

## THE PRACTICALITY OF TRANSCUTANEOUS CO<sub>2</sub> MONITORING DURING POLYSOMNOGRAM RECORDING IN A SLEEP UNIT

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### Abstract:

The transcutaneous CO<sub>2</sub> (tcCO<sub>2</sub>) monitoring has demonstrated a good correlation with the arterial CO<sub>2</sub> value, and is better than pulseoxymeter for to detect hypoventilation episodes. The tcCO<sub>2</sub> monitoring is not routine in our environment. The aim of our study was to evaluate the utility of tcCO<sub>2</sub> monitoring in our sleep unit, in basal studies and in non invasive ventilation settings. We performed a prospective study. We measured the tcCO<sub>2</sub> values in basal polysomnographies (PSG) and in CPAP or BIPAP settings in patients with diagnosis of OSAS, obesity-hypoventilation Syndrome and COPD. We included 102 studies in 89 patients. There were 45 basal studies, 21 CPAP settings and 34 BIPAP settings. The most frequent pathology was OSAS. The mean pressure in CPAP settings was 9.6 H<sub>2</sub>Ocm, while in BIPAP settings the mean IPAP was 15.7 and the mean EPAP was 7.4. The mean desaturation index was 27, the mean peripheral O<sub>2</sub> value was 91.8%, and the mean cumuled time under 90% (CT90) of O<sub>2</sub> peripheral saturation was 22.9%. The mean tcCO<sub>2</sub> was 45.6 and the maximum was 49.2. Conclusions: tcCO<sub>2</sub> monitoring is a non invasive method for to detect hypoventilation episodes in patients with sleep pathology and in non invasive ventilation settings, although the peripheral oxygen saturation remains in normal values.

**Key words:** Hypoventilation, non-invasive ventilation, transcutaneous monitoring of CO<sub>2</sub>

### UTILIDAD DE LA MONITORIZACIÓN TRANSCUTÁNEA DE CO<sub>2</sub> DURANTE EL REGISTRO POLISOMNOGRÁFICO EN UNA UNIDAD DE SUEÑO

#### Resumen

Los trastornos respiratorios del sueño son frecuentes en la población general y generan un alto consumo de recursos por ingresos, consultas y uso crónico de las terapias ventilatorias. La medición de CO<sub>2</sub> transcutánea (tcCO<sub>2</sub>) ha mostrado buena correlación con la presión arterial de CO<sub>2</sub> (PCO<sub>2</sub>) y es superior al pulsioxímetro para detectar hypoventilación. Su uso está poco extendido en nuestro medio. Nuestro objetivo fue valorar su utilidad en estudios de sueño basales y en titulaciones de CPAP y BIPAP, aplicadas a pacientes con síndrome de apneas del sueño (SAHS) y síndrome de obesidad-hipoventilación (SOH). Usamos el medidor tcCO<sub>2</sub> en polisomnografías (PSG) basales de pacientes con sospecha de patología respiratoria del sueño y en titulaciones de CPAP o BIPAP de pacientes ya diagnosticados. Se realizaron 102 estudios a 89 pacientes. Hubo 45 estudios basales, 21 titulaciones de CPAP y 34 de BIPAP. La patología más frecuente fue el SAHS. La presión media de las titulaciones de CPAP fue de 9,6 cmH<sub>2</sub>O. En las titulaciones de BIPAP la IPAP media fue de 15,7 y la EPAP media de 7,4. El índice de desaturación (IDH) medio fue de 27. La SpO<sub>2</sub> media fue de 91,8% y el CT90 del 22,9%. La tcCO<sub>2</sub> media fue de 45,6 y la máxima de 49,2. No hubo efectos secundarios a la monitorización tcCO<sub>2</sub>. Conclusiones: observamos hipercapnia latente en muchos pacientes y el medidor fue bien tolerado. Creemos que la monitorización tcCO<sub>2</sub> puede ser útil como método no invasivo para detectar hypoventilación, aun con cifras normales de SpO<sub>2</sub>.

