Noninvasive Ventilation for Severe Acute Asthmatic Attacks

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Abstract

Asthma is a chronic disease characterized by reversible airway obstruction caused by bronchial smooth muscle contraction, airway inflammation, and increased secretion. In most patients, control of disease activity is easily achieved with medical therapy. However, in a small minority, asthmatic attacks may be fatal. Some patients with severe asthmatic attacks are refractory to standard treatment, and a few of these patients have a history of severe asthmatic attacks that necessitated mechanical ventilation. In addition to the usual complications of mechanical ventilation, invasive mechanical ventilation in asthmatic patients is associated with other risks. These patients are often difficult to ventilate, have low compliance with high inspiratory pressures, and have frequent patient-ventilator asynchrony. Noninvasive ventilation (NIV) has been increasingly used to treat acute respiratory failure in the past two decades. It is now considered as standard first-line therapy in chronic obstructive pulmonary disease exacerbations and acute pulmonary edema. The increase in knowledge and experience has revived the use of NIV in asthma, which has previously been thought to be contraindicated. The purpose of this article is to review the up-to-date information on the use of NIV during severe acute asthmatic attacks. Nowadays, although sufficient data are not present to recommend the use of NIV in severe asthmatic attacks, there are some interesting and promising results about NIV. In conclusion, new well-designed studies including cases with respiratory acidosis and hypercapnia are necessary to eliminate the controversy. *(JAEM 2015; 14: 30-4)*

Key words: Noninvasive ventilation, acute respiratory failure, asthma attack

Noninvasive ventilation (NIV) is a supportive therapy used in respiratory failure cases and is generally applied with facial or nasal masks without placement of a tube in the patient. It is possible to lower the mortality and morbidity rates by preventing complications and infectious complications, especially those caused by intubation, which may arise during invasive mechanical ventilation (IMV) without having to resort to changes in ventilation support to the patient through NIV use in appropriate patients. Although the incidence of ventilator-associated pneumonia during IMV is 30% during the first 3 days, it increases by 1% each following day. However, the rate of the pneumonia complication in NIV is below 5%. Although the mortality rate in ventilator-associated pneumonia is about 50%, it accounts for 30% of total mortality rates (1).

Noninvasive ventilation has been increasingly popular and used to treat respiratory failure in the past two decades (2-4). Prospective randomized studies now point out the efficiency of NIV in acute exacerbations of chronic obstructive pulmonary disease (COPD), acute cardiogenic pulmonary edema, hypoxemic respiratory failure seen in immunosuppressed patients, and the weaning stages of patients with COPD, and these studies also advise NIV to be used as first-line ventilatory support (5). With the increase in NIV use, the accumulation of knowledge and experience about the method has also increased. The fact that the method is available to be used in emergency service units, intermediate intensive care, and services besides intensive care units (ICUs) has enabled an increase in application rates and therefore has lead to even more increases in experience. Due to the increase in knowledge and experience, today, NIV can be utilized in various clinical conditions such as severe asthmatic attacks, postoperative respiratory failure, bronchoscopy, preintubation oxygenization, postextubation respiratory failure, failure in extubation, and palliative therapy, and it can also be used more aggressively in cases such as hypercapnic COPD, for which it is advised to be used as a first-line ventilatory support option. Suggestions for the use, place of application, and application of NIV in acute respiratory failures according to the efficiency levels are summarized in Table 1.

Asthma is a chronic disease characterized by reversible airway obstruction caused by bronchial smooth muscle contraction, airway inflammation, and increased secretion. In most of asthmatic patients, the attacks can be controlled with medical therapy. However, in a very small group of patients, asthmatic attacks can be fatal (near-fatal asthma). Severe asthmatic attacks can be resistant to therapy in this patient group, and mechanical ventilation therapy is called for in some of these patients.

