CONTINUOUS POSITIVE AIRWAY PRESSURE IN CLINICALLY STABLE PATIENTS WITH MILD-TO-MODERATE OBESITY-HYPOVENTILATION SYNDROME AND OBSTRUCTIVE SLEEP APNEA

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SUMMARY AT A GLANCE

This study shows a progressive improvement in night-time oxygenation and daytime hypercapnia with CPAP use in clinically stable mild-to-moderate OHS patients, also suffering from OSA. CPAP can be a safe first-line treatment in these selected patients, although early monitoring is essential to detect treatment failure.

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ABSTRACT

Background and Objective: The use of continuous positive airway pressure (CPAP) treatment in patients with obesity hypoventilation syndrome (OHS) and obstructive sleep apnea (OSA) was evaluated and factors that might predict CPAP treatment failure were determined.

Methods: A sleep study was performed in 29 newly diagnosed, clinically stable OHS patients. CPAP treatment was commenced if the apnea-hypopnea index was >15. Lung function, night-time oximetry, blood adipokine and C-reactive protein levels were assessed prospectively on enrollment and after 3 months. Treatment failure at 3 months was defined as daytime $PaCO_2$ >45 mmHg and/or oxygen saturation (SpO_2) <90% for >30% of the night-time oximetry study.

Results: All patients had severe OSA (median apnea-hypopnea index (AHI) = 74.7(62-100) with a nocturnal mean SpO_2 of 81.4±7) and all patient were treated with CPAP. The percentage of time spent below 90% saturation improved from 8.4% (0.0-39.0%) to 0.3% (0.4-4.0%). Awake $PaCO_2$ decreased from 50 (47-53) mmHg to 43 (40-45) mmHg. Seven patients failed CPAP treatment after three month. $PaCO_2$ at 1 month and mean night-time SpO_2 during the first night of optimal CPAP were associated with treatment failure at 3 months [ODDS ratio 1.4(1.03-1.98); p=0.034 and 0.6(0.34-0.93); p=0.027].

Conclusions: CPAP treatment improves night-time oxygenation and daytime hypoventilation in selected clinically stable OHS patients who also have OSA. Patients with worse night-time saturation while on CPAP and higher daytime $PaCO_2$ at one month were more likely to fail CPAP treatment.

Key words: obesity hypoventilation syndrome, obesity, obstructive sleep apnea syndrome, continuous positive airway pressure, nighttime oxyhemoglobin saturation

Short title: CPAP and mild-to-moderate OHS and OSA

Abbreviations

ABG = arterial blood gas

AHI = apnea-hypopnea index

BMI = body mass index

BVS = bilevel ventilatory support

COPD= chronic obstructive pulmonary disease

CPAP = continuous positive airway pressure

CRP = C-reactive protein

ELISA = enzyme-linked immunosorbent assay

FVC = forced vital capacity

IQR = interquartile range

MVV = maximal ventilatory ventilation

OHS = obesity hypoventilation syndrome.

OR= Odds ratio

OSA = obstructive sleep apnea

$PaCO_2$ = partial pressure of carbon dioxide, arterial

PaO_2 = partial pressure of oxygen, arterial

PImax = maximal inspiratory pressure

PEmax = maximal expiratory pressure

PSG = Polysomnography

SpO_2 = arterial oxyhemoglobin saturation measured by pulse oximetry

RP = respiratory polygraphy

TLC = total lung capacity

INTRODUCTION

The worldwide obesity epidemic (1) is leading to obesity-related respiratory complications (2). Obesity is the main risk factor for obstructive sleep apnea (OSA) (3) and a determining factor for obesity hypoventilation syndrome (OHS) (4). OHS is associated with OSA and approximately 90% of OHS patients also have upper-airway obstruction during sleep (5). The limited evidence available shows that non-invasive ventilation (6-7), particularly bi-level ventilatory support (BVS), is effective in the majority of OHS patients, while CPAP is effective in a poorly defined subgroup with mild-moderate OHS and OSA (8-9). In the only randomized trial comparing CPAP and BVS, both treatments improved daytime hypercapnia in patients with mild OHS and associated OSAS (10). It remains unclear whether these treatments correct night-time hypoxemia. One study in severely obese patients with OSA and OHS showed that during the first night of CPAP treatment, sleep architecture and obstructive events improved, but oxygen desaturation remained in 43% of the patients (11). Whether night-time hypoxemia persists after longer-term CPAP treatment is still matter of debate.

