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Gender Difference in Apnea and Hypopnea Component in Obstructive Sleep Apnea

Obstrüktif Uyku Apnesinde Apne ve Hipopne İçeriğindeki Cinsiyet Farkı

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Summary

Introduction: We aimed to analyze the apnea and hypopnea structure separately with demographic parameters and sleep architecture in men and women with sleep apnea.

Materials and Methods: Patients referred for snoring, witnessed apnea and/or day time sleepiness to Dışkapı Yıldırım Beyazıt Research and Educational Hospital Sleep Center and gone under polysomnography (PSG) between December 2010 and June 2012 were taken in order. PSG reports were analyzed retrospectively. The patients with sleep efficiency less than 40% were excluded. The BMI, neck circumference (NC), abdominal circumference (AC) and PSG values were recorded.

Results: Totally 406 patients (250 male, 156 female patients) were studied. NC was found more in males whereas AC and BMI were found significantly more in females. Mean age, apne-hypopnea index (AHI), oxygen desaturation index (ODI) for 3% were similar in two genders. Percentage of total light sleep (Stage 1+2) was significantly more in males while Stage 3 (slow wave sleep: SWS) was more in females. Total apneas were significantly more in males and hypopneas were significantly more in females. The factors associated with AHI were NC and BMI in males and AC and BMI in females.

Discussion: We found that, females are more hypopneic and men are more apneic, in a study group of similar apne-hypopnea indexed patients. The different distribution of fat in genders seems to effect the apnea/hypopnea predominance. The clinical significance of the apnea and hypopnea indexes separately can be related with SWS percentage. Prospective studies are needed to evaluate the effect of apneas and hypopneas on morbidity and mortality in both genders. (*JTSM 2014;1:16-21*)

Key Words: Obstructive sleep apnea syndrome, apnea, hypopnea, gender

Özet

Giriş: Obstrüktif uyku apneli kadın ve erkeklerde demografik verilerle beraber apne ve hipopne yapısını ayrı olarak incelemeyi amaçladık.

Gereç ve Yöntem: Dışkapı Yıldırım Beyazıt Araştırma ve Eğitim Hastanesi Uyku Merkezi'ne horlama, tanıklı apne ve/veya uykululuk ile Aralık 2010-Haziran 2012 tarihleri arasında başvuran ve polisomnografi (PSG) yapılan hastalar sırayla çalışmama alındı. PSG raporları retrospektif olarak değerlendirildi. Uyku etkinlikleri %40'ın altında olanlar çalışma dışı bırakıldı. Vücut kitle indeksi (VKİ), boyun çevresi (BÇ), karın çevresi (KÇ) ve PSG değerleri kaydedildi.

Bulgular: Toplam 406 hasta (250 erkek, 156 kadın) çalışmaya alındı. BÇ erkeklerde, KÇ ve VKİ anlamlı olarak yüksek bulundu. Ortalama yaş, apne-hipopne indeksi (AHİ) ve %3 oksijen desaturasyon indeksi (ODİ) iki cinsiyette benzerdi. Erkeklerde total yüzeyel uyku (Evre 1+2) daha fazlayken Evre 3 (Yavaş Dalga Uykusu: YDU) kadınlarda daha fazlaydı. Erkeklerde total apne sayısı, kadınlarda hipopneler anlamlı derecede fazlaydı. AHİ'ini erkekte etkileyen faktörler BÇ ve VKİ iken kadınlarda KÇ ve VKİ idi.

Sonuç: Benzer apne-hipopne indeksi olan bir grup hastada kadınların daha hipopneik, erkeklerin daha apneik olduğunu saptadık. Cinsiyetlerde yağ dağılımındaki farklılığın apne/hipopne ağırlığında etkili olması muhtemel gözükmektedir. Apne ve hipopne indekslerinin ayrı ayrı önemi YDU yüzdesi ile ilişkilendirilebilir. Apne ve hipopnelerin her iki cinsiyette morbidite ve mortalite üzerindeki etkilerini değerlendirmek için prospektif araştırmalara ihtiyaç vardır. (*JTSM 2014;1:16-21*)

Anahtar Kelimeler: Obstrüktif uyku apne sendromu, apne, hipopne, cinsiyet

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by repetitive upper airway collapse during sleep associated with reversible arterial oxygen desaturation. OSAS leads to repetitive night awakenings and excessive daytime sleepiness (1). The prevalence rate of OSA (Obstructive Sleep Apnea) with AHI>5 is found as 2% in women and 4% in men (2). OSA is strongly related with obesity (3-5), neck circumference (6-8), fat distribution pattern (9-12) which show discrepancy between men and women.