Patients with asthma are at a risk of contracting other complications in addition to the ordinary complications of IMV. In these patients, enabling appropriate ventilation even in high inspiratory pres-

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Table 1. The use of NIV in acute respiratory failures according to its efficiency levels

Efficiency level	Place	Suggestions
A: Numerous randomized controlled trials and meta-analyses		
COPD exacerbation	ICU, Res IC, Service	First-line vent. support option in select patients
Weaning acceleration in COPD	ICU, Res. IC	In appropriate patients, with close follow-up
Cardiogenic pulmonary edema	ICU, Res. IC	First-line vent. support option in select patients
Hypoxemic immunodeficient patient	ICU, Res. IC	First-line vent. support option in select patients
B: Limited controlled studies, case-control series, or cohort studies		
Postoperative respiratory failure	ICU	In appropriate patients, with close follow-up
Preintubation oxygenization	ICU	In a very limited number of very carefully selected patients, with very close follow-up
During bronchoscopy	ICU, Res. IC	In appropriate patients, with close follow-up
Postextubation respiratory failure prevention	ICU	In a very limited number of very carefully selected patients, with very close follow-up
Asthmatic attacks	ICU, Res. IC	In appropriate patients, with close follow-up
C: Case series or conflicting data		
Palliative	Service, Res. IC	In appropriate patients, with close follow-up
Pneumonia	ICU, Res. IC	In a very limited number of very carefully selected patients, with very close follow-up
ARDS	ICU	In a very limited number of very carefully selected patients, with very close follow-up
Extubation failure	ICU	In appropriate patients, with close follow-up

NIV: noninvasive ventilation; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; ARDS: acute respiratory distress syndrome

sures can be difficult, and patient-ventilator asynchrony is frequently seen. Thus, deep sedation and, most of the time, neuromuscular blockage are needed to overcome these challenges. Despite all these approaches, however, patients who are subjected to IMV are at a high risk of contracting morbidities such as permissive hypercapnia and barotrauma (pneumothorax). Further, endotracheal intubation itself and some of the agents used for sedation-analgesia can deteriorate bronchospasm or provoke laryngospasm. All these complications, in turn, elongate mechanical ventilation durations, extend intensive care stays, and increase mortality rates.

The use of NIV and the increase in knowledge and experience have brought forward the issue that NIV might be used in diseases such as asthma, which has previously been thought to be contraindicated. Today, NIV use in severe asthmatic attacks causing respiratory failure is still a controversial issue, and the number of randomized controlled trials (RCTs) on the subject is very low. Current studies do not have a sufficient number of cases, and their methodologies are problematic. It has been reported, however, that NIV use could prove to be helpful in selected patients with severe asthmatic attacks through careful and close monitoring as a result of these studies.

Selecting the right patient is the condition for NIV to be successful in severe asthmatic attacks. Table 2 displays a summary of the contraindications and indications of NIV use in severe asthmatic attacks.

Patients with asthma who are at the risk of respiratory failure and resistant to standard medical therapy should be detected at an early stage because NIV treatment can be useful in these patients at the early stages, and they can be protected from the potential complications of IMV. The place of application of NIV is a factor that affects success. Although the place of application of NIV is still a controversial issue, there are many reports supporting the use of NIV in ICUs, which prove to be the most effective and secure place of NIV application and which have the most clinical experience (6, 7). It can, however, be used at places where there are trained and experienced healthcare professionals and where it would be easy to performed close monitoring, intubation, and IMV. Today, it is advised that NIV application should be initiated at emergency service units and hospital services at an early stage in patients with mild acidosis (pH>7.30) (8, 9). In patients with more severe acidosis (pH<7.30), however, the results are not the same as the results in those with mild acidosis, and more intubation is needed. Therefore, the severity of the disease should be determined correctly at an early stage to refer patients to a place where they can receive the best and most effective treatment.

Edema, bronchospasm and inflammation seen in severe asthma attacks where the forced expiratory volume in first second (FEV1) is below taken that 25% of the expected values, the resulting flow limitation in the airways and dynamic hyperinflation impairs gas exchange, the respiratory mechanics and hemodynamics. Tachypnea causes respiratory muscles to work more and increases respiratory workload by shortening expiration duration and dynamic hyperinflation and therefore leading to positive-end expiratory pressure (PEEP) (10). The increase in respiratory workload and physiological dead space becomes a vicious circle and elevates intrinsic PEEP even more by causing an increase in the respiratory rate and CO_2 production and shortening the duration of expiration. As this vicious circle progresses, muscle fatigue and ventilation failure occur. NIV can be efficient by breaking this vicious circle, which rapidly deteriorates.

