Comparison of Partial Pressure of Carbon Dioxide in Arterial Blood and Transcutaneous Carbon Dioxide Monitorizaiton in Patients with Obstructive Sleep Apnea and Sleep Related Hypoventilation/Hypoxemia Syndromes

Obstrüktif Uyku Apne ve Uykuyla İlişkili Hipoksemi-Hipoventilasyon Sendromlu Hastalarda Arteriyel Kan Parsiyel CO_2 Basıncı ile Transkutanöz CO_2 İzleminin Karşılaştırması

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Summary

Objective: There is limited number of studies conducted on the use of capnography for CO_2 monitorization in sleep laboratories. In this study, it was aimed to investigate the correlation between the CO_2 value measured by transcutaneous carbon dioxide ($tcCO_2$) monitorization and partial pressure of carbon dioxide ($PaCO_2$) levels measured with arterial blood gas analysis in patients diagnosed with obstructive sleep apnea syndrome (OSAS) and Sleep-related hypoventilation/hypoxemic syndromes (SRHHS).

Materials and Methods: Patients with bilevel positive airway pressure (BiPAP) treatment indication who were diagnosed with OSAS and SRHHS via polysomnography (PSG), were prospectively included in the study. Four arterial blood gas analyses were conducted from all participants (pre- and post-PSG, before and after manual bi-level positive airway pressure titration) in order to find $PaCO_2$ levels against $tcCO_2$ monitorization.

Results: Totally 30 patients with sleep-related respiratory disease (SRRD), consisting of 18 patients with OSAS and COPD, and 12 patients with OSAS and obesity hypoventilation syndrome (OHS), were included in the study. A correlation was detected between average $tcCO_2$ level and average $PaCO_2$ level in night PSG (r=0.600; p<0.0001). Similarly, we found a correlation between average $tcCO_2$ level and average $PaCO_2$ level in BiPAP titration night measurements as well (r=0.812; p=0.001). Finally, a correlation was detected between the average $PaCO_2$ value obtained from four blood gas samples measured in both nights and the average $tcCO_2$ value taken from two capnographies (r=0.783; p<0.001).

Conclusion: Comparing $tcCO_2$ and $PaCO_2$ values, it was determined that the average CO_2 values measured by capnography correlated with the average of simultaneous arterial CO_2 values measured before and after BiPAP titration.

Keywords: Transcutaneous carbon dioxide, Obstructive sleep apnea syndrome, polysomnography, capnography

Öz

Amaç: Uyku laboratuvarlarında kapnograf ile CO_2 monitörizasyon kullanımıyla ilgili az sayıda çalışma vardır. Bu çalışmada Obstrüktif uyku apnesi sendromu (OSAS) ve Uykuyla ilişkili hipoksemi-hipoventilasyon sendromu (UHHS) tanılı hasta grubunda transkutanöz yol ile ölçülen $tcCO_2$ değerinin kan gazı ile ölçülen $PaCO_2$ değerleri ile korelasyonunu araştırmayı hedefledik.

Gereç ve Yöntem: Polisomnografi (PSG) ile OSAS ve UHHS tanısı alan ve bilevel pozitif hava yolu basıncı (BiPAP) tedavi endikasyonu olan hastalar prospektif olarak çalışmaya alındı. Hastalardan PSG öncesi, sonrası ve manuel BiPAP titrasyonu öncesi ve sonrası toplam 4 kez arteriyel kan gazı örneği alındı ve hastaların $PaCO_2$ düzeylerine bakıldı, eşzamanlı olarak $tcCO_2$ monitörizasyonu ile CO_2 ölçümü yapıldı.

Bulgular: Çalışmaya 18'i OSAS ve KOAH, 12'si OSAS ve Obezite hipoventilasyon sendromu (OHS) tanılı toplam 30 uykuyla ilişkili solunum bozukluğu hastası (UİSB) dahil edildi. PSG gecesi ortalama $tcCO_2$ düzeyi ile ortalama $PaCO_2$ düzeyi arasında korelasyon saptandı (r=0,600; p<0,0001) (Şekil 1). Benzer şekilde BiPAP titrasyonu gecesi ölçümlerinde de ortalama $tcCO_2$ ve ortalama $PaCO_2$ değerleri arasında korelasyon saptantı (r=0,812; p=0,001). Her iki gecedeki toplam dört kan gazından elde edilen ortalama $PaCO_2$ ve toplam iki kapnogramdan elde edilen ortalama $tcCO_2$ değerleri arasında da korelasyon saptanmıştır (r=0,783; p<0,001).

