Nocturnal Noninvasive Mechanical Ventilation

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Szymon Skoczyński and Patrycja Rzepka-Wrona

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Abbreviations

ABG	Arterial blood gas analysis
AHI	Apnea-hypopnea index
ARF	Acute respiratory failure
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
EPAP	Expiratory positive airway pressure
FVC	Forced vital capacity
MEP	Maximum expiratory pressure
MIP	Maximal inspiratory pressure
MV	Minute ventilation
NIV	Noninvasive ventilation
ODI	Oxygen desaturation index

S. Skoczyński (✉) · P. Rzepka-Wrona
Department of Pulmonology, School of Medicine, The Medical University of Silesia, Katowice, Poland

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OSA	Obstructive sleep apnea
$PaCO_2$	Arterial carbon dioxide partial pressure
PEEP	Positive end expiratory pressure
PFTs	Pulmonary function tests
PS	Pressure support
PSG + CAPNO	Polysomnography + capnography
RF	Respiratory failure
S/T	Spontaneous over timed mode
SNIP	Sniff nasal inspiratory pressure
SpO_2	Oxygen saturation
T	Timed mode
$TcCO_2$	Transcutaneous carbon dioxide
TV	Tidal volume

39.1 Introduction

It is vital to acknowledge disease specific aspects of nocturnal ventilation that impact the ventilation settings. For example, patients with early-stage obese hypoventilation syndrome (OHS) coupled or not with obstructive sleep apnea (OSA) do not face challenges with diurnal ventilation. Therefore, it is nocturnal ventilation that poses clinical challenges, such as hypoventilation, which may present itself as clusters of desaturations due to subdued breathing. This is why settings should be adjusted during sleep. Capnography might be of great help. The current guidelines of the American Thoracic Society [1] suggest that arterial blood gas (ABG) can serve as a guideline for whether capnography should be performed. For patients who have low or moderate risk of developing OHS (<20%), serum bicarbonate level should be assessed to decide whether to perform capnography: in individuals with serum bicarbonate (HCO^{3-}) levels <27 mmol/L, it is possible to forego capnography, as the diagnosis of OHS seems very unlikely, whereas in individuals with serum arterial oxygen saturation (HCO^{3-}) ≥ 27 mmol/L, it is generally advised to perform capnography to rule out or confirm the diagnosis of OHS.

39.2 Neuromuscular Diseases

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease with a prevalence of about 6 in 100,000. It usually results in progressive hypoventilation stemming from respiratory muscle weakening and is associated with poor survival, cognitive impairment, and poor quality of life [2]. Hypoventilation in ALS patients may worsen during sleep as a result of apneas and hypopneas, hypotonia of respiratory muscles, weakening of the diaphragm, supine position, and probably dysfunctions of the central respiratory drive. In patients with ALS, different muscular parts may be affected in a random way, which means that in some individuals there is

predominance of bulbar muscles weakness, whereas in other cases respiratory muscles weakness may play a major role. In patients with bulbar problems, predominance of obstructive apneas may be expected. To address this pathology, using a mode with auto continuous positive airway pressure (CPAP) is advised. In this case, the ventilator will adjust PEEP based on upper airway measured patency. It is important to avoid a maximal PEEP setting at more than 12 cm H_2O because above this limit there is a large risk of aerophagia which can cause stomachache or even vomiting, which all together would decrease compliance and increase the risk of aspiration pneumonia. On the other hand, in patients with a predominance of respiratory muscle weakness, the home-ventilator should be adjusted in a hybrid mode, in which a target TV is set and the device adjusts pressure support (PS), based on the currently estimated TV. During sleep, in the situation of neuromuscular dysfunction, TV may decrease significantly and unexpectedly; therefore, adjusting settings to a wide range of PS will improve stability during nighttime ventilation. Importantly, VC < 60% predicted value is associated with hypopneas in REM sleep in the course of neuromuscular diseases. VC < 40% and maximum inspiratory pressure <30 cmH_2O are strongly associated with hypoventilation during both REM and NREM sleep phases. Diurnal hypoventilation develops after VC decrease below 25% of predicted value. Nocturnal NIV effectively improves the lowest oxygen desaturation values (nadir SaO_2), apnea-hypopnea index (AHI), and oxygen desaturation index (ODI). Moreover, the occurrence of episodes of desaturation <90% and <80% is reduced [3]. Both nocturnal average end-tidal CO_2 and duration of nocturnal hypercapnea are associated with the severity of nocturnal respiratory symptoms (measured by disease-specific orthopnea-questionnaire scores). Use of NIV may prolong life and positively impact its quality, but only in case of good compliance (NID daily use >4 h). Therefore, for long-term ventilation, it is vital to adjust ventilator settings so that maximal effectiveness is achieved using minimal possible pressures. As respiratory failure is more pronounced at night, disease progression may not be obvious. Therefore, in this patient population, two points of care are essential – reading of both diurnal and nocturnal ventilator reports. This requires assessment of the detailed report downloaded from the ventilator and timely conduction of polysmnography with transcutaneous capnometry (PSG + CAPNO) to assess and optionally adjust ventilator settings. Based on this assessment, it is often necessary to set night and day time device modes to meet different needs at different times of day. Based on this assessment, medical professionals may foresee the need to consider tracheotomy and shifting to invasive ventilation.