Table 2. Indications and contraindications of NIV in asthmatic attacks

Contraindications	**Indications (Risky patients for whom NIV can be effective)**
Specific contraindications	**Diagnostic criteria for severe asthma (at least one)**
- Urgent need for endotracheal intubation	- Use of accessory respiratory muscles
- Mental fog	- Pulsus paradoxus>25 mmHg
- Extreme secretion and risk of aspiration	- Pulse>110/min.
- Mask-face discrepancy	- Respiratory rate>25-30/min.
Relative contraindications	- Difficulty speaking
- Hemodynamic instability	- PEF or FEV_1<50% (expected)
- Severe hypoxia and/or hypercapnia (PaO_2/FiO_2<200, $PaCO_2$>60 mmHg)	- Arterial oxygen saturation<91-92%
- Cooperation disorder	**Risk factors for severe asthmatic attacks**
- Severe agitation	- Recent hospitalization
- Lack of sufficient experience	-Previous ICU stay necessitating mechanical ventilation
- Noncompliance to treatment	
- Exposure to an extreme level of allergens	

NIV: noninvasive ventilation; PEF: peak expiratory flow; ICU: intensive care unit

Moreover, NIV can cause bronchodilatation by mechanical effects, enabling bronchodilator medication to reach more peripheral airways. Formed bronchodilatation improves or accelerates the improvement of respiratory functions by decreasing airway resistance, adding to the ventilation of atelectatic areas and elevating the clearance of secretions.

Within the framework of NIV therapy, the load of the respiratory muscles is relieved, the efficiency of inspiratory effort is increased, and respiratory workload is decreased through supporting inspiration by pressure (IPAP), in addition to the expiratory positive airway pressure (EPAP) applied to overcome PEEP (intrinsic PEEP-Oto-PEEP) caused by dynamic hyperinflation (10). Respiratory workload can be decreased by 30-70%, transdiaghragmatic pressure by 50-75%, diaphragmatic electromyography (EMG) results by 20-90%, and dyspnea by 30-65% through the use of NIV (Figure 1) (11). As a result, improvement in blood gasses and a decrease in labored breathing, the respiratory rate, and the use of accessory respiratory muscles are achieved.

In the following part of the study, we will review articles, case series, and RCTs published to date on the use of NIV in severe asthmatic attacks in the adult population.

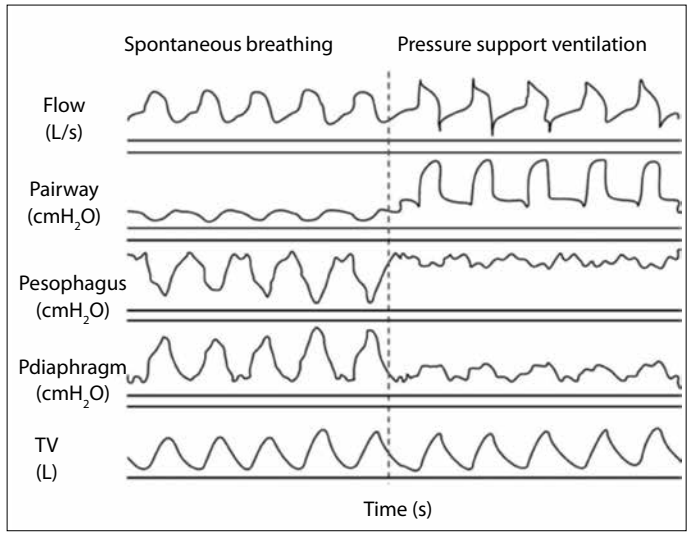

Figure 1. The effects of pressure support in noninvasive ventilation
TV: tidal volume