Sonuç: Çalışmamızda $tcCO_2$ ile $PaCO_2$ değerleri karşılaştırılması sonucu; kapnograf ile ölçülen ortalama CO_2 değerlerinin BiPAP titrasyonu öncesi ve sonrasında alınan simultane arteryal pCO_2 değerleri ortalaması ile korelasyon gösterdiğini tespit edildi.

Anahtar Kelimeler: Transkutanöz karbondioksit, Obstrüktif uyku apne sendromu, polisomnografi, kapnograf

Introduction

It is important to know carbon dioxide partial pressure ($PaCO_2$) in arterial blood to determine the sufficiency of alveolar ventilation (1). $PaCO_2$ monitoring is conducted with varying frequencies in sleep laboratories in order to evaluate the efficiency of diagnosis and treatment, and to apply apnea and pulmonary stress tests (2-8).

Today, examination of the arterial blood gas is the gold standard method in $PaCO_2$ measurement. Since it is an invasive method that results in such side effects as severe pain, susceptibility to infection, thrombosis, there are ongoing efforts to develop alternative methods that constantly measure intensive care patients and sleep laboratories (9). Even though the $PaCO_2$ measurement with arterial catheterization is easy to repeat, it still requires expensive equipment, specially-trained staff, and in most of the cases, an intensive care environment. It also causes morbidity on a slight but significant level (10).

Non-invasive CO_2 monitoring ($tcCO_2$) with transcutaneous capnography is an almost 30-year-old method that relies on high resolution CO_2 measurement which is applied by placing locally heated electrochemical sensors on the skin without an invasive process (11).

A correlation was detected in most of the studies that involve various patient groups during the evaluation of the results of the studies comparing $PaCO_2$ measurements and the measurements carried out with the transcutaneous method (11-13). However, most of these studies included different patient groups, and were not practiced in sleep laboratories. In our study, we referred to our sleep laboratory, and examined the consistency of the average $PaCO_2$ level in arterial blood gas obtained in both polysomnography (PSG) and bi-level positive airway pressure (BiPAP) titration applications and the average CO_2 value that is measured by nightlong $tcCO_2$ monitoring in the same nights in patients with Obstructive sleep apnea syndrome (OSAS) and Sleep related hypoventilation/hypoxemia syndromes (SRHHS) diagnosis.

Materials and Methods

A total of 68 cases referred to the sleep outpatient clinics in our hospital between July 2011 and February 2012 were evaluated. Fifty-four patients diagnosed with sleep related respiratory disorders, 24 cases of whom with certain congestive cardiac failure diagnosed via echocardiogram were excluded from the study. Patients with BPAP treatment indication and diagnosed with overnight PSG, OSAS, SRHHS were included prospectively in the research. OSAS and SRHHS diagnoses relied on the International Classification (ICSD-2) in American Sleep Academy (14). Informed consent was received from the patients in both nights of diagnosis and treatment. The study protocol was approved by the Institutional Review Board of the research hospital.

Polysomnography

Patients were taken to the sleep laboratory at 8:00 pm and they underwent standard PSG. PSG was measured via Compumedics E-Series (Compumedics Limited, Australia) Profusion PSG 2 (Compumedics Limited, Australia) program and included four electroencephalography (EEG) channels (C3 to A1, C4 to A2, O1 to A2, and O2 to A1), right and left electrooculography (EOG) channels, one chin electromyography (EMG) channel and four tibialis anterior EMG channels, finger pulse oximeter, strain gauges for thoracoabdominal movements, one electrocardiography (ECG) lead, a nasal airflow (pressure cannula), a nasal thermistor and a digital microphone to detect snoring. PSG records were scored in 30-second durations of sleep, breathing and oxygenation according to the standard criteria determined by the American Academy of Sleep Medicine (AASM) (14). Obstructive apnea was defined as a 90% cessation of oro-nasal airflow for at least 10 seconds in the presence of chest-wall motion. Hypopnea was defined as a 50% or higher reduction in the airflow associated with 3% or higher arterial oxygen desaturation and/or arousal, or a 30% or higher reduction in respiratory airflow associated with 4% or higher arterial oxygen desaturation and/or arousal for at least 10 seconds. Apnea hypopnea index (AHI) was calculated as the total number of apneas and hypopneas per hour of sleep. Diagnosis of OSA relied on PSG findings, according to the International Classification of sleep disorders 2 (ICSD-2) (15). Subjects with an Apnea-hypopnea index (AHI) ≥5 were considered to have OSA, and OSA severity was classified as mild (5≤ AHI <15), moderate (15≤ AHI <30), or severe (AHI ≥30). The Oxygen desaturation index (ODI) measuring the number of oxygen desaturations ≥3% per hour of sleep was determined.

