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DERLEME/REVIEW

Nocturnal Noninvasive Positive Pressure Ventilation in Stable Severe Chronic Obstructive Pulmonary Disease

Kronik Obstrüktif Akciğer Hastalığında Noktürnal Noninvaziv Pozitif Basınçlı Ventilasyon

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ABSTRACT

Chronic Obstructive Pulmonary Disease is characterized as a progressive and irreversible inflammatory response in the airways and alveoli because of exposure to noxious particles or gases. Excessive inflammation causes progressive, persistent, and not fully reversible structural changes and airflow limitation. Although COPD is a significant public health problem, diagnosis and treatment stages need to be improved.

Nocturnal Noninvasive Positive Pressure Ventilation is one of the treatment modalities of choice for COPD exacerbation, and the role and benefits of NPPV in COPD exacerbation are well defined, but the use of nocturnal NPPV on stable severe COPD individuals is controversial, and the evidence is not sufficient yet. This review evaluates the effects of nocturnal NPPV on stable COPD patients.

Keywords: Chronic obstructive pulmonary disease, nocturnal noninvasive positive pressure ventilation, COPD, NPPV

ÖZET

Kronik obstrüktif akciğer hastalığı (KOAH), zararlı gaz ve partiküllerin akciğerde yol açtığı inflamasyon nedeniyle hava yollarında ve alveollerde daralma ve solunum problemlerinin geliştiği, ilerleyici, kalıcı ve geri dönüşü olmayan bir hastalıktır. Önemli bir halk sağlığı sorunu olmaya devam etmesine rağmen tanı ve tedavi basamakları geliştirilmeye muhtaçtır.

Noninvaziv pozitif basınçlı ventilasyonun KOAH alevlenmesindeki rolü ve faydaları literatürde iyi tanımlanmıştır. Stabil ilerlemiş KOAH hastalarında noktürnal NPPV kullanımı ise tartışmalı bir konu olmaya devam etmekte ve bununla ilgili literatürde henüz yeterli veri ve kanıt bulunmamaktadır. Bu derlemede stabil ilerlemiş KOAH hastalarında noktürnal NPPV kullanımının etkilerinin değerlendirilmesi amaçlandı.

Anahtar kelimeler: Kronik obstrüktif akciğer hastalığı, noktürnal noninvaziv pozitif basınçlı ventilasyon, COPD, NPPV

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is the third cause of mortality globally, affecting women and men equally. In the case of concomitant comorbidities, morbidity and mortality rate increases. COPD is a common preventable and treatable pulmonary disorder, approximately 10% of adults over the age of forty have COPD, and frequency increases with age[1].

Significant exposure to noxious particles or gases (primarily tobacco smoke and biomass) causes abnormal inflammatory responses in the airways and alveoli. Excessive inflammation causes progressive, persistent, and not fully reversible structural changes and airflow limitation[2]. Increased work of breathing, sleep-related disordered breathing, respiratory muscle fatigue, and chronic alveolar hypoventilation are the main respiratory findings of severe COPD[3]. With the progression of the disease, nocturnal gas exchange is impaired; in addition, COPD is frequently associated with sleep-related breathing disorders (SRBD), such as sleep-related hypoxemia, obstructive sleep apnea, and sleep-related hypoventilation[4].

The effect of nocturnal NPPV on stable COPD remains a controversial issue. The evidence about the benefits of long-term nocturnal NPPV in COPD patients is conflicting[5-7]. A few studies about this issue exist in the literature, and the reported results about the benefit of nocturnal NPPV on survival, daytime blood gas values, gas exchange, quality of life, and sleep architect are various[6,8,9]. These varied outcomes have been found to lead to variation in long-term nocturnal NPPV administration[10]. Positive results of nocturnal NPPV have been reported with the use of high-intensity NPPV then the perspective on nocturnal NPPV in stable COPD patients has changed[11].

Knowledge gaps on this issue of patient selection and NPPV administration procedures remain. Comprehensive studies are required, and stable severe COPD patients should be carefully evaluated for nocturnal Noninvasive Positive Pressure Ventilation (NPPV) as a nonpharmacological treatment choice[12].

Nocturnal NPPV in Stable Severe COPD Patients-Patient Selection

Nocturnal NPPV is suggested for patients with daytime hypercapnia (Partial Pressure of Arterial CO2 (PaCO2) ≥52 mmHg) and hypoxemia (Peripheral Oxygen Saturation≤88 % for ≥5 minutes of ≥2 hours of sleep oximetry)13. Long-term nocturnal NPPV decision is not recommended during the acute on chronic hypercapnic stage. Reassessment for long-term NPPV is recommended 2-4 weeks after exacerbation13.