**Palabras clave:** Hipoventilación, ventilación no invasiva, medición transcutánea de CO<sub>2</sub>.

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## INTRODUCTION

Sleep-related breathing disorders are common in the general population. They generate a high use of resources for the health care system in terms of hospitalizations, addressing consults or emergencies and the chronic use of respiratory therapy. Sleep apnea-hypopnea syndrome (SAHS) is defined as a clinical picture of excessive drowsiness; cognitive-behavioral, respiratory, cardiac, metabolic or inflammatory disorders occurring as side effects of repeated episodes of upper airway obstruction during sleep<sup>1</sup>. It is a common disorder, present in 2-4% of the adult population<sup>2</sup>. Respiratory poligraphy or polysomnography (RP or PSG) is necessary for diagnosis. To make the diagnosis, an apnea-hypopnea index (AHI) >5 and symptoms related to the disease must be present<sup>1</sup>. Another common disease is obesity hypoventilation syndrome (OHS), defined as the combination of daytime hypercapnia (partial carbon dioxide pressure, PCO<sub>2</sub> >45 mmHg) and suffering from obesity (body mass index >30 Kg/m<sup>2</sup>), in which losing weight would reverse the alterations in sleep, pulmonary hypertension and shortness of breath associated with OHS<sup>3</sup>.

As we know, during PR recording sensors tracking body position, respiratory effort, airflow and pulse oximetry and other data are generally placed on the patient<sup>4</sup>. The extension of the use of pulse oximetry has allowed for the non-invasive monitoring of pulse and the oxygen in the arterial hemoglobin. Capnography, for its part, allows for the measurement of CO<sub>2</sub> in exhaled air and non-invasive transcutaneous monitoring. The transcutaneous measurement of CO<sub>2</sub> in humans was first described in 1960 by Severinghaus and consists of placing an electrode on the skin, which it heats to 42° C, vaporizing the capillary CO<sub>2</sub> in the subcutaneous tissue. This is the concentration which is measured by an infrared light transceiver/reader of a specific wavelength which is absorbed by the CO<sub>2</sub> in the tissue. The amount of light that reaches the reader is proportional to the amount of CO<sub>2</sub> present in the tissue. These measurements are read on a continuous reading monitor that is connected to the electrode<sup>5</sup>.

Its use is increasingly widespread, used on patients with alveolar hypoventilation both in sleep units and outpatient clinics, hospital stays and neonatal and adult intensive care units where invasive and non-invasive mechanical ventilation (IMV and NIV) are used.

Currently, arterial blood gas (ABG) is still the most exact method to

measure arterial oxygen pressure (PO<sub>2</sub>) and PCO<sub>2</sub> as well as the acid-base balance, allowing us to know the degree of oxygenation in the blood and pulmonary ventilation<sup>6</sup>.

Since the end of the last century, multiple studies have compared the gold standard, arterial blood gas, with transcutaneous CO<sub>2</sub> measurement.

Reviewing the literature, the highest number of studies on tcCO<sub>2</sub> has been in neonatal<sup>7</sup> patients and children, both in acute<sup>8</sup> and diagnostic processes while undergoing poligraphy<sup>9</sup>. The number of studies in adults continues to increase, including the study by Moronta and Gutiérrez<sup>6</sup> in which stable individuals went to outpatient clinics for respiratory diseases where they underwent baseline ABG and a single measurement of tcCO<sub>2</sub>. The average difference between diagnostic techniques was 1.08% and capnographic values were 1.1% (p <0.01) higher than those from blood gas. Similarly, the literature includes studies on patients in acute respiratory failure being treated with non-invasive mechanical ventilation with continuous CO<sub>2</sub> monitoring. In this case, while tcCO<sub>2</sub> measurement is not recommended as a substitute for that of PCO<sub>2</sub>, there are recommendations for it to have a changing role and be a response to treatment.

The development and extension of transcutaneous CO<sub>2</sub> measurements draws from the premise of being a continuous nocturnal recording, in comparison with ABG which is an occasional measurement and can thus mask nocturnal hypoventilation<sup>11</sup>.

Some studies have looked at tolerance for the device, initially recommending a change in the recording point after 4 hours and the recalibration of the machine to avoid scalding the skin<sup>12</sup> since, as mentioned previously, the machine increases temperature to 42 or 43°C to work correctly. However, more recent studies have measured tcCO<sub>2</sub> over 8 hours of continuous recording, without noting discomfort or side effects such as skin burns<sup>13,14</sup>.

The objective of this study was to evaluate the practicality of transcutaneous monitoring as a non-invasive tool to detect hypoventilation episodes in baseline sleep studies in patients with suspected sleep-related breathing disorders as well as CPAP or BIPAP titration in patients who have already been diagnosed with a sleep-related breathing disorder.