Arterial Blood Gas

The first arterial blood gas sample was taken in supine position prior to the night polysomnography recording, the second was taken at the end of recording; the third was taken before manual BPAP titration started and the fourth was taken in the morning after titration in the same position from radial artery via heparinized tubes to the amount of 2 ml. The process was carried out by duly trained assistant staff. Samples were evaluated with Rapidlab Analyzer 860 (Bayer Health Care Systems-Siemens, USA) device.

Measurement with Capnography

Sentec V-Sign digital transcutaneous CO_2 probe was used in Sentec digital monitoring system (Sentec AG, Therwil, Switzerland) which measures with transcutaneous method, in order to measure arterial carbon dioxide pressure non-invasively and constantly. $TcCO_2$ was measured in line with the manufacturer's recommendations. The probe was secured on the earlobe with a clip. The skin was heated with the probe up to 42 degrees in order to improve arterialization. The gas coming out of the skin and passing through a gas permeable membrane, according to the working principle of the device, changes the pH value of the electrolyte located under the membrane. The difference between the reference electrode and the measuring electrode is equivalent to the arterial partial carbon dioxide pressure according to pH value logarithms and the Sveringhaus effect. These values were calculated by being transferred to VSTAT software. When recording finished, a report was prepared indicating the highest, the lowest and average CO_2 values. Calibration integration was performed automatically by the calibration system.

Other Measurements

Respiratory function test measurements were performed via ZAN 100 (Flow handy, Germany) device, afoot and using nose clips. Minimum 3 maximum 5 tests were applied until three acceptable tests were obtained. The highest forced vital capacity and the first second forced expiratory volume were recorded. Excessive daytime sleepiness was defined as the score of Epworth sleepiness scale >10 (16).

Statistical Analyses

All data were analyzed by using SPSS for Windows version 17. Constant variables were stated in median (inter-quarters rate), categorical variables were stated in numbers (%). Comparisons were made by using the square tests for categorical variables, and the Mann-Whitney U tests for constant variables. The Spearman correlation test was used for correlation analysis. P<0.05 was accepted as the significance threshold.

Results

Eighteen patients diagnosed with the OSA syndrome and COPD, and 12 with the OSA syndrome and Obesity Hypoventilation Syndrome (OHS), totally 30 patients with SRHHS (Sleep-Related Hypoventilation/Hypoxemic Syndromes) were included in the study. The most commonly determined symptoms were snoring (90%) and daytime sleepiness (75%). Patients' demographic data are given in Table 1.

Considering pre-BPAP PSG and post-BPAP titration PSG data, we observed treatment effect on a statistically significant level in almost all patients (Table 2). Duration through which patients had oxygen saturation below 90% decreased significantly (p<0.001), a significant increase was observed in minimum and average O_2 saturation (p<0.001, p<0.001 respectively). We detected a statistically significant reduction in the number of obstructive and NREM AHI (p<0.001 both). Relevant data are presented in Table 2.

Comparing the BPAP value obtained from the patients in the PSG night before the recording started and in the morning after the recording, and the arterial blood gas values obtained the night before and after titration, a significant decrease in patients' $PaCO_2$ (p<0.001) and a significant increase in patients' PaO_2 (p:0.012) was observed. Relevant data are given in Table 3 and Table 4.

