Noninvasive ventilation for neuromuscular respiratory failure: when to use and when to avoid

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Purpose of review
Neuromuscular respiratory failure can occur from a variety of diseases, both acute and chronic with acute exacerbation. There is often a misunderstanding about how the nature of the neuromuscular disease should affect the decision on how to ventilate the patient. This review provides an update on the value and relative contraindications for the use of noninvasive ventilation in patients with various causes of primary neuromuscular respiratory failure.

Recent findings
Myasthenic crisis represents the paradigmatic example of the neuromuscular condition that can be best treated with noninvasive ventilation. Timely use of noninvasive ventilation can substantially reduce the duration of ventilatory assistance in these patients. Noninvasive ventilation can also be very helpful after extubation in patients recovering from an acute cause of neuromuscular respiratory failure who have persistent weakness. Noninvasive ventilation can improve quality of survival in patients with advanced motor neuron disorder (such as amyotrophic lateral sclerosis) and muscular dystrophies, and can avoid intubation when these patients present to the hospital with acute respiratory failure. Attempting noninvasive ventilation is not only typically unsuccessful in patients with Guillain–Barre syndrome, but can also be dangerous in these cases.

Summary
Noninvasive ventilation can be very effective to treat acute respiratory failure caused by myasthenia gravis and to prevent reintubation in other neuromuscular patients, but should be used cautiously for other indications, particularly Guillain–Barre syndrome.

Keywords
Guillain–Barre syndrome, mechanical ventilation, myasthenia gravis, neuromuscular respiratory failure, noninvasive ventilation

INTRODUCTION

Multiple forms of neuromuscular disease can produce respiratory failure and require mechanical ventilation. This can occur with acute neuromuscular disease and with chronic progressive neuromuscular conditions in the setting of acute exacerbations or superimposed acute cardiopulmonary disease. The prognosis of patients with primary neuromuscular respiratory failure is primarily determined by the specific cause of the neuromuscular weakness [1▪]. The ideal ventilator strategy is also determined by the same factor [2].

Noninvasive ventilation (NIV) represents a valuable option for some patients with neuromuscular respiratory failure. The role of NIV in the management of neuromuscular diseases is better recognized for advanced stages of chronic progressive conditions such as amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy [3▪,4]. However, NIV can also be very helpful in the ED and the ICU to treat select patients with acute weakness from exacerbation of chronic conditions, most notably myasthenia gravis [5▪,6▪▪].

The keys to optimizing the use of NIV for neuromuscular patients are adequate recognition of the neuromuscular disease in question and timely intervention. Although some neuromuscular conditions lend themselves well to the application of NIV, attempts at implementing NIV in other situations can be potentially hazardous. Meanwhile, timing can make the difference between success and failure of NIV. In patients who are getting fatigue but who

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KEY POINTS

- The choice of ventilatory support in patients with neuromuscular disease should be made based on the knowledge of the specific diagnosis.
- NIV with BiPAP can avert intubation and shorten the duration of hospitalization in patients with myasthenia gravis, but only if initiated early (optimally before development of hypercapnia).
- NIV should be avoided in patients with GBS manifested with rapidly progressive weakness and labile dysautonomia.
- NIV ventilation may reduce the risk of reintubation in patients with improving weakness from various neuromuscular conditions who initially required invasive mechanical ventilation.

can still recover if the work of breathing is reduced, NIV can be highly effective and prevent intubation. Instead, NIV is likely to fail once these patients have developed severe fatigue with frank hypercapnia. Rapid assessment of the level of consciousness, amount of secretions, and cardiopulmonary status (concomitant signs of pulmonary edema, respiratory infection, and large atelectasis) is also necessary to make the right decision regarding the appropriateness of a trial of NIV.

It is important to recognize the early clinical features and pathophysiological phases of neuromuscular respiratory failure to ensure timely initiation of ventilator support [2,7,8]. This review will provide a quick overview of these topics. The technical aspects of NIV have been the subject of recent comprehensive reviews [9**,10], and therefore, this article will also refer to a few points specifically pertinent to neuromuscular patients. Most of the review will be focused on discussing the neuromuscular indications and relative contraindications for the use of NIV, including practical advice whenever possible.

TEXT OF REVIEW

Clinical recognition of neuromuscular respiratory failure

Patients with neuromuscular respiratory failure appear typically tired, dyspneic, and diaphoretic. Often they cannot complete full sentences with a single breath (a sign known as staccato speech). Respiratory rate is fast and usually they are also tachycardic. In some cases, they may exhibit difficulty handling oral and respiratory secretions and their cough may be weak. Use of accessory muscles (sternocleidomastoid, intercostal, and abdominal) can be easy to visualize, but palpation may make it more evident. Yet, the most reliable sign of impending respiratory failure is the presence of a paradoxical breathing pattern (i.e., the inward rather than outward movement of the abdomen with each inspiration) (Rabinstein Warning signs).

A focused neurological examination may be extremely valuable to identify the cause of the neuromuscular failure and is also necessary to determine if the patient had bulbar muscle weakness that may increase the risk of aspiration [11,12]. Ophthalmoparesis and ptosis can be seen with myasthenia gravis or Guillain–Barre syndrome (GBS). Absent reflexes favor the latter. Preservation of oculomotor function with profound weakness of the extremities can be seen with spinal cord injury, ALS, and myopathies. Bulbar muscle weakness (oropharyngeal and laryngeal weakness) can be prominent with GBS, myasthenia gravis, ALS, diphtheria, and botulism. Weakness of neck flexion is often considered to correlate with the degree of diaphragmatic weakness, but this is true mostly for neuropathic disorders.

