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Original Article

Clinical and Polysomnographic Features of Rapid Eye Movement–Specific Sleep-Disordered Breathing

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ABSTRACT

Objective: The aim of this study was to analyze the clinical and polysomnographic features of rapid eye movement (REM)–specific sleep disordered-breathing (SDB).
Patients and Methods: All cases of sleep apnea-hypopnea syndrome (SAHS) (apnea-hypopnea index [AHI] ≥ 10/h) diagnosed using over night polysomnography during the period 2004 to 2006 were analyzed retrospectively. Those cases in which the ratio of AHI during REM sleep to AHI during non-REM sleep was more than 2 were classified as REM-specific SDB. We recorded the following data: clinical signs and symptoms related to SAHS, PSG results, cardiovascular risk factors, and previous cardiovascular events. Logistic regression analysis was used to identify predictors of REM-specific SDB and to analyze the possible interactions between variables.
Results: A total of 419 patients were analyzed, of whom 138 (32.9%) presented REM-specific SDB. This condition was more common in patients with mild to moderate SAHS than in those with more severe cases (odds ratio, 8.21; 95% confidence interval, 4.83–14.03). The variables independently associated with REM-specific SDB in the logistic regression analysis were female sex, lower AHI, and higher body mass index. No interactions between the main variables studied were found. There were no differences between patients with REM-specific SDB and those with non-REM-specific SDB with regard to signs and symptoms related to SAHS, excessive daytime sleepiness, sleep architecture, cardiovascular risk factors, or history of cardiovascular episodes.

Características clínicas y polisomnográficas del síndrome de apneas durante el sueño localizado en la fase REM

Palabras clave:
Síndrome de apneas del sueño
Sueño REM
Hipersomnia diurna
Sexo femenino

RESUMEN

Introducción: El objetivo de este estudio ha sido analizar las características clínicas y polisomnográficas del síndrome de apneas-hipopneas durante el sueño (SAHS) localizado en la fase REM (SAHS-REM).
Pacientes y métodos: Se han analizado retrospectivamente todos los casos de SAHS —índice de apneas-hipopneas (IAH) ≥ 10/h— diagnosticados mediante polisomnografía completa en el período 2004–2006. Se catalogaron como SAHS-REM aquellos en que la razón IAH-REM/IAH-no REM fue mayor de 2. De todos los pacientes se recogieron los siguientes datos: clínica de SAHS, resultados de la polisomnografía, factores de riesgo cardiovascular y eventos cardiovasculares previos. Se realizó un análisis de regresión logística para identificar las variables predictoras de SAHS-REM, así como para analizar posibles interacciones entre variables.
Resultados: Se analizaron en total 419 casos, de los que 138 (32,9%) presentaban SAHS-REM. Esta entidad fue más frecuente en pacientes con SAHS leve-moderado que en los casos graves (*odds ratio* = 8,21; intervalo de confianza del 95%, 4,83–14,03). En el análisis de regresión logística, las variables que se asociaron de forma independiente al SAHS-REM fueron el sexo femenino, un menor IAH y un mayor índice de masa

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corporal, y no se detectaron interacciones entre las principales variables estudiadas. No se encontraron diferencias entre los pacientes con SAHS-REM y SAHS-no REM en cuanto a la clínica del SAHS, hipersomnia diurna subjetiva, estructura de sueño, factores de riesgo cardiovascular o antecedentes de episodios cardiovasculares.

Conclusiones: El SAHS-REM podría considerarse un estadio inicial del SAHS, que acontece preferentemente en mujeres obesas con trastorno del sueño leve-moderado y que carece de características específicas en cuanto a presentación clínica, estructura de sueño o comorbilidad cardiovascular.

