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Sleep-related breathing disorders in obese patients presenting with acute respiratory failure

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Summary *Introduction*: The study was conducted to assess the clinical and polysomnographic characteristics of patients with sleep-related breathing disorders who presented to the intensive care unit (ICU) with acute respiratory failure and the practicability of performing polysomnography for such patients.

Material and methods: We analyzed clinical presentation, cause of admission to the ICU, ICU course and outcome of 11 subjects with acute respiratory failure who were diagnosed to have sleep disordered breathing based on polysomnography between October 1999 and January 2003. Subjects were compared to 11 patients with obstructive sleep apnea syndrome matched to each subject using body mass index, age and apnea hypopnea index measured at the time of diagnosis (matched comparison group). Repeated arterial blood gases and polysomnography were done for 8 subjects compliant to treatment 6–8 months after discharge from ICU.

Results: The reason for ICU admission for all subjects was hypercapnic respiratory failure. pH and daytime PaO_2 were significantly lower in studied subjects compared to the matched comparison group while awake daytime $PaCO_2$ was significantly higher. Subjects had frequent episodes of hypoventilation. Follow up arterial blood gases and polysomnography 6–8 months after treatment (non-invasive ventilation) in compliant subjects showed significant improvement in all blood gases parameters.

Conclusions: Early polysomnography (or portable cardio-respiratory monitoring) allows accurate diagnosis and institution of the appropriate ventilation method Further studies should assess the evolution of respiratory drive in patients with sleep disordered breathing and hypercapnia under therapy (non-invasive ventilation).

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Introduction

Sleep disordered breathing is a relatively common disorder.[1] Serious complications like hypertension,[2] ischemic heart disease,[3] stroke[4] and pulmonary hypertension[5] have been reported secondary to sleep disordered breathing. Patients with obstructive sleep apnea syndrome have been shown to have increased mortality,[6] which has been attributed to comorbid conditions and complications of obstructive sleep apnea syndrome like obesity, hypertension and ischemic heart disease. The association between sudden death and sleep disordered breathing has been reported earlier in patients labeled with the diagnosis of "*Pickwickian syndrome*".[7] The relationship between sleep disordered breathing and acute respiratory failure is not well established. Few papers in the literature addressed the issue of acute respiratory failure in patients with sleep disordered breathing.[8–10] Patients with sleep disordered breathing and respiratory failure may be misdiagnosed as having chronic obstructive pulmonary disease (COPD) or chronic heart disease resulting in delay in receiving the appropriate treatment.

This study was conducted to describe the clinical and polysomnographic characteristics of patients with sleep-related breathing disorders who present to the ICU with acute respiratory failure and to assess the practicability of performing polysomnography in this group of patients.

Material and methods

The study was conducted at King Khalid University Hospital (KKUH), which is a 650 beds tertiary care hospital that accepts referrals from different regions of Saudi Arabia. Around 60–70 patients a year are admitted to the medical intensive care unit (ICU) for respiratory failure. Data from eleven subjects with acute respiratory failure diagnosed to have sleep-related breathing disorders (based on polysomnography) between October 1999 and January 2003 during ICU admission were analyzed for clinical presentation, reason for ICU admission, management, response to treatment and outcome. The diagnosis of obstructive sleep apnea was already established in one subject and continuous positive airway pressure (CPAP) was prescribed, however, he was not compliant to treatment. The remaining ten subjects were not known to have sleep-related breathing disorders before.