Night-time hypoxemia could add to obesity, potentially increasing the burden of chronic inflammation and its pro-atherogenic effects (12-14). A previous study comparing eucapnic obese patients to OHS patients found OHS to be associated with endothelial dysfunction with increased pro-inflammatory markers and decreased adiponectin (15).

The response to CPAP or BVS treatment remains unclear, since the only controlled study comparing BVS with conservative treatment did not show a difference (16).

The primary objective of the study was to evaluate the response of night-time arterial oxyhemoglobin saturation and daytime $PaCO_2$ after 3 months of CPAP treatment in OHS patients with associated OSA, and to explore factors that might predict the failure of CPAP in this population. In addition, we analyzed the response to CPAP on the pro-inflammatory markers adipokine and C-reactive protein [CRP].

METHODS

Study Design, Setting and Participants

This prospective 27 months long study enrolled patients aged 18 to 75 years, who fulfilled OHS diagnostic criteria. Patients with acute onset of respiratory failure were enrolled after 4 weeks of a clinically stable condition without BSV. The study protocol was approved by the Institutional Review Board of the Hospital de la Santa Creu i Sant Pau (Protocol number EC No 04.092.476) and written informed consent was obtained from all participants.

OHS was determined by a $PaCO_2$ at rest >45 mmHg and a body mass index (BMI) >30 kg/m^2 in the absence of other causes of hypoventilation, such as neuromuscular or chest-wall disorders. We excluded patients with major psychiatric disorders, untreated hypothyroidism or chronic obstructive pulmonary disease, and those who were taking sedatives (17).

Measurements

All patients were evaluated at enrolment and after 3 months of CPAP treatment. Sleepiness was assessed on the Epworth Sleepiness Scale. Arterial blood gas (ABG) samples were taken while the subject was seated, breathing room air for more than 4 hours since wakening (daytime ABG). Blood samples were collected between 8:00 and 9:00 am after overnight fasting and were immediately centrifuged; serum was kept frozen at –70°C until assayed. Serum adiponectin, leptin and soluble leptin receptor concentrations were measured with a solid-phase enzyme-linked immunosorbent assay (ELISA) (Quantikine, R&D Systems Inc, Minneapolis, MN and Mediagnost, Reutlingen, Germany). Serum CRP was measured by an automated particle-enhanced immunoturbidimetric assay (CRPLX, Cobas, Roche Diagnostics GmbH, Mannheim, Germany).

Sleep Study Recordings, Titration Studies and Treatment

All patients underwent overnight diagnostic studies with either polysomnography (PSG) (Siesta, Compumedics, Melbourne, Australia) or respiratory polygraphy (RP) (Sibelhome, Sibel, Barcelona, Spain). Night-study interpretation was assessed according to standard criteria (19-20).

We initiated a CPAP trial on subjects with AHI >15 during a second overnight PSG for titration. The mean nocturnal SpO_2 was measured again while the patient used CPAP at the determined setting. We took an early morning aterial boold gas, as an indirect measurement of night-time hypoventilation (21). The sleep study was repeated after 3 months of treatment. The protocol stipulated that patients who showed a mean night-time SpO_2 <85% during the first night of treatment, would be switched to BVS. At the

end of the first month patients were reassessed for clinical stability and an ABG sample was extracted. Objective treatment compliance was determined by calculating the average number of hours recorded by the CPAP device's built-in hour meter. Patients with an average use time <4 hours per night were considered non-compliant.

Endpoints

Treatment failure after 3 months was defined by a daytime $PaCO_2$ >45 mmHg and/or SpO_2 <90% for > 30% of the night. We based this definition of desaturation on the definition applied to COPD patients (22), as no references to night oxygenation in OHS patients are available.