It is important to determine the etiology of hypercapnia. Hypoxemic and hypercapnic patients should be evaluated for cardiac pathologies and sleep-related respiratory problems. Evaluation of patients with polysomnography to exclude sleep apnea is critical13. Polysomnography is unnecessary if the patient is cachectic without signs of obstructive sleep apnea. Cardiac pathologies such as heart failure and pulmonary hypertension may also cause gas exchange abnormalities. Patients should be evaluated for cardiac pathologies and medical treatments for cardiac pathologies before the nocturnal NPPV decision3,14.

Management of Patients with COPD and SRBD

COPD is highly associated with SRBD. SRBD is a problem in nearly 40 % of COPD patients4. Expiratory snoring, insomnia, awakening with the sensation of gasping or choking, daytime sleepiness, fatigue, oxygen responsive morning headaches, and decline in cognitive status are the cardinal symptoms of SRBD15,16. Patients with these symptoms should be evaluated in terms of SRBD. Also, obesity (Body mass index>30 kg/m2), increased neck circumference (>43 cm for male, >41 cm for female), reduced daytime peripheral oxygen saturation (<93%), daytime hypercapnia, pulmonary hypertension, right heart failure, polycythemia is concluded as the indication for evaluating COPD patients regarding SRBD and nocturnal NPPV17.

SRBD may result in progressive hypercapnic respiratory failure and death in COPD patients. There are four main titles of SRBD associated with COPD:

- Sleep-Related Hypoxemia has been reported in nearly 70% of COPD patients.
- Coexisting Obstructive Sleep Apnea may be present in 10 to 30% of COPD patients.
- Sleep-Related Hypoventilation is the increase of $PaCo_2$>10mmHg during sleep.
- Respiratory Effort Related Arousals is the sleep fragmentation due to impaired respiration.

In COPD patients with existing SRBD, nocturnal NPPV improves dyspnea and corrects nocturnal hypoxemia, hypercapnia, and sleep[5,18-20].

Positive Effects of Nocturnal NPPV in COPD Patients

The beneficial effects of nocturnal NPPV are not solely due to an improvement in gas exchange[8]. Positive effects of nocturnal NPPV on stable COPD patients can be listed below:

1. Reversal of hypoventilation,
2. Respiratory muscle unloading,
3. Reduce the frequency of exacerbations and hospitalizations,

4. Cardiovascular function improvement,
5. Improving patients' survival,
6. Improving patient's nutritional status,
7. Improving patients' exercise tolerance,
8. Improving patients' Health-Related Quality of Life,
9. Reduce economic burden.

1. Reversal of Hypoventilation

According to physiological and clinical studies in stable hypercapnic COPD patients, nocturnal NPPV improves alveolar ventilation and lung function by increasing tidal volume, reducing respiratory rate and hyperinflation. These physiological changes result in a significant and sustained amelioration of daytime blood gas pressures (decline in PaCO2, an increase of PaO2); patients with higher baseline PaCO2 benefit more from higher inspiratory positive airway pressure levels and longer ventilation per day[4,13-17,21].

2. Respiratory Muscle Unloading

Respiratory muscle weakness occurs in severe COPD. Some points can be cited as the reason. Decreased elastic recoil results in hyperinflation. Hyperinflation caused by diaphragmatic disconfiguration is a mechanical disadvantage for the respiration[22]. Respiratory muscle exhaustion due to increased work of breathing can be cited as another reason[23].

Nocturnal NPPV provides ventilatory support, reduces respiratory muscle load and energy expenditure in acute and chronic respiratory failure, and improves respiratory performance[24-27].

3. Reduce the Frequency of Exacerbations and Hospitalizations

COPD exacerbation is defined as " a worsening of the patient's respiratory symptoms and a change in medication". Acute change in one or more of the following symptoms is required[28].

- Increased cough frequency and severity
- Increased sputum production and/or change of sputum character
- Increased dyspnea

Nocturnal NPPV increases hospitalization-free days survival in patients with daytime persistent hypercapnia after a recent hospitalization and also significantly reduces the exacerbations, general practitioner visits, rate, and length of admission, total days in hospital[13,29,30].

4. Cardiovascular Function Improvement

Nocturnal NPPV ameliorates cardiac functional performance, improves heart rate variability, and reduces circulating natriuretic peptide levels in patients with stable severe COPD. Thus, nocturnal NPPV contributes to reducing cardiac comorbidities in stable COPD patients[31].

5. Improving Patients' Survival

Data about the effect of nocturnal NPPV on survival in stable severe COPD patients is heterogeneous, and although evidence is not enough yet, in a meta-analysis, it is demonstrated that there is no increase in mortality[4]. Long-term NPPV produces more significant benefits for patients displaying more severe disease[13,15]. In another randomized controlled trial, the one- year death rate was significantly lower than the patients without nocturnal NPPV[7].