39.3 Chronic Obstructive Pulmonary Disease (COPD)

COPD is the third leading cause of *death* worldwide. The disease has two phenotypes, COPD in patients with normal body weight is less frequently complicated by type 2 respiratory failure (RF) (its likelihood increases when FEV_1 is below 0.5 L) – those patients require high PS settings after type 2 RF development, but their diurnal and nocturnal ventilator requirements remain similar. On the other hand, in

obese individuals with COPD, development of type 2 RF is much more frequent. In general, in those patients the ventilator should be set in an auto-EPAP mode, or the level of PEEP should be predefined during CPAP titration. Moreover, in those patients as the respiratory drive decreases, there is an increasing need for assured respiratory rhythm; therefore, the settings should include timed or spontaneous/timed modes for sleep ventilation.

Due to epidemics of obesity in developed countries, the number of obese COPD patients receiving home ventilation is rising. In a cross-sectional observational study on >3500 individuals with COPD, aimed at the assessment of self-perceived sleep quality (SLEPICO study) [4], it was revealed that the COPD assessment test (CAT) and the pulmonary function tests-based disease severity score may predict the decrease in sleep quality as assessed by COPD and asthma sleep impact score – CASIS score. The results of the SLEPICO study reveal that age, disease duration and stage, and most importantly CAT score ≥10 may be indicators for deterioration of sleep quality.

Various factors impact ventilation of individuals with COPD reduced chemo sensitivity, increased resistance of upper airways, and diminished activity of the respiratory muscles. These phenomena are predominant in individuals who report orthopnea during wakefulness and experience shift in ventilation/perfusion ratio and redistribution of body fluids. These changes result in a significant decrease in TV and, consequently, hypoventilation. Nocturnal hypoventilation may lead to retention of carbon dioxide during daytime. Nocturnal NIV is aimed at reduction (or, preferably, correction) of hypoventilation by at least 20% because it was proven than chome NIV may prolong the patient's life only when substantial reduction or normalization of daytime $PaCO_2$ is achieved. Therefore, nowadays, clinical goals are set based on parameters measured during wakefulness. Ventilatory capacities in COPD are impaired due to airway obstruction and dynamic hyperinflation stemming from intrinsic positive end expiratory pressure (PEEP) and because of increased work of respiratory muscles. The capacity of inspiratory muscles is diminished in the course of COPD. Pulmonary hyperinflation leads to a decrease in diaphragm strength. COPD is frequently associated with dysfunction of the diaphragm.

Nocturnal NIV reduces the resistance of upper airways (due to PEEP), reduces nighttime hypoventilation because of PS and PEEP, and results in relaxation of respiratory muscles (due to PS). Therefore, after successful nighttime ventilation, during daytime the patient is able to maintain acceptable spontaneous minute ventilation and obtain improved quality of life and daytime activities.