A secondary objective was to evaluate tolerance to the device and if discomfort or side effects presented at the point where the electrode was applied on patients studied during continuous nocturnal recording.

## MATERIAL AND METHODS

An observational prospective study was done on baseline polysomnography and CPAP and BIPAP titration with respiratory polygraphy or polysomnography control done in the sleep unit at Hospital Puerta del Mar. The equipment for the sleep study incorporated the TOSCA 500 (Radiometer Medical ApS, Copenhagen) brand transcutaneous CO<sub>2</sub> meter. All patients were recruited from a sleep unit with a suspected sleep-related breathing disorder (SAHS, OHS) or had an existing diagnosis. Patients underwent CPAP or BIPAP titration from 1 March 2013 to 31 August 2014.

The study was carried out in the sleep unit at Hospital Puerta del Mar in Cadiz. The TOSCA 500 transcutaneous CO<sub>2</sub> meter was connected to one of the Jaeger SleepLab 1000p (Jaeger, Warwick, UK) polysomnograms at our disposal. Thus, all of the studies were carried out in the same PSG bed with the same polysomnography equipment using the same transcutaneous CO<sub>2</sub> meter, after calibrating the device to avoid measurement errors. For all of the studies, the transcutaneous meter signal was obtained for three values: minimum, average and maximum tcCO<sub>2</sub> for each patient.

Our study carried out a continuous recording throughout the night, without recalibration nor change in sensor placement throughout the entirety of the test.

The following were inclusion criteria: adults over the age of eighteen with one of the following characteristics:

- Immunocompetent patients with obesity (BMI >30 Kg/m<sup>2</sup>) with a suspected sleep-related breathing disorder.
- Patients diagnosed with amyotrophic lateral sclerosis (ALS) with suspected alveolar hypoventilation after a suspicious baseline nocturnal pulse oximetry done during diagnosis or during follow-up at our ALS unit or through daytime hypercapnia detected in a baseline arterial blood gas for patients with alterations in forced vital capacity during pulmonary function tests.
- Suspected SAHS.
- Suspected OHS.
- Patients diagnosed with SAHS or OHS for CPAP or BIPAP titration.

Exclusion criteria were patients declining to participate in the study and/or declining to receive nocturnal respiratory support via the informed consent for said treatment.

Demographic data for patients was collected as well as tobacco use, presence of COPD (with spirometry values if affirmative) and the presence of cardiovascular risk factors: arterial hypertension (AHT), dyslipidemia, diabetes mellitus type 2 (DM2) and obesity. Obesity was defined as those patients with BMI >30 Kg/m<sup>2</sup>. Patients were classified into three groups according to degree of obesity: moderate obesity (BMI 30 - 35 Kg/m<sup>2</sup>), severe obesity (BMI 35 - 39.9 Kg/m<sup>2</sup>) and morbid obesity (>40 Kg/m<sup>2</sup>). The Charlson comorbidity index was also included. The Epworth Sleepiness Scale was used for all patients. The study was nocturnal and collected the following variables for analysis: AHI, 4% IDH, average and minimum peripheral capillary oxygen saturation (SpO<sub>2</sub>), CT90, average and maximum transcutaneous CO<sub>2</sub> values (tcCO<sub>2</sub>) throughout the night of the study. First, the characteristics and values of the aggregate sample were analyzed, followed by those based on diagnosis where patients with SAHS, OHS, COPD and neuromuscular disease were analyzed.

Variables were collected based on data and analyzed using the SPSS statistics software package, version 15.0. A statistical analysis was done for all variables included in the study. Qualitative variables are expressed as absolute frequency and percentages, while the quantitative variables are expressed as averages and standard deviations. The correlation between quantitative variables was measured using Pearson's correlation coefficient. The chi-square was used to measure association and compare proportions between qualitative variables.

The selection of independent variables for the multivariate analysis was based on the degree of statistical significance obtained in the univariate analysis. The presence of hypercapnia was considered to be the main variable. Differences with a p value of 0.05 or less associated with the contrast test were considered significant in all cases.

The study was done respecting the ethical principles for medical research involving human subjects from the Declaration of Helsinki by the World Medical Association as well as applicable laws for clinical trials with medical products, having received authorization from the center's clinical research ethics committee.

## RESULTS

### Aggregate sample analysis

A total of 89 patients were included, for whom a total of 102 nocturnal sleep studies with tcCO<sub>2</sub> measurement were conducted. Of the 89 patients, 52.5% were women. The average age was 64 (range: 20-90). The average score on the Epworth Scale was 6.5 points.