Table 1. Demographic data of the patients included in the study	
SRHHS (n=30)	
Sex	
Male Female	14 (46%)* 16 (54%)*
Age (year) (average±SD)	57±9
Additional disease	
HT DM Other No additional disease	13 (43%)* 5 (16%)* 5 (16%)* 7 (23%)*
BMI (kg/m^2)	41 (30-55)**
*: Colon percentage **: Median (min-max), HT: Hypertension, DM: Diabetes mellitus, BMI: Body-mass index, SRHHS: Sleep-related hypoventilation/ hypoxemic syndromes	

Table 2. Comparison of the patients' overnight polysomnography and manual bi-level positive airway pressure titration data

	PSG median (min-max)	Titration with BPAP median (min-max)	p value
Duration of oxygen saturation under 90% (min)	191(121-299)	51 (3-139)	<0.001
Minimum O2 saturation (%)	63 (47-74)	81 (65-85)	<0.001
Average O2 saturation (%)	85 (77-89)	92 (89-93)	<0.001
t AHİ	39 (23-74)	14 (8-21)	<0.001
o AHİ	24 (3-58)	0 (0-4)	<0.001
c AHİ	0 (0-0)	0 (0-0)	0.726
m AHİ	0 (0-0)	0 (0-0)	0.046
REM AHİ	23 (0-68)	11 (5-22)	0.061
Supine AHİ	48 (29-79)	13 (8-21)	<0.001
NREM AHİ	42 (23-78)	15 (9-20)	<0.001
t AHI: Total apnea hypopnea index (events/hr), o AHI: Obstructive apnea hypopnea index, c AHI: Centre apnea hypopnea index, m AHI: Mix apnea hypopnea index, PSG: Polysomnography, BPAP: Bi-level positive airway pressure, REM: Rapid eye movement sleep, NREM: Non-rapid eye movement sleep			

Table 3. Comparison of the arterial blood gas values before and after polysomnography, and before and after bi-level positive airway pressure

	Before PSG	After PSG	p value	Before BPAP	After BPAP	p value
pH	7.38 (7.27-7.51)	7.39 (7.23-7.55)	0.745	7.38 (7.31-7.47)	7.37 (7.32-7.43)	0.936
PO$_2$ (mmHg)	59.5 (34-105)	63.5 (35-112)	0.274	61.5 (34-108)	73.1 (45-109)	0.012
PCO$_2$ (mmHg)	46 (34-69)	49 (38-67)	0.004	47.7 (32-72)	51.2 (40-84)	<0.001
HCO$_3$ (mEq/L)	26.9 (18-40)	28 (20.1-35)	0.397	27.5 (19.8-36)	28.7 (23-37)	0.26
O2 Sat (%)	90.2 (63.8-97.8)	92.3 (63.5-99)	0.141	88.8 (65-98)	91.9 (81-97.7)	0.02
PSG: Polysomnography, BPAP: Bi-level positive airway pressure						

A correlation was detected between average $tcCO_2$ level and average $PaCO_2$ level measured in the PSG night (r: 0.600; p<0.0001) (Figure 1). Similarly, there was a correlation between average tcCO2 level and average $PaCO_2$ level in the BPAP titration night measurements as well (r:0.812; p:0.001) (Figure 2). We found a correlation between the $PaCO_2$ value obtained from total four blood gas samples in both nights and the tcCO2 value taken from two capnograms in total (r:0.783; p<0.001). Relevant correlation curves are presented respectively (Figure 1, 2).

Discussion

WWe performed a $tcCO_2$ monitoring on our patients diagnosed with OSAS and SRHHS and investigated whether it was correlated with $PaCO_2$ measurement. A comparison of $tcCO_2$ and $PaCO_2$ values conducted within the scope of our study indicated that average CO_2 data measured by capnography correlated with the average of simultaneous arterial CO_2 values measured before and after BPAP titration. Based on the results, we believe that measurements can be made in sleep laboratories with transcutaneous capnography without disturbing the patients regarding the patient group diagnosed with OSAS and UHSS, and results compatible with arterial CO_2 values can be obtained.

Capnographies are devices capable of performing both end tidal and transcutaneous measurements. The end tidal capnography, which is particularly used in intensive care units, both exposes the patient to an invasive procedure such as $PaCO_2$ monitoring via arterial blood gas or catheterization, and we know that it may yield false results in the cases with increased dead gap respiration (17). For these reasons, we preferred measuring with transcutaneous capnography method which offers rather non-invasive measurements.

