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Sleep and non-invasive ventilation in patients with chronic respiratory insufficiency

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Abstract *Objective:* Noninvasive ventilation with pressure support (NIV-PS) therapy can augment ventilation; however, such therapy is fixed and may not adapt to varied patient needs. We tested the hypothesis that in patients with chronic respiratory insufficiency, a newer mode of ventilation [averaged volume assured pressure support (AVAPS)] and lateral decubitus position were associated with better sleep efficiency than NIV-PS and supine position. Our secondary aim was to assess the effect of mode of ventilation, body position, and sleep–wakefulness state on minute ventilation ($\dot{V}_E$) in the same patients. *Design:* Single-blind, randomized, cross-over, prospective study. *Setting:* Academic institution. *Patients and participants:* Twenty-eight patients. *Interventions:* NIV-PS or AVAPS therapy. *Measurements and results:* Three sleep studies were performed in each patient; prescription validation night, AVAPS or NIV-PS, and crossover to alternate mode. Sleep was not different between AVAPS and NIV-PS. Supine body position was associated with worse sleep efficiency than lateral decubitus position (77.9 ± 22.9 and 85.2 ± 10.5%; $P = 0.04$). $\dot{V}_E$ was lower during stage 2 NREM and REM sleep than during wakefulness ($P < 0.0001$); was lower during NIV-PS than AVAPS ($P = 0.029$); tended to be lower with greater body mass index ($P = 0.07$), but was not influenced by body position. *Conclusions:* In patients with chronic respiratory insufficiency, supine position was associated with worse sleep efficiency than the lateral decubitus position. AVAPS was comparable to NIV-PS therapy with regard to sleep, but statistically greater $\dot{V}_E$ during AVAPS than NIV-PS of unclear significance was observed. $\dot{V}_E$ was determined by sleep–wakefulness state, body mass index, and mode of therapy.

Keywords Artificial respiration · Sleep · Obesity hypoventilation syndrome · Respiratory insufficiency · Respiratory failure

Introduction

Patients with pulmonary or extra-pulmonary disorders that cause nocturnal alveolar hypoventilation—such as severe chronic obstructive pulmonary disease and morbid obesity—may develop derangements in daytime gas exchange characterized by hypoxia and hypercapnia [1, 2]. Such patients are said to have chronic respiratory insufficiency. In patients with chronic respiratory insufficiency, the failure to achieve adequate ventilation and gas exchange during sleep can lead to sleep disruption and consequent daytime sleepiness, early morning

headache (due to hypercapnia), dyspnea, and fatigue [1, 2]. Correction of such ventilatory and gas exchange abnormalities using noninvasive ventilation with pressure support (NIV-PS) is a popular method for improving sleep quality, health-related quality of life, functional status, and daytime gas exchange [1–3].

In patients with chronic respiratory insufficiency, NIV-PS can improve minute ventilation ($\dot{V}_E$) by augmenting the inspired tidal volume on a breath-by-breath basis through application of a higher inspiratory and lower expiratory PAP (IPAP and EPAP) [3]. However, such pressure settings are fixed at a certain level and may not adapt to the varying needs of a patient within a given night [3]. For example, it has been previously described that during spontaneous breathing, $\dot{V}_E$ progressively decreases from wakefulness through various stages of sleep: non-rapid eye movement [NREM] 1, 2, slow wave and REM sleep [4]. Moreover, in morbidly obese patients, during spontaneous respiration, $\dot{V}_E$ may decrease in the supine position when compared to the lateral decubitus position at any given sleep–wakefulness state [5]. Whether such changes in $\dot{V}_E$ occur during NIV-PS therapy in patients with chronic respiratory insufficiency is unknown. Conceivably, the effectiveness of NIV-PS therapy may be limited by changes in sleep–wakefulness state or body position.

Our primary aim was to test the hypothesis that in patients with chronic respiratory insufficiency a newer mode of ventilation [averaged volume assured pressure support (AVAPS)] and the lateral decubitus position were associated with better sleep efficiency than conventional non-invasive ventilation (NIV-PS) and the supine position. Our secondary aim was to assess the effect of mode of ventilation, body position, and sleep–wakefulness state on minute ventilation in patients with chronic respiratory insufficiency.