Introduction

Sleep apnea-hypopnea syndrome (SAHS) is characterized by repeated episodes of upper airway obstruction that disturbs normal sleep architecture and is associated with daytime sleepiness as well as neuropsychiatric, breathing, and cardiovascular disorders.[1] While obstruction can occur during any stage of sleep, apneas tend to be more prolonged and are associated with greater desaturation during rapid eye movement (REM) sleep. The particular vulnerability of this stage of sleep is probably due to diminished respiratory drive, more irregular ventilation, and generalized muscle hypotonia, which predisposes the patient to upper airway obstruction due to the loss of tone in pharyngeal dilator muscles.[2,3] It is thus logical that a greater number of respiratory events occur in this stage than in others. In some cases, however, there is an excessive concentration of such events during REM sleep compared to non-REM stages, and this disorder is referred to as REM-specific sleep-disordered breathing (SDB). The study of this condition is of particular interest, as the selective clustering of respiratory events—in which REM sleep is interrupted, but other sleep stages barely affected—may represent a variant of SAHS with its own particular features. To date, however, few studies on the characteristics of this condition have been published.[4-8] The aim of this study was to analyze whether there are any specific clinical or polysomnographic features that distinguish REM-specific SBD from non-REM-specific SDB.

Patients and Methods

All patients diagnosed with obstructive SAHS (apnea-hypopnea index [AHI] $\geq$ 10/h) using conventional overnight polysomnography (PSG) in the pulmonology department of Hospital de Valme in Seville, Spain, from January 2004 to December 2006 were analyzed retrospectively. They had all been referred to the specialized sleep disorder clinic due to suspected SAHS and were in stable condition. Patients whose sleep studies had not been analyzed manually, in whom the degree of daytime sleepiness had not been assessed using the Epworth scale, or in whom fewer than 15 minutes of REM sleep had been recorded, were excluded. The study was approved by the hospital ethics committee.

Clinical Evaluation

For all patients, an initial medical history was taken using a standard protocol, and weight, height, and body mass index (BMI) were recorded during a physical examination. The patients were interviewed about the presence of snoring, witnessed apneas, morning headache, and quality of sleep. Any history of stroke, arrhythmia, ischemic heart disease, or myocardial disease was recorded. Patients were classified as having hypertension, diabetes, or dyslipemia if they had been previously diagnosed with any of these diseases, were taking specific medication for any of them, or had ambulatory systolic blood pressure higher than 140 mm Hg or diastolic blood pressure higher than 90 mm Hg on at least 2 occasions, fasting glucose concentrations greater than 110 mg/dL on at least 2 tests, or fasting cholesterol/triglyceride levels higher than 200 mg/dL. We also interviewed them about the habitual use of drugs with a potential sedating effect, such as benzodiazepines, antihistamines, and sleeping pills. The degree of daytime sleepiness was assessed subjectively in all cases using the Spanish version of the Epworth scale.[9]

Sleep Study

SAHS was diagnosed by attended overnight PSG in the sleep laboratory using the Ultrasom system (Nicolette Biomedical Inc, Madison, Wisconsin, USA) or the Compumedics PS system, (Compumedics, Melbourne, Australia). We recorded electro encephalogram, electro-oculogram, electromyogram, oronasal airflow, chest and abdominal movements, electrocardiogram, snoring, and arterial oxygen saturation (SaO_2). A thermistor and nasal pressure cannula were used to monitor oronasal airflow and thoracic bands to monitor chest and abdominal movements.

All studies were reviewed manually by an expert. Sleep stages were classified according to the criteria of Rechtschaffen and Kales.[10] Respiratory events were classified according to standard criteria.[1] Apnea was defined as a decrease of more than 90% in the respiratory signal for at least 10 seconds, and classified as obstructive or central in function of the presence or absence of respiratory movements. Hypopnea was defined as a decrease of 30% to 90% in respiratory signal for at least 10 seconds, followed by an arousal and/or desaturation of 3% or more. AHI was defined as the total number of apneas and hypopneas per hour of sleep and was calculated during REM and non-REM sleep. An overall AHI of 10 to 30 was considered to be diagnostic of mild to moderate SAHS and an overall AHI higher than 30 was considered to be diagnostic of severe SAHS. Following the criteria used by most authors, patients were considered to have REM-specific SBD if the ratio of REM AHI to non-REM AHI was more than 2, and to have non-REM-specific SBD if the ratio was 2 or less.[5-7,11] Minimum SaO_2 and cumulative percentage of sleep time with SaO_2 less than 90% were recorded as indices of nighttime hypoxemia.