Statistical Analysis

Statistical analysis was performed with SPSS 15 software (SPSS Inc., Chicago, IL). Continuous data were tested for normality (Kolmogorov-Smirnov test). Data were presented as mean ± standard deviation, median and interquartile range (IQR), depending on their normality. The paired T, Wilcoxon and McNemar tests were used to compare normal, skewed and categorical variables before and after treatment. To analyze the significance of $PaCO_2$ and SpO_2 global tendency over time, we used the Friedman test. In the bivariate analysis either the non-paired T test Mann-Whitney *U* test or a chi-square test was performed. Binary logistic regression was used to assess the ability of factors to predict the failure of treatment. A p-value of <0.05 was considered significant.

RESULTS

Thirty-six patients diagnosed with OHS (30 from the sleep laboratory and 6 from the respiratory ward) were candidates for enrolment. A final 29 patients were enrolled, after 2 declined to participate, 2 still required BVS at discharge, 1 died during the acute episode and 2 were excluded (1 for hypothyroidism and 1 for use of sedatives; Figure 1). Table 1 shows the characteristics and comorbidities of these 29 participants.

Twenty six patients underwent PSG and three RP. All presented with concomitant OSA with an AHI >15 [median AHI:74.7 (IQR, 62-100)] and a mean night-time SpO_2 of 81.4 ± 7%. The median optimal positive airway pressure was 11 (IQR, 10-12) cmH_2O. No patient was switched to BVS because of persistent oxygen desaturation during the first night of CPAP treatment. Significant improvement in sleep architecture was seen on CPAP with increased percentages of deep sleep and rapid eye movement sleep and correction of obstructive events and sleepiness (Table 2 ,3).

Two patients were lost to follow-up (Figure 1). A slight weight loss was seen during the 3-month study period [mean difference of 4.0 Kg; 95% CI (0.5-7.6)]. No changes were observed in adipokines or CRP after treatment (Table 3). Mean treatment adherence at 3 months was 6.0 (4.5-7) h/night. Only two of the 27 patients were considered non-compliant.

After 3 months, CPAP treatment had led to significant amelioration of night-time oxygen desaturation (Figure 2, Table 4), daytime $PaCO_2$ (Figure 3) and early morning PaO_2, $PaCO_2$ (Table 4). At the end of the study seven patients met the criteria for

treatment failure: six for daytime $PaCO_2$ >45 mmHg and one for oximetry time >30% and SpO_2 <90%. CPAP failure patients had a lower baseline daytime PaO_2, a higher daytime $PaCO_2$ at 1 month and a lower mean night-time SpO_2 following optimal CPAP treatment (Table 5). When adjusted for age, sex and weight change, the binary logistic regression analysis showed that daytime $PaCO_2$ at 1 month was associated with treatment failure [OR = 1.4 (1.03-1.98); p=0.034], while higher mean night-time SpO_2 during the first night protected against treatment failure [OR= 0.6(0.34-0.93); p=0.027].

When we separately analyzed the clinical characteristics of seven patients (26%) who fulfilled the criteria for treatment failure, three had a $PaCO_2$ of 46 mmHg, only 1 mmHg above the cut point for BVS treatment. These patients had optimal night-time SpO_2 correction and were clinically asymptomatic and, consequently, CPAP treatment was maintained. The patient with SpO_2 <90% for more than 30% of the total sleep time was normocapnic, so oxygen was added to nocturnal CPAP treatment. Another patient was one of the two non-compliant patients. The two remaining patients who failed CPAP were switched to BSV (7%).

DISCUSSION

Our clinically stable mild-to-moderate OHS patients with OSA experienced improvement in obstructive events, night-time SpO_2, daytime hypercapnia and sleepiness after 3 months of night-time CPAP treatment. However, these improvements were not accompanied by changes in pro-inflammatory markers. Patients with worse overnight SpO_2 during the fixed optimal CPAP on the first night of treatment

(established in the previous titration test) and higher daytime $PaCO_2$ at one month were shown to be at higher risk of treatment failure. An important contribution of our study, not previously analyzed, is that mean night-time SpO_2 and daytime $PaCO_2$ improved progressively, starting from the titration polysomnography and continuing throughout the three months of treatment (Figure 2,3).