There are several studies and reviews evaluating the gender difference in OSA patients (4,6,9,11,12,13-18). OSA prevalence and AHI is higher in males whereas females have more frequently obesity and hypertension. Additionally, males have more frequently upper-body pattern obesity, especially more fat distribution in the neck. Females are less susceptible than males to develop apnea or hypopnea in response to hypercapnia during sleep. The differences in airway collapsibility seem to be the most likely physiologic mechanism that could explain the male predominance of OSAS. Up to now, there is no knowledge about the apnea/hypopnea structures separately in men and women with OSA.

We aimed to analyze the sleep pattern, apnea and hypopneas separately and the factors associated with the severity of apneas and hypopneas in the two genders with sleep apnea.

Materials and Method

Study Sample

Patients referred for snoring, witnessed apnea and/or day time sleepiness to Dışkapı Research and Educational Hospital Sleep Center and undergone polysomnography (PSG) between December 2010 and June 2012 were taken in order. PSG reports were analyzed retrospectively. The study was approved by the local ethics committee of Dışkapı Research and Educational Hospital. The patients with sleep efficiency less than 40% were excluded. The BMI, neck circumference (NC), abdominal circumference (AC), arterial blood gas (ABG), Epworth sleepiness scale (ESS), and polysomnographic (PSG) values were recorded.

Polysomnography

The participants underwent polysomnography using Compumedics E series (Compumedics®, Melbourne, Victoria, Australia). At least 6 hours of recording was taken. The polysomnography recordings included 6-channel electroencephalography, 2-channel electrooculography, 2-channel submental electromyography, oxygen saturation by an oximeter finger probe, respiratory movements via chest and abdominal belts, airflow both via nasal pressure sensor and oro-nasal thermistor, electrocardiography, and leg movements via bilateral tibial anterolateral electrodes. Sleep stages and respiratory parameters were scored according to the standard criteria of the American Academy of Sleep Medicine (AASM). Based on the guidelines of the AASM published in 2007, apnea is defined as a ≥90% decrease in airflow persisting for at least 10 seconds according to the basal amplitude. Hypopnea is defined as a ≥50% decrease in the airflow amplitude relative to the baseline value with an associated ≥3% oxygen desaturation or arousal, persisting for at least 10 s. (16).

Apnea-hypopnea index (AHI) was calculated based on the following formula: total index of obstructive apneas + hypopneas / total sleep time (h). Sleep stage scoring was done according to AASM criteria using software (Profusion PSG 3) in 30-s-epochs by a certified registered polysomnographic technologist (16).

Other Measurements

Body weight was recorded in erect position without shoes and wearing light indoor dressings, with an electronic scale. Height was also measured and body mass index (BMI) was calculated as body weight/height2 (kg/m^2). Abdominal circumference (AC) was measured at the level of umbilicus in erect position. Neck circumference (NC) was measured at the level of cricothyroid membrane. Arterial blood gas was taken as below: First the patient was informed about the possible complications (bleeding, bruising, arterial thrombosis, infection and pain); then consent was obtained to proceed. Routine sampling was taken from the radial artery of the non-dominant arm by heparinized syringe with cap and 20-22 G needle in the sitting position.

The Turkish version of ESS was used. ESS was validated in Turkish OSA patients (19).

Statistical Analysis

Data analysis was performed by using SPSS for Windows, version 18.0 (SPSS Inc., Chicago, IL, United States). Normal distribution of continuous variables was tested by Shapiro Wilk test. Levene test was used for the evaluation of homogeneity of variances. Continuous variables between two groups were compared by independent sample t-test. Mann Whitney-U test was applied for comparisons of the median values, in case of non-normal distribution. Nominal data (questions with yes/no answer) were analyzed by Pearson's Chi-square test. The non-parametric Jonckheere-Terpstra Test was used to test the ordered differences of apnea index, hypopnea index and AHI, among BMI groups, as the distributions were not normal. A p value less than 0.05 was considered statistically significant.