Materials and methods

Patients

Thirty-nine patients with a diagnosis of chronic respiratory insufficiency were recruited. Institutional Review Board of the University of Arizona approved the study and written informed consent was obtained from each participant. Patients with chronic respiratory insufficiency (obesity hypoventilation syndrome with or without obstructive sleep apnea, chronic obstructive pulmonary disease, neuromuscular disease) who were currently receiving home ventilation (NIV-PS) for at least 2 months and adherent to such therapy (>4 h per night by compliance download) were considered eligible (Tables 1, 2). Exclusion criteria were: (1) Clinically unstable [hemodynamically unstable (systolic blood pressure <90 mmHg)] or acute respiratory failure [hypoxemia; SpO_2 <88% despite O_2 supplementation up to 4 lpm] or impending respiratory failure [respiratory rate >35 breaths per min and use of accessory muscles of respiration]; (2) history of heart failure or Cheyne–Stokes respiration; (3) inability to clear secretions; (4) acute sinusitis, otitis media, facial trauma, burns and other anatomic abnormalities interfering with mask fit; (5) inability to remove face mask due to neurological impairment. None of the patients were fully ventilator dependent (i.e., requiring greater than 6 h of ventilation per 24 h). The study was conducted in the hospital ward.

Table 1 Inclusion criteria

History of underlying condition that could cause chronic respiratory insufficiency
1. Morbid obesity
2. Chronic obstructive pulmonary disease (COPD)
3. Neuromuscular disease
4. Kyphoscoliosis
Plus one or more of the following symptoms prior to ventilatory therapy elicited by history
1. Excessive fatigue
2. Daytime sleepiness
3. Dyspnea
4. Morning headache
5. Cognitive change or memory loss
6. Supplemental oxygen use
7. Breathing problems
Plus one or more of the following documented test results
• Previous diagnosis of elevation of arterial carbon dioxide levels
• Decreased oxygen levels at night or during sleep
• Abnormal pulmonary function testing
Chronic respiratory insufficiency undergoing nocturnal NIV-PS therapy for at least 2 months and adherent to such therapy (>4 h per night by compliance download)

Table 2 Demographic data, primary diagnosis and underlying disease, of study population ($n = 28$, all male)

Variables	Values
Age (years)	63 ± 9
BMI (Kg/m^2)	39 ± 8.5
FEV1 (L)	2.4 ± 0.7
FEV1(% pred)	67 ± 16
FVC (L)	3.3 ± 0.7
FVC (% pred)	71 ± 14
Underlying disease[a]	**Number of patients[a]**
Obesity hypoventilation syndrome	20
Chronic obstructive pulmonary disease	7
Poliomyelitis	1
Diaphragm paralysis	1
Obstructive sleep apnea	14

Values are expressed as mean ± SD

BMI Body Mass Index, *FEV1* forced expiratory volume in 1 s, *FVC* forced vital capacity, *% pred* percentage of predicted, *L* liter

[a] The total count exceeds 28 because some patients suffered from more than one listed condition

Study design

All modes of ventilation were provided by the same device using a full-face mask (AVAPS/BiPAP Synchrony; Respironics Inc; Murrysville, PA). Each subject underwent three consecutive overnight sleep studies: (1) Conventional NIV-PS set at the respective patients' prescription settings in order to validate the prescription pressure and serve as an acclimatization night, (2) AVAPS or NIV therapy assigned randomly, and (3) and crossed over to alternate therapy mode (Fig. 1). Patients underwent randomization only if their prescription pressure did not change significantly (>5 cm H_2O) during the first sleep study.

Measurements

Polysomnography

Standard full-night polysomnography (Sandman, Ontario, CA) entailed EEG (C4-A1, C3-A2, O1-A2, and O2-A1), left and right EOG, sub-mental EMG, ECG, thoraco-abdominal movement by inductance plethysmography, leg movements by bilateral anterior tibialis EMG, body position by a small sensor attached to the chest belt, naso-oral airflow using thermistor, flow and tidal volume output from the ventilator monitoring, and finger pulse-oximetry. Sleep was manually staged in 30-s epochs according to standard criteria [6], and respiratory events according to consensus conference recommendations [7].