A noteworthy aspect of the study was the diagnosis of OSA syndrome in all patients recruited, which confirms the important role of obstructive events in the pathogenesis of hypoventilation in obese patients. Kessler *et al* (5) described a prevalence of 88% of OSA syndrome in OHS patients. Perez de Llano *et al* (23) also detected OSAS in 87% of 54 OHS subjects when they performed PSG after hospital discharge of patients in a clinically stable condition; 30% of their patients could be switched to CPAP. This finding endorses the reassessment of patients after stabilization of the intercurrent processes at a time when polysomnography might detect sleep apnea (3).

BSV (23-24) and CPAP (8-9) have been successfully used to treat OHS patients in a stable condition. Although the use of CPAP is recommended by some expert panels (26-27), most studies with CPAP have been small and retrospective. The study of Banerjee et al (11) was the first with a prospective design that demonstrated the relief of airway obstruction and improvement in sleep architecture on the first CPAP titration night, although they emphasized the failure to correct oxygen desaturation in 43% of patients. There is only one randomized trial to date by Piper and colleagues, in which a comparison of CPAP with BSV in a selected population of OHS patients with OSA showed similar effects on daytime $PaCO_2$ at 3 months (10). Their patients had a higher degree of hypercapnia and obesity than those in our study, and their night-time

oxygenation correction with CPAP in the titration study was worse than ours. No data on night-time oxygenation with either CPAP or BSV was shown in the follow-up at 3 month, so this study was unable to conclude that CPAP treatment could improve persistent hypoxemia.

Although is not fully proven, the correction of night-time oxygenation could be an important goal for treatment, particularly in light of a 4-year follow-up study of 130 OHS patients treated with BSV, which found that supplementary oxygen therapy was the only independent predictor of mortality (28). To improve our assessment of night-time hypoxemia, we added a second monitored night on optimal CPAP, as data from the first titration night are of limited value due to the variable time needed to identify the optimal pressure. Night-time oxygen saturation and daytime $PaCO_2$ in the first month proved useful in detecting patients more likely to fail after 3 months of treatment, underlining the importance of early monitoring with two feasible and commonly used tests. It is important to identify those patients with OHS who will benefit from long-term treatment with CPAP therapy, as this requires simpler clinical management than BSV. Overall, CPAP is effective in stable OHS patients with mild-to-moderate hypercapnia OSA, and it is a candidate for first-line treatment. BSV should be strongly considered, however, in patients who fail a CPAP trial, in OHS patients without OSA and in severe hypercapnic OHS where CPAP has not proved effective.

To study one of the physiopathological pathways of OHS, we explored the responses of leptin, adiponectin and CRP to CPAP; we did not detect any changes after 3 months of treatment. Previous studies have suggested that, in addition to the pro-inflammatory role of leptin, central leptin resistance may also play a role in inducing hypercapnia (29).

The ability of OHS treatment to modify leptin levels is still a matter of debate, as the only two studies undertaken to date have yielded contradictory results (30-31). Budweiser and colleagues found CRP decreased in OHS patients on long-term BSV (32). However, the only controlled trial to explore the response of OHS treatment to metabolic, inflammatory markers and adipokines, in a very mild hypercapnic population, failed to demonstrate any changes when comparing BSV to conservative short-term treatment (16). Our study also found a lack of response with respect to adipokines and CRP levels over a longer treatment period. These results can be attributed to several factors. Firstly, our patients formed a clinical study group by undergoing active hypolipemiant, anti-hypertensive and hypoglycemiant treatment, which could interfere with the determination of metabolic profiles and biomarkers and minimize the difference produced by both these factors. Secondly, although leptin, adiponectin and CRP protein can change with moderate weigh loss (33), the associated comorbidities, such as metabolic syndrome and obesity, could have an overwhelming effect on the activation of inflammatory pathways and adipokines.

A limitation of the study is that we included patients with mild-to-moderate hypercapnia, representing a less severe manifestation of the disease; consequently, our results are not applicable to patients with a higher degree of hypercapnia, or those with clinical instability. Another limitation is the lack of randomization of patients to a control group. Moreover, there was a slight but statistically significant weight loss after the third month of treatment. It seems improbable, however, that this weight loss could explain the overall improvement in hypoventilation. Nevertheless, we controlled this confounding factor by binary logistic regression analysis. Finally, the absence of night-time transcutaneous capnography measurements to monitor sleep hypoventilation under CPAP treatment should be considered as another weakness. Instead, we followed a

simpler approach (21,34) and analyzed blood gas measurements as soon as the patient woke up.