The effect of independent variables on dependent variables was tested with linear regression method. Logarithmic transformation was applied for independent variable, which did not have normal distribution. The significance of the regression models were tested with ANOVA test.

Results

Totally 406 patients (250 male, 156 female patients) with mean ages of 54.8±14.1 in males and 56.4±11.7 in females were studied. NC was higher in males and AC and BMI were significantly higher in females. Mean age, ESS, day time ABG values (pO2, pCO2, oxygen saturation) were not different in two genders (Table 1).

Sleep efficiency, total sleep time (TST), percentages of Stage 1 and Stage REM did not show difference between males and females. The percentages of Stage 2, total light sleep (Stage 1+2) were more in males while Stage 3 percentage (deep sleep) was significantly more in females. PLMI was higher in males. 153/250 (61.2%) male patients and 97/156 (62.1%) female patients had AHI>15 (Table 2).

Mean AHI values were similar in males and females. Mean oxygen values, duration less than 90% saturation, oxygen desaturation index (ODI) for 3% in PSG also did not show statistically significant difference between two genders. Total apneas were significantly more in males (101.2±9.8 versus 42.5±6.9) and hypopneas were significantly more in females (155.5±9.6 versus 128.9±60) (Figure 1). The mean duration of both apneas and hypopneas were more in males (15.8±7.2 sec. vs. 12.8±6.2 sec. for apneas, p<0.001 and 23.7±9.5 sec vs 21.2±7.2 sec. p=0.01 for hypopneas). REM/NREM AHI was significantly more in females (Table 3). The mean apnea-hypopnea duration in REM did not differ between males and females (14.4±10 sec. vs. 13.9±10 sec. respectively), while the mean apnea-hypopnea duration in NREM stage was significantly longer in males (77.4±5 sec. vs. 53.4±4.4 sec. in males and females respectively). The total apnea index was highest especially in patients with BMI>35 in males while the total hypopnea index was highest in patients with BMI>35 in females (Figure 2, 3).

The main factors associated with AHI in males were BMI and neck circumference (NC). The R square value was 0.296 between BMI, NC and AHI in males. The regression model was statistically significant (p=0.000) in ANOVA test. BMI (p=0.000) and NC (p=0.001) were related to AHI in males. The main factors associated with AHI were BMI and abdominal circumference (AC) in females. The R square value was 0.295 between BMI, AC and AHI in females. The regression model was statistically significant (p=0.000) in ANOVA test. BMI (p=0.000) and AC (p=0.017) were related to AHI in females. The formulas below were found from the regression analysis.

For Females: AHI= -59.58+1.281*BMI+0.42*AC

For Males: AHI=-79.43+1.846*BMI+1.43*NC

NC was not related to AHI in females (p=0.119), while AC was not associated with AHI in males (p=0.079).

The main factors associated with AI were BMI and NC in males. The R square was 0.161 between BMI, NC and AI in males. The regression model was statistically significant (p=0.000) in ANOVA test. BMI (p=0.002) and NC (p= 0.006) were related to AI in males. The main factor associated with AI was BMI in females. The R square was 0.084 between BMI and AI in females. The regression model was statistically significant (p=0.000) in ANOVA test. BMI (p=0.000) was effective on AI in females. AC was not related to AI in males and females.

The main factors associated with HI were BMI and AC in males. The R square value was 0.161 between BMI, AC and HI in males. The regression model was statistically significant (p=0.000). BMI (p=0.04) and AC (p=0.036) were effective on HI in males. The main factors associated with HI were BMI and AC in females. The R square value was 0.283 between BMI, AC and HI in females. The regression model was statistically significant (p=0.000). BMI (p=0.006) and AC (p=0.002) were effective on HI in females. NC was not associated with HI in males and females.