Validation of device tidal volume output

In a bench study, with the ventilator used to deliver AVAPS and PS connected to an artificial lung simulator (ASL 5000^{TM}, Ingmar Medical, Pittsburgh, PA) via a heated calibrated pneumotachograph (Hans-Rudolf, Kansas City, MO), we validated the accuracy of the tidal volume output generated by the device [8]. Three separate runs at different tidal volume settings (500, 750, and 1,000 ml) were conducted for 5 min each and the tidal volume output of the device was compared to that measured by the pneumotachograph (gold standard). The bias (<6%) and precision (<1%) errors of the device V_T output were excellent.

Device settings

In each patient, NIV-PS settings were confirmed to be adequate during the first sleep study and remained at such settings during the subsequent NIV-PS therapy night. For AVAPS settings, maximum IPAP ($IPAP_{max}$) was set at 10 cm H_2O above the prescription IPAP or at 30 cm H_2O; whichever was the lowest. The minimum range for the IPAP ($IPAP_{min}$) was set 5 cm H_2O below the prescribed IPAP level. During AVAPS, the actual IPAP level fluctuated between $IPAP_{max}$ and $IPAP_{min}$ to ensure adequate "*target*" tidal volume averaged over a 1-min period (*principle of operation*). *Preferred* target tidal volume was tailored for each patient by determining breathing comfort when tidal volume was set at 110% of baseline

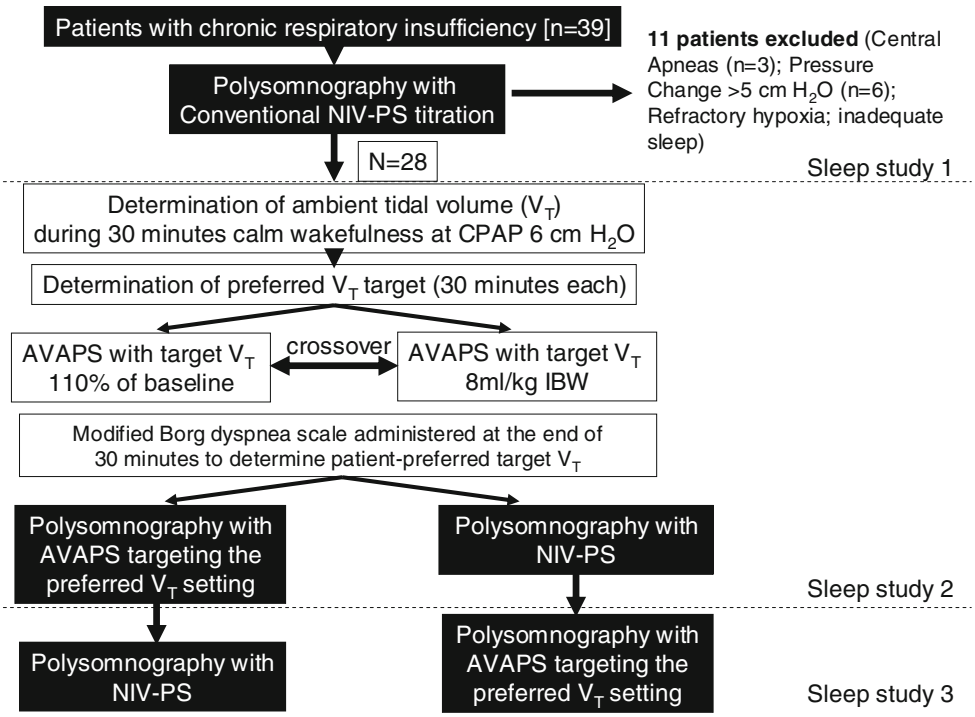

Fig. 1 Schematic diagram showing flow of patients through the study. *Dashed horizontal lines* delineate as to which sleep study night the respective procedures were performed. At the start of the second sleep study night, the technician determined the baseline tidal volume (V_T) over the last 1 min of a 30-min period during calm wakefulness at CPAP setting of 6 cm H_2O. Subsequently, the subjects were given two 30-min trials of AVAPS, while the target V_T was set at 110% of the baseline V_T or at a V_T derived from ideal body weight (8 ml/Kg ideal body weight). The target V_T setting with the lowest dyspnea score was chosen as the preferred target V_T. In the event that the subjects gave the same rating to both (target V_T) trials they were queried as to which trial they preferred most