We conclude that once upper airway obstruction has been confirmed as a significant component of OHS in patients with both mild-to-moderate hypercapnia and a stable condition, it is reasonable to attempt to treat them with CPAP alone, rather than with BVS. We found that in such selected, clinically stable OHS patients long-term CPAP will progressively improve night-time oxygen saturation, daytime gas exchange and hypoventilation symptoms. CPAP can be considered a safe, first-line therapeutic option in these patients, although early monitoring of night-time oximetry and daytime $PaCO_2$ will be essential in the first months of treatment for the early detection of any treatment failure.

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Figure legends

Figure 1: Flow diagram of patient recruitment and follow-up.

Figure 2: Change in patients' mean night-time SpO_2 from baseline to 3 months after starting CPAP treatment.

Figure 3: Daytime $PaCO_2$ after 3 months of CPAP treatment

Table 1: Characteristics of the 29 OHS patients

Age, (years) [#]	59 (47-65)
Women, n (%)	17 (59%)
BMI (kg/m^2)	43.7 ±7.4
Neck circumference (cm)	45.8 ± 4
Waist circumference (cm)	133 ±14
Hypertension, n (%)	22 (75.9%)
Diabetes, n (%)	10 (34.5%)
Dyslipidemia, n (%)	10 (34.5%)
Ischemic heart disease, n (%)	2 (6.9%)
Stroke, n (%)	4 (13.8%)
Smoking, n (%)	16 (55.2%)
Metabolic Syndrome (NCEP-ATP III), n (%)	20 (69%)

Values are presented as mean±SD, median (interquartile range) for normal or non-normal data[#] and number of patients (%) for categorical data .BMI = body mass index; NCEP-ATP III = National Cholesterol Education Program's Adult Treatment Panel III.

Table 2: Diagnostic and titration night sleep variables of the 29 OHS patients

	Diagnostic Study (n=29)	CPAP Titration Study (n=29)	p value
Sleep efficiency * (%)	79,4 ± 11	84.9 ± 10	0.001
Arousal index* ($n.h^{-1}$)	63.4 ± 26	12 ± 8	<0.001
Apnea hypopnea index ($events.h^{-1}$)[#]	74.7 (62-100)	12.2 (3-22)	<0.001
Stage I*(%)[#]	16.5 (11-26)	4.6 (3-7)	<0.001
Stage II* (%)	59.9 ± 14	37.3 ± 13	<0.001
Stage III-IV*(%)[#]	6.6 (1.6-17)	28.0 (26-46)	<0.001
REM sleep* (%)	10.3 ± 7	25.4 (11)	<0.001
Mean night SpO_2 (%)	81.4 ± 7	90.8 ± 4	<0.001
Minimum nocturnal SpO_2 (%)[#]	53.0 (47.8-66)	77 (63-85)	<0.001
TST with SpO_2 < 90% (%)[#]	58.0 (39-74)	7.0 (0.7-40)	<0.001

* N = 26 (some data were not available for 3 patients who underwent respiratory polygraphy for diagnosis). N=29 in all other cases. Values are presented as mean±SD or median (interquartile range) for normal or non-normal data[#]. Paired T test and Wilcoxon test were used to detect differences in normal and skewed data. REM = rapid eye movement; TST = total study time (polysomnography or polygraphy); SpO_2 = arterial oxygen saturation by pulse oximetry.

Table 3: Anthropometrical, clinical and biological data on enrollment and after 3 months of CPAP treatment

	On enrollment (n=27)	After 3 months of CPAP treatment (n=27)	p value
BMI, kg/m^2	43.4 ±7.5	42.0 ± 6.4	0.035
Waist, cm	132 ± 14	130 ±14	0.013
Weight, kg	115.7 ± 25	111.6 ± 21	0.028
Epworth sleepiness scale[#]	17 (12-18)	4 (2-8)	<0.001
Morning Headache, n (%)	11 (40.7)	0 (0)	<0.001
PaO_2 (mmHg)	66.0 ± 11	73.3 ± 12	0.001
$PaCO_2$ (mmHg) [#]	50.0 (47-53)	43.0 (40-45)	<0.001
Leptin (ng/ml)** [#]	38.8 (24-66)	38.4(23-78.2)	0.781
Leptin receptor (ng/ml)**	4.02 ± 0.8	3.96 ± 0.85	0.760
C reactive protein (mg/l)** [#]	6.98 (3.4-9.5)	6.03 (3.1-9.2)	0.476
Adiponectin (ng/ml)**	94.1 ± 55	93.4 ± 53	0.924

