Respiratory Patterns During Sleep in Obesity-Hypoventilation Patients Treated With Nocturnal Pressure Support: A Preliminary Report

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Respiratory Patterns During Sleep in Obesity-Hypoventilation Patients Treated With Nocturnal Pressure Support*

A Preliminary Report

Yan Fei Guo, MD; Emilia Sforza, MD, PhD; and Jean Paul Janssens, MD

Background: **The obesity-hypoventilation syndrome (OHS), commonly defined as a combination of obesity and diurnal hypercapnia, is efficiently treated using nasal positive pressure ventilation (NPPV). The present study aimed to determine whether nocturnal polysomnography allows detection of respiratory disturbances occurring in patients with OHS treated with NPPV that may interfere with the quality of sleep and of ventilatory support, and are not detected by nocturnal pulse oximetry and capnography.**

Methods: **Twenty OHS patients in stable clinical condition treated by NPPV for at least 3 months with a bilevel pressure support ventilator were studied. All patients underwent single-night polysomnography under NPPV including transcutaneous measurement of P_{CO_2} (TcP_{CO_2}). Four types of respiratory events were defined and quantified: patient/ventilator desynchronization, periodic breathing (PB), autotriggering, and apnea-hypopneas.**

Results: **Eleven patients (55%) exhibited desynchronization occurring mostly in slow-wave sleep and rapid eye movement sleep and associated with arousals but not inducing significant changes in TcP_{CO_2} or oxygen saturation using pulse oximetry (Sp_{O_2}). Eight patients (40%) showed a high index of PB, mostly occurring in light sleep and associated with more severe nocturnal hypoxemia. Autotriggering was sporadic and usually limited to one or two breaths, although prolonged and asymptomatic autotriggering occurred in one patient during 10.6% of total sleep time.**

Conclusions: **Patient/ventilatory asynchrony and PB are respiratory patterns occurring frequently in OHS patients treated using NPPV. Nocturnal monitoring of Sp_{O_2} and TcP_{CO_2}, commonly used to assess the efficacy of ventilatory support, do not adequately explore this aspect of therapy that might influence its efficacy as well as sleep quality.** ***(CHEST 2007; 131:1090–1099)***

Key words: obesity-hyperventilation syndrome; positive airway pressure, intermittent; sleep-disordered breathing

Abbreviations: ABG = arterial blood gas; AHI = apnea/hypopnea index; BMI = body mass index; NPPV = noninvasive positive pressure ventilation; NREM = non-rapid eye movement; ODI = oxygen desaturation index; OHS = obesity-hypoventilation syndrome; PB = periodic breathing; PVA = patient/ventilator asynchrony; REM = rapid eye movement; Sp_{O_2} = oxygen saturation measured using pulse oximetry; TcP_{CO_2} = transcutaneous P_{CO_2}; TST = total sleep time; WASO = wake after sleep onset; WOB = work of breathing

The obesity-hypoventilation syndrome (OHS) is commonly defined as a combination of obesity (body mass index [BMI] > 30 kg/m^2) and arterial hypercapnia during wakefulness ($Pa_{CO_2} > 45$ mm Hg) without any other known cause of hypoventilation.[1,2] Patients may present with symptoms such as daytime sleepiness, fatigue, and morning headaches, which are similar to those seen in sleep-disordered breathing, frequently associated with OHS. However, pulmonary hypertension, cor pulmonale, and recurrent episodes of hypercapnic respiratory failure develop in patients with OHS. Indeed, OHS without ventilatory support is associated with a substantial morbidity and early mortality.[3]

Weight loss improves the severity of OHS, but noninvasive positive pressure ventilation (NPPV) with either volume-cycled or bilevel pressure respirators is the mainstay of treatment.[4–6] The past years have seen an increase in the use of bilevel pressure respirators for this indication.[7] After treatment with NPPV, breathlessness on exertion, quality of sleep, daytime sleepiness and fatigue, and early morning headaches improve.[6] Furthermore, nocturnal and daytime arterial blood gas (ABG) levels improve, often within the first few days of treatment.[4,5,8]

Some patients with OHS are not adequately treated using bilevel pressure respirators; possible contributing factors include insufficient correction of alveolar hypoventilation, intolerance related to mask discomfort, sensation of excessive air pressure, or claustrophobia. The negative impact of mouth leaks on transcutaneous P_{CO_2} (TcP_{CO_2}) and sleep structure has also been reported.[9] We know that leaks, which cause patient-ventilator asynchrony (PVA), are a major cause for NPPV failure during daytime.[10] Efficacy of NPPV requires an optimal interaction between the patient's ventilatory drive and the ventilator. PVA may result from ineffective inspiratory triggering or ineffective termination of inspiratory pressure support (cycling asynchrony), leading to a mismatch between neural (patient) and mechanically assisted (ventilator) breaths.[11,12] Work of breathing (WOB) may increase because of PVA and approach or exceed WOB imposed by the underlying disease.[13] Pulse oximetry, capnography (TcP_{CO_2}), daytime ABG levels, and questionnaires evaluating improvement in quality of life, sleep disturbances, and sleepiness are commonly used to evaluate efficacy of NPPV in patients treated on a long-term basis.[14,15] Although these methods measure the benefit of treatment on subjective symptoms as well as nocturnal hypoventilation, they are, however, unable to identify respiratory disturbances occurring during sleep such as PVA, which may affect the efficacy of treatment. A still unanswered question, therefore, is whether the occurrence of PVA or other respiratory disturbances during the night may compromise the efficacy of NPPV and have a deleterious effect on sleep structure. The aim of the current study was to evaluate whether nocturnal polysomnography allows the detection of respiratory disturbances occurring in NPPV-treated patients with minimal or no alteration in either nocturnal oxygen saturation measured by pulse oximetry (Sp_{O_2}) or TcP_{CO_2}, contributing to increased sleep disruption.