[9] (determined during CPAP of 6 cm H_2O and calm wakefulness) or 8 mL/Kg of Ideal Body Weight (Fig. 1). Calm wakefulness was defined as a period when the subjects were supine with eyes closed and there was EEG evidence for alpha rhythm (8–12 Hz) with no evidence for movement based upon EMG and video assessment. Breathing comfort was assessed by modified Borg dyspnea scale at the end of 30 min of each setting. The target V_T setting with the lowest dyspnea score was chosen as the preferred target V_T. In the event that the subjects gave the same rating to both (target V_T) trials, they were queried as to which trial they preferred most. In our study, 16 patients preferred 110% of the baseline V_T whereas, 12 patients preferred 8 mL/Kg of ideal body weight. During AVAPS, EPAP level was the same as that during NIV-PS therapy.

Titration of pressure during prescription validation

During polysomnography (first sleep study), the EPAP setting was begun at 4 cm H_2O with a minimum IPAP of 8 cm H_2O, which translates to a NIV-PS level of 4 cm H_2O. Subsequently, both IPAP and EPAP were increased by 2 cm H_2O increments in response to (a) obstructive apneas, (b) hypopneas (defined as 50% reduction in flow signal accompanied by 3% desaturation by pulseoximetry), (c) inspiratory flow limitation events identified by flow waveform, or (d) snoring. IPAP level alone was increased by 2 cm H_2O increments when persistent evidence for hypoventilation [$SpO_2 < 88\%$ for 3 continuous epochs (90 s) was present in the absence of above-mentioned obstructive events].

Measurement of $\dot{V}_E$

Breath-by-breath measurements of tidal volume output "recorded simultaneously with the conventional tracings of the polysomnography" were analyzed over one-min blocks during various stages of sleep and body position. Care was taken to ensure that such time periods were devoid of arousals during sleep and movement during wakefulness (*calm wakefulness*). Tidal volume, respiratory rate, and minimum SpO_2 (min SpO_2) were measured and $\dot{V}_E$ calculated as the product of tidal volume and respiratory rate.

Data analysis

Results are reported as mean ± SD unless otherwise specified. One-way or two-way repeated-measures analysis of variance (ANOVA) was performed to identify significant covariates that influenced $\dot{V}_E$. Multivariate regression models were constructed with $\dot{V}_E$ as dependent variable after significant determining variables were identified by univariate regression techniques (a probability of 0.05 was regarded as significant). Multicollinearity among independent variables was verified, and in the event of collinearity only the strongest predictor variable was included.

Results

Twenty-eight of 39 patients were found to have adequate pressure settings and went on to receive NIV-PS or AVAPS on separate nights (Tables 1, 2). IPAP level during NIV-PS remained fixed at 17 ± 4 cm H_2O. During AVAPS therapy, set $IPAP_{min}$ and $IPAP_{max}$ were 13 ± 4 and 26 ± 3 cm H_2O, respectively. During AVAPS therapy, the mean IPAP pressure was 18 ± 5 cm H_2O which tended to be higher than IPAP during NIV-PS (17 ± 4 cm H_2O; $P = 0.08$; paired t test), and the IPAP during AVAPS therapy was noted to fluctuate between a low of 14 ± 6 cm H_2O and a high of 21 ± 5 cm H_2O.

Sleep architecture

Neither NIV-PS nor AVAPS significantly modified sleep architecture, quality, or quantity (Table 3). However, supine body position was associated with worse sleep efficiency than the lateral decubitus position (77.9 ± 22.9 and 85.2 ± 10.5%; $P = 0.04$). Further analysis for the possible mechanisms that underlie such association revealed that the apnea-hypopnea index was greater during supine (median 6.3, IQR 1.8, 60 per hour) than during lateral position (median 0.6, IQR 0, 3.7 per hour; $P < 0.0001$).