Statistical Analysis

The statistical package SPSS version 13.0 was used for data processing and statistical analysis. The results were expressed either as percentages or means (SD), depending on whether the data were qualitative or quantitative. Means were compared using the *t* test when the data were normally distributed; otherwise the nonparametric Mann-Whitney test was used. For the comparison of qualitative variables, the χ^2 test with the Yates correction was used, and when necessary, the 2-tailed Fisher exact test. Variables with a *P* value less than .10 in the univariate analysis were entered into a multivariate logistic regression analysis in order to identify those that were independently associated with REM-specific SBD and to analyze the possible interactions between variables that might

reinforce or otherwise modify the effect of some on others. Statistical significance was set at a value of *P* less than .05.

Results

During the study period, 460 patients were diagnosed with SAHS. In 16 cases, the sleep study had not been reviewed manually; in 5, a daytime sleepiness score had not been entered into the patient's medical history; and in 20, fewer than 15 minutes of REM sleep had been recorded. These patients were therefore excluded from the study. We finally analyzed 419 patients (281 men and 138 women), with a mean (SD) age of 53.9 (11.4) years, and a BMI of 34.1 (6.1) kg/m^2.

A total of 138 patients (32.9%) had REM-specific SBD, while in the remaining 281 (67.1%), respiratory events did not occur predominantly during REM sleep. Overall, patients with REM-specific SBD had less severe SAHS (with a lower AHI and less nighttime desaturation) than those with non-REM-specific SBD (Table 1). REM-specific SBD was significantly more common in patients with mild to moderate SAHS than in those with more severe disease (114/217 compared to 24/202; odds ratio [OR], 8.21; 95% confidence interval [CI], 4.83-14.03). The ratio of REM to non-REM respiratory events was 3.4 (2.2) in the REM-specific SBD group compared to 0.8 (0.5) (*P*<.0001) in the non-REM-specific SBD group. With regard to sleep architecture, patients with REM-specific SBD spent a shorter time in stage I sleep and a longer time in deep and REM sleep than patients with non-REM-specific SDB. No differences between the 2 groups were observed with regard to time in supine position (Table 1).

When we compared the clinical and anthropometric characteristics of the 2 groups, we observed that REM-specific SDB was more common in women, in more obese patients, in those who took drugs with a sedating effect, in those who complained of morning headache, and in those with fewer witnessed breathing pauses (Table 2). No differences, however, were found between those with REM-specific SBD and those with non-REM specific SBD in terms of subjective daytime sleepiness measured using the Epworth scale (11.7 [4.6] vs 11.9 [4.1], respectively; *P*=.76) or in cardiovascular comorbidity or previous cardiovascular events (Table 2).

The variables independently associated with REM-specific SDB in the logistic regression analysis were female sex, lower AHI, and higher BMI (Table 3). There was no evidence of any interaction between sex, AHI, and BMI, or that these interacted with the other variables included in the logistic regression analysis.

Discussion

The present study showed that as many as a third of the patients in our series who underwent PSG for suspected SAHS had REM-specific SDB. The variables independently associated with this variant of SAHS were female sex, lower AHI, and higher BMI. Patients with REM-specific SDB did not differ from those with non-REM-specific SDB in terms of signs or symptoms of sleep apnea, sleep architecture, degree of daytime sleepiness, cardiovascular comorbidity, or previous cardiovascular events.