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Materials and Methods

Study Population

All patients followed up by the Division of Pulmonary Diseases of Geneva University Hospital for OHS (defined as BMI ≥ 30 kg/m^2 and diurnal $Pa_{CO_2} \geq 45$ mm Hg) and treated by home NPPV between August 1, 2003, and April 15, 2004, were eligible for this study (n = 29): 20 patients agreed to participate and fulfilled the following inclusion criteria: (1) stable clinical condition; (2) home treatment with a bilevel pressure respirator for at least 3 months; and (3) NPPV initiated after at least one episode of acute hypercapnic respiratory failure. Exclusion criteria were as follows: association with COPD, any unstable respiratory condition, comorbidities, and/or poor compliance defined by a daily use of ventilator of < 4 h. As previously described,[7] adjustment of ventilator settings and oxygen supplementation aimed to obtain the lowest possible value for daytime Pa_{CO_2} (or nocturnal TcP_{CO_2}) with the ventilator, and a mean nocturnal $Sp_{O_2} > 90\%$, with $< 20\%$ of the nocturnal total recording time having $< 90\%$ of Sp_{O_2}. Expiratory positive airway pressure values were titrated to normalize the desaturation index under NPPV. The study protocol was approved by the Ethics Committee for Medical Research of Geneva University Hospital, and written informed consent was obtained from all participants.

Nocturnal Recording

Standard polysomnography was performed (Brainlab; Schwartzer; Munich, Germany) using seven EEGs, right and left electrooculograms, and one electromyogram of chin muscle for conventional sleep staging. Respiratory airflow was monitored with a nasal cannula connected to a pressure transducer (Protech 2; Protech; Minneapolis, MN); thoracic and abdominal respiratory movements were monitored with piezoelectric strain gauges, and tracheal sound by microphone. Sp_{O_2} was continuously measured with a pulse oximeter and a finger probe. Positive pressure level was continuously measured at the mask and recorded during the nocturnal study.

TcP_{CO_2} measurements were performed using a capnograph (Tina TCM3; Radiometer; Copenhagen, Denmark). The calibration of the electrode was performed before each new measurement, with a standard (5% CO_2, 20.9% O_2) calibration gas. To ensure optimal performance, the membrane of the electrode was changed for each recording. The electrode was positioned on the anterior chest wall. The temperature of the electrode was set at 43°C.[15]

Polysomnographic Scoring

All polysomnographic studies were manually scored both for sleep and respiratory parameters by an experienced sleep specialist (E.S.).

Sleep Parameters

Sleep was scored according to standard criteria[16] using 20-s epochs, an epoch duration commonly used in our laboratory. The following sleep parameters were defined: total sleep time (TST); sleep efficiency, defined as TST/total recording time × 100; percentage of each sleep stage; wake after sleep onset (WASO); and sleep latency. As indexes of sleep fragmentation, we considered the number of awakenings, the sleep stage shifts, the sleep fragmentation index (number of awakenings lasting ≥ 20 s plus sleep stage shifts/TST in hours),[17] and the index of microarousals. Microarousals were scored according to American Sleep Disorders Association criteria[18] as a return to α or fast frequency, well differentiated from the background EEG. The duration was, however, extended to include arousals lasting ≥ 1.5 s and < 3 s[19] in order to better estimate sleep fragmentation.

Respiratory Parameters

Capnography and polysomnography were synchronized before lights out, allowing matching of data during subsequent analysis. Figure 1 depicts a period of stable ventilation in non-rapid eye movement (NREM) sleep under nocturnal ventilation. The following respiratory disturbances were identified (mouth leaks, although most certainly frequent in these patients, are underestimated by the methods used in our polysomnographic evaluation, and are thus not quantified):

Apneas and Hypopneas: Scoring of apneas and hypopneas was done using combined analysis of nasal pressure and respiratory effort. Using standard criteria,[20] hypopneas were defined as ≥ 50% reduction in nasal pressure signal from baseline value lasting at least 10 s, associated with either an oxygen desaturation of > 3% or an arousal and associated with concomitant variation of respiratory effort, either reduction (central hypopneas) or progressive increase (obstructive hypopneas). Apnea was defined as being central, obstructive, or mixed on the basis of absence or persistence of respiratory efforts measured with the thoracic and abdominal strain gauges associated with a reduction in nasal pressure to at least 20% of the baseline value. Periods with prolonged absence of nasal pressure signal were considered as probable air leaks and discarded from the analysis.

Periodic Breathing: Periodic breathing (PB) was defined as the recurrence of a crescendo-decrescendo pattern of respiratory depth on thoracoabdominal wall movement tracings, lasting at least 10s. The total number of PB episodes, the PB index (number/h of sleep), the percentage of TST during which PB occurred, and the sleep stage during which each event occurred were recorded.

Desynchronization: Desynchronization was identified by observing uncoupling of the patient's respiratory efforts and onset of ventilator pressure support (Fig 2) for at least 10 s and three consecutive breaths. The end of the event was defined by the occurrence of three consecutive synchronized breaths. The ventilator rhythm was derived from the flow and pressure curves. The patient's respiratory efforts were derived from the thoracoabdominal wall movements. The number of events and their length were recorded. The percentage of TST spent with PVA was computed for each case, and the sleep stage during which each event occurred was recorded.

Autotriggering: Autotriggering was defined as the occurrence of at least three rapid successions of pressurizations at a respiratory rate > 40 breaths/min, and clearly above that of the patient's respiratory rate (Fig 3). This type of event is suggestive of either a defect in inspiratory effort sensing by the machine (which may be related to leaks), or an overly sensitive inspiratory trigger. The number of events and the ratio of their total length to the total time of recording were calculated.