Minute ventilation

During NIV-PS therapy in the supine position (Fig. 2; left panel, closed symbols), $\dot{V}_E$ decreased progressively from wakefulness through various stages of sleep: stage 1, stage 2, and REM (one-way ANOVA with repeated measures; $P = 0.0001$). During NIV-PS therapy in the lateral decubitus position (Fig. 2; right panel; closed symbols), $\dot{V}_E$ decreased progressively from wakefulness through various stages of sleep: stage 1, stage 2, and REM (one-way ANOVA with repeated measures; P = 0.018). During AVAPS in the supine position, however, $\dot{V}_E$ did not change from wakefulness to every sleep stages [$P = 0.2$; (Fig. 2, left panel; open symbols)]. Moreover, during AVAPS in the lateral decubitus position, $\dot{V}_E$ tended to decrease across sleep–wakefulness states [$P = 0.10$; (Fig. 2; right panel; open symbols)]. The changes in $\dot{V}_E$ across the various sleep–wakefulness states were different between AVAPS and NIV-PS therapy (2-

Table 3 Sleep variables

	NIV-PS	AVAPS	*P* value
Sleep efficiency (%)	86 ± 9	82 ± 12	0.2
Total sleep time (min)	388 ± 65	373 ± 85	0.4
Wake (min)	41.5 (IQR; 18.6, 81)	56.3 (IQR; 25.6, 96.5)	0.2
NREM stage 1 (min)	53 ± 20	62 ± 31	0.13
NREM stage 2 (min)	263 ± 49	240 ± 70	0.12
REM (min)	70 ± 26	64 ± 29	0.4
Awakenings per hour	21 ± 11	24 ± 11	0.5
REM periods per night	3.3 ± 1.4	3.3 ± 1.3	0.9
REM latency (min)	87 (IQR; 50, 124)	100 (IQR; 57, 152)	0.6
Apnea hypopnea index	3.2 (IQR; 0.5, 6.5)	3.2 (IQR; 0.8, 6.7)	0.8
Sleep onset latency (min)	7.3 (IQR; 4, 11.1)	10.4 (IQR; 5.3,15.3)	0.2
Mean nocturnal SpO_2 (%)	96.3 ± 2.6	96.4 ± 2.4	0.8
Minimum SpO_2 (%)	80.3 ± 19.1	84.9 ± 5.8	0.3
Early morning headache	25%	7%	0.14
Daytime fatigue (VAS)	71.5 ± 14.7	70.7 ± 16.8	0.8
Daytime sleepiness (SSS)	1.9 ± 0.9	1.7 ± 0.8	0.5

Values are presented as either mean ± SD or median and inter quartile range (IQR) Early morning headache, expressed as proportion of patients. Daytime fatigue, measured by Visual Analogue Scale (VAS). Daytime sleepiness, measured by Stanford Sleepiness Scale (SSS)

SpO_2 Oxygen saturation by pulseoximetry, *REM* rapid eye movement, *NREM* non-rapid eye movement, *NIV-PS* non-invasive ventilation with pressure support, *AVAPS* averaged volume assured pressure support, *min* minutes

way ANOVA with repeated measures; $P = 0.02$; Fig. 2). Changes in body position did not influence $\dot{V}_E$ ($P = 0.9$). For both modes of therapy and body positions combined, $\dot{V}_E$ progressively decreased from 8.7 ± 2.3 during wakefulness to 7.8 ± 1.8, 7.4 ± 1.6, and 7.3 ± 1. 7 L/min during stage 1, stage 2, and REM sleep, respectively ($P < 0.0001$, ANOVA). Moreover, regardless of body position or sleep–wakefulness state, $\dot{V}_E$ during AVAPS (8.0 ± 1.9 L) was greater than during NIV-PS therapy (7.6 ± 2.0 L; $P = 0.03$).