In literature review we found that very few studies have been conducted in a sleep laboratory. In one of these studies, Sanders et al. compared all three methods but failed to detect any correlation between $PaCO_2$ and $tcCO_2$ (18) . However, their

research included a patient group with sleep diseases associated with neuromuscular diseases, restrictive and obstructive lung diseases, displaying quite heterogeneous CO_2 values. Therefore, the cases presented quite a wide CO_2 range. They suggested
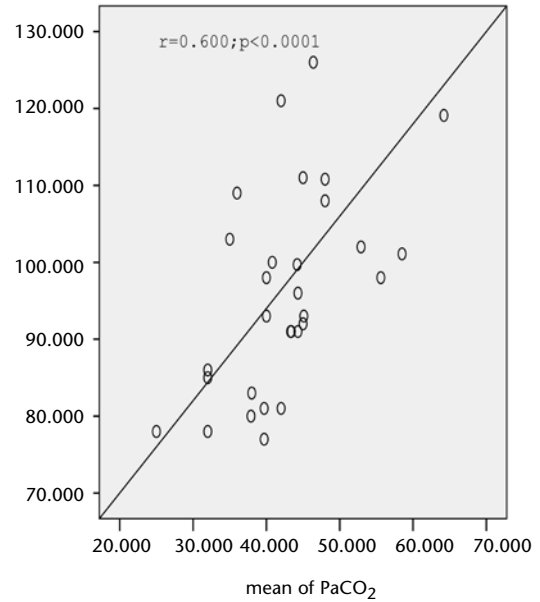

Figure 1. Polysomnography night correlation curve

$tcCO_2$: The CO_2 value measured by transcutaneus carbondioxide monitorization, $PaCO_2$: Partial pressure of carbon dioxide levels measured with arterial blood gas analysis
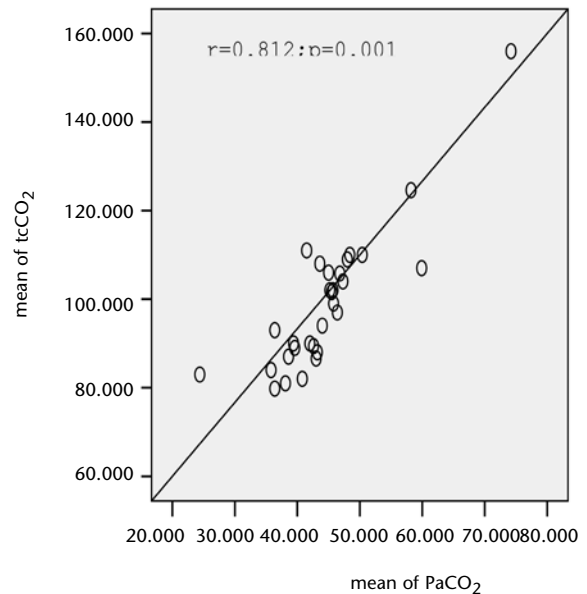

Figure 2. Bi-level positive airway pressure night correlation curve

$tcCO_2$: The CO_2 value measured by transcutaneus carbondioxide monitorization, $PaCO_2$: Partial pressure of carbon dioxide levels measured with arterial blood gas analysis

Table 4. Minimum, maximum and average carbon dioxide values measured with transcutaneous capnography during polysomnography and bi-level positive airway pressure titration

	PSG Median (min-max)	BPAP Median (min-max)	p value
Average CO_2 (mmHg)	42.6 (25-64.2)	44.5 (24.4-74.2)	0.285
Minimum CO_2 (mmHg)	30.3 (16.9-55)	32.4 (19.5-70)	0.267
Maximum CO_2 (mmHg)	55.4 (38.4-95)	55.9 (40-122)	0.734
PSG: Polysomnography, BPAP: Bi-level positive airway pressure, CO_2: Carbon dioxide			

that correlated results can be found in a patient group with a narrower CO_2 range. Our patient group consisted of cases with more homogeneous CO_2 values. Similarly, studies with narrower CO_2 ranges also indicated a correlation as presented in our study (19,20). As mentioned above, we may have detected a correlation due to the values on a narrower range. Nevertheless, both our study and the one conducted by Sanders et al. included a limited number of patients, thus further studies with higher numbers of patients, including specifically the sub-groups with narrow and wide CO_2 ranges, are required. It can still be considered as an effective method in monitoring the patients displaying a narrower CO_2 range.

Pillsbury et al. (12) found a correlation between $PaCO_2$ and $tcPCO_2$ values in the study they conducted among healthy subjects with a normal CO_2 range. Healey et al. (13) stated in their study conducted on 20 patients with stable CO_2 values who were monitored under mechanic ventilation that both end tidal and transcutaneous capnography could be alternative methods to arterial blood gas. This study conducted by Healey et al. (13) found a correlation in narrow CO_2 results. Our study aimed to research the effectiveness of capnography in monitoring non-invasive mechanic ventilation treatment for obstructive and restrictive respiratory diseases. Our study did not include healthy subjects. Intensive care patients, similar to the patients suffering from sleep-related diseases, need long term monitoring as well. Therefore, use of non-invasive methods such as within the scope of our study should be taken into consideration for patient comfort.