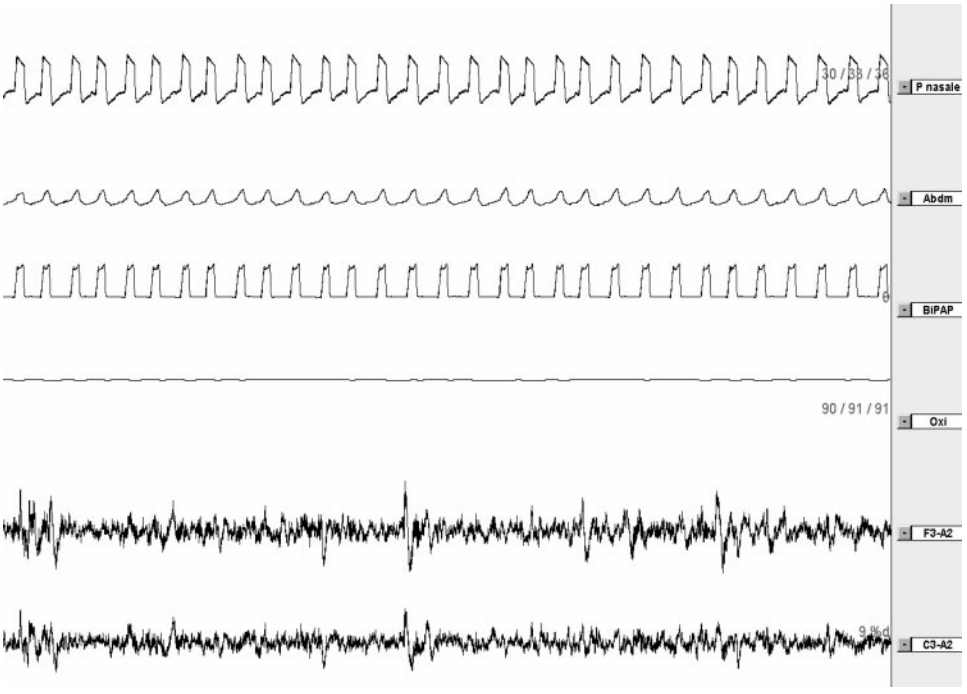

FIGURE 1. Polysomnographic recording of a subject with normal ventilation under NPPV during slow-wave sleep. From *top* to *bottom*: pressure flow signal (P nasale); abdominal movements (Abdm); pressure signal from ventilator (BiPAP); SpO_2 (Oxi); and EEG (F3-A2 and C3-A2). Time span = 2 min.

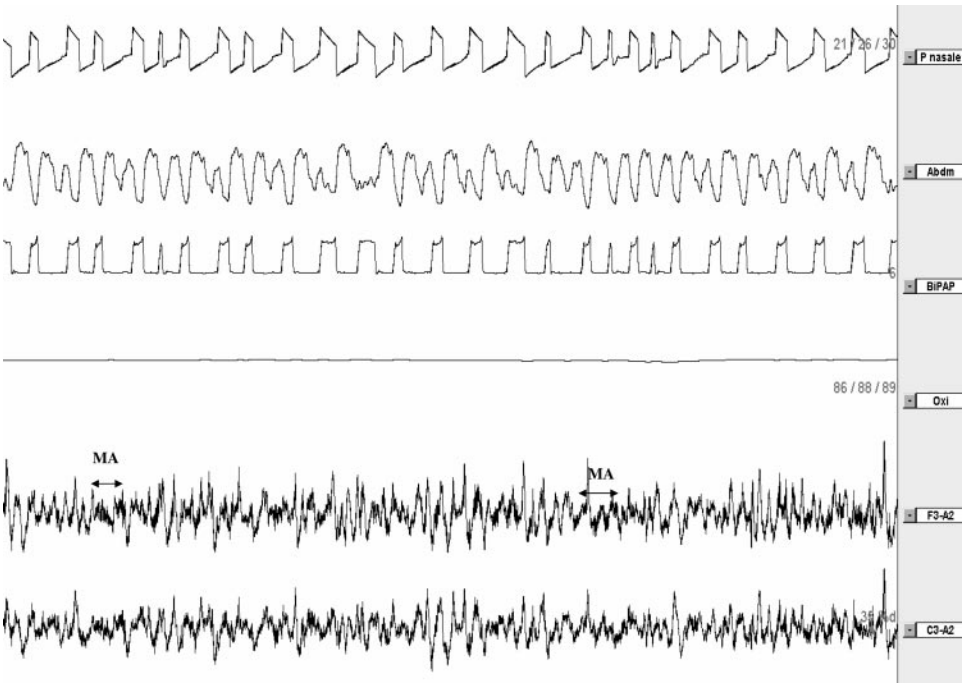

FIGURE 2. Polysomnographic recording of a subject with persistent PVA in slow wave sleep. From *top* to *bottom*: pressure flow signal; abdominal movements; pressure signal from ventilator; Spo_2; and EEG. Time span = 2 min. The occurrence of asynchrony induces in some cases the appearance of microarousals (MA). See Figure 1 legend for expansion of abbreviations.

Spo_2 and $TcPco_2$ Analysis

Minimal and mean Spo_2, percentage of TST with $Spo_2 < 90\%$, oxygen desaturation index (ODI) [transient desaturation defined as a decrease in Spo_2 of $\geq 4\%$], and mean, median, maximal, and minimal $TcPco_2$ values were recorded.

Statistical Analysis

All statistical analysis was performed using statistical software (SPSS for Windows 11.0; SPSS; Chicago, IL). Significance was taken at $p \leq 0.05$ for all tests after Bonferroni corrections. Results are presented as mean ± SD.

According to presence of asynchrony or PB, patients were stratified into two groups: those with a higher percentage of asynchrony or PB, and those without these respiratory patterns. Comparison between these two groups was done using an unpaired Student *t* test.

RESULTS

Patients

Patient characteristics and baseline ventilator settings are shown in Table 1. The study group included 8 women and 12 men (mean age, 63.5 ± 11.6 years; average BMI, 43 ± 7 kg/m^2). Four types of bilevel pressure-cycled ventilators were used: the VPAP II ST and III ST (ResMed; North Ryde; Australia); the Synchrony (Respironics; Murrysville, PA); the Moritz II (MAP; Martinsried, Germany); and the BiPAP ST (Respironics; Murrysville, PA). Ventilators were all set in the spontaneous/timed mode (assist pressure support with a back-up respiratory rate). Assisted ventilation was initiated during an acute episode of hypercapnic respiratory failure in 15 patients, and electively because of progressive hypercapnia in 5 patients. In all patients, adjustment of ventilator parameters had been performed to obtain maximal improvement of daytime ABG levels, nocturnal Spo_2, and $TcPco_2$ (Table 1). During the study night, ventilatory assistance was provided through a nasal mask (n = 17) or facial mask (n = 3). In four patients, supplemental oxygen was administered with NPPV.

