetes mellitus, central diabetes insipidus, or congestive heart failure), or drugs cannot explain it. This suggestion especially applies to older adults, where the traditional hallmarks of OSAS (ie snoring, increased body mass index and neck circumference) are much weaker than in adults [3].

Nocturia is potentially harmful and deserves intervention because either, it negatively impacts the health status and increases the risk of developing depression by fragmenting sleep [4], or because it is associated with morbidity (eg hypertension) [5] and mortality [6]. Continuous positive airway pressure (CPAP) treatment is effective in reducing night-time voiding frequency and improves patients' quality of life [7], moreover reduced voiding after CPAP may be also used as a surrogate index of the response of hypertension to treatment [5].

Emerging evidence in animal models highlight different effects of intermittent and chronic hypoxia on human body. Genetic regulation studies have shown [8] that cycles of intermittent hypoxia/re-oxygenation affect tissues such brain, fat or muscle [9,10] and even gut microbiota [11]. While data in SDB patients suggest a relationship between nocturia and apnea/hypopnea index (AHI) [12], as of yet no clinical study has investigated whether this association is mediated by nocturnal hypoxia frequency or

Abbreviations: SDB, sleep-disordered breathing (SDB); AHI, apnea/hypopnea index (AHI); ODI, oxygen desaturation index (ODI); TST_{90}, sleep time with an oxygen saturation below 90%.

* Corresponding author. Department of Geriatrics Campus Bio-Medico University, Via Alvaro del Portillo, 200, 00128, Rome, Italy. Fax: +39 06 22 541 456.
E-mail address: p.finamore@unicampus.it (P. Finamore).

https://doi.org/10.1016/j.sleep.2018.01.009
1389-9457/

length and severity. Notably, Fanfulla et al., analyzing the relationship between daytime hypoxemia and nocturnal hypoxia in OSAS patients, demonstrated that hypoxia length and severity, expressed by a sleep time with an oxygen saturation below 90% (TST_{90}) is the likely determinant of the positive correlation observed between AHI and daytime hypoxemia [13]. Thus, TST_{90} might be an overall measure of biological impact of OSAS and, then, also a correlate of OSAS-related nocturia.

Therefore, the aim of our study is to evaluate whether nocturia occurrence is associated with intermittent desaturations or hypoxia length and severity.

2. Methods

Two-hundred-seventy-five subjects attending the pulmonary medicine outpatient clinic of the University Hospital "Campus Bio-Medico" were consecutively recruited to perform sleep polysomnography (PSG) in the suspicion of SDB. The clinical suspicion of SDB was based on the presence of any of the following known clinically predictive signs and symptoms: snoring, dry mouth, abnormal sleep duration and schedule, daytime nap habits, excessive daytime sleepiness, increased neck circumference, morbid obesity (BMI>36), facial or oropharyngeal dysmorphisms (macroglossia, micrognathism, uvulopalatal hypertrophy, or velopharinx collapse), and sleep apneas (referred by patients or their partners) [14,15]. All patients were also screened for excessive daytime somnolence using the Epworth Sleepiness Scale-ESS.

The investigation conforms to the principles outlined in the Declaration of Helsinki. All the study participants provided written informed consent. The study protocol was approved by the local Ethical Committee (protocol number: 47/11 CBM, Rome).

2.1. Nocturia

Nocturia was defined as a self-reported average frequency of voiding $\geq$ two per night in the previous year, because this threshold of nocturnal voids is considered to be clinically meaningful, reducing quality of life and correlating with negative outcomes [5,6].

2.2. Respiratory parameters

Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS), a self-administered eight question questionnaire with a total score ranging from 0 to 24. An ESS score higher than ten is associated with excessive daytime sleepiness [16].