Palmisano et al., (21) in the study which evaluated 756 samples taken from 251 cases, investigated quite different disease groups falling in an age interval of 4 weeks-60 years, and measured varying ranges of CO_2. They pointed out that as the difference between CO_2 values increases, consistency of measurements decreases. Although the number of patients was very remarkable, heterogeneity of the groups made us think that new studies should be conducted in further sub-groups.

Healey et al. (13) reported for intensive care patients and Hanly et al. reported for congestive cardiac failure patients that their $tcCO_2$ measurements were negatively affected by low cardiac output or vasoconstrictor agents, hypothermia or hypovolemia or increased cardiogenic hypotension-related cutaneous vascular resistance. In cases with cardiac index below 1.5 L/min, the difference between $tcCO_2$ and $PaCO_2$ was observed to increase dramatically. Further, it was stated that in intensive care units especially in which inotropic agents such as dopamine was used, measurement results could be detected incorrectly due to vasoconstriction, and thus transcutaneous measurement should not be performed (22). Our patient group did not display any serious cardiac failure or cases treated with inotrope. Therefore, in contrast to these studies, we can assume that the $tcCO_2$ values measured also during the BPAP monitoring correlated with the $PaCO_2$ values measured with ABG analysis.

Even though it seems to be a useful method for the patients suffering from sleep-related diseases and intensive care patients who need constant monitoring, the method has its own difficulties such as calibration before measurements, constant replacement of the membranes, skin burns etc. It is known that especially the probes placed on the stomach skin in the new capnographies which are being used for the first time are heated up to 43°C-44°C for measurement, and they often cause skin burns. This was an important limitation reason until the introduction of new generation probes (23). The sensor we preferred in our study has recently been developed and which measures from earlobe. Given that earlobe is an area with thin skin and subcutaneous fat tissue, the sensor was heated up to 42°C. This is a new technology, and in our opinion, it will eventually replace the method whereby the probe is heated up to 43°C for optimal measurement and placed on stomach skin. We did not encounter any skin burn in our study. The necessity of calibrating the capnographies once in every 4 hours also constitutes an important limitation factor. It increases the workload and disturbs patients. Moreover, it is very likely to have an impact on the results and sleep quality in sleep laboratories, as was in our study. The probe we used in our study has a calibration time of 8 hours so this offered an optimal recording time for the sleep laboratory. Domingo et al. stated that limitations have decreased thanks to the improvements witnessed in the past two decades, such as smaller probes, shorter alteration time, lower heat, and less calibration requirement; and the aforementioned method has displayed an increasing clinical usage (24).

We detected a significant increase in PaO_2 and a significant decrease in $PaCO_2$ values after titration in BPAP pressure values with 13 mmHg EPAP and 17 mmHg IPAP when we compared and evaluated the BPAP values taken from patients in the PSG night before starting recording and in the morning after finishing record, and the arterial blood gas values taken the night before and after titration. However, no statistically significant difference could be found between the minimum, average, and maximum CO_2 values of the patients measured with capnography both in the diagnosis PSG and titration BPAP nights. We think that low $PaCO_2$ value (37 mmHg), a narrow range (30-47 mmHg) and suboptimal pressure application until effective BPAP pressure is attained (13 mmHg EPAP and 17 mmHg IPAP) may constitute the reasons for the absence of a difference.

One of the limitations in our study pertains to the small number of patients. Capnography records included highest, lowest and average CO_2 values observed during recording. Therefore, we compared the average CO_2 value measured by capnography and the CO_2 value detected by blood gas. Inability of the capnography to show instantaneous values constitutes another limitation of our study. Although blood gas samples were taken by well-trained staff, it is also possible that sufficient standardization could not have been achieved due to the human factor.

Conclusion

In conclusion, this study compared $tcCO_2$ and $PaCO_2$ values in both diagnostic PSG night and titration night with BPAP in patients with OSAS and SRHHS. Our results suggested that $tcCO_2$ monitoring during PSG and BPAP titration can be introduced to clinical practice. However, further studies are needed in order to determine the subgroup of patients in which it can be effective.

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