Sleep Data

Details of sleep parameters are given in Tables 2, 3. WASO, sleep efficiency, and percentage of different sleep stages indicated disturbed sleep, with a high number of awakenings and sleep stage transitions, as well as low sleep efficiency and increased WASO. Light sleep (stages 1 and 2) and rapid eye movement (REM) sleep were increased compared to slow wave sleep. Comparison of patients with PVA or PB vs without PVA or PB showed that patients with PVA or PB had a more disturbed sleep, with a greater amount of light (stages 1 and 2) sleep and a

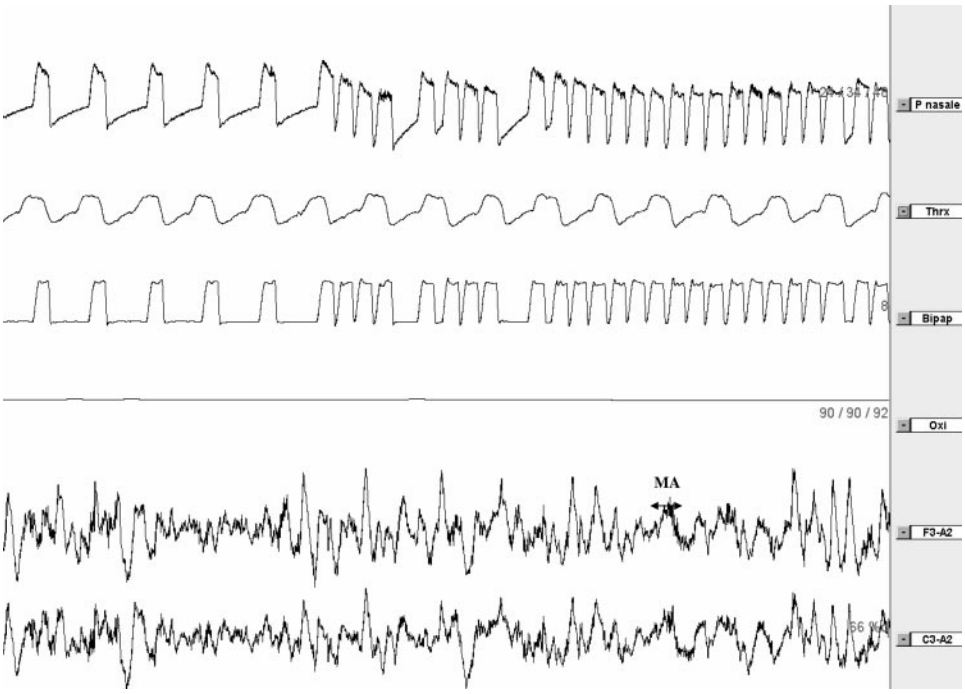

FIGURE 3. Polysomnographic recording of a subject with ventilator autotriggering during slow wave sleep, inducing occasional microarousals. From *top* to *bottom*: pressure flow signal; thoracic movements (Thrx); pressure signal from ventilator; Spo_2; and EEG. Time span = 2 min. See Figure 1 legend for expansion of abbreviations.

lower amount of slow wave sleep, differences however reaching significance only in PVA patients (Tables 4, 5).

Respiratory Data: $TcPco_2$, and Spo_2

In spite of the fact that apnea and hypopnea were uncommon, oxygen desaturations were relatively frequent in study patients (ODI from polysomnography: 6.6 ± 6.4/h; range, 0 to 20.2/h). As shown in Table 3, nine patients showed an average nocturnal $Spo_2 < 90\%$. The mean nadir Spo_2 was 79 ± 6% (range, 68 to 91%), and mean Spo_2 was 90 ± 3% (range, 83 to 95%). Four patients received supplemental oxygen therapy. Two of these patients had severe oxygen desaturations despite oxygen supplementation with an average nocturnal Spo_2 and minimal Spo_2 being, respectively, 89% and 74 to 76%. Correction of alveolar hypoventilation was on average satisfactory: mean $TcPco_2$ was 44 ± 5 mm Hg (range, 36.5 to 54.9 mm Hg) [Table 3]. We did not find any significant relationship between average Spo_2 or nadir Spo_2 and $TcPco_2$ ($r = -0.004$ and 0.007; $p = 0.986$ and 0.977, respectively; Spearman correlation).

Apnea and Hypopneas

The evaluation of data analyzed by polysomnography showed that the apnea-hypopnea index (AHI) under noninvasive ventilation varied markedly among patients, with an average value of 5.2 ± 5.0/h (range, 0 to 16/h) [Table 3]. Four patients still had an AHI > 10/h under bilevel pressure respiration. In one case, respiratory events occurred during episodes of autotriggering of the ventilator. One patient showed a clear predominance of obstructive hypopneas, and three patients had obstructive and central hypopneas.

PVA

Polysomnographic data showed that 11 patients (55%) exhibited desynchronization with their ventilator (Table 4, Fig 2), the average sleep time with PVA being 31.7 ± 22.9% of TST (range, 6.1 to 72.6%). The association between desynchronization and sleep stage varied substantially between patients. Average percentage of time spent with PVA was 58.2% for stages 1–2 sleep, 22.2% for stages 3–4, and 19.6% for REM sleep.

Despite the occurrence of PVA for a substantial proportion of TST, oxygen desaturations were infrequent in these patients (four patients, however, received supplemental oxygen). When comparing patients with or without PVA, we did not find any statistically significant difference in terms of average nocturnal Spo_2, nadir Spo_2, or ODI. $TcPco_2$ was also practically identical for the two groups, suggesting that PVA did not have deleterious effects on