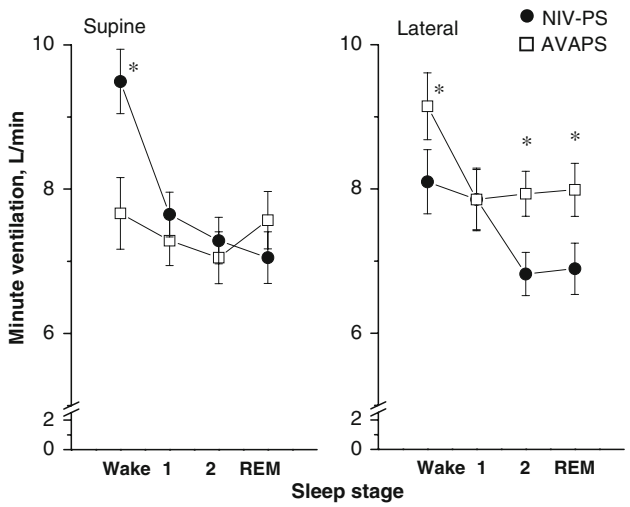

Fig. 2 Minute ventilation during supine (*left panel*) and lateral decubitus position (*right panel*) while receiving bilevel positive airway pressure (NIV-PS; *closed symbols*) or averaged volume assured pressure support (AVAPS; *open symbols*). Minute ventilation associated with wakefulness and different stages of sleep are shown. Each symbol is derived from minute ventilation measured at a given body position, sleep–wakefulness state, and mode of PAP therapy in 28 patients. Post hoc comparison are represented by *asterisk* symbol if statistically significant (Neuman–Keuls; $P < 0.05$)

Univariate regression with various determining variables revealed that sleep–wakefulness state, mode of therapy (AVAPS or NIV-PS) and to a lesser extent body mass index (BMI) influenced $\dot{V}_E$ (dependent variable) (Table 4). Multivariate regression revealed that NIV-PS therapy; sleep; and greater BMI were associated with lower $\dot{V}_E$ (model $R^2 = 0.09$, $P < 0.0001$; Table 4).

Tidal volume

The reduction in $\dot{V}_E$ in relation to various sleep states appeared to be primarily the result of a reduction in V_T from wakefulness through the various sleep stages ($P < 0.0001$; one-way ANOVA). Changes in body position did not influence V_T ($P = 0.17$). For both modes of therapy and body positions combined, V_T was reduced from wakefulness (619 ± 163 mL) to stage 1 (546 ± 156 mL), stage 2 (513 ± 135 mL) and REM sleep (505 ± 150 mL) ($P < 0.0001$).

Univariate regression revealed that sleep-wakefulness state, mode of therapy (AVAPS or NIV-PS), body mass index (BMI), and O_2 therapy influenced V_T (Table 5). Multivariate regression revealed that NIV-PS therapy, sleep, and greater BMI were independently associated with lower V_T (model $R^2 = 0.13$, $P < 0.0001$; Table 5).

Table 4 Determinants of minute ventilation ($\dot{V}_E$)

Variable	B	SE	*P* value
Univariate regression			
BMI	−0.023	0.01	0.081
Body position	−0.02	0.2	0.933
Sleep stage	0.46	0.09	<0.0001
AVAPS[a]	0.43	0.2	0.032
Multivariate regression (BMI, sleep stage, AVAPS therapy); $R^2 = 0.09$; $P < 0.0001$			
BMI	−0.023	0.013	0.07
Sleep stage	0.462	0.087	<0.0001
AVAPS[a]	0.418	0.191	0.029

BMI Body Mass Index, *AVAPS* averaged volume assured pressure support, *NIV-PS* non-invasive ventilation with pressure support, *SE* standard error, *B* coefficient

[a] Compared to NIV-PS (non-invasive ventilation with pressure support)

Table 5 Determinants of tidal volume (V_T)

Variable	B	SE	*P* value
Univariate regression			
BMI	−3.8	1.09	0.001
Body position	−22.49	16.59	0.17
Sleep stage	38.07	7.28	<0.0001
AVAPS therapy[a]	59.37	16.36	<0.0001
O_2 therapy	−11.18	6.6	0.091
Multivariate regression (BMI, sleep stage, AVAPS therapy) $R^2 = 0.13$; $P < 0.0001$			
BMI	−3.67	1.15	0.002
Sleep stage	37.81	7.07	<0.0001
AVAPS therapy[a]	58.62	15.6	<0.0001
O_2 therapy	−1.89	6.89	0.78

BMI Body Mass Index, *AVAPS* averaged volume assured pressure support, O_2 oxygen, *SE* standard error, *B* coefficient, *O_2* oxygen

[a] Compared to NIV-PS (non-invasive ventilation with pressure support)