39.4 Kyphoscoliosis

The severity of the deformity is evaluated by measuring the Cobb angle on an X-ray of the spine. This angle is measured at the intersection of two lines, one parallel to the top and the other parallel to the bottom vertebrae of the scoliotic

curve. The greater the angle, the more advanced the spinal deformity; angles >100 are associated with respiratory symptoms, and angles>120 are associated with respiratory failure. In this setting, the ability to distend is severely impaired, causing restriction, especially when the Cobb angle exceeds. Hypercapnia is initially associated with sleep or physical exercise; as the deformity progresses, it may occur at rest during wakefulness. Nocturnal hypoxemia usually precedes the onset of respiratory failure in kyphoscoliosis. Hypoventilation during sleep is the most common dysfunction and results from a decreased neural drive to the respiratory muscles in the REM phase. Because kyphoscoliotic patients depend solely on diaphragm activity to maintain alveolar ventilation during sleep, they are at risk of developing hypoxemia and hypercapnia. However, the degree of nocturnal desaturation may not always correlate with the Cobb angle. Prevalence of obstructive sleep apnea is similar to that of the general population. OSA further aggravates respiratory failure [5]. Distortion of the trachea may predispose patients with advanced kyphoscoliosis to obstructive sleep apnea occurrence. Kyphoscoliotic patients with RF are often treated with hybrid NIV modalities. This treatment mode has been proven to positively impact both diurnal and nocturnal PaO_2 soon after treatment introduction. Furthermore, unloading of respiratory muscles is reflected in an increase in forced vital capacity (FVC) after 12 months of treatment.

Furthermore, in kyphoscoliotic individuals treated with diurnal mouthpiece pressure ventilation (MPV) and nocturnal NIV, a significant improvement of clinical and ABG parameters (arterial.

oxygen tension (PaO_2)/fractional inspired oxygen (FiO_2) ratio, $PaCO_2$ and pH as well as a significant increase in FVC, FEV_1, maximal inspiratory pressure (MIP), maximum expiratory pressure (MEP), sniff nasal inspiratory pressure (SNIP), TV, and breathing frequency) were noted. The 6-minute walk test (6MWT) distance also improved, but insignificantly. Importantly, quality of life is improved after with MPV + NIV treatment initiation. Although, according to data from clinical trials, NIV is strongly indicated in patients with kyphoscoliosis, as it benefits patients both in terms of CO_2 reduction, as well as outcomes and quality of life, a change in chest elastic recoil in different body positions must be taken into consideration. It may happen that effective minute ventilation may be obtained only in one body position, e.g., on the right or left side. This can be easily observed during daytime, but it may be responsible for nighttime NIV failure. That is why in the case of NV failure, patients with kyphoscoliosis should be observed at different body positions during both wakefulness and sleep. This may be responsible for significant diurnal body position related TV changes in the case of pressure-controlled settings, or for a significant change in inspiratory pressure during volume-controlled settings. This may be suspected in a situation when usually implemented NIV settings are not followed by $PaCO_2$ reduction. In those patients, the best option is NIV set after capnometric and PSG assessment is performed in a respiratory center or sleep lab (Table 39.1).

Table 39.1 NIV disease-related treatment options

	Night time changes in respiration	Position related changes in ventilation (supine/prone)	Acute respiratory acidosis	Chronic respiratory acidosis
COPD	Diminished chemosensitivity, increased upper airway resistance, decreased respiratory muscles' activity, a change in ventilation/perfusion ratio, redistribution of body fluids decrease in TV	**Worsening of airflow obstruction,** increase in hyperinflation and/or atelectasis can cause hypoventilation. Secondary hyperinflation increase in work of breathing, increased arousability and sleep disturbance	Mostly during acute exacerbation	Occurs due to changes in respiratory mechanics; shortening of respiratory muscles (due to hyperinflation) and expiratory airflow reduction, respiratory muscle fatigue
			Hypercapneic in respiratory failure, NIV allows to avoid intubation and mechanical ventilation and decrease mortality, during invasive MV which focus on avoiding ventilator-induced lung injury and minimizing intrinsic positive end-expiratory pressure iPEEP	In less severe bronchial obstruction RF is caused frequently by overlap with OSA. NIV is the treatment of choice
OHS	Hypoventilations, apneas, hypopneas, clusters of desaturation	As OHS usually co-exists with OSA: higher incidence of apneas and hypopneas, positional OSA: 50% increase in AHI in supine sleep position compared to the non-supine position	Leading cause: congestive heart failure, associated with older age, compromised PFTs, low VC associated with ICU admission risk; NIV: first-line treatment	RFis probably underreported, alveolar hypoventilation during sleep → nocturnal hypercapnia and hypoxia → resetting of the respiratory drive → diurnal hypercapnia and hypoxemia
Kyphoscoliosis	Prolonged central apneas, clusters of desaturation mostly in REM sleep, severely decreased TV	Impact of sleep positions on patients with compromised PFTs; clusters of desaturation mostly during REM sleep, inhibited accessory respiratory muscles esp. in REM sleep	May be precipitated by a respiratory infection (pneumonia), blood stream infection, decompensation of pulmonary hypertension (cor pulmonale).The risk of ARF development during infection is associated with the extent of chest deformity and decrease in VC	NIV is first-line treatment due to impaired chest mechanics, improves survival, chronic respiratory failure usually occurs in teenage years/young adults. Body position related differences in ventilation effectiveness and compliance are frequently seen

