

Araştırma

The Effects of Undiagnosed Nocturnal Hypoxia on the Intensive Care Unit Admission Scores

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ABSTRACT

Objective: Undiagnosed obstructive sleep apnea syndrome (OSAS) which is characterized with nocturnal hypoxia (NH) is commonly seen in population. Furthermore, it is associated with postoperative complications, prolonged hospital stay and nocturnal death. Hence, in this study, it was aimed to investigate the effects of undiagnosed NH on the ICU admission scores.

Material and Methods: This study was designed as a prospective observational study. Sleep apnea test (SAT) was performed on 64 patients with the diagnosis of pneumonia at the 6th month after hospital discharge. Demographic data, ICU admission scores, length of hospital stay, apnea-hypopnea index (AHI), minimum SpO₂ (min-SpO₂), percentage of NH (NH%), minimum and maximum heart rates were recorded.

Results: For all patients, the median values of APACHE II score, Charlson comorbidity index (CCI), AHI, min-SpO₂, NH%, max-HR and length of hospital stay were 18, 5, 21.5, 78%, 33.2%, 121 min⁻¹, and 11 days. NH% was positively correlated with APACHE II score, CCI and length of hospital stay. In patients with NH%≥18%, while CCI, APACHE II, AHI, max-HR, length of ICU and hospital stay were significantly higher; min-SpO₂ was significantly lower than patients with NH%<18%. In multivariate analysis, length of hospital stay increased by each unit increase in CCI, APACHE II score and NH%.

Conclusion: Most of the patients admitted to the ICU can have undiagnosed NH. Increase in NH% may be a reason for increased ICU admission scores and prolonged hospital stay.

Keywords: nocturnal hypoxia, APACHE II score, apnea-hypopnea index

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ÖZ

Tanısı Konulmamış Gece Hipoksisinin Yoğun Bakım Giriş Skorları Üzerine Etkileri

Amaç: Gece hipoksisi (GH) ile karakterize olan tanısı konulmamış obstrüktif uyku apnesi sendromu (OUAS) toplumda sık görülmektedir. Ayrıca, postoperatif komplikasyonlar, uzamış hastane kalış süresi ve gece ölümü ile ilişkilidir. Bu nedenle, bu çalışmada tanısı konulmamış GH'nin yoğun bakım giriş skorları üzerine etkilerinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Çalışma prospektif gözlemsel olarak dizayn edilmiştir. Çalışmaya dahil edilen 64 pnömoni tanılı hastaya hastaneden taburcu olduktan 6 ay sonra uyku apnesi testi (UAT) uygulanmıştır. Demografik veriler, yoğun bakım giriş skorları, hastane kalış süresi, apnea-hipopne indeksi (AHI), minimum periferik oksijen satürasyonu (min-SpO₂), GH yüzdesi (%GH), minimum ve maksimum kalp hızı kaydedilmiştir.

Bulgular: Tüm hastaların APACHE II skoru, Charlson comorbidity indeksi (CCI), AHI, min-SpO₂, %GH, maksimum kalp hızı ve hastane kalış süresi median değerleri 18, 5, 21.5, %78, %33.2, 121 dk⁻¹ ve 11'di. %GH ile APACHE II skoru, CCI ve hastane kalış süresi arasında pozitif korelasyon vardı. %GH ≥%18 olan hastalarda CCI, APACHE II skoru, maksimum kalp hızı, yoğun bakım ve hastane kalış süreleri anlamlı yüksek; min-SpO₂ anlamlı düşük bulundu. Çok değişkenli analizde, CCI, APACHE II skoru ve %GH'deki her bir birim artış hastane kalış süresini arttırdı.

Sonuç: Yoğun bakıma alınan hastaların önemli bir kısmı yoğun bakım girişinde tanısı konulmamış GH'ye sahip olabilirler. %GH'deki artış, artmış yoğun bakım giriş skorları ve uzamış hastane kalış süresi için bir neden olabilir.

Anahtar kelimeler: gece hipoksisi, APACHE II skoru, apne-hipopne indeksi

INTRODUCTION

Hypoxia is related to the organ dysfunction which leads to a decrease in the delivery of oxygen (DO_2)^[1,2]. Obstructive sleep apnea syndrome (OSAS) which is characterized with nocturnal hypoxia (NH) is also associated with hypertension, diabetes mellitus, atrial fibrillation, pulmonary hypertension, postoperative complications, prolonged hospital stay and nocturnal death because of chronic nocturnal hypoxia^[3-9]. Moreover, OSAS is known to have a high prevalence in population, and a significant amount of these cases are undiagnosed OSAS^[10]. According to 2009 Guidelines, apnea hypopnea index (AHI) is a diagnostic parameter for OSAS and it is determined by performing polysomnography^[11]. Nevertheless, in the guideline, portable monitors (PMs) are also defined as monitors which record AHI, minimum-peripheral oxygen saturation (min- SpO_2) and duration of $\text{SpO}_2 \leq 90\%$ ^[11,12]. Ambulatory monitorization have been already performed in different clinical situations during ICU (intensive care unit) stay^[13]. NH can also be directly determined based on the duration of $\text{SpO}_2 \leq 90\%$ by using PMs. In the present study, our hypothesis was that being in a situation of undiagnosed NH in daily sleep period before ICU admission can be associated with the ICU admission scores.