Case Series

The first study on the use of NIV in hypercapnic acute asthmatic attacks was published by Meduri et al. (12) in 1996. The authors of the article reported their experience with 17 patients who had received NIV at the ICU because of respiratory acidosis related to severe asthmatic attacks. The average values of patients were pH of 7.25±0.07 and $PaCO_2$ of 65±11 mmHg; their respiratory rate was 29±5/min; their mean NIV pressures were EPAP of 4±2 cmH_2O and IPAP of 14.5±5 cmH_2O. The conditions of 2 of 17 patients (12%) necessitated intubation and IMV, while the remaining 15 patients got better rapidly within hours. It was stated that 2 of 15 patients who showed rapid improvement needed sedation, and that the duration of NIV was 16±21 h, while their ICU stay was limited to 51±73 h. Consequently, the authors stressed that NIV was very effective in rapid improvement in the respiratory rate and arterial blood gasses with low pressures in asthmatic attacks leading to hypercapnic respiratory failure.

Five years after the above mentioned article, Fernandez et al. (13) published their own experience over a 7-year period (1992-1998) with 22 patients with severe asthma who had distinct respiratory acidosis and were suitable for NIV for the onset of ventilation support. In this study, the authors described the inclusion criteria for patients suitable for NIV as follows: 1-severe labor breathing at rest, 2-respiratory rate>30/min, 3-PaO_2 while breathing room air<60 mmHg or taking in oxygen<80 mmHg, 4-$PaCO_2$≥50 mmHg, 5-pH≤7.30, 6-using accessory respiratory muscles or having at least two of the abdominal paradox movement criteria. The mean values of 22 patients who met the above criteria and who received NIV support were calculated

to be pH of 7.28±0.008 and $PaCO_2$ of 63±24 mmHg, and their respiratory rates were 32±6/min, and 3 of these patients (14%) necessitated intubation and IMV. It was underlined that although the number of patients using NIV in this patient group increased year by year over a 7-year period, the number of patients receiving invasive ventilation decreased.

In a retrospective study published in 2010 by Murase et al. (14), the authors categorized their experience with severe asthmatic attacks as pre-NIV period (1999-2003) and post-NIV period (2004-2008). In the pre-NIV period, 9 of 50 cases received IMV because of hypoxemia (PaO_2/FiO_2 rate, 241.8±160.9) and hypercapnia ($PaCO_2$, 79.0±39.7), while in the post-NIV period, 17 of 57 cases received NIV because of hypoxemia (PaO_2/FiO_2 rate, 197.1±132.3) and hypercapnia ($PaCO_2$, 76.8±29.9). A total of 2 of the 17 cases with NIV needed intubation. In their article, the authors stressed that the onset of NIV use was shorter than the onset of IMV (171.7±217.9 min versus 38.5±113.8 min, $p<0.05$), the duration of hospitalization in patients using NIV was shorter (12.6±4.2 days versus 8.4±2.8 days, $p<0.01$), there was a decrease in mechanical ventilation duration (36.9±38.4 h versus 20.3±35.8 h, $p=0.09$), and there was also a decrease in intubation rates. As a result, the authors stated that NIV was a rewarding and user-friendly treatment option that could be used to stabilize severe asthmatic attacks.

Randomized Controlled Trials

The total number of RCTs published up to date on the effects of NIV on severe asthmatic attacks in the adult population is 6, the first being published in 2001 and the latest in 2013.

In the first RCT published in 2001 by Holley et al. (15), patients referred to the ER with an acute asthmatic attack were randomized as patients with nasal NIV and standard treatment and those only receiving standard treatment. In contrast to the initial expectation, only 35 patients were covered by the study. A total of 19 patients were in the NIV group, while the remaining 16 were in the control group. The results of this study, however, are not reliable because of the major bias in patient selection. The mean values of patients who received NIV were stated to be pH of 7.35±0.04 and $PaCO_2$ of 40±11, and the respiratory rate was 28±5/min. While 1 patient in the NIV group needed IMV (5%), 2 patients in the control group needed IMV (13%). The authors reported that there was no significant difference between the two groups with regards to all the measured results.