The diagnosis of sleep disordered breathing was entertained based on clinical suspicion with a typical history obtained from relatives (snoring, witnessed apnea by family members or excessive daytime sleepiness), body habitus associated with witnessed apneas by the ICU staff or repetitive desaturation using pulse oximeter with fast sampling rate (3–10 s) and negative history for alcohol, hypnotic or psychotropic drug dependence. Apart from occasional linear atelectasis, chest radiographs showed no other abnormalities. Polysomnography was performed before discharge from ICU. For one subject, polysomnography was performed in the ICU. The remaining subjects were transferred to the nearby sleep disorders center accompanied by an ICU nurse. Polysomnography was not performed for subject number 5 as he was diagnosed before in another hospital to have obstructive sleep apnea syndrome. Critical care monitoring was continued while in the sleep disorders center. No polysomnography was performed for patients during mechanical ventilation. None of the other subjects was known to have chronic lung diseases nor history of skeletal or neuromuscular diseases. Ventilated patients received sedation during intubation only. After that, no sedation was given to them. For ventilated patients, polysomnography was performed 3–4 days after extubation. While in the ICU before polysomnography was performed, subjects were started on Bi-level positive airway pressure (BilevelPAP) (IPAP 10 cm H_2O and EPAP 6 cm H_2O). Treatment modality and pressures were adjusted later based on the polysomnographic findings.

Subjects were compared to 11 patients with obstructive sleep apnea syndrome matched to each subject using body mass index, age and apnea hypopnea index measured at the time of diagnosis (matched comparison group). The comparison group comprised of consecutive patients referred electively to the sleep disorders center during the study period for obstructive sleep apnea syndrome diagnosis.

A data entry sheet was completed for each subject assessing; demographic data, reason for ICU admission, duration of ICU stay, co-morbid conditions, medications, investigations, and mechanical ventilation methods. Repeated arterial blood gas analysis and polysomnography were done for eight subjects compliant to treatment (CPAP or bilevel positive airway pressure (BilevelPAP)) 6–8 months after discharge from ICU. Pulmonary function testing (FEV_1, FVC) was performed for subjects before discharge from the hospital.

Polysomnography

Alice-4 diagnostic equipment from Respironics, Inc, Murrysville, Pennsylvania, USA was used in data

acquisition. Data were then downloaded in to IBM-PC. The patient was connected to the monitoring machine by a trained technician. The technician stayed with the patient throughout the study.

During the study, the following parameters were monitored: four electro-encephalography (EEG) (C1-A4, C2-A3, O1-A4, O2-A3), chin electromyography (EMG), electro-oculography (EOG) (eye movement), leg EMG, electro-cardiography (ECG), oxygen saturation, chest and abdominal wall movements, two air flow signals (nasal prong pressure and thermistor), sleep position, and microphone for snoring.

During polysomnography the following protocol was used. During the initial 1–3 h, the patient was studied without intervention to identify the nature and severity of the underlying sleep disordered breathing. After that, treatment was started. CPAP (Respironics Inc, Muraysville, PA) was attempted initially. BilevelPAP (Respironics Inc, Muraysville, PA) was started if the patient could not tolerate CPAP due to persistent massive mask air leakage or discomfort exhaling against positive pressure, or the patient had frequent episodes of hypoventilation without airway obstruction (revealed as a plateau on the inspiratory flow signal using nasal prong pressure without a thoracoabdominal paradox). Pressure titration was performed according to a described protocol.[11] Oxygen supplementation was added if the patient continued to have hypoxemia despite complete elimination of the obstructive respiratory events. Once the mode of support, pressure level and level of oxygen supplementation have been determined, the patient was transferred back to the ICU. The needed support measures were instituted in the ICU using mechanical ventilators in the ICU with internal alarms and monitors.

All sleep studies were analyzed by the principal author to maximize the inter-scorer and intra-scorer reliability.

Analysis and scoring of the sleep studies

Analysis and scoring of the electronic raw data was done manually page by page evaluating time in bed, total sleep time (TST), sleep stages, and arousal index according to established criteria.[12,13] Reports were generated using the Alice-4 software. Standard definitions were used to classify central, obstructive apneas and hypopneas and central hypoventilation.[14] Apnea was defined as the cessation of airflow $\geqslant$10 s, and hypopnea as a recognizable, transient reduction of airflow ($>$50%) for $\geqslant$10 s using nasal prong pressure flow signal. The diagnosis of obstructive sleep apnea syndrome was based on history of snoring and excessive daytime sleepiness and apnea hypopnea index of $>$10 h. Hypoventilation was defined as sustained oxygen desaturation that was not associated with obstructive apneas or hypopneas or periodic breathing.[15–17] Patients with hypoventilation were labeled as having sleep hypoventilation syndrome (SHVS).