MATERIALS and METHODS

Study design

Upon the approval of Acibadem University Ethic Committee (ATADEK), the present study was designed as a prospective observational study. All patients with pneumonia admitted to the ICU between June 1st 2014, and June 1st 2015 were evaluated. Patients who were <18-year old, non-survivor patients, cases with diagnosis of trauma, chronic obstructive pulmonary disease (COPD), congestive heart failure, cerebrovascular disease, cancer and tracheotomized patients were excluded. Sixty-four patients with pneumonia who were included in the study were called back in the 6th month after hospital discharge. After their consent was obtained, sleep apnea test (SAT) was performed in a special room by using PM (ApneaLinkTM, RESMED-Munich, Germany). All NH parameters such as AHI, min- SpO_2 , duration of $\text{SpO}_2 \leq 90\%$ were recorded during sleep period by

ApneaLinkTM. In the morning of the day after, ApneaLinkTM software Version 7.0.

Database

In the ICU period, the patient's age (years), gender, body mass index (BMI) (kg m^{-2}), APACHE II (Acute Physiology and Chronich Health Evaluation) score, Charlson comorbidity index (CCI), clinic pulmonary infection score (CPIS), isolated microorganisms identified, norepinephrine, steroid, invasive mechanical ventilation (IMV) and renal replacement therapy (RRT) requirements, length of ICU and hospital stay (days) were recorded. During application of SAT, patients' duration of SAT (minute), AHI (h^{-1}), min- SpO_2 (%), duration of $\text{SpO}_2 \leq 90\%$ (minute), the percentage of NH (NH%), minimum and maximum heart rate (min-HR and max-HR) were also recorded.

Definitions

According to Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine, a PM should include an oronasal thermal sensor to detect apneas, a nasal pressure transducer to measure hypopneas; oximetry and inductance plethysmography to record the respiratory effort^[11]. The ApneaLinkTM (RESMED-Munich, Germany) is a PM which can measure, and record AHI, min- SpO_2 , duration of $\text{SpO}_2 \leq 90\%$, minimum and maximum HR during sleep^[12].

The SAT was defined as a sleep test which NH markers could be recorded by using PM. Apnea was a non-breathing period lasting over 10 seconds. Hypopnea was defined as a breathing period with a 50% decrease in amplitude and a more than 4% decrease in oxygen saturation^[11]. Min- SpO_2 was the lowest saturation during the application of SAT. The duration of $\text{SpO}_2 \leq 90\%$ was the sum of the $\text{SpO}_2 \leq 90\%$ periods during the application of SAT. The NH% was defined as the ratio between the duration of $\text{SpO}_2 \leq 90\%$ and the SAT application time (duration of $\text{SpO}_2 \leq 90\% \div$ duration of SAT).

Statistical analysis

Statistical analysis was performed with the Wizard Pro Version 1.7.20. All of the variables in the database were summarized by using descriptive statistics. The

results were given as the percentage (%) and median (quartiles). All variables were tested for normal distribution using Kolmogorov-Smirnov test. Pearson correlation test was performed to determine the correlations and expressed as r². According to the first quartile of NH%, two NH% groups were defined and Student-t and Mann-Whitney U tests were used for the comparison between NH% groups. The multivariate regression model included age, BMI, APACHE II score, CCI, AHI, min-SpO₂ and NH% to estimate an increase in the length of hospital stay. These parameters were added to the regression model by using enter method. A type 1 error was established at 0.05.

RESULTS

Sixty-four patients with pneumonia were included in this study. For all patients, the median values of age, APACHE II, CCI, AHI, min-SpO₂, NH%, max-HR, length of hospital stay were 69, 18, 5, 21.5, 78%, 33.2%, 121 min⁻¹, and 11 days, respectively (Table 1). The first quartile of NH% was 18% (Table 1). In patients with NH% ≥18%, CCI, APACHE II, AHI, max-HR and length of hospital stay were significantly higher; min-SpO₂ was significantly lower than patients with NH% <18% (Table 2). NH% was positively correlated with APACHE II, CCI and length of hospital stays (r²=0.16; r²=0.26; r²=0.43 respectively, p<0.001 for all) (Figure 1). In multivariate analysis, length of hospital stay was increased by an increase in CCI, APACHE II and NH% (p=0.015; p<0.001; p=0.012, respectively) (Table 3).