** n=21

Values are presented as mean±SD or median (interquartile range) for normal or non-normal data[#]. Paired T test, Wilcoxon and McNemar tests were used for normal, skewed and categorical data. BMI = body mass index;; $PaCO_2$ = arterial partial pressure of carbon dioxide; PaO_2 = arterial partial pressure of oxygen; TLC = total lung capacity.

Table 4: Night-time saturation and 7:00 am arterial gas measurements after the first night of CPAP treatment and after 3 months in 27 OHS patients

	After the first night of optimum CPAP treatment (n=27)	After 3 months of CPAP treatment (n=27)	p value
Study time with SpO_2 <90% (%)[#]	8.4 (0.0-39.0)	0.30 (0.4-4.0)	0.011
Mean night-time SpO_2 (%)	92.3± 3.0	94.1% ± 2.8	0.001
Early morning PaO_2 (mmHg)	74.6 ± 16	81.1 ± 15	0.038
Early morning $PaCO_2$ (mmHg) [#]	53.0 (49-55)	48.0 (46-51)	0.009

Values are presented as mean±SD or median (interquartile range) for normal or non-normal data[#]. Paired T test and Wilcoxon test were used to detect differences in normal and skewed data. PaCO2 = arterial partial pressure of carbon dioxide; PaO2 = arterial partial pressure of oxygen; SpO2 = arterial oxygen saturation by pulse oximetry.

Table 5: Clinical and respiratory function data for CPAP-successful patients and CPAP-failed patients 27 OHS patients

	CPAP success (n=20)	CPAP failure (n=7)	p value
BMI (kg/m^2)	43.3 ±8.0	43.8 ± 6.7	0.892
Waist circumference (cm)	132.0 ± 14	133,8 ±16	0.768
Age (years)	58.3 ± 9	57.8 ± 11	0.929
Gender, women (%)	10 (66.7)	5 (33.3)	0.326
Epworth sleepiness score[#]	17 (14-18)	15 (11-18)	0.725
Change in Epworth sleepiness score	-10.2 ± 6	-7.6 ± 8	0.378
FVC (% predicted)	73.0 ± 15	69.0 ± 11.4	0.527
TLC (% predicted)	86.9 ±16	79.3 ± 10	0.249
PaO_2 (mmHg)	68.0 ± 12	58.1 ± 4.8	**0.009**
$PaCO_2$ (mmHg) [#]	47.0 (46.3-52)	51.0 (50-54)	0.081

Apnea hypopnea index (events/hr) [#]	74.6 (66-98)	64.3 (45-90)	0.263
Hypopnea index (events/hr)	19.1 (12-48)	25.4 (10-53)	0.959
Basal mean night SpO_2 (%)	82.5 ± 6.1	80.0 ± 9.7	0.433
Basal TST < 90% of SpO_2 (%)	53.9 ± 26	54.3 ± 35	0.972
Basal Minimum nocturnal SpO_2 (%)	56.8 ± 15)	58.8 ± 13	0.758
Apnea hypopnea index with optimal CPAP (events/hr) [#]	10.7 (2.8-33)	15.9 (5-22)	0.766
1st day CPAP treatment TST < 90% of SpO_2 (%)	3.9 (0-19)	39 (1-54)	0.130
1st day CPAP treatment mean night-time SpO_2 (%)	93.1 ± 2.7	90.0 ± 2.9	**0.020**
1st day CPAP treatment, early morning PaO_2 (mmHg)	77.2 ±17	67.3 ±9.9	0.160
1st day CPAP treatment, early morning $PaCO_2$ (mmHg)	51.9 ± 4,8	56.4 ± 6.1	0.054
Daytime PaO_2 1st month (mmHg)*	69.8 ± 10.0	67.3 ± 13	0.613
Daytime $PaCO_2$ 1st month (mmHg)*	45.8 5.2	51.2 ± 3.5	**0.004**
Baseline Leptin (ng/ml)*	43.5 ± 29	51.2±3.8	0.445
CPAP use h/night [#]	6 (4-7)	7 (5-7)	0.219

*n= 25

Values are presented as mean±SD, median (interquartile range), number of patients (%) for normal, non-normal data and categorical data.[#.] Unpaired T test, Mann-Whitney *U* and chi-squared tests were used to detect differences in normal, skewed and categorical data..