Table 1
Polysomnographic Features of Patients With Rapid Eye Movement (REM)–Specific Sleep Disordered-Breathing (SDB) and With Non-REM-Specific SDB[a]

Variables	REM-Specific SDB (n=138)	Non-REM-Specific SDB (n=281)	*P*
TST, min	322.5 (68.2)	310.3 (63.6)	.06
Sleep efficiency, %	75.1 (14.0)	75.2 (13.1)	.90
Stage I, %	35.0 (15.8)	42.8 (17.9)	<. 0005
Stage II, %	37.0 (11.9)	34.9 (12.8)	.10
Stages III-IV, %	14.5 (9.0)	10.5 (8.9)	.0001
REM stage, %	12.9 (6.1)	10.8 (5.3)	.0007
Time in supine position, %	44 (13)	43 (20)	.52
Total AHI, n	21.7 (9.7)	45.3 (25.3)	<. 0005
REM AHI, n	53.2 (8.5)	38.3 (24.6)	<.0005
Non-REM AHI, n	15.5 (8.6)	43.1 (24.2)	<.0005
REM/non-REM AHI ratio	3.4 (2.2)	0.8 (0.5)	<.0001
Minimum SaO_2, %	76.7 (9.7)	74.9 (12.5)	.11
CT_{90}, %	5.9 (12.4)	13.3 (20.3)	.0002

Abbreviations: AHI, apnea-hypopnea index; CT90, cumulative percentage of time with arterial oxygen saturation less than 90%; SaO_2, arterial oxygen saturation: TST, total sleep time.

[a] Data are shown as means (SD).

Table 2
Baseline Clinical and Anthropometric Features of Patients With Rapid Eye Movement (REM)–Specific Sleep Disordered-Breathing (SDB) and With Non-REM-Specific SDB[a]

Variables	REM-Specific SDB (n=138)	Non-REM-Specific SDB (n=281)	*P*
Female sex	64 (46.3)	74 (26.3)	<.0005
Age, y	54.6 (11.3)	53.4 (11.4)	.30
BMI, kg/m^2	35.0 (6.9)	33.6 (5.7)	.02
Epworth score	11.7 (4.6)	11.9 (4.1)	.76
Use of sedatives	35 (25.3)	47 (16.7)	.06
Alcohol consumption, g/d	11.9 (22.0)	15.2 (25.5)	.17
Smokers	58 (42)	166 (59)	.01
Hypertension	84 (60.8)	154 (54.8)	.28
Diabetes mellitus	29 (21.0)	65 (23.1)	.71
Hyperlipemia	85 (61.5)	152 (54.0)	.17
Cardiovascular events[b]	32 (23.1)	59 (20.9)	.69
Snoring	135 (97.8)	275 (97.8)	.73
Witnessed breathing pauses	96 (69.5)	233 (82.9)	.002
Morning headaches	57 (41.3)	86 (30.6)	.03
Restorative sleep	43 (31.1)	92 (32.7)	.83

[a] Data are shown as means (SD) or number of patients (percentage).

[b] These include stroke, arrhythmia, ischemic heart disease, and myocardial disease.

Table 3
Predictors of Rapid Eye Movement–Specific Sleep-Disordered Breathing. Logistic Regression Analysis

Variables	Exp (B)	95% CI	*P*
Female sex	1.96	1.05–3.57	.03
BMI	1.07	1.02–1.13	.002
AHI	0.92	0.89–0.94	<.0005

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval.

The rate of REM-specific SDB in our series was high: as many as 32.9% of patients who underwent PSG for suspected SAHS presented this variant of the disease. Although this figure does not necessarily reflect the prevalence in our area (since not all patients undergo overnight PSG), it is similar to rates reported in other retrospective studies that used similar diagnostic criteria (33.5%-36.4%).[5,6] The definitions of REM-specific SDB used by other authors, such as Siddiqui et al[12] and Loadsman and Wilcox,[13] were based on a less strict criterion—merely a greater number of events in REM sleep than in non-REM sleep. In our opinion, such a criterion is too permissive, as it would include patients without a clear significant predominance of events in REM sleep. Using the above-mentioned definition, 60.8% of our series would have REM-specific SDB. This percentage is slightly higher than the 50% reported in the 2 studies.[12,13]

Despite this high rate of cases, the literature on this topic is scarce.[4-8] REM-specific SDB was first described in 1996 by Kass et al,[4] who suggested that it was a specific entity distinct from SAHS and that it could be the cause of excessive daytime sleepiness in patients with an overall AHI lower than 10. This hypothesis was not subsequently confirmed, and the condition appears rather to be a variant of SAHS that occurs in patients with specific characteristics. In our series, these characteristics were female sex, obesity, and nonsevere SAHS.