All patients underwent an unattended overnight type II sleep study (SOMNOscreen™, SOMNOmedics, Italy) at the University Hospital "Campus Bio-Medico". The recorded parameters were oximetry, respiratory monitoring (including chest and abdominal effort), airflow and cardiac monitoring (including single lead EKG and heart rate), actigraphy, and light sensor and body position. Subjects were recommended to avoid caffeinated food and drinks, as well as alcohol which could interfere with sleep architecture. Subjects with a length of registration < 6 h were excluded from the analysis. Respiratory parameters were scored according to the standard criteria of the American Academy of Sleep Medicine (AASM). Apnea was defined as a reduction of the respiratory airflows >90% for at least 10 s, while hypopnea was defined as a $\geq$50% decrease in ventilation that was accompanied by a $\geq$ 3% decrease in oxygen saturation. Oxygen desaturation index (ODI) was defined as the number of instances of desaturation $\geq$ 4% recorded per hour of sleep. OSAS was diagnosed in subjects with a number of apnea and hypopnea events per hour of sleep (AHI index) $\geq$ 5. Dual efforts thoraco-abdominal piezoelectric belts were used for detection of respiratory efforts (RE) that we used as a proxy for breathing events unrelated to hypoxia.

Total sleep time with SpO_2<90% (TST_{90}) is the percentage of the sleep time spent with a SpO_2 lower than 90% and represents an arbitrary, but conventionally adopted, measure of hypoxic burden [17].

2.3. Statistical analysis

Data were recorded using a dedicated software with automatic coding of drugs and diagnoses. Statistical analyses were performed using SPSS for Mac 20.0. Differences were considered significant at the $P < 0.050$ level. Data of continuous variables are presented as mean values and standard deviation (SD). Medians and interquartile ranges were provided for non-normally distributed variables. Spearman's rho correlation analysis was performed to assess the correlation between ODI, AHI, RE, TST_{90}.

Analysis of variance (ANOVA) of patients grouped according to the occurrence of nocturia for normally distributed variables was usually performed; otherwise, the nonparametric Mann–Whitney U test was adopted. The two-tailed Fisher exact test was used for dichotomous variables. The covariates to be entered into analyses were chosen as explanatory according to available reviews and meta-analyses from the electronic databases of PubMed (MEDLINE) and Cochrane Library, based upon their efficiency and cheapness. AHI and ODI were expressed as number of events per hour of sleep. Severe OSAS was considered when AHI >30/h, as an independent variable. Educational level was expressed as years of school attendance. Diagnoses were coded according to the International Classification of Diseases, ninth edition, Clinical Modification codes. Drugs were coded according to ATC classification. On admission, adjudicated disease diagnoses were based on self-reported history, clinical documentation, clinician's judgment, and medication use. Body Mass Index (BMI) was calculated as weight (Kg) divided by height squared (m^2). Dry mouth and snoring were either self or bed-partner reported.

Multivariable logistic regression analysis was used to assess the association of experience of nocturia, with age, sex, ODI, and all those variables which differed significantly ($P < 0.050$) in univariate analyses. Abnormally distributed variables were analyzed after log transformation. Logistic regression analysis was also adopted to evaluate the association of increasing ODI tertiles with the occurence of nocturia. To rule out any role of TST_{90} in the association of nocturia with ODI, interaction term ODI $\times$ TST_{90} was performed.

Collinearity diagnostics, estimated by correlation matrices, indicated the absence of collinearity between the covariates entered into the model (all correlation matrices <0.8); for such a reason, AHI as well as RE were excluded from the model due to their collinearity with ODI (both correlation matrices >0.8). Furthermore, in logistic regression the test of goodness of fit, performed by the Hosmer and Lemeshow Test, indicated a good fit of the model (P value > 0.050).

3. Results

Sixty-six out of the 275 participants (24%) complained of nocturia in the previous year. Mean age of the sample was 63 (SD:12) years, 38% were females, and mean BMI was 31.8 (SD:5.8) Kg/m^2.The median AHI was 15 (7–34), median RE was 22 (12–38), median ODI was 15 (8–31), and the median TST_{90} was 6.9% (1.3–23). General characteristics of the study population, as well as main characteristics according to the occurrence of nocturia, are shown in Table 1.

Specifically, patients who reported nocturia complained of significantly more prevalent snoring ($P = 0.042$) and dry mouth