BMI = body mass index; FVC = forced vital capacity; TLC = total lung capacity; PaO_2 = arterial partial pressure of oxygen; $PaCO_2$ = arterial partial pressure of carbon dioxide; SpO_2 = arterial oxygen saturation by pulse oximetry.

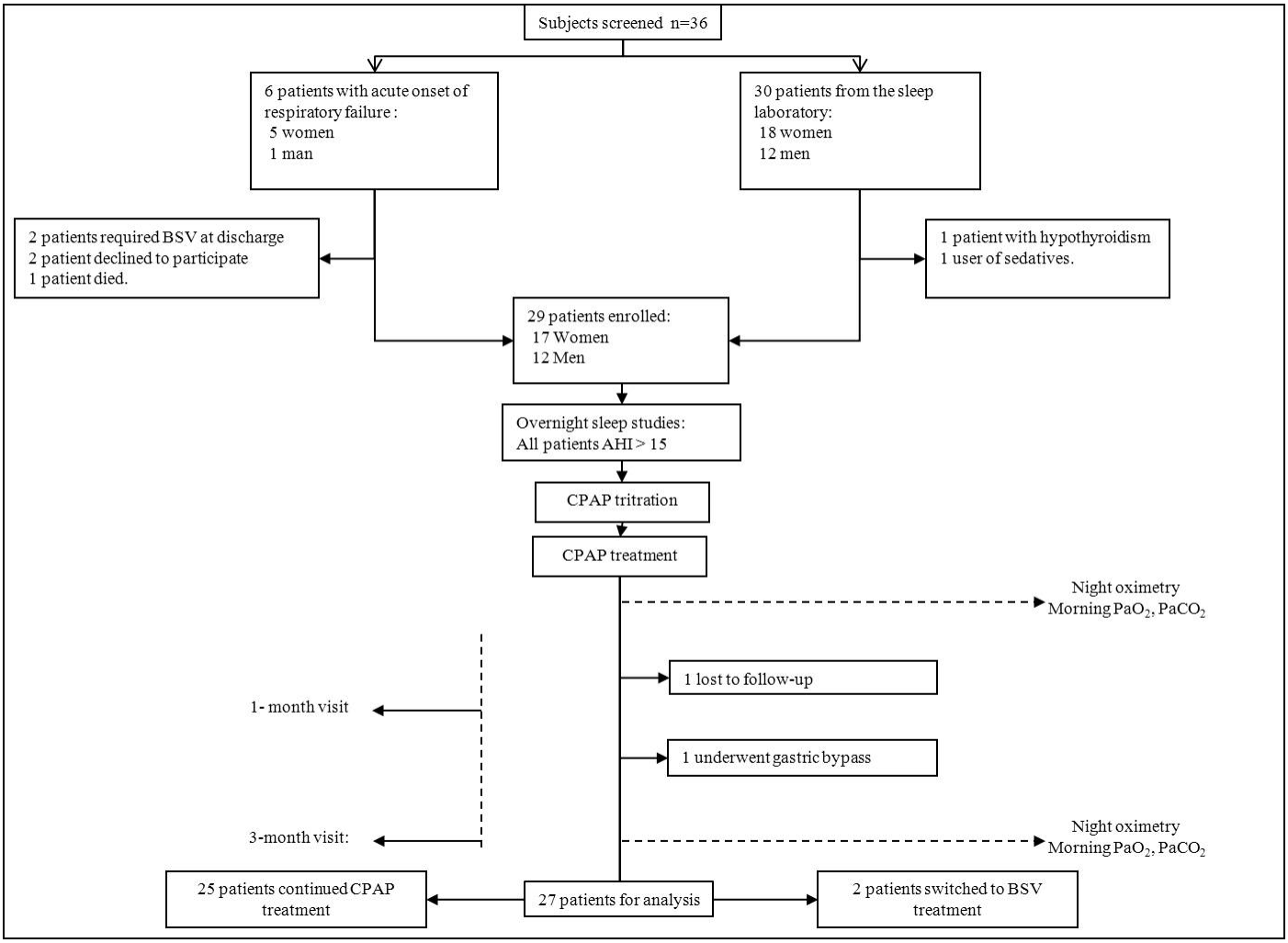
Subjects screened n=36
6 patients with acute onset of respiratory failure :
5 women
1 man
30 patients from the sleep laboratory:
18 women
12 men
2 patients required BSV at discharge
2 patient declined to participate
1 patient died.
1 patient with hypothyroidism
1 user of sedatives.
29 patients enrolled:
17 Women
12 Men
Overnight sleep studies:
All patients AHI > 15
CPAP tritration
CPAP treatment
Night oximetry
Morning PaO_2, $PaCO_2$
1 lost to follow-up
1- month visit
1 underwent gastric bypass
3-month visit:
Night oximetry
Morning PaO_2, $PaCO_2$
25 patients continued CPAP treatment
27 patients for analysis
2 patients switched to BSV treatment