Half of the participants had a history of tobacco use, primarily among men (62.5%) versus women (37.5%),  $p < 0.001$ . The average BMI was 35.7 Kg/m<sup>2</sup> (range: 16.4 to 61), with 73.7% of participants suffering from obesity. Of these, 39.5% were morbidly obese, with a BMI greater than 40.

As far as other cardiovascular factors analyzed, their presence was quite significant within the sample. The prevalence of arterial hypertension was 68.8%, dyslipidemia was present in 40% and 37.5% of patients suffered from diabetes mellitus.

With regard to the distribution of different cardiovascular risk factors between genders, males were significantly associated with tobacco use and suffering from COPD ( $p < 0.05$ ), similar to obesity and tobacco use, which were more prevalent among men (54.1% and 62.5%, respectively,  $p < 0.04$ ). Arterial hypertension, dyslipidemia and diabetes were more frequent among women (58.1%, 53.1% and 53.3%, respectively). The distribution of risk factors for patients involved in the study is reflected in Table 1.

The presence of other comorbidities was evaluated using the Charlson comorbidity index, the average value of which was 3.8. In fact, 65% of patients had a Charlson index greater or equal to 3 points. For patients prescribed continuous home oxygen therapy, the average Charlson index was 5.08.

The distribution of sleep studies done with transcutaneous CO<sub>2</sub> monitoring is summarized in Table 2. The 102 studies were distributed as follows:

- 45 baseline studies.
- 14 split nights. Of these, 10 were BIPAP trials/titrations, 3 for CPAP and 1 with supplementary O<sub>2</sub>, all of which were administered in the second part of the study.

- 21 CPAP adjustment/titrations.
- 34 BIPAP adjustment/titrations.
- 1 volumetric ventilator titration.
- 1 nocturnal O<sub>2</sub> monitoring as separate treatment.

No cases of intolerance to the device or side effects were recorded in the area where the transcutaneous CO<sub>2</sub> meter was applied, and thus no changes were made to sensor placement. The meter was also not recalibrated during the recording as it was not considered necessary since, in addition to not needing to change sensor placement, no data collection errors were registered in any study that would require recalibration.

When analyzing disease distribution in the aggregate sample, SAHS was the most frequent (61 patients, 68.5%), followed by OHS (31 patients, 34.8%), COPD (25 patients, 28%), patients diagnosed with neuromuscular disease (4 patients, 4.4%) and patients with no sleep-related breathing disorders after completing a baseline study (7 patients, 8%). SAHS and OHS overlapped in 19 patients. Of the 25 patients with COPD, 20 of them were associated with SAHS (overlap syndrome) and 5 with OHS. Table 3 shows the distribution by disease.

With regard to the data obtained in the sleep studies, the average AHI in the aggregate sample was 11.9 and the average IDH was 27. The average global SpO<sub>2</sub> was 91.8% and the minimum was 78.8%. The average CT90 was 22.9%. Average tcCO<sub>2</sub> values in the aggregate sample were 45.6, with maximums of 49.2. In CPAP titration, the average pressure was 9.5 cmH<sub>2</sub>O (range: 9 to 13 cmH<sub>2</sub>O). In BIPAP titration, the average IPAP was 15.7 cmH<sub>2</sub>O (range: 9 to 20) and the average EPAP was 7.4 cmH<sub>2</sub>O (range: 4 to 11).

As for the patients who were not diagnosed with respiratory disease after the baseline sleep study, statistically significant differences were observed in pulse oximetry values with respect to the aggregate sample, with an average SpO<sub>2</sub> of 94.3% ( $p: 0.04$ ), a minimum value of 87.4% ( $p < 0.001$ ) and a CT90 value of 1.1% ( $p < 0.001$ ). However, no differences were observed in the average and maximum tcCO<sub>2</sub> values (46.2 and 48.5, respectively), being very similar to those for the aggregate sample.

**Table 1. Aggregate sample risk factor distribution**

Risk factors/Comorbidities	(%)	% Women	p*
Obesity (BMI >30)	73.7	45.9	NS
Tobacco use	50	37.5	0.002
Arterial hypertension	68.8	58.1	NS
Dyslipidemia	40	53.1	NS
Diabetes mellitus	37.5	53.3	NS
COPD	28	32	0.001

(\*): p values in function of different comorbidities between males and females.