6. Improving Patients' Nutritional Status

It is essential to screen the nutritional status of COPD patients. Body mass index (BMI) is one of the crucial determinants of survival in COPD patients. It is essential to follow up on patients' BMI, weight loss (Weight

loss is identified as weight loss of ≥%10 in the past six months or weight loss of ≥%5 in the last month), and nutritional status to intercept malnutrition and muscle wasting that are common[32].

In the advanced stages of COPD, protein and energy metabolism are impaired due to hyperinflation and hypercapnia, which results in high energy consumption. Prolonged energy deficit, an imbalance between protein synthesis and protein breakdown, results in weight loss, muscle wasting, and malnutrition which are considered one of the main reasons for dyspnea, decreased ventilatory capacity, and exercise tolerance. It is essential to manage this stage with adequate nutritional therapy, exercises, and anabolic stimuli[33]. Also, data about significant weight gain in malnourished COPD patients after initiation of NPPV supports the use of NPPV for hypercapnic COPD patients[34,35].

7. Improving Patients' Exercise Tolerance

Exertional dyspnea is a troublesome symptom for COPD patients, a crucial physiological burden to limit activities. During exercise, healthy subjects differ from COPD patients. Muscle oxygen uptake and ATP consumption is higher in COPD patients than the healthy ones[34]. Nocturnal NPPV ameliorates hypoventilation, lung function, and gas exchange and improves the six-minute walking test[3,4,31,36,37]. Besides, implementing NPPV during exertion in stable COPD patients could play an important role[20,26,36]. NPPV can be used for patients who are receiving pulmonary rehabilitation programs to augment the effects of rehabilitation.

8. Improving Patients' Health-Related Quality of Life

Health-Related Quality of Life (HRQL) assessment is essential for critically ill patients to monitor treatment success[38].Quality of life refers to global life satisfaction regarding health, housing, employment, security, interpersonal relationships, education, and leisure pursuits. It is expressed as HRQL, mainly when applied to the life problems most affected by health or disease. In the literature, improvement of HRQL with NPPV in COPD patients is demonstrated[29,39].

9. Reduce Economic Burden

The use of nocturnal NPPV in highly selected stable severe COPD outpatients with recurrent hospital admissions is beneficial in reducing hospital readmissions and minimizing the costs[26,30].

Table 1. The outcome of Long-term Nocturnal NPPV in Stable Severe COPD

Study (Year)	Study Design	The Outcome of Long-term Nocturnal NPPV in Stable COPD
Renson etal[26] (1994)	RCT	İmproves exercise capacity and dyspnea, no significant difference in arterial PaO2 and PaCO2
Gay et al [41] (1996)	RCT	Lung function, nocturnal oxygen saturation, and sleep efficiency, blood gas tensions remained unchanged
Jones et al [13] (1998)	Prospective observational	General practitioner visits and hospital admissions are decreased
Casanova et al[5] (2000)	RCT	Over one year, the natural course of the disease was similar; only dyspnea rating decreased
Garrod et al[37]. (2000)	RCT	Significantly improve the mean shuttle walk test
Budweiser et al [15] (2005)	Retrospective, explorative	Long-term reduction of hyperinflation improved daytime blood gas
Sin et al (2007) [31]	RCT	Improves heart rate variability
Duiverman et al[40] (2008)	RCT	Augments the benefits of pulmonary rehabilitation, improves HRQOL, functional status, and gas exchange
Köhnlein et al [42]. (2009)	RCT	Significant improvement for FEV1, lung hyperinflation, HRQOL, blood gas, exercise tolerance
Dreher et al[11]. (2010)	RCT	High-intensity NPPV is superior to low intensity
Struik et al[7]. (2014)	RCT	Prolongs the time of readmission and death in 12 months

Adverse Effects of Nocturnal NPPV in COPD Patients

Various adverse effects may occur with the use of nocturnal NPPV. For many COPD patients who start to use nocturnal NPPV, adaptation difficulty is a significant problem, and understanding the problems and providing solutions will contribute to the adaptation process and increase the usage rate[39].

Irritation of interface contact areas is the most common problem. Appropriate interface and avoiding overtightening may help relieve the injuries[39].

The nose and mouth dryness can be resolved with humidification, nasal spray, or nasal gel. Nasal congestion can be resolved with nasal glucocorticoids, antihistamine therapy, or nasal decongestant therapy[40].

Gastric insufflation may occur. It is essential to balance pressure support, air leak, and tidal volume to reduce gastric insufflation[2,4].

Conclusion

Long-term nocturnal NPPV support should be applied to selected COPD patients with the sense that it will improve the patient-oriented clinical outcomes such as dyspnea, exercise tolerance, HRQL, and survival to reduce the frequency of attacks and the need for health care services. The current literature of randomized controlled trials and cohort studies is not sufficient yet to provide convincing evidence about long-term nocturnal NPPV use for stable COPD patients. The need to prove the effectiveness remains and comprehensive studies are required.

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