Table 1—*Patient Characteristics and Ventilator Settings

Patient No.	Sex	Age, yr	BMI, kg/m^2	Duration of NPPV, yr	Initiation of NPPV	FEV_1, % Predicted	FVC, % Predicted	FEV_1/FVC, % Predicted	Ventilator	IPAP, cm H_2O	EPAP, cm H_2O	Respiratory Backup Rate, min	O_2, L/min
1	F	69	48.8	2.1	Acute	67	66	102	Synchrony	22	6	15	1.5
2	M	77	34.2	7.4	Acute	56	66	85	Synchrony	18	6	14	
3	M	71	42.8	0.3	Acute	85	87	98	VPAPIII S/T	18	6	14	
4	F	75	35.7	2.4	Elective	76	82	93	VPAP II S/T	18	8	12	
5	M	64	39.9	0.4	Acute	60	67	90	VPAPIII S/T	14	4	16	
6	M	54	39.1	3.4	Acute	52	57	91	VPAP II S/T	18	5	12	
7	M	72	38.5	0.3	Acute	52	55	95	Synchrony	24	8	12	
8	M	57	53.2	8.4	Elective	106	98	108	BiPAP S/T	10	6	14	
9	M	38	32.2	0.3	Elective	85	79	108	BiPAP S/T	18	6	15	
10	F	63	48.5	0.3	Elective	52	60	87	VPAP II S/T	12	4	12	
11	M	61	45.5	7.2	Acute	76	85	90	BiPAP S/T	18	8	18	
12	M	44	53.1	6.7	Acute	71	72	99	Synchrony	28	8	10	3
13	M	61	45.9	3.4	Elective	52	46	113	VPAP II S/T	22	7	15	
14	F	65	47.9	3.2	Acute	82	88	93	VPAP II S/T	25	5	14	
15	F	77	39	0.5	Acute	NA	NA	NA	Moritz S/T	15	4	14	
16	F	49	40.1	3.3	Acute	102	100	102	VPAP II S/T	16	6	12	
17	M	57	41.9	1.8	Acute	55	64	85	VPAP II S/T	22	7	18	
18	F	78	32.6	8.6	Acute	101	114	89	BiPAP S/T	18	8	12	2
19	M	59	41.2	0.9	Acute	87	76	114	VPAP II S/T	12	6	10	
20	F	79	57.3	3.2	Acute	61	80	76	VPAP II S/T	22	7	15	1
Mean		63.5	42.9	3.4		72.5	75.9	96		18.5	6.3	13.7	
SD		11.6	7.0	2.9		18.3	17.1	10		4.6	1.4	2.2	

*F = female; M = male; IPAP = inspiratory positive airway pressure; NA = not available; EPAP = expiratory positive airway pressure.

blood gas levels (Table 4). Although alveolar ventilation seemed little affected by PVA, patients who desynchronize with the machine had a worse sleep quality, with more stage 1 and 2 sleep, more arousals, less slow wave sleep and REM sleep, and low sleep efficiency when compared to the patients without

Table 2—*Parameters Recorded During Sleep Study

Patient No.	TST, min	Stage 1, %	Stage 2, %	Slow Wave Sleep, %	REM Sleep, %	SL, min	SE, %	WASO, min	Stage Changes, No.	SFI, No./h	MAI, No./h
1	405.0	15.9	53.7	13.6	16.9	2	75	24.5	337	63	18
2	326.0	21.6	58.8	11.7	8.0	14	74	37.2	337	78	29
3	275.0	12.6	45.8	28.8	12.6	20	51	46.1	196	55	22
4	402.0	21.8	56.1	11.9	10.3	3	70	29.3	564	113	27
5	336.0	16.6	63.9	7.9	11.8	17	54	44	240	54	48
6	384.0	10.9	49.3	27.9	12.2	19	75	16.8	177	35	16
7	323.0	20.2	39.5	28.4	12.1	4	62	36.1	264	62	26
8	383.0	15.9	43.5	22.3	18.6	27	69	26.2	305	62	26
9	362.0	9.6	46.2	36.7	7.7	17	67	30.9	131	28	29
10	324.0	13.3	42.5	33.2	11.0	5	64	35	196	47	26
11	494.0	11.5	63.8	13.9	10.7	17	89	10.6	288	44	31
12	437.0	9.6	61.1	16.7	12.6	10	82	12.9	211	34	24
13	423.0	11.1	38.3	24.0	26.7	10	76	21.4	141	26	10
14	494.0	13.9	76.1	3.2	6.7	49	83	9.7	251	38	30
15	462.0	15.5	57.5	6.6	20.5	9	78	21.1	336	54	32
16	452.0	20.0	54.9	9.1	16.1	4	80	19.3	392	65	31
17	347.0	25.9	55.8	6.5	12.0	9	58	40.2	395	91	35
18	406.0	11.4	42.7	26.4	19.5	12	75	26.4	178	30	18
19	285.0	18.9	52.6	18.9	9.8	6	69	28.9	262	71	29
20	402.0	9.2	32.6	28.9	29.4	4	75	23.5	142	27	8
Mean	386.1	15.3	51.7	18.8	14.3	13	71	27	267	54	26
SD	63.8	4.8	10.5	10.0	6.1	11	10	11	107	23	9

*MAI = microarousal index; SL = sleep latency; SE = sleep efficiency; SFI = sleep fragmentation index.

Table 3—*Nocturnal Respiratory Parameters

Patient No.	AHI, /h	Mean $TcPCO_2$, mm Hg	Median $TcPCO_2$, mm Hg	$TcPCO_2$ Awake, mm Hg	SpO_2 Awake, %	SpO_2 Minimum, %	SpO_2 Mean, %	ODI, /h
1	4.3	48.9	49	51	91	81	90	2.3
2	0	42.2	42.5	51	91	80	90	10.9
3	3.5	40.6	40.6	NA	87	68	83	10.7
4	6.2	41.6	43	41	85	71	85	9.2
5	11.1	37.1	38	44	94	75	88	6.3
6	2.1	43.9	45.2	48	91	78	90	6.5
7	5.1	36.6	35.2	43	92	83	89	0.9
8	9.9	41.6	41.6	NA	95	84	94	20
9	11	41.9	42.2	44	95	68	88	8.7
10	0.8	44.1	44.4	40	92	84	91	11.4
11	5.3	48.5	48.3	54	93	82	91	1.1
12	15.9	54.9	55.5	56	90	74	89	20.2
13	0.8	39.2	40.2	42	91	84	88	1.1
14	4.5	51.4	51.5	50	92	80	90	2.4
15	1.2	53.7	53.5	56	92	83	88	1.8
16	16.1	45.1	45.2	44	93	82	93	14.3
17	3.6	36.5	36.2	42	97	82	95	2.8
18	3	41	41.2	36	92	80	90	0.7
19	0.5	44.1	44.4	37	96	91	95	0
20	0	49.3	49.5	50	90	76	89	0.9
Mean	5.2	44.1	44.4	46.1	92.0	79.3	89.8	6.6
SD	5.0	5.4	5.5	6.2	2.8	5.8	3.0	6.4

*See Table 1 for expansion of abbreviation.