Figure1

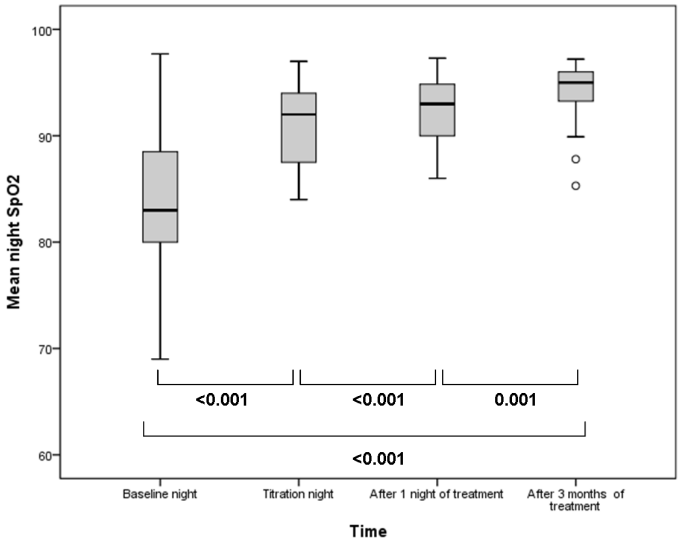
100
90
80
70
60
Mean night SpO2
<0.001
<0.001
0.001
<0.001
Baseline night
Titration night
After 1 night of treatment
After 3 months of treatment
Time

Figure2

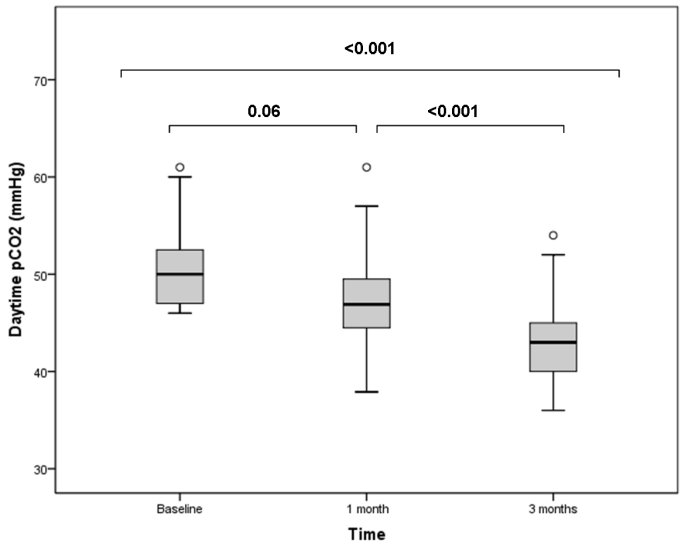
<0.001
0.06
<0.001
70
60
50
40
30
Daytime pCO2 (mmHg)
Baseline
1 month
3 months
Time

Figure3