Female predominance leads us to believe that there might be differences between the sexes with regard to upper airway stability and that these differences may, at least in part, be attributable to hormonal factors. It is known that in the waking state, women have greater genioglossus activity than men,[14] and that during non-REM sleep men show greater upper airway resistance and collapsibility than women.[15] Higher concentrations of progesterone and other female sex hormones might, on the one hand, act as respiratory stimulants, and on the other hand, protect against upper airway obstruction by increasing pharyngeal dilation muscle tone.[16,17] During REM sleep, which is characterized by decreased muscle tone and ventilatory response, the protective effect of sex hormones may be negligible, and this could explain the clustering of most respiratory events in that stage. Other authors have also observed a higher prevalence of REM-specific SDB in women.[5,11] In a retrospective study of 1540 patients (601 women) with SAHS, Koo et al,[11] grouped patients by age (<55 years and >55 years), and found significantly more cases of REM-specific SDB in the older group. Ours was a retrospective study, and we could therefore not determine the menopausal status of the female patients. If, like Koo et al, we take 55 years as a cutoff point for menopause, it can be seen that female patients under this age more frequently had REM-specific SDB than older ones (57.8% vs 38.2%; OR, 2.09; 95% CI, 0.99-4.40; *P*=.052), but the difference was not significant. This would add strength to the theory that hormonal factors play a role. The lack of significance is probably attributable to the small number of women in our study compared to that of Koo et al. In contrast, Haba-Rubio et al[6] did not find an association between female sex and REM-specific SDB in a retrospective study of 415 patients. However, they did note that 46.4% of the women had REM-specific SDB compared to 16.5% with non-REM-specific SDB. These percentages are very similar to those in our study.

The other variable associated with REM-specific SDB was lower overall severity of SAHS. This association suggests that in mild to moderate SAHS, most respiratory events would first be concentrated in REM sleep and would then extend to other non-REM stages as SAHS severity increases, with a gradual lowering of the ratio of REM AHI to non-REM AHI.

The role of BMI is less clear. Obesity is one of the most widely known risk factors for SAHS. Various mechanisms have been described, including the narrowing of the upper airways due to fat deposits on the pharyngeal wall, a reduction in lung volume, and, possibly, decreased respiratory drive.[18-22] While obesity is a risk factor for SAHS in general—in fact, both groups in our series had a BMI within the obese range—its particular association with REM-specific SDB in the multivariate analysis could be explained by the fact that in patients with milder SAHS, obesity would have a sufficiently intense effect on the upper airways to provoke obstructive events during REM sleep because of the atony of the pharyngeal dilation muscle and poorer respiratory control. In other studies, however, obesity was not found to be associated with REM-specific SDB,[5,6] although in one of them BMI in the series was comparatively low (31.3 [6.3] kg/m^2). In our study, both groups were considerably obese and the difference in BMI between them was 1.4 kg/m^2. Further studies are needed to evaluate the clinical significance of this variable.

Of particular interest is the fact that patients with REM-specific SDB and non-REM-specific SDB had similar characteristics in terms of subjective daytime sleepiness, SAHS symptoms, cardiovascular comorbidity, and history of cardiovascular events. While in the univariate analysis REM-specific SDB was associated with certain clinical variables such as morning headache or fewer witnessed breathing pauses, these associations disappeared in the logistic regression analysis. The final multivariate model did not show apparently better sleep architecture (less time in stage I sleep and more in deep sleep) or longer duration of REM sleep to be independently associated with REM-specific SDB. Such differences must therefore be attributed to the lower severity of SAHS in this group. Thus, except for female sex and higher BMI, we found no particular features that would allow a priori identification of patients who might present REM-specific SDB. This similarity between the groups would indicate, in effect, that REM-specific SDB is not a specific entity with its own peculiar features, but rather a variant of SAHS mediated by sex and disease severity. An interesting hypothesis suggested by our results is that REM-specific SDB could be considered an initial stage of SAHS in patients with mild to moderate forms of the disease. In this case, respiratory events might at first be restricted to REM sleep but then be distributed more evenly throughout all sleep stages as the disease becomes more severe and the ratio of REM AHI to non-REM AHI gradually decreases.