Respiratory rate and oxygenation

Respiratory rate, however, was not altered by changes in sleep–wakefulness state or body position. In 11 patients who did not receive oxygen supplementation, minimum oxygen saturation (min SpO_2) was 92.8 ± 3.6% and a 230 mL decrement in $\dot{V}_E$ was associated with a 1% decrement in SpO_2 ($r^2 = 0.01$; $P = 0.038$). In such patients, min SpO_2 tended to be higher during AVAPS night (93.2 ± 2.5%) than during NIV-PS night (92.4 ± 3.6%; $P = 0.10$). Arterial blood gases were not different following the nights when patients received either NIV-PS or AVAPS therapy (Table 6).

Discussion

Sleep–wakefulness state

In spontaneously breathing healthy subjects, respiratory drive, and consequently $\dot{V}_E$, decreases progressively from wakefulness through various stages of sleep [4]. In disease states, decrements in $\dot{V}_E$ during various stages of sleep has been measured in patients with COPD [10, 11], cystic fibrosis [12, 13] and may result in oxygen desaturation [14] and hypercarbia [15]. Whether such hypoventilation occurs during non-invasive PAP therapy, however, is less clear. Milross and colleagues [12] found decrements in $\dot{V}_E$ in patients with cystic fibrosis while receiving NIV-PS therapy; however, they did not adjust for BMI or body position. Moreover, in the same study, $\dot{V}_E$ decreased by only 10% with deeper stages of sleep as compared to wakefulness. In the current study, however, deeper stages of sleep were associated with up to 24% drop in $\dot{V}_E$ when compared to wakefulness (Fig. 2) and such changes were adjusted for influences from BMI and body position. While some of the drop in $\dot{V}_E$ could be physiological, a 24% drop in $\dot{V}_E$ appears to be in greater than expected.

Conversely, one could interpret the $\dot{V}_E$ data to suggest that during NIV-PS therapy $\dot{V}_E$ is greater during wakefulness than during sleep (Fig. 2). Such a higher level of $\dot{V}_E$ following sudden change from sleep to wakefulness—"ventilatory overshoot"—may, in some patients, set the stage for central apneas and sequelae [16–19]. Nevertheless, the inability of NIV-PS therapy to "adapt" to changes in sleep–wakefulness state may be a limitation. In our study, however, such lack of adaptation translated only to minor changes in oxygen saturation and there was no effect on sleep (Table 3). The lack of benefit to sleep measures may be attributable to the study design that potentially favored NIV-PS therapy; patients had been using NIV-PS therapy for over 2 months but were naïve to AVAPS. In contrast, Storre and colleagues [20] recruited patients naïve to NIV and found that sleep quality was better during AVAPS than during NIV-PS

Table 6 Arterial blood gas

	pH	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	HCO_3 (mEq/L)	SpO_2 (%)
AVAPS	7.40 ± 0.02	73.3 ± 9.4	41.2 ± 5.3	25.3 ± 2.7	92.8 ± 2.7
NIV-PS	7.39 ± 0.03	72.4 ± 12	41.9 ± 6.01	24.8 ± 2.6	91.4 ± 8.4

Arterial blood gas values were not different following night of AVAPS and NIV-PS ($P > 0.5$)

AVAPS Averaged volume assured pressure support, *NIV-PS* non-invasive ventilation with pressure support

therapy. Moreover, the fact that NIV-PS setting was confirmed to be adequate during the first sleep study makes unlikely the probability of finding clinically significant differences compared to AVAPS during the subsequent night. Conceivably, it may be possible to set a ventilator mode in a certain way so as to obtain proper ventilatory support for the patient. The only difference is the complexity of the procedure of setting the ventilator for each mode. AVAPS might be easier to be set to obtain adequate ventilation compared to NIV-PS.

Other investigators have studied patients with chronic respiratory insufficiency while receiving NIV-PS therapy and noticed variability in $\dot{V}_E$ [21], albeit less than that during proportional assist ventilation. In our study, we report less variability in $\dot{V}_E$ during AVAPS than during NIV-PS therapy. Such lack of variability may be important in guaranteeing $\dot{V}_E$ in patients with chronic respiratory insufficiency.