During follow up visits, compliance to treatment (CPAP, BilevelPAP and home oxygen) was assessed by asking family members who are living with the patient. Good compliance was defined as using CPAP or BilevelPAP more than five nights per week, poor compliance as less than three nights per week, and intermediate compliance between 3 and 5 nights per week. For one patient, his machine was provided with a data-recording card that allowed objective assessment of compliance during every visit.

Statistical analysis

Data are expressed in text and tables as mean $\pm$ standard error of mean (SEM). Comparisons between subjects and their matched comparison group were made using *t*-test. For comparing the studied subjects before and after treatment, paired *t*-test was used. Results were considered statistically significant at the $P<0.05$.

Results

Eleven subjects were included in the study, 6 males and 5 females. Table 1 shows the characteristics of all 11 subjects on admission. All subjects were admitted to the ICU due to hypercapnic respiratory failure. All studied subjects were discharged to the ward, in which ten of them were discharged home later. Subject number 5 required re-admission to ICU two days after transfer to the ward as he refused to use CPAP. On his second admission, he developed severe sepsis and expired after 3 days. Subject number 3, was sent home in a stable condition on BilevelPAP and home oxygen. However, she was not compliant to treatment and refused to use BilevelPAP or to have tracheostomy. Three months after discharge, she developed hypercapnic respiratory failure and congestive heart failure necessitating intubation and mechanical ventilation. The patient expired during that admission. Unfortunately, the details of her last admission were unavailable since she was admitted to another hospital. Subject number 10 refused to

Table 1 Characteristics of the studied subjects.

Subject No	Sex	Reason for admission	Cor-pulmonale	Apnea known	BP	GCS	APACHE score	Mechanical ventilation	PSG diagnosis	ICU stay (days)	Outcome
1	M	Hypercapnic RF	Yes	No	130/70	13	24	No	SHVS+OSA	4	Discharged
2	M	Hypercapnic RF	Yes	No	145/69	11	17	No	SHVS+OSA	7	Discharged
3	F	Hypercapnic RF	Yes	No	140/90	7	17	Yes	SHVS+OSA	11	Discharged*
4	M	Hypercapnic RF	Yes	No	147/70	15	24	No	SHVS+OSA	5	Discharged
5	M	Hypercapnic RF	Yes	Yes	136/58	7	10	Yes	OSA	7	Discharged**
6	M	Hypercapnic RF	Yes	No	120/80	15	19	No	SHVS+OSA	3	Discharged
7	M	Hypercapnic RF	Yes	No	160/70	15	32	No	OSA	6	Discharged
8	F	Hypercapnic RF	Yes	No	160/100	15	25	No	SHVS+OSA	14	Discharged
9	F	Hypercapnic RF	Yes	No	130/70	15	30	No	SHVS+OSA	4	Discharged
10	F	Hypercapnic RF	Yes	No	150/70	11	21	Yes	SHVS	8	Discharged
11	F	Hypercapnic RF	Yes	No	124/60	13	21	No	SHVS+OSA	3	Discharged
Mean (SEM)					140/74 (4.1/3.7)	12.5 (0.9)	21.8 (1.9)			6.5 (1)	

CHF: congestive heart failure; GCS: Glasgow coma scale (range from 3 (poor)-15 (good)); APACHE: Acute Physiology and Chronic Health Evaluation score (range 0–71, increasing score represents a greater severity of illness); RF: respiratory failure; SHVS: sleep hypoventilation syndrome; OSA: obstructive sleep apnea.

*Discharged home but readmitted again to ICU few months later and expired.

**Discharged to the ward and readmitted few days later with septic shock and expired.

use BilevelPAP. She was admitted 4 times that year following her diagnosis. Subject number 11 did not come for follow up.