**Table 2. Distribution of sleep studies done with tcCO<sub>2</sub> recording**

Type of study	Frequency	(%)
Baseline PSG	45	44.1
Split night*	14	13.7
CPAP adjustment/titration	21	20.6
BIPAP adjustment/titration	34	33.3
Volumetric ventilator adjustment/titration	1	1
Separate nocturnal O <sub>2</sub> adjustment/titration	1	1

\* Split nights included CPAP or BIPAP adjustment/titration in the second half of the night.

**Table 3. Distribution of patient disease in the aggregate sample.**

Distribution by disease	Frequency	(%)
OSAHS	61	68.5
OHS	31	34.8
COPD	25	28
Neuromuscular	4	4.4
No disease	7	7.8

More detailed results for the global parameters from the sleep studies are included in Table 4.

**Table 4. Parameter values for sleep recording**

Average parameter values for sleep study	
IAH	11.9
IDH	27
Average SpO <sub>2</sub>	91.8%
Minimum SpO <sub>2</sub>	78.8%
CT90	22.9%
Average / maximum global tcCO <sub>2</sub>	45.6/49.2
Baseline study average / maximum tcCO <sub>2</sub>	44.5/48.03
tcCO <sub>2</sub> in CPAP titration	45.87/49.22
Average / maximum tcCO <sub>2</sub> in BIPAP titration	45.41/49.25
Patients with nocturnal O <sub>2</sub> (with/without BIPAP) (n=12)	45.8/48.92
Average CPAP	9.6
Average IPAP	15.7
Average EPAP	7.4

### Analysis by diagnostic subgroup

The results for each diagnostic subgroup are described in detail below. Table 5 shows the average values for the parameters analyzed in the study for each subgroup.

### SAHS

As mentioned previously, subjects with SAHS accounted for 68.5% of diagnoses, in a total of 61 patients. The average score on the Epworth Scale was 6.9 points. The average BMI was 36.6 (range: 17 to 61). Of the SAHS patients suffering from obesity, 36.8% had a BMI of >40. The average AHI in the diagnostic studies for SAHS was 34.1 (range: 5.1 to 80.9), while the average IDH was 56.84. The average global SpO<sub>2</sub> was 90.6% and the minimum was 74.5%. The average CT90 was 33.2%. With regard to the transcutaneous CO<sub>2</sub> values for these patients, the average value was 44.8 and the maximum

was 48.9.

77% of SAHS patients (47 patients) received nocturnal treatment. Of these, 22 patients (46.8%) received CPAP treatment with an average pressure of 9.9 cmH<sub>2</sub>O, while the remaining subjects (25 patients, 53.2%) received BIPAP treatment with an average IPAP pressure of 15.9 cmH<sub>2</sub>O and an average EPAP pressure of 7.5 cmH<sub>2</sub>O.

### OHS

As we mentioned in the global results, the second most frequent diagnosis was OHS, occurring in 34.8% of cases (31 patients). The average score on the Epworth Scale was 5.5 points. The average BMI for patients diagnosed with OHS was 39 (range: 31 to 56), with 42.8% being morbidly obese with a BMI >40. The average AHI for these patients at the time of diagnosis was 11.2, with an IDH value of 31. The average SpO<sub>2</sub> was 90.5, and the minimum was 76.4. The average CT90 was 38.7%.

The average transcutaneous CO<sub>2</sub> value was 45.2 and the maximum was 49.8. As for the stratification by degree of obesity, an average tcCO<sub>2</sub> of 40.2 was observed in patients with moderate obesity, while patients with severe and morbid obesity respectively had averages of 45.2 and 45.1. The same is observed in maximum tcCO<sub>2</sub> values, which were 46.68 in patients with moderate obesity, while the severely and morbidly obese had respective values of 49.5 and 49.1.

Of patients diagnosed with OHS, 67.7% (21 patients) received nocturnal treatment. Of these, 3 patients received CPAP treatment with an average pressure of 13.3 cmH<sub>2</sub>O, while the 18 remaining subjects received BIPAP treatment with an average IPAP of 15.5 cmH<sub>2</sub>O and an average EPAP of 5.9 cmH<sub>2</sub>O.

### COPD

Of the total number of patients studied, 25 suffer from COPD, making up 28% of the total sample. For these patients, the average FEV1 was 1,042 ml (range: 590 ml to 2,130 ml), with an average obstruction percentage of 44% of the theoretical value. As a result, the majority of COPD patients had severe airflow limitation. Men constituted 68% of COPD patients. The majority were also obese (75%) which is a similar percentage to the number of obese patients in the aggregate sample.