Sleep and body position

Our finding that supine body position was associated with worse sleep efficiency than the lateral decubitus position during assisted ventilation is novel. Further analysis for the possible mechanisms that underlie such association revealed that the apnea-hypopnea index was greater during supine than during lateral decubitus position. Because IPAP and EPAP levels were titrated to control obstructive apneas and obstructive hypopneas during the first "prescription validation" sleep study, only patients whose obstructed ventilation was successfully controlled were allowed to remain in the study. Consequently, the respiratory events that resulted in differences between supine and lateral position were primarily central apneas and non-obstructive hypopneas (as evidenced by the lack of a flow-limitation pattern in the inspiratory portion of the flow tracing). This finding is in line with our prior work that demonstrated that occurrence of central apneas was associated with worsening of sleep efficiency [16].

Interestingly, we did not observe any effect of body position on $\dot{V}_E$ (Table 5). The respiratory effects of body position during sleep have been widely studied in normal subjects and in patients breathing spontaneously [22, 23], in patients with OSA [24] and in stable chronic hypercapnic COPD patients [25]. Some investigators [26] observed that V_T, $\dot{V}_E$ and lung compliance significantly decreased whereas, respiratory resistance increased while supine when compared to sitting position in spontaneously breathing healthy subjects. In awake patients with COPD, however, body position does not significantly influence breathing pattern and respiratory muscles function during NIV-PS therapy [25]. Similarly, our data shows that in patients with chronic respiratory insufficiency, who were receiving NIV-PS therapy, changes in posture did not influence $\dot{V}_E$. Therefore, the present study provides evidence that NIV-PS therapy is able to achieve adequate ventilation despite changes in body position. Moreover, since respiratory mechanics differ between wakefulness and sleep [13], results obtained during diurnal NIV-PS therapy in awake COPD patients [25] cannot apply to the night time use during sleep, our data provides additional useful information.

Mode of therapy

The finding that changes in $\dot{V}_E$ were primarily due to changes in V_T rather than respiratory rate calls for a mode of ventilation that corrects the variance in V_T. In line with such reasoning, the decrement in $\dot{V}_E$ was greater during NIV-PS therapy than AVAPS, the latter being capable of adjusting IPAP to achieve target V_T. In the 11 patients who were not receiving supplemental O_2, minimum SpO_2 was higher during AVAPS when compared to NIV-PS therapy. This indicates that AVAPS therapy, through increments in V_T, is able to prevent hypoventilation, and, thus, attenuate oxygen desaturation.

Limitations

Statistically greater $\dot{V}_E$ during AVAPS than NIV-PS may not necessarily represent a clinical advantage. Moreover, although differences in $\dot{V}_E$ between NIV-PS and AVAPS were statistically significant, they appear clinically minor. There are other limitations to our study. Our failure to adjust the V_T measurements for air leak on a breath-by-breath basis is a limitation. However, the algorithms operating in the device are meant to adjust for the "baseline drift" in the integrated volume signal derived from flow inputs as a surrogate measure of air leak. More importantly, our inferences derived from differences in $\dot{V}_E$ and daytime arterial blood gases are limited by the lack of measures of arterial PCO_2 during sleep. Lastly, we caution that while mechanistic underpinnings between critically ill patients and patients with chronic respiratory insufficiency may be the similar, the presented data cannot be extrapolated to patients with acute respiratory failure without further study. Specifically, subjective perception of dyspnea that were obtained during AVAPS in our study limit the extrapolation of our results to critically ill patients. Moreover, our failure to obtain similar dyspnea ratings during NIV-PS may have favored the AVAPS mode.

Conclusions

In conclusion, in patients with chronic respiratory insufficiency, supine position was associated with worse sleep efficiency than the lateral decubitus position.

AVAPS was comparable to NIV-PS therapy with regards to sleep, but statistically greater $\dot{V}_E$ during AVAPS than NIV-PS of unclear significance was observed. $\dot{V}_E$ was determined by sleep–wakefulness state, body mass index, and mode of therapy, but not by body position. Changes in $\dot{V}_E$ during NIV-PS therapy were independent of effects of body position and BMI and was primarily due to decrements in tidal volume rather than in respiratory rate; and was less likely during AVAPS than NIV-PS therapy.

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