All subjects were diagnosed to have pulmonary hypertension based on clinical picture and echocardiographic findings. Repeated echocardiography for subject numbers 1 and 4 one year after treatment revealed normalization of the pulmonary artery pressure (no data was available for other subjects).

Table 2 summarizes the characteristics of subjects and their matched comparison group. Mean age for subjects was 53 ± 4.9 years and body mass index was $47.7 \pm 4.1\,kg/m^2$. Mean age of the comparison group was 54.2 ± 3.1 years and body mass index was $44.1 \pm 1.9\,kg/m^2$. Two subjects were known to have hypothyroidism and were on thyroid hormone replacement at the time of admission. Thyroid function was normal for the remaining subjects and the matched comparison group. Both subjects and their matched comparison group were identical in the apnea hypopnea index. However, compared to the comparison group, subjects spent more time with $PaO_2 < 90\%$, had higher desaturation index and their lowest recorded oxygen saturation was significantly lower. Desaturation index was higher in subjects because this group had frequent episodes of sustained oxygen desaturation that was not associated with obstructive apneas, hypopneas or periodic breathing. Those episodes were not scored as apneas or hypopneas and were labeled as episodes of hypoventilation. The affected subjects were diagnosed to have sleep hypoventilation syndrome. Nine subjects were labeled as having sleep hypoventilation syndrome.

pH was significantly lower in subjects (7.29 ± 0.02) compared to their matched comparison group (7.4 ± 0.01) ($P < 0.05$). Awake daytime PaO_2 was also significantly lower in subjects compared to their matched comparison group ($P < 0.05$). All subjects had daytime hypercapnia with $PaCO_2$ ranging from 52.2 to 116 mmHg (77.9 ± 5.1).

Pulmonary function testing was performed in all subjects before discharge from the hospital. It showed obstructive pattern in subject numbers 3, 8 and 11. Pulmonary function measurements were within normal limits for the rest of the subjects.

Table 3 summarizes the treatment modalities used. Ten of the studied subjects required BilevelPAP and supplemental oxygen. One subject was controlled by CPAP alone. Eight subjects were compliant to treatment. Six to eight months after treatment, all compliant subjects did not require oxygen supplementation while awake. However, three of them continued to need nocturnal oxygen hooked to BilevelPAP during sleep.

Table 4 summarizes the arterial blood gas parameters on admission and 6–8 months after treatment in compliant subjects. It demonstrates significant improvement in all parameters.

Discussion

Obesity is known to be a major risk factor for a range of respiratory disorders.[18] The present study describes an unusual cause of acute respiratory failure necessitating ICU admission in obese patients. We described 11 subjects with sleep-related breathing disorders who developed severe hypercapnic respiratory failure necessitating ICU admission. Early diagnosis allowed early institution of appropriate treatment, hence, avoiding the need for invasive mechanical ventilation in most subjects. This study stresses the importance of early sleep study in patients with acute respiratory failure suspected of having sleep-related breathing

Table 2 Comparison between subjects and their matched comparison group (reported polysomnographic findings upon diagnosis and arterial blood gases parameters upon admission to the ICU).

	Subjects	Comparison group	*P* value
Age	53.3 ± 4.9	54.2 ± 3.1	NS
Body mass index	47.7 ± 4.1	44.1 ± 1.9	NS
Apnea hypopnea index	45.4 ± 9.0	48.8 ± 5.8	NS
Time with oxygen saturation $<90\%$ (% of total sleep time)	76.9 ± 6.9	33.4 ± 7.9	<0.05
Desaturation index	78.5 ± 10.3	56.1 ± 3.8	<0.05
Minimum oxygen saturation	63.1 ± 3.5	76.6 ± 8.4	<0.05
pH	7.29 ± 0.02	7.4 ± 0.01	<0.05
$PaCO_2$ (mmHg)	77.9 ± 5.1	36.3 ± 1.7	<0.05
PaO_2 (mmHg)	48.3 ± 2.9	76.2 ± 3.3	<0.05
HCO_3 (mmol/L)	38.8 ± 2.2	24.3 ± 3.6	0.05

Table 3 Treatment modalities for studied subjects on diagnosis and 6-8 months after treatment.