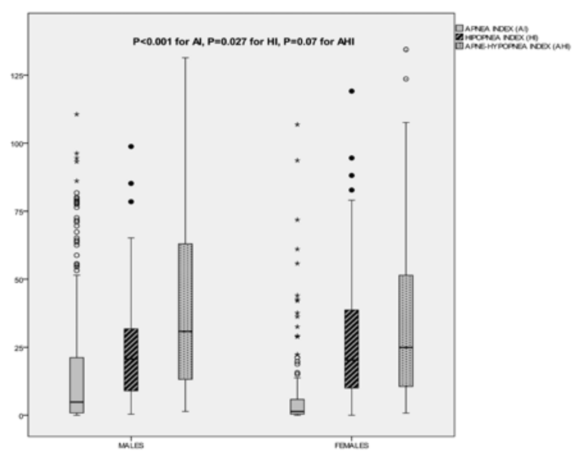

Figure 1. Apne index, hypopnea index and apnea-hypopnea index in male and female patients with OSA.

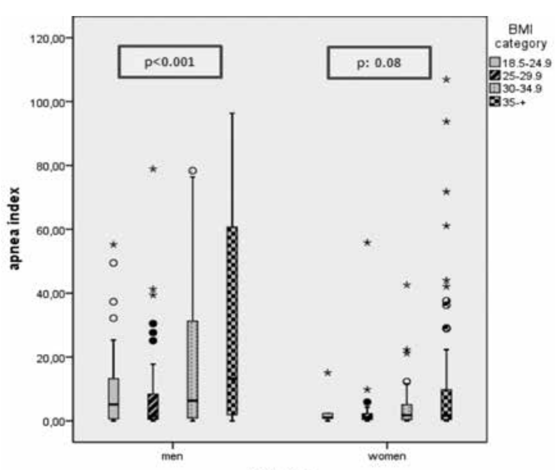

Figure 2. Apnea index in males and females in respect to BMI.

*: Values within 95% distribution range o: Outside 95% distribution range.

Discussion

In our study, we found that females are more hypopneic and men are more apneic, in a study group of patients with similar apnea-hypopnea indices, Mean ODI for 3% and the duration below 90% were also similar. But when analyzed separately, the males were found to have more apneas and females to have more

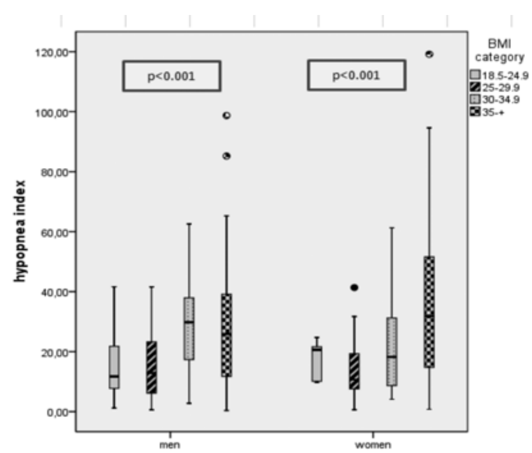

Figure 3. Hypopnea indexes in males and females in respect to BMI.

*: Values within 95% distribution range o: Outside 95% distribution range

hypopneas. There are studies (4,6,9,13-15,20-24) concerning the gender difference in sleep architecture in OSA, but there is no study that emphasizes the difference in apnea/hypopnea component in two genders. Neck circumference and BMI were the most associated with parameters to AHI in males whereas abdominal circumference and BMI were the most associated with parameters to AHI in females in the linear regression analysis. When taken separately, apnea index was mostly affected by BMI and neck circumference in males, while BMI was the only factor associated with apneas in females. Additionally, HI was mostly affected by BMI and abdominal circumference in females and only BMI in males in linear regression analysis.

Females had significantly more deep sleep than males despite a similar total index of apnea-hypopnea events and males had more light sleep (stage 2 covering the larger part) in polysomnography. One explanation can be the hypopneas which cover the most of the respiratory events in females, giving permission to the deeping of the sleep stage. Both the total index and the duration of apnea-hypopneas in NREM were higher in males. But, the mean duration of apnea-hypopnea events in REM and total index of hypopneas were similar in males and females, different from NREM stage. REM stage seems to be a worsening factor of the respiratory events. Both the total index and the duration (the ability of ending the event) were worsened with REM sleep especially in females. Females were more obese than the males in our study group. This finding is consistent with the study which reported that increased BMI was associated with longer apnea events in REM sleep more than stage 2 sleep (22). In the same study, the worsening of the respiratory events females and reducing the sex difference in apnea frequency and duration were linked with the less collapsible airway as a result of greater muscle tone; REM sleep caused decrease in muscle tone and led to worsening of the respiratory events especially in females.