The average score for COPD patients on the Epworth Scale was 5.5. The

average BMI for COPD patients was 35.4 (range: 17 to 61). Of these subjects, 33% were morbidly obese. The average AHI was 21.8, with an SAHS percentage of 80% (20 of 25 COPD patients), while the average IDH was 36.5. The average SpO<sub>2</sub> was 86.8 (significantly lower than the global average,  $p < 0.05$ ) and the minimum value was 77.2. The average CT90 was 26% without statistically significant differences from the aggregate sample values. The average transcutaneous CO<sub>2</sub> value in COPD patients was 42.6 and the maximum was 49.

A total of 12 patients received nocturnal treatment, making up 48% of cases. Of these, 7 patients were treated with BIPAP with an average IPAP of 16.4 cmH<sub>2</sub>O and an average EPAP of 6.8 cmH<sub>2</sub>O. Those who received CPAP treatment (5 patients) had an average pressure of 10.4 cmH<sub>2</sub>O.

### AMYOTROPHIC LATERAL SCLEROSIS

Throughout the time of the study, 4 patients diagnosed with amyotrophic lateral sclerosis were included, with an average age of 54 (range: 20-75). The average score on the Epworth Scale was 1.5 points. The average BMI for these patients was 20 (range: 18 to 22). Of the 4 patients with a diagnosis of ALS included in the study, 3 underwent BIPAP titration and a baseline sleep study was only done for one of them to evaluate the presence of nocturnal hypoventilation. Taking this into account, the average AHI for these patients was 11.5 and the IDH was 6.7.

Significantly higher pulse oximetry values were also observed in comparison with the aggregate sample, with an average SpO<sub>2</sub> of 94.2% ( $p: 0.05$ ), a minimum value of 83.4% ( $p: 0.02$ ) and a CT90 of 3.2% ( $p < 0.001$ ). Slightly higher average tcCO<sub>2</sub> values (46.9) and maximum tcCO<sub>2</sub> values (50.4) were also observed with respect to the global average, despite the fact that 3 out of the 4 patients underwent a BIPAP titration study, as mentioned previously. All of them received ventilation through a nasal mask, with average IPAP pressure of 11.5 cmH<sub>2</sub>O and an average EPAP of 5.5 cmH<sub>2</sub>O.

### Multivariate analysis

Although significant differences were observed for some of the parameters analyzed between the different subgroups, none of the factors studied were related to the presence of hypercapnia in the multivariate analysis.

**Table 5. Parameter values obtained in the study for different diagnostic subgroups**

	SAHS	OHS	COPD	ALS*	Aggregate sample
BMI	36.6	39	35.4	20	35.7
Epworth Scale	6.9	5.5	5.5	1.5	6.5
AHI	34.1	11.2	21.8	11.5	11.9
IDH	56.8	31	36.4	6.7	27
Minimum SpO <sub>2</sub>	74.5	76.4	77.2	83.4	78.8
Average SpO <sub>2</sub>	90.6	90.4	86.4	94.2	91.8
CT90 (%)	33.2	38.7	26	3.2	22.9
Average tcCO <sub>2</sub>	44.8	45.2	42.6	46.9	45.6
Maximum tcCO <sub>2</sub>	48.9	49.8	49	50.4	49.2
Average CPAP pressure	9.9	13.3	10.4	-	9.5
Average IPAP pressure	15.9	15.5	16.4	11.5	15.7
Average EPAP pressure	7.5	5.9	6.8	5.5	7.4

\*The study was BIPAP titration for three out of four patients with ALS.

## DISCUSSION

Although it may be considered a limitation of the study, a daytime baseline blood gas was not conducted in patients before leaving the hospital since, although it was initially a secondary objective of the study to evaluate the correlation between transcutaneous capnography and blood gas values, due to the organization of the unit and changes with regard to unit staff throughout the study, this point was carried out at the beginning of the study but was not conducted again. The results section does not refer to the comparative ABG analysis done at the end of the study for patients who underwent the test due to the limited number of patients. However, the correlation between the measurement of transcutaneous CO<sub>2</sub> and arterial PCO<sub>2</sub> values has already been studied in other work, such as the study by Dawson et al.<sup>15</sup> and another by Parker and Gibson<sup>16</sup>. In the latter, the same transcutaneous CO<sub>2</sub> meter was used as the one available in our sleep unit. Both studies found a good correlation between arterial PCO<sub>2</sub> values and those obtained through measuring tcCO<sub>2</sub>. Correlation studies for both values have even been carried out in

patients hospitalized for respiratory disease<sup>17</sup> and patients with sleep-related breathing disorders such as SAHS or OHS<sup>18,19</sup>, obtaining good results both in basal sleep studies and CPAP and BIPAP titration.