Treatment modality						Follow up after 6–8 months		
Subject no	Treatment modality	IPAP cmH_2O	EPAP cmH_2O	Need for daytime O_2	Compliance with treatment	Need for PPV	Need for daytime O_2	Need for nocturnal O_2
1	BiPAP+O_2	8	4	Yes	Good	Yes	No	Yes
2	BiPAP+O_2	8	4	Yes	Good	Yes	No	No
3	BiPAP+O_2	10	6	Yes	Poor	Yes	Yes	Yes
4	BiPAP+O_2	20	16	Yes	Good	Yes	No	Yes
5	BiPAP+O_2	10	6	Yes	Poor	No data	No data	No data
6	BiPAP+O_2	18	14	Yes	Good	Yes	No	No
7	CPAP	—	12	No	Good	Yes	No	No
8	BiPAP+O_2	8	4	Yes	Good	Yes	No	No
9	BiPAP+O_2	12	8	No	Good	Yes	No	No
10	BiPAP+O_2	10	6	Yes	Poor	Yes	Yes	Yes
11	BiPAP+O_2	10	6	Yes	No data	No data	No data	No data

IPAP: inspiratory positive airway pressure, EPAP: expiratory positive airway pressure; BiPAP: bilevel positive airway pressure, O_2: Oxygen.

Table 4 Arterial blood gases parameters in compliant subjects, before treatment with non-invasive ventilation and 6–8 months after treatment.

	Before treatment	After treatment	*P* value
pH	7.3 ± 0.01	7.4 ± 0.004	<0.05
$PaCO_2$ (mmHg)	79.4 ± 8.1	49.1 ± 4.6	0.05
PaO_2 (mmHg)	45.7 ± 3.7	71.1 ± 3.2	<0.05
HCO_3 (mmol/L)	40.5 ± 2.9	27.1 ± 0.8	<0.05

disorders. In the present study, we used full polysomnography due to the vicinity of the sleep disorders center to the ICU. However, portable sleep diagnostic system may suffice. Sleep disordered breathing is overlooked as a cause of acute respiratory failure.[9,10] In obese patients with unexplained hypercapnic respiratory failure, sleep disordered breathing should be considered as a possible cause. Ventilating this group of patients via non-invasive ventilation is safe and very effective in this setting.

Although the apnea hypopnea index, body mass index and age were comparable in studied subjects and their matched comparison group, all but two subjects had sleep hypoventilation syndrome and hypercapnia compared to none in the comparison group. Our findings contrast with Eugene et al.[8] who reported obstructive sleep apnea syndrome only in their group of apnea patients with acute respiratory failure. However, later reports[9,10] concurred with our findings where high prevalence of sleep hypoventilation syndrome was reported in patients with sleep disordered breathing admitted to the ICU with acute respiratory failure. Therefore, it seems that the severity of the apnea hypopnea index may not be a good predictor of apnea patients who may develop respiratory failure. Based on our data and previous reports (Table 5), it seems that middle-aged obese patients with sleep disordered breathing, hypercapnia and hypoxemia are at a higher risk of having acute respiratory failure. Clinicians should be alert in managing apneic patients with hypoventilation, daytime hypercapnia and hypoxemia, as these patients may have a greater risk tendency to develop respiratory failure. Our findings demonstrate that CPAP may not be effective in some patients due to the persistent hypoventilation. This stresses the importance of performing polysomnography to document the pattern of breathing and response to treatment. All studied subjects but one had a combination of obstructive sleep apnea and sleep hypoventilation syndrome. That explains the high EPAP used in some cases. EPAP is needed to prevent upper airway closure during expiration. Fibro-optic imaging studies in patients

Table 5 Comparison of our findings with previously reported data.