PVA (Table 4). The periods of desynchronization, varying from 10 s to several minutes in length, were frequently associated with arousals. Desynchronization-related arousals mostly occurred in stages 1 and 2 (68% of PVA episodes were associated with arousals). In contrast, few arousals occurred during desynchronization periods in slow wave sleep and REM sleep.

Table 4—*Sleep and Respiratory Parameters in Patients With and Without PVA

Variables	Patients With PVA (n = 11)	Patients Without PVA (n = 9)	p Value†
TST, min	379 ± 64	395 ± 66	NS
Sleep efficiency, %	74.1 ± 11.0	69.1 ± 11.0	NS
Stage 1, %	17.6 ± 5.1	12.4 ± 2.2	0.008
Stage 2, %	56.2 ± 9.4	46.2 ± 9.5	0.031
Slow wave sleep, %	15.0 ± 10.0	23.6 ± 8.4	0.05
REM sleep, %	11.3 ± 3.3	17.9 ± 6.9	0.022
AHI, /h	5.1 ± 4.5	5.4 ± 5.9	NS
ODI, /h	7.6 ± 7.5	5.4 ± 5.0	NS
MAI, /h	30 ± 8	21 ± 9	0.032
Minimal SpO_2, %	79 ± 7	80 ± 6	NS
Mean SpO_2, %	90 ± 3	91 ± 3	NS
Mean $TcPCO_2$, mm Hg	45 ± 6	43 ± 6	NS
Median $TcPCO_2$, mm Hg	45 ± 6	44 ± 6	NS

*Data are presented as mean ± SD. MAI = microarousal index; NS = not significant.
†Student *t* test.

PB

Polysomnography data showed that for 40% (n = 8) of OHS patients, the PB index (number per hour) was > 5/h (mean ± SD, 10.0 ± 4.8/h; range, 5 to 20.5/h) and the mean percentage of TST with PB was 6.3 ± 4.4% (range, 1.5 to 16.2% of TST) [Table 5]. Among the eight patients with PB, four patients had a PB index > 10/h. The occurrence of PB was greater in light sleep (81% occurred in stage 1 and 2 of NREM sleep) and did not induce severe sleep fragmentation, only 22.5% of PB events being associated with arousals. Comparison of patients with vs without PB showed no significant differences in mean or median $TcPCO_2$. There was a trend toward more severe nocturnal hypoxemia in patients with greater PB; these patients showed lower minimal SpO_2 (76.4% vs 82.3%, p = 0.04) and a higher ODI (10.8 vs 3.8, p = 0.01).

Autotriggering

When applying the criteria of three consecutive breaths to score an autotriggering episode, few episodes were detected in the group of patients as a whole; autotriggering was most frequently sporadic and limited to one or two breaths. In one case, we found persistent (and asymptomatic) autotriggering during sleep (Fig 3), occurring during 10.6% of the TST. Persistent autotriggering occurred more frequently in stages 1 and 2 (72% of all episodes) and

Table 5—*Sleep and Respiratory Parameters in Patients With and Without PB

Variables	Patients With PB (n = 8)	Patients Without PB (n = 12)	p Value†
PB index, /h	10.1 ± 4.8	1.8 ± 1.5	< 0.0001
TST, min	423 ± 71	361 ± 46	0.05
Sleep efficiency, %	75.1 ± 11.3	68.8 ± 8.2	NS
Stage 1, %	15.1 ± 4.2	15.4 ± 5.3	NS
Stage 2, %	55.1 ± 12.6	49.5 ± 8.8	NS
Slow wave sleep, %	14.5 ± 9.6	21.7 ± 9.6	NS
REM sleep, %	15.4 ± 15.8	13.5 ± 6.7	NS
ODI, /h	10.8 ± 6.7	3.8 ± 4.6	0.01
Minimal Spo_2, %	76.4 ± 8.1	82.3 ± 4.0	0.04
Mean Spo_2, %	89.5 ± 3.4	91.3 ± 1.7	NS
Mean $TcPco_2$, mm Hg	42.8 ± 5.6	44.9 ± 6.0	NS
Median $TcPco_2$, mm Hg	43.3 ± 5.6	45.0 ± 6.1	NS

*Data are presented as mean ± SD. See Table 4 for expansion of abbreviation.
†Student *t* test.

less in slow wave sleep (23%) or REM sleep (5%). The autotriggering episodes were associated with a higher AHI (16.1/h), higher ODI (14.3), and lower sleep efficiency (69%). Interestingly, occurrence of autotriggering did not induce appearance of arousals.

Polysomnography vs Capnography and Oximetry for the Detection of PVA

Five patients (25%) had neither PVA, PB, apneas, nor autotriggering; 15 patients had either PVA or PB; and 5 patients had PVA and PB. Of 11 patients with PVA, 6 patients (55%) had a normal mean nocturnal Spo_2 (≥ 90%) and 6 patients (55%) had normal $TcPco_2$ values (≤ 45 mm Hg). When combining both criteria, three patients (27%) had $TcPco_2$ values ≤ 45 mm Hg and Spo_2 > 90% (Fig 4).