In a later study, it was found that females had significantly higher percentage of SWS and lower NREM AHI than men (25). Increasing age and male gender were associated with less SWS and SWS percentage was significantly less in more severe OSA patients (26).

The clinical significance of the apnea/hypopneas is unclear. In a recent review about untreated obstructive sleep apnea and long-term adverse outcomes, it is reported that evidence exists in men for a relationship between OSA and all-cause mortality and a composite cardiovascular outcome. The effect of AHI was attenuated with female gender (27). The local fat distribution specific to gender can cause more apneas or hypopneas. The higher neck circumferences were shown to be effective in apneas in males, but not in females in our study. Predominant apneas in the respiratory events may be a cause for worse outcomes in men. The longer duration of the apneas and hypopneas in males and less SWS can be additive worsening factors in males.

We found that, females were more hypopneic and men were more apneic, with similar apnea-hypopnea index. The different distribution of fat in genders seems to effect the apnea/hypopnea predominance. The clinical significance of the hypopneas/apneas separately can be related with SWS percentage, which is significantly higher in the female patients. The elucidation of the relation between apneas/hypopneas and cardiovascular consequences require prospective studies in OSA.

Table 1. Demographic data for male and female patients

Variables	Male patients (250)	Female patients (156)	P
Age	54.8± 14.1	56.4± 11.7	NS
Neck circumference (cm)	42.2±4.6	38.3±3.6	<0.001
Abdominal circumference (cm)	108.1±14.9	112.4±15.6	0.006
Epworth	9.1±5.5	8.7±6.2	NS
BMI (kg/m^2)	31.6±6	36.1±7.7	<0.001
pO2 (mmHg)	76.3±12.2	75.3±11.6	NS
pCO2 (mmHg)	37.6±5.6	37.2±6.3	NS
Oxygen saturation (%)	94.4±4.5	94±4.3	NS

NS: Nonsignificant

Table 2. Sleep parameters for male and female patients

Variables	Male patients	Female patients	p
Total Sleep Time	351.6±67.4	355.7±60.5	NS
Stage 1 (%)	8.9±6.7	8±6.3	NS
Stage 2 (%)	58.4±13.6	52.4±12.6	<0.001
Stage 1+2 (%)	67.2±14.9	60.6±14.4	<0.001
Stage 3 (%)	19.2±11.1	26.2±12.5	<0.001
Stage REM (%)	13.1±6.4	13.2±6.2	NS
PLMI	42.4±2.4	31.5±2.3	0.002

PLMI: Periodic Leg Movement Index, NS: Nonsignificant

Table 3. Sleep parameters related with sleep apnea for male and female patients

Variables	Male patients	Female patients	p
AHI	39.2±1.9	33.9±2.2	NS
Apne index	16.5±1.5	7.4±1.3	<0.001
Hypopnea index	22.6± 1.1	26.8± 1.7	0.03
Mean Oxygen % sat.	88.8±5.5	88.9±6	NS
Duration<%90(min)	87.7±6.7	95.1±8.6	NS
ODI %3	34.5±1.9	29.4±2.2	NS
Total apne-hypopnea event number/Night	230.1±11.8	197.6±13	NS
Total apnea number/N	101.2±9.8	42.5±6.9	<0.001
Total hypopnea number/Night	128.9±6	155±9.6	0.01
Total REM Apnea number/Night	11.3±1.2	7.7±1	0.025
Total REM Hypopnea Number/Night	18±1	28.3±2	<0.001
Total NREM Apnea number/Night (N)	90.8±9.1	34.9±6.6	<0.001
Total NREM Hypopnea Number/N	111.7±5.7	126.7±9.2	NS
REM/NREM AHI	1.8±0.2	2.5±0.2	0.008
REM AHI	37.9±1.7	44.3±2.4	0.029
NREM AHI	38.3±1.9	31.4±2.3	0.02

ODI: Oxygen Desaturation Index, NS: Nonsignificant

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