We would still need to explain why patients with mild to moderate sleep disorders showed similar cardiovascular comorbidity to that of the non-REM-specific SDB group, in which SAHS is generally more severe. One possibility is that a higher REM AHI might account for the cardiovascular consequences of SAHS. When we analyzed our series, we observed that patients who were hypertense did indeed have a higher REM AHI than those who were not (46.2 [24.1] vs 34.5 [24.4] respectively, *P*<.0005), but we did not find this association with diabetes (44.8 [23.8] vs 40.0 [25.1], respectively; *P*=.08), dyslipemia (40.7 [25.0] vs 41.4 [24.8], respectively; *P*=.68), or history of cardiovascular events (40.7 [25.2] vs 42.3 [23.6], respectively; *P*=.56). Another hypothesis, which we were unable to analyze, is that respiratory events occurring during REM sleep might have specific characteristics that make them more harmful—for example, longer duration—and that could lead to more serious cardiovascular consequences, independently of AHI.

The present study has certain limitations. The first of these is that the study sample was evaluated retrospectively. Our series, however, consisted of patients with suspected SAHS who were all evaluated in a similar way, according to the standard protocol used in our clinic that included expert manual revision of the sleep studies. Second, it is possible that by using a subjective rather than an objective instrument for the evaluation of daytime sleepiness, some differences between the 2 groups may have been overlooked. However, the Epworth scale is the instrument normally used to evaluate sleepiness in clinical practice and to provide the information to guide treatment decisions. Other authors using the maintenance of wakefulness test, an objective instrument, found no differences between patients with REM-specific SDB and those with non REM-specific SDB in terms of excessive daytime sleepiness.[6] In contrast, Punjabi et al[8] found non-REM AHI, but not REM AHI, to be associated with greater daytime sleepiness. However, these authors used a different method: rather than using an index to define REM-specific SDB, they grouped AHI scores in quartiles, applied survival analysis techniques, and used a different instrument to assess daytime sleepiness (the multiple sleep latency test). In any event, we cannot rule out the possibility that more subtle differences between the 2 groups might have been made apparent by the use of quality-of-life questionnaires, cognitive tests, or more complex questionnaires. Finally, in our study we required a minimum of 15 minutes of REM sleep (which was approximately 5% of total sleep time in the group with non-REM-specific SDB), a criterion recommended by other authors.[7,11] While other studies either included all patients in whom REM sleep, no matter how brief, was detected,[12] or required higher percentages of REM sleep, we believe that the time requirement we used was sufficient to eliminate the risk of artifacts in the sample produced by marginal cases with only a few minutes of REM sleep. We also believe that requiring a higher percentage of REM sleep might have excluded too many patients; bearing in mind that in our series the mean time spent in REM was 11.5% of total sleep time (36 minutes). In any event, when the 20 patients excluded because they had spent less than 15 minutes in REM sleep were analyzed, the results were not affected (data not included).

To sum up, REM-specific SDB was relatively common in our series and was associated mainly with female sex, greater obesity, and mild to moderate forms of SAHS. We were unable to identify any other distinguishing clinical or polysomnographic features or a difference in repercussions on cardiovascular disease in the REM-specific group compared to the non-REM-specific SDB group.