DISCUSSION

This is the first study which the effects of undiagnosed NH on critically ill patients were evaluated. The present study showed that undiagnosed NH in daily sleep period was associated with higher ICU admission scores and poor outcomes.

It is known that all tissues use NADH for the production of mitochondrial energy which precipitates the need for oxygen [1,2]. Hence, hypoxia should be directly related to the organ dysfunction via delivery of oxygen because if the oxygen saturation decreases, DO₂ also decreases [14]. In recent studies, it was already demonstrated that NH was associated with morbidity and mortality [3,4,15]. In this study, the most important

Table 1. Demographic data, outcomes and apnea test markers.

Demographic data	
Age, (years)	69 (65-78)
Male, n (%)	44 (68.8)
BMI, (kg m ⁻²)	28 (26.4-0.1)
CCI	5 (4-6)
APACHE II	18 (14-24)
CPIS	7 (7-8)
Microorganisms, n (%)	
<i>Klebsiella pneumonia</i>	18 (28.1)
<i>Streptococcus pneumonia</i>	14 (21.9)
<i>Enterococcus</i>	10 (15.6)
<i>Candida albicans</i>	9 (14.1)
<i>Non-albicans candida</i>	5 (7.8)
<i>E. coli</i>	3 (4.7)
Unidentified	5 (7.8)
Medications and supports, n (%)	
The usage of norepinephrine	27 (42.2)
IMV requirement	22 (34.4)
The usage of steroid	20 (31.3)
RRT requirement	4 (6.3)
Outcomes	
Length of ICU stay, (day)	6 (4-8)
Length of hospital stay, (day)	11 (8-13)
Apnea Test markers	
Duration of AT, (minute)	388 (365-411)
AHI (h ⁻¹)	21.5 (16-29)
min-SpO ₂ (%)	78 (74-83)
Duration of SpO ₂ ≤ 90% (minute)	132.5 (73-168)
NH% (%)	33.2 (18-43.9)
min-HR	58 (52-66)
max-HR	121 (102-134)

AHI: apnea hypopnea index, APACHE II: acute physiology and chronic health evaluation, AT: apnea test, BMI: body mass index, CCI: charlson comorbidity index, CPIS: clinical pulmonary infection score, HR: heart rate, ICU: intensive care unit, max: maximum, min: minimum, NH: nocturnal hypoxia. Results were given as percentage and median (interquartile).

Table 2. Comparison of NH% groups.

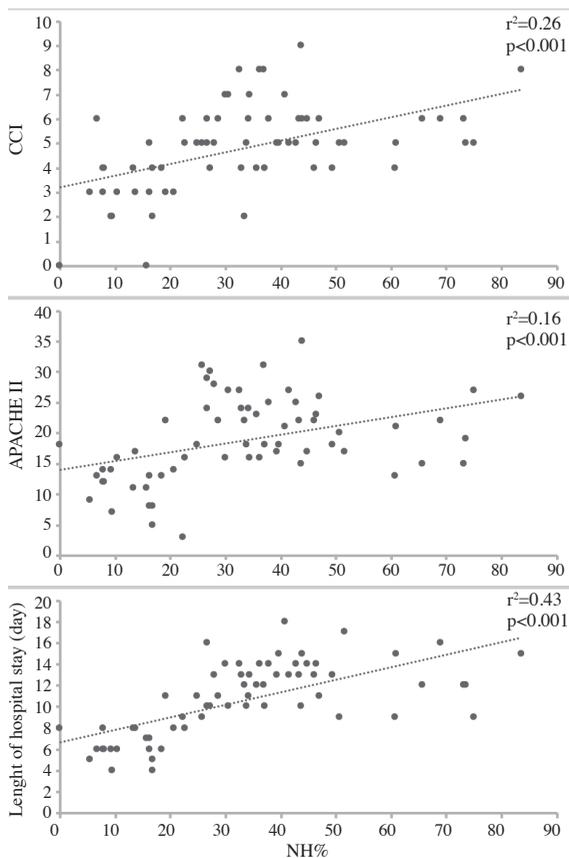
	NH% < 18% (n=16)	NH% ≥18% (n=48)	p
Age (year)	68±11	71±10	0.261
Male, n (%)	9 (56.2)	35 (72.9)	0.213
BMI, (kg m ⁻²)	27.9±3.5	29±4.2	0.340
CCI	3 (2-4)	5 (5-6)	<0.001
APACHE II	12±4	21±6	<0.001
CPIS	8 (7-9)	7 (7-8)	0.349
Duration of SAT, (min.)	389 (365-408)	387 (367-418)	0.620
AHI (h ⁻¹)	16 (14-18)	24 (18-32)	<0.001
min-SpO ₂ (%)	87.5 (79-88)	77 (73-82)	<0.001
Duration of SpO ₂ ≤ 90% (min.)	36 (28-62)	145.5 (122-177)	<0.001
NH% (%)	11±5	41±16	<0.001
min-HR	55±10	59±10	0.214
max-HR	98±13	127±20	<0.001
The usage of norepinephrine, n (%)	1 (6.2)	26 (54.2)	<0.001
IMV requirement, n (%)	1 (6.2)	21 (43.8)	0.006
The usage of steroid, n (%)	1 (6.2)	19 (39.6)	0.013
Length of ICU stay, (day)	3 (3-4)	7 (6-8)	<0.001
Length of hospital stay, (day)	6 (6-8)	12 (10-14)	<0.001