Discussion

This is to our knowledge the first study of sleep structure and nocturnal respiratory events in a homogeneous group of OHS patients treated by home

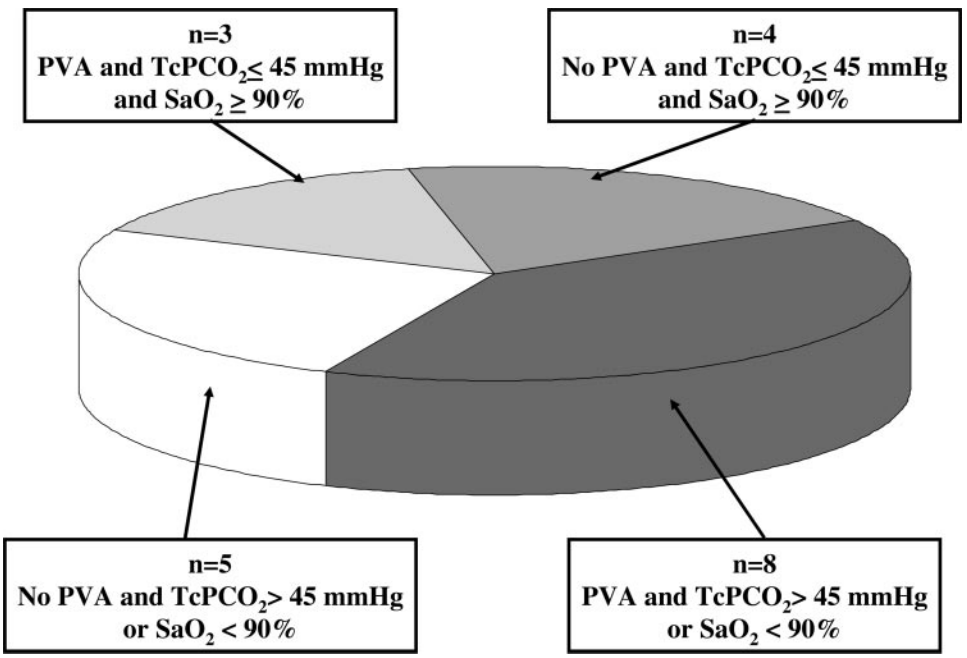

Figure 4. Agreement between mean nocturnal $TcPco_2$, nocturnal Spo_2 values, and presence of PVA assessed by polysomnography (see text for definition); n = 20 patients. Three patients with PVA (27% of those with PVA) had normal nocturnal Spo_2 and $TcPco_2$ findings. Sao_2 = arterial oxygen saturation.

NPPV with a bilevel pressure respirator. The most interesting finding of this study was that specific and sometimes severe respiratory disturbances could occur under NPPV and not necessarily be associated with drops in Spo_2 or increases in $TcPco_2$. Among these events, the most frequently detected were intermittent or persistent PVA, ventilator-induced PB and, to a lesser degree, autotriggering of the ventilator. The major adverse consequence of these events is increased sleep fragmentation, as demonstrated by the close association between episodes of PVA and arousals.

The most common pattern of respiratory disturbances was PVA, detected in 55% of patients studied, occurring mainly in stages 1 and 2 of NREM sleep, and in four cases, lasting $>40\%$ of TST. Although in acute care settings, PVA may contribute to failure of NPPV,[13,21] PVA was not, in this study, associated with significant decreases in Spo_2 or increases in $TcPco_2$ when compared with patients without PVA (Table 4). However, PVA was associated with more fragmented sleep and a decrease in slow wave sleep and REM sleep. Two thirds of PVA episodes were associated with microarousals in stage 1 and 2 of NREM sleep, often followed by resynchronization of patient and ventilator. PVA-associated arousals occurred much less frequently in slow wave sleep or REM sleep, probably because of a higher arousal threshold during these sleep stages. PVA may result from defective inspiratory triggering (causing delayed pressurization or unrewarded inspiratory efforts) or either delayed or premature cycling.[11,12] In patients without increased intrinsic positive end-expiratory pressure, major leaks are probably the most important contributors to these events. Mouth leaks were underestimated by the methods used in our polysomnography evaluation and were not quantified. The relevance of detecting PVA is, in the present study, mainly related to its deleterious impact on sleep structure, and its theoretical negative impact on WOB and relief of respiratory muscles. Indeed, Fanfulla et al[22] showed how two different ventilator settings, which did not induce significantly different diurnal patterns of breathing, blood gas levels, or respiratory mechanics, could affect quite differently nocturnal patient/ventilator synchrony, nocturnal blood gas levels, and sleep quality (sleep efficiency, amount of REM sleep, number of arousals). The authors suggest that inappropriate settings of home ventilators leading either to ineffective inspiratory efforts or central apnea may be more easily detected by sleep studies than through daytime assessment. In fact, the later study[22] and the study by Collard et al[23] both suggest that for patients receiving long-term mechanical ventilation, sleep studies are necessary for determining appropriate ventilator settings thus minimizing PVA, and improving ABG levels and sleep architecture. Furthermore, detection of PVA may orient the clinician toward the following: (1) mouth leaks, and (2) defective inspiratory triggering, or cycling, which are adjustable parameters in many recent bilevel pressure respirators.

The second interesting finding is that 40% of our patients presented periods of PB, more frequent in unstable (stage 1 and 2) sleep, and associated neither to changes in $TcPco_2$ nor to sleep fragmentation (Table 5). Our hypothesis was that occurrence of PB would be associated with ventilator-induced hypocapnia and/or high pressure settings. "Overassistance" by the ventilator and higher pressure settings have been suggested as causes of central apnea.[22] Both PB and central apneas can be due to glottic closure, which depends partly on chemosensitivity of respiratory centers to $Paco_2$, and can lead to different ventilatory patterns with the same $TcPco_2$ levels. This has been described in healthy subjects submitted to NPPV with a bilevel pressure respirator at increasing inspiratory positive airway pressure (IPAP) levels.[24] The ventilator-induced decrease in glottic width can be offset by increasing the inspired Pco_2.[25] In the present study, however, we found that mean and median nocturnal $TcPco_2$ values were not significantly lower in patients with PB vs without PB. Furthermore, differences in ventilator settings (IPAP values) could not explain occurrence of PB. Thus, the physiopathology of PB in these patients remains unclear. Is a higher apnea threshold or sensitivity to carbon dioxide in patients involved? Is there individual variability in terms of sensitivity to increased pressure and/or flow in upper airways?