	Number of subjects	Age (SD)	BMI (SD)	AHI (SD)	PH (SD)	$PaCO_2$ (SD)	PaO_2 (SD)	PSG diagnoses (number of subjects)
Fletcher et al.[8]	8	57	41.6	90	45	82	45	All OSAS
Buckle et al.[10]	9	51.6 (14.7)	43.6 (14.8)	No data	7.3 (0.03)	80.8 (8.6)	48.1 (6.8)	OHS+OSAS (2), OHS (2), OSAS (2), CSA (3)
Resta et al.[9]	14	57.1 (12.9)	42.7 (9.6)	25.9	7.28 (0.04)	65.9 (11.9)	42.1 (5.6)	OHS+OSAS (5), OHS (2), OSAS (5), CSA (2)
Present study	11	53.3 (4.9)	47.7 (4.1)	45.4 (9.0)	7.29 (0.02)	77.9 (5.1)	48.3 (2.9)	SHVS+OSAS (8), SHVS (1), OSAS (2)

OSAS: obstructive sleep apnea syndrome; OHS: obesity hypoventilation syndrome; CSA: central sleep apnea; SHVS: sleep hypoventilation syndrome; BMI: body mass index; AHI: apnea hypopnea index.

with obstructive sleep apnea have demonstrated that upper airway narrowing begins prior to inspiration in sleeping humans.[19]

Subjects compliant to therapy had significant improvement in their daytime $PaCO_2$. Six of them did not require daytime oxygen supplementation 6–8 months after institution of nocturnal non-invasive ventilation treatment. Earlier studies using tracheostomy and then CPAP led to the clear recognition that treating obstructive sleep apnea syndrome may lead to improvement in hypercapnia.[20,21] Nocturnal non-invasive ventilation may help normalize $PaCO_2$ due to changes in respiratory drive that occurs as a consequence of improved upper airway mechanics.[22] Sullivan et al., have previously reported that patients with obstructive sleep apnea and daytime hypercapnia have low or absent hypoxic responsiveness.[23] Moreover, in a group of 13 obese patients with obstructive sleep apnea (half of them were hypercapnic), Garay et al.[24] have observed a diminished ventilatory response to hypoxia and hypercapnia in patients who were hypoxemic and hypercapnic, respectively. These results suggest that repeated apnea could favor a diminished ventilatory response to hypoxia and hypercapnia.[25] Several factors might have contributed to the improvement in daytime PaO_2. Theoretically, positive pressure ventilation might have improved lung mechanics by decreasing the incidence of atelectasis. Moreover, the reduction in pulmonary artery pressure and the daytime $PaCO_2$ will result in improvement in daytime PaO_2.

Our study also demonstrated the safety and feasibility of performing polysomnography in the sleep disorders center for ICU patients with clinical suspicion of sleep-disordered breathing. We described the protocol used to perform polysomnography in such patients. Performing polysomnography for ICU patients with acute respiratory failure and clinical suspicion of sleep-disordered breathing will allow a more accurate diagnosis and appropriate institution of management protocols. However, if performing full polysomnography is not feasible, portable sleep diagnostic system can be used.

This study has some limitations. The number of studied subjects is relatively small. However, previous studies reported small number of patients with the largest reporting 14 patients only[8–10] (Table 5). Another limitation is the unavailability of follow up data on all subjects as some subjects did not come for follow up.

In summary, this study showed that sleep disordered breathing can be the cause of acute respiratory failure in obese patients admitted to the ICU. Intensivists and respirologists should have

a high index of suspicion especially in obese patients with hypercapnia. Our study also shows that polysomnography is feasible and efficacious in acutely ill patients. Early polysomnography (or portable cardio-respiratory monitoring) allows accurate diagnosis and institution of appropriate ventilation method, which may lead to avoidance of mechanical ventilation and reduction in morbidity. Compliance to treatment results in improvement of daytime hypercapnia and hypoxemia. Further studies with a larger number of subjects and sufficient records of follow up visits should be done to supplement, explore and confirm our observations. Furthermore, we need more studies on the evolution of respiratory drive in patients with sleep disordered breathing and hypercapnia under therapy (non-invasive ventilation).

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