AHI: apnea hypopnea index, APACHE II: acute physiology and chronic health evaluation, BMI: body mass index, CCI: charlson comorbidity index, CPIS: clinical pulmonary infection score, HR: heart rate, ICU: intensive care unit, IMV: invasive mechanical ventilation, max: maximum, min: minimum, NH: nocturnal hypoxia, SAT: sleep apnea test. Results were given as mean (±sd), percentage and median (interquartiles).

Table 3. Multivariate linear regression model for length of hospital stay.

	Coefficient (95 % CI)	p
Age (year)	-0.05 (-0.10; 0.01)	0.086
BMI (kg m ⁻²)	-0.05 (-0.20; 0.09)	0.464
CCI	0.57 (0.11; 1.04)	0.015
APACHE II	0.17 (0.08; 0.27)	<0.001
AHI (h ⁻¹)	0.001 (-0.07; 0.07)	0.974
min-SpO ₂ (%)	-0.07 (-0.17; 0.04)	0.194
NH%	0.06 (0.01; 0.11)	0.012

AHI: apnea-hypopnea index, APACHE: acute physiology and chronic health evaluation, BMI: body mass index, CCI: charlson comorbidity index, CI: confidence interval, min-SpO₂: minimum peripheral oxygen saturation, NH: nocturnal hypoxia.

**Figure 1. NH% Correlations.**

APACHE II, acute physiology and chronic health evaluation; CCI, charlson comorbidity index; NH, nocturnal hypoxia.

result was that median values of AHI and NH% were 21.5 and 33.2%, respectively (Table 1). Furthermore, 2 patients with AHI<5 and one patient with NH%=0 were detected which signifies that the majority of the patients admitted to the ICU had undiagnosed NH and these patients could be exposed to hypoxia being un-

aware of this effect every night before ICU admission. Thus, we can ask this question; “Can ICU admission scores be affected by undiagnosed NH?”. It is known that ICU admission scores such as APACHE II help us to predict the likelihood of mortality at the ICU admission [16,17]. Li et al. [18] demonstrated that per 5 point increase in APACHE II score was related to risk of death in the ICU. We observed that NH% in daily sleep period was positively correlated with APACHE II score and CCI at the ICU admission and also positively correlated with length of hospital stay (Figure 1). Furthermore, when the first quartile of NH% was determined as a cut-off value, we observed that ICU admission scores, norepinephrine, steroid and IMV requirements, length of ICU and hospital stays in patients with NH% \geq 18% were higher than those of the patients with NH%<18% (Table 2).

In fact, AHI has been suggested to be used as a diagnostic parameter for OSAS in accordance with the Guideline [11]. Yet, the different hypoxia definitions in OSAS have been still discussed [19]. In the present study, we didn't find any relationship between AHI and each of CCI, APACHE II score and length of hospital stay ($r^2=0.04$ $p=0.118$; $r^2=0.06$ $p=0.068$; $r^2=0.05$ $p=0.092$ respectively). Therefore, we think that NH% may be a better parameter than AHI to define the NH because NH can be directly demonstrated.

BMI is expectedly related to worse outcomes, on the contrary there are some studies which had obtained different results [20,21]. Onal et al. [22] found a negative correlation between BMI and outcomes. Yang et al. [23] demonstrated that CCI was also a predictive factor for mortality. We also found that length of hospital stay increased by only increases in APACHE II, CCI and NH% (Table 3). Furthermore, there was not any correlation between NH% and BMI ($r^2=0.002$ $p=0.738$). If these results can be accepted as evidence for the effects of NH on critically ill patients, then it can be concluded that the patient with worse clinical status at the ICU admission can have undiagnosed NH and they should be also treated after hospital discharge.

CONCLUSION

Most of the admitted patients to the ICU can have undiagnosed NH. Increased NH% in daily sleep period may be a reason for the worse clinical status at

the ICU admission and increased length of hospital stay. NH% may be the better parameter than AHI to demonstrate the NH. Determining and treating undiagnosed NH before ICU admission may improve clinical status of the patients at the ICU admission.

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Conflict of Interest

The authors declare that they have no conflict of interest

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