Study Limitations

In the discussion of our results, some methodologic limitations should be considered. First, the limited number of subjects studied and the analysis restricted to just one night may have overestimated the occurrence of respiratory disturbances and the associated sleep fragmentation. However, the differences found in sleep structure between patients with or without these respiratory events suggest that the "first-night effect" alone could not contribute to the occurrence of these alterations. Secondly, criteria used to define asynchrony, PB, apneas-hypopneas, and autotriggering are somewhat arbitrary, and may explain in some cases the low number of events such as apneas or hypopneas. However, in the absence of formally established criteria for polysomnography scoring under ventilation, we tried to determine whether specific respiratory events, previously proposed as markers of partial efficacy of therapy,

occurred in our patients.[22] The use of these criteria in a larger sample of patients could open a new way to analyze efficacy of therapy in OHS patients receiving long-term mechanical ventilation. Finally, our results could be criticized because of the absence of direct quantitative flow measures necessary to evaluate the role of pressure drops and air leaks in the occurrence of asynchrony and PB. However, since our study was an exploratory analysis in a small group of patients, we believe that application of new techniques allowing simultaneous recording of sleep, pneumotachograph and a pressure transducer, could in the future allow a better understanding of respiratory disturbances in patients receiving mechanical ventilation.

In conclusion, we chose to analyze arbitrarily defined respiratory events occurring under bilevel pressure support ventilation that could be physiologically relevant, and their impact on sleep structure, $TcPCO_2$, and SpO_2. Among these events, nocturnal PVA and PB were common. Nocturnal PVA appears to be clinically relevant because it induces sleep fragmentation and decreases REM and slow wave sleep, which was not the case for PB or autotriggering. These findings suggest that end points in the evaluation of NPPV should not be restricted only to monitoring of nocturnal SpO_2 or $TcPCO_2$ and daytime blood gas levels, but should seek for respiratory disturbances occurring under ventilation that affect sleep quality. Future studies are needed to establish whether recognition of these respiratory-related disturbances affect either the efficacy of therapy or compliance.

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References

1 Kessler R, Chaouat A, Schinkewitch P, et al. The obesity-hypoventilation syndrome revisited: a prospective study of 34 consecutive cases. Chest 2001; 120:369–376
2 Sharp J, Barrocas M, Chokroverty S. The cardiorespiratory effects of obesity. Clin Chest Med 1980; 1:103–123
3 Nowbar S, Burkart KM, Gonzales R, et al. Obesity-associated hypoventilation in hospitalized patients: prevalence, effects, and outcome. Am J Med 2004; 116:1–7
4 Piper AJ, Sullivan CE. Effects of short-term NIPPV in the treatment of patients with severe obstructive sleep apnea and hypercapnia. Chest 1994; 105:434–440
5 Perez de Llano LA, Golpe R, Ortiz Piquer M, et al. Short-term and long-term effects of nasal intermittent positive pressure ventilation in patients with obesity-hypoventilation syndrome. Chest 2005; 128:587–594
6 Masa JF, Celli BR, Riesco JA, et al. The obesity hypoventilation syndrome can be treated with noninvasive mechanical ventilation. Chest 2001; 119:1102–1107
7 Janssens JP, Derivaz S, Breitenstein E, et al. Changing patterns in long-term noninvasive ventilation: a 7-year prospective study in the Geneva Lake area. Chest 2003; 123: 67–79
8 Pankow W, Hijjeh N, Schütter F, et al. Influence of noninvasive positive pressure ventilation on inspiratory muscle activity in obese subjects. Eur Respir J 1997; 10:2847–2852
9 Teschler H, Stampa J, Ragette R, et al. Effect of mouth leak on effectiveness of nasal bilevel ventilatory assistance and sleep architecture. Eur Respir J 1999; 14:1251–1257
10 Carlucci A, Richard JC, Wysocki M, et al. Noninvasive versus conventional mechanical ventilation: an epidemiologic survey. Am J Respir Crit Care Med 2001; 163:874–880
11 Chao DC, Scheinhorn DJ, Stearn-Hassenpflug M. Patient-ventilator trigger asynchrony in prolonged mechanical ventilation. Chest 1997; 112:1592–1599
12 Yamada Y, Du HL. Analysis of the mechanisms of expiratory asynchrony in pressure support ventilation: a mathematical approach. J Appl Physiol 2000; 88:2143–2150
13 Leung P, Jubran A, Tobin MJ. Comparison of assisted ventilator modes on triggering, patient effort, and dyspnea. Am J Respir Crit Care Med 1997; 155:1940–1948
14 Janssens JP, Howarth-Frey C, Chevrolet JC, et al. Transcutaneous PCO_2 to monitor noninvasive mechanical ventilation in adults: assessment of a new transcutaneous device. Chest 1998; 113:768–773
15 Janssens JP, Perrin E, Bennani I, et al. Is continuous transcutaneous CO_2 ($PtcCO_2$) monitoring reliable over an 8 hour period? Respir Med 2001; 95:331–335
16 Rechtschaffen A, Kales A. A manual of standardized terminology, technique and scoring system for sleep stages of human sleep. Los Angeles, CA: Los Angeles Brain Information Service. Brain Information Institute, 1968
17 Haba-Rubio J, Ibanez V, Sforza E. An alternative measure of sleep fragmentation in clinical practice: the sleep fragmentation index. Sleep Med 2004; 5:577–581
18 American Sleep Disorders Association. EEG arousal: scoring rules and examples. Sleep 1992; 5:577–581
19 Martin SE, Engleman HM, Kingshott RN, et al. Microarousals in patients with sleep apnoea/hypopnoea syndrome. J Sleep Res 1997; 6:276–280
20 Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research; the report of an American Academy of Sleep Medicine task force. Sleep 1999; 22:667–689
21 Jubran A, Van de Graaff WB, Tobin MJ. Variability of patient-ventilator interaction with pressure support ventilation in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1995; 152:129–136
22 Fanfulla F, Delmastro M, Berardinelli A, et al. Effects of different ventilator settings on sleep and inspiratory effort in patients with neuromuscular disease. Am J Respir Crit Care Med 2005; 172:619–624
23 Collard P, Dury M, Delguste P, et al. Movement arousals and sleep-related disordered breathing in adults. Am J Respir Crit Care Med 1996; 154:454–459
24 Parreira VF, Jounieaux V, Aubert G, et al. Nasal two-level positive-pressure ventilation in normal subjects: effects of the glottis and ventilation. Am J Respir Crit Care Med 1996; 153:1616–1623
25 Jounieaux V, Aubert G, Dury M, et al. Effects of nasal positive-pressure hyperventilation on the glottis in normal awake subjects. J Appl Physiol 1995; 79:176–185