Neuromuscular diseases	Hypopneas in REM sleep, hypercapnia, nocturnal hypoxemia, sleep atonia, reduced lung volumes, and chemosensitivity, decreased airway dilator contribute to the occurrence sleep-disordered breathing events	Even in normal individuals, the supine position reduces the vital capacity by as much as 19% and the functional residual capacity by about 25%. Diaphragmatic weakness is more pronounced in VC in supine position (>25%). VC and supine VC: crucial criteria for the diagnosis of diaphragmatic function impairment and initiation of NIV	Mostly caused by **Guillain-Barré syndrome and myasthenia gravis** PFTs which predict the need for mechanical ventilation: VC, peak inspiratory pressure, peak expiratory pressure	The most common cause of morbidity and mortality; reduction in inspiratory muscle strength, ineffective alveolar ventilation, expiratory muscle weakness, impaired secretions clearance leading to chronic respiratory insufficiency. Bulbar problems especially in ALS may lead to NIV failure, however intubation is controversial due to poor disease related quality of life and no effective treatment. Cough assist physiotherapy may improve NIV effectiveness and tolerance
Invasive ventilation via tracheotomy	Can be postponed/ avoided thanks to implementation of NIV In some settings should be the first-line treatment, e.g., septic shock-induced ARF in neuromuscular diseases NIV may be used as weaning from invasive ventilation	In invasive MV it is less relevant because prosthesis of the upper airways with the intubation tube protects against apnea occurrence	Tracheostomy is usually performed after 7 day of intubation and mechanical ventilation in the ICU, in patients with poor prognosis for fast decannulation; however, in patients with COPD and OHS weaning from tracheotomy in short period of time (few months) is usually possible with the use of NIV	In patients with neuromuscular disease acute tracheotomy is frequently associated with shifting to chronic invasive ventilation. Chronic NIV may be considered as sealing treatment in ALS; however, occurrence of bulbar syndrome makes NIV extremely difficult and frequently poorly tolerated

39.5 Conclusions

To conclude, it is important to remember spontaneous ventilation during wakefulness and sleep vary. This is more important in chronic respiratory failure, where it is suggested to increase ventilation at night but not necessarily at the cost of patient's quality of life (although large discrepancies are observed in the intensity of NIV settings in different countries). During chronic treatment, it is crucial to restore physiological sleep, sometimes with a slight increase in patient's MV (acceptance of permissive hypercapnia). This will prevent the development of nighttime acidosis. The mechanism of hypoventilation may differ significantly; therefore, chronic home NIV should be performed according to disease-specific recommendations. In acute respiratory failure, the treatment should be targeted at a rapid increase of MV leading to resolution of decompensated respiratory acidosis. In this situation, settings should be adjusted based on the severity of acidosis and the patient's neurological status. This kind of treatment usually lasts for a few hours or days, after which the patient usually requires diminishing of ventilator settings. Therefore in acute respiratory acidosis the ventilator settings are usually based on timed (T) or spontaneous over timed (S/T) modes. Treatment implementation should be performed in a secured setting, optimally aided by multiorgan monitoring (ECG, SpO_2, transcutaneous capnometry T_CCO_2). Those patients should be constantly monitored by a nurse experienced in NIV and mask adjustment. In chronic patients, especially those who have significant diurnal minute ventilation changes (individuals with OHS, neuromuscular diseases), automatic hybrid modes are frequently required. These modalities have the capacity to target optimal minute ventilation even in patients with changing respiratory drive, upper airway patency, and chest compliance. Therefore, in most cases of patients using mostly nighttime NIV, the ventilator settings should be adjusted during sleep. In patients using NIV during day- and nighttime (no matter on the disease leading to respiratory failure) night and day specific settings may increase treatment effectiveness and patient compliance.

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