References

1. Grupo Español de Sueño (GES). Consenso nacional sobre el síndrome de apneas-hipopneas del sueño. Arch Bronconeumol. 2005;41 Supl 4:1-100.
2. Millman RP, Knight H, Kline LR, Shore ET, Cheung DCC. Changes in compartmental ventilation in association with eyes movements during REM sleep. J Appl Physiol. 1988;65:1196-202.
3. Gould GA, Gugger M, Molloy J, Tsara V, Shapiro CM, Douglas NJ. Breathing pattern and eyes movement density during REM sleep in man. Am Rev Respir Dis. 1988;138:874-7.
4. Kass JE, Akers SM, Bartter TC, Pratter MR. Rapid-eye-movement-specific sleep disordered breathing: a possible cause of excessive daytime sleepiness. Am J Respir Crit Care Med. 1996;154:167-9.
5. O'Connor C, Thornley KS, Hanly PJ. Gender differences in the polysomnographic features of obstructive sleep apnea. Am J Respir Crit Care Med. 2000;161:1465-72.
6. Haba-Rubio J, Janssens JP, Rochat T, Sforza E. Rapid eye movement-related disordered breathing: clinical and polysomnographic features. Chest. 2005; 128:3350-7.
7. Resta O, Carpagnano GE, Lacedonia D, Di Gioia G, Giliberti T, Stefano A, et al. Gender difference in sleep profile of severely obese patients with obstructive sleep apnea (OSA). Respir Med. 2005;99:91-6.
8. Punjabi NM, Bandeen-Roche K, Marx JJ, Neubauer DN, Smith FL, Schwartz AR. The association between daytime sleepiness and sleep-disordered breathing in NREM and REM Sleep. Sleep. 2002;25:307-14.
9. Chiner E, Arriero JM, Signes-Costa J, Marco J, Fuentes I. Validación de la versión española del test de somnolencia de Epworth en pacientes con síndrome de apneas del sueño. Arch Bronconeumol. 1999;35:422-7.
10. Rechtschaffen A, Kales A. A manual of standardized terminology and scoring system for sleep stages of human subjects. Los Angeles: Brain Information Service/ Brain Research Institute, University of California at Los Angeles, 1968.
11. Koo B, Dostal J, Ioachimescu O, Budur K. The effects of gender and age on REM-related sleep-disordered breathing. Sleep Breath. 2008;3:259-64.
12. Siddiqui F, Walters AS, Goldstein D, Lahey M, Desai H. Half of patients with obstructive sleep apnea have higher NREM AHI than REM AHI. Sleep Med. 2006; 7:281-5.
13. Loadsman JA, Wilcox I. Is obstructive sleep apnea a rapid eye movement-predominant phenomenon? Br J Anaesth. 2000;85:354-8.
14. Popovic RM, White D. Influence of gender on waking genioglossal electromyogram and upper airway resistance. Am J Respir Crit Care Med. 1995;152:725-31.
15. Trinder J, Kay A, Kleiman J, Dunai J. Gender differences in airway resistance during sleep. J Appl Physiol. 1997;83:1986-97.
16. Popovic R, White D. Upper airway muscle activity in normal women: influence of hormonal status. J Appl Physiol. 1998;84:1055-62.
17. Zwillich CW, Natalino M, Sutton F. Effect of progesterone on chemosensitivity in normal man. J Lab Clin Med. 1978;92:262-9.
18. Jones RL, Nzekwu MMU. The effects of body mass index on lung volumes. Chest. 2006;130:827-33.
19. Bloom JW, Kaltenborn WT, Quan SF. Risk factors in a general population for snoring. Importance of cigarettes smoking and obesity. Chest. 1988;93:678-83.
20. White DP, Lombard RM, Cadieux RJ, Zwillich CW. Pharyngeal resistance in normal humans: influence of gender, age, and obesity. J Appl Physiol. 1985;58:365-71.
21. Shelton KE, Woodson H, Gay S, Suratt PM. Pharyngeal fat in obstructive sleep apnea. Am Rev Respir Dis. 1993;148:462-6.
22. Campo A, Frühbeck G, Zulueta JJ, Iriarte J, Seijo LM, Alcaide AB, et al. Hyperleptinaemia, respiratory drive and hypercapnic response in obese patients. Eur Respir J. 2007;30:223-31.