Regarding tolerance to the transcutaneous CO<sub>2</sub> meter and the possible side effects from the device in the area where the meter was applied on the skin, this study did not register any case of discomfort or side effects, agreeing with the results obtained by other authors who have completed continuous 8-hour monitoring<sup>13,14</sup>.

If we analyze the average and maximum tcCO<sub>2</sub> values detected in the aggregate sample, we find slightly elevated levels despite having a normal average SpO<sub>2</sub>. It was only among subjects who underwent a baseline study for suspected sleep-related breathing disorders and in which the test ruled out any disorder that we found normal tcCO<sub>2</sub> values as well as higher average and minimum SpO<sub>2</sub> values and a lower CT90. The fact that average and maximum tcCO<sub>2</sub> values similar to the aggregate sample were seen for patients who were ultimately not diagnosed with any sleep-related breathing disorder after the baseline study may be justified because there were only 7 cases, a very small number of patients to establish differences.

Obesity is a known independent risk factor for suffering from SAHS. In fact, two thirds of patients with SAHS are obese<sup>19</sup>. Additionally, 90% of hypercapnic obese patients suffer from SAHS, while 11 to 15% of obese patients with SAHS show signs of hypercapnia, a figure which increases to 23-27% when BMI >40<sup>19,20</sup>. In our study, the average and maximum tcCO<sub>2</sub> levels were observed to be higher corresponding to higher BMI, although they did not reach statistical significance. There was a very similar distribution of disease among the obesity subgroups, except for ALS patients where the BMI was noticeably lower. This may be explained by the fact that when they arrive at the sleep unit to begin non-invasive ventilation, ALS patients already have a significant deterioration in muscle function as well as muscle mass.

With regard to the finding that 80% of COPD patients presented symptoms of SAHS (overlap syndrome), this may be due to several factors. First, the main indication to complete the sleep study was suspected SAHS, and thus the sample is biased. In other words, the objective of the study was not to evaluate the existence of SAHS in COPD patients in general. On the contrary, patients who have clinical symptoms compatible with SAHS, regardless of COPD, were candidates to participate in the study. Secondly, the percentage of obesity among COPD patients included in the study was 75%, quite

a high number, although the percentage was similar to the aggregate sample. Despite the fact that these patients had an average SpO<sub>2</sub> lower than the other subgroups, with a higher CT90, the minimum SpO<sub>2</sub> was similar to the other groups, along with average and maximum transcutaneous CO<sub>2</sub> levels. This mild hypoxemia, without higher hypercapnia than the other groups, could be explained by these patients' low lung function.

In a study by Lee et al.<sup>11</sup> on neuromuscular patients, which followed hospitalization and included a baseline blood gas and later continuous recording of tcCO<sub>2</sub>, patients with normocapnia in the baseline ABG were shown to display hypercapnia in nocturnal CO<sub>2</sub> measurements, concluding that ABG is not sufficient as the only tool to detect ventilator mechanics problems in these patients. Our study was only able to recruit 4 patients with neuromuscular disease and of them, a baseline study was only done for one. The other 3 patients underwent BIPAP titration. The average tcCO<sub>2</sub> level for these patients was 47, slightly higher than the aggregate sample, along with a maximum tcCO<sub>2</sub> of 50.4. However, while this is a small number of patients to be able to reach conclusions, it seems that these patients may be especially interested in transcutaneous CO<sub>2</sub> monitoring, as hypoventilation can often go unnoticed.

## CONCLUSIONS

The results of the study reveal that the presence of latent nighttime hypercapnia in patients with respiratory disease is frequent while sleeping, both in diagnostic studies and in CPAP or BIPAP titration studies. In addition, we have not found problems with device tolerance stemming from continued use throughout the night. Thus, it can be used to reveal latent hypercapnia in different diseases during adult sleep, in addition to the observed lack of discomfort and side effects at the local level.

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