The second RCT was published in 2003 by Soroksky et al. (16), and the authors of the study included 30 patients who had presented to the ER with complaints of acute asthmatic attack. Patients were randomized into two groups, with 15 patients in each, as follows: those receiving NIV and standard treatment and those only receiving standard treatment. It was stated in the study that there was no difference between the groups regarding basal values, and the mean values of the NIV group were pH of 7.41±0.04, $PaCO_2$ of 33.39±3.48, and PaO_2 of 82.85±38.72 mmHg, and the respiratory rate was 34.8±1.8/min. The authors concluded that the respiratory function test (FEV_1 and PEF) results of the NIV group showed more rapid improvement and decreased the need for hospitalization. However, the study group of this trial covered patients with milder asthmatic attacks who had respiratory alkalosis and hypocapnia.

The third RCT was published in 2008 by Soma et al. (17), and the authors randomized patients presenting to the ER with asthmatic attacks into 3 groups, which is different from the previous studies. The first group comprised 14 patients receiving IPAP of 8 cmH_2O and EPAP of 6 cmH_2O, and the second group comprised 12 patients receiving IPAP of 6 cmH_2O and EPAP of 6 cmH_2O, while the control group comprised 14 patients receiving only oxygen therapy. None of patients in the trial needed intubation. The results of the study revealed that in the NIV groups (high and low pressure), labor breathing improved more rapidly in comparison with that in the control group (which was measured using the Borg Scale), and in the group with high NIV pressure, improvement in FEV_1 values was more rapid than that in the control group. In this trial, however, regulated pressure support (PS) was set at a very low level (2 cm H_2O). Its value was almost close to CPAP support. Moreover, the population of the trial included patients with very mild asthmatic attacks (respiratory rate, about 20/min).

The RCT published in 2009 by Brandao et al. (18) evaluated the effects of NIV on bronchodilator nebulization in asthmatic attacks, which is different from the other RCTs. Thirty-six patients presenting to the ER with FEV_1 level below 60% were evaluated after randomization into 3 groups. The first group included patients receiving bronchodilator nebulization of IPAP of 15 mmHg and EPAP of 5 mmHg NIV pressure, and the second group included those receiving bronchodilator nebulization of IPAP of 15 mmHg and EPAP of 10 mmHg NIV pressure, while the control group included those receiving nebulization without PS. Although none of patients needed intubation, the authors observed significant improvements in respiratory function tests during 30 min of the initiation of treatment. This trial, like the others, was conducted with a small number of patients and included patients with mild asthmatic attacks.

The study published in 2010 by Gupta et al. (19) was conducted at a respiratory ICU, which is different from the previous 4 studies, and covered 53 patients with severe asthmatic attacks who had a history of asthma for at least a year and who were tachypneic (>30/min), tachycardic (>100/min), and hypoxemic ($PaO_2<60$ mmHg). Patients were randomized into two groups as follows: those receiving medical treatment (25 patients) and those receiving NIV treatment in addition to standard medical treatment (28 patients). The NIV population included hypocapnic patients ($PaCO_2=37$ mmHg) with respiratory alkalosis (pH=7.42). NIV pressure was set at IPAP of 12 cmH_2O and EPAP of 5 cmH_2O. The authors concluded that NIV added to standard medical treatment in severe asthmatic attacks accelerated improvement in respiratory functions, decreased the need for inhaled bronchodilator, and decreased hospitalization durations and stays in the ICU.

The latest RCT was recently published in 2013, and the authors evaluated the effects of NIV on the pulmonary distribution of nebulized bronchodilators using pulmonary scintigraphy (20). Twenty-one patients who had presented to the ER with moderate-severe asthmatic attacks were randomized into two groups as follows: those receiving NIV and bronchodilator nebulization (10 patients) and the control group receiving nebulization without PS (11 patients). The results of the study revealed that clinical NIV showed better improvement in respiratory function tests but had no effect on the pulmonary distribution of bronchodilators.

Our literature review points out that there are some interesting and encouraging results, although today, there are no sufficient data to advise NIV use in severe asthmatic attacks. NIV accelerates improvement in labor breathing and respiratory functions in mild-moderate asthmatic attacks and decreases the need for inhaled bronchodilators and hospitalization rates (21-24). Therefore, NIV can be carefully used with close monitoring at ICUs, where emergency intubation can

be handled, in carefully selected patients with life-threatening severe asthmatic attacks. Well-designed new RCTs with a large number of patients with respiratory acidosis and hypercapnia, which have no methodological problems, are needed to eliminate contradictions.

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