Lung examination may reveal signs of consolidation (most commonly from atelectasis or pneumonia from aspiration). Signs of airway obstruction or pulmonary edema are not present unless the patient has coexistent comorbidities such as chronic obstructive pulmonary disease or heart failure. Physical examination should be complemented with bedside spirometry to measure forced vital capacity, maximal inspiratory pressure (sometimes referred to as negative inspiratory force) and maximal expiratory pressure; arterial blood gases and a chest radiograph.

Basic pathophysiology of neuromuscular respiratory failure

Neuromuscular diseases cause a restrictive pattern of respiratory failure. The earliest abnormality produced by weakness of respiratory muscles is the development of microatelectasis in the lung bases. Patients at this stage may be tachypneic with respiratory alkalosis and a normal or slightly reduced PO_2. As the fatigue of the respiratory muscles progresses, generalized alveolar hypoventilation ensues. This is first manifested by a high respiratory rate with normal P_{CO_2}, which precedes the occurrence of hypercapnia with respiratory acidosis. Only later does the profound hypoxemia complete the picture as alveoli continue to collapse. This downward spiral of worsening ventilation–perfusion mismatch and increasing work of breathing (further overloading the already fatigued muscles)

can be sometimes reversed by timely intervention with NIV, but otherwise results in the need for tracheal intubation and invasive mechanical ventilation.

Therefore, correct assessment of the stage of the neuromuscular respiratory failure demands integration of data from the physical examination, arterial blood gases, bedside spirometry, and chest radiograph [2,8,12]. This thorough initial evaluation is necessary whenever neuromuscular failure is suspected. Especially patients with chronic neuromuscular conditions may be able to compensate severe degrees of respiratory muscle weakness seemingly well, and only careful evaluation can reveal the true degree of ventilator compromise in these cases.

Bulbar muscle weakness introduces another level of concern in neuromuscular patients. Upper airway obstruction and aspiration are added risks in these cases. Yet, the presence of bulbar muscle weakness should not be necessarily seen as an immediate indication for intubation. Some of these patients may do well with NIV if their ventilatory failure is not too advanced and it is deemed still reversible. It is important to be cautious in patients who have pooling of respiratory secretions, but even some of these patients can be treated with NIV.

Noninvasive ventilation in neuromuscular patients: general concepts

NIV can be used to deliver continuous positive airway pressure or bilevel positive airway pressure (BiPAP) [9▪▪,10]. Continuous positive airway pressure can help overcome upper airway resistance and keep alveoli open, thus improving gas exchange. However, this mode of ventilation provides little support to the respiratory muscles, and therefore, it is not ideal in patients with respiratory muscle fatigue. In such instances, using BiPAP is the best strategy. Inspiratory positive airway pressure and expiratory positive airway pressure, as well as the flow of oxygen, should be tailored to the individual situation and a backup rate should be prescribed [13]. In addition to pressure support ventilation, NIV can deliver pressure control ventilation and proportional assist ventilation, although these techniques are less often employed [13]. However, the most crucial – and often the most challenging – element to the successful delivery of NIV is the fitting of the mask (the interface) to provide ventilation with sufficient comfort to the patient while minimizing air leaks [9▪▪].

In the ED and ICU, we prefer the use of oronasal masks. They are more stable than nasal masks and cause less claustrophobia than total face masks. Also patients with neuromuscular disease often breathe through their mouth, which renders nasal masks ineffective. Having an experienced and dedicated respiratory therapist is essential to find the ideal fit for the patient among the various models of oronasal masks available. In addition to preventing leaks, optimal fitting reduces the occurrence of pressure skin sores over the nasal bridge, a common limiting factor when NIV needs to be used continuously for several days.

An important practical point to keep in mind is that patients with facial oropharyngeal muscle weakness are actually easier to ventilate with NIV because they do not 'fight' the delivery of gas. This lack of resistance to the inspiratory pressure allows for the maintenance of good tidal volumes and diminishes patient discomfort. Thus, when evaluating a patient in the ED or the ICU who has bilateral facial weakness and a weak tongue, the clinician should not feel dissuaded from trying NIV; in fact, these patients may be good candidates for this ventilatory modality.

Patients who are unable to swallow and are pooling oral and respiratory secretions should be monitored carefully, but may still be cautiously tried on NIV. We have treated myasthenic patients with these characteristics quite a few times with excellent results. Generally it becomes evident within minutes whether these patients will tolerate NIV. Although extremely agitated patients who must be sedated are not good candidates for NIV, patients with acute neuromuscular weakness are often restless. Yet, this restlessness is because of air hunger and can improve once they wear the NIV mask and their ventilation improves.

When to try noninvasive ventilation in a patient with neuromuscular disease

The possible indications for NIV in neuromuscular respiratory failure are listed in Table 1. In the acute setting, NIV is most useful in patients with myasthenic crisis (i.e., myasthenia gravis exacerbation causing respiratory failure and requiring ventilatory assistance).

Myasthenia gravis is an autoimmune disorder characterized by a failure of neuromuscular transmission [14]. The most common autoantibodies block the postsynaptic nicotinic acetylcholine receptors in the muscle membrane [15]. Although much less common, patients with antibodies against muscle-specific tyrosine kinase should be recognized because they have more bulbar involvement and may have a higher predisposition to develop respiratory failure [16]. Patients with myasthenia gravis have fluctuating muscle weakness with

Table 1. Indications and relative contraindications for the use of noninvasive ventilation in patients with neuromuscular respiratory failure

Indications
Myasthenic exacerbation/crisis (before hypercapnia)
Improving neuromuscular failure with persistent weakness after extubation
Neuromuscular disorders with exacerbated COPD or CHF
Motor neuron disease (e.g., ALS)
Muscular dystrophies
Relative contraindications
Guillain–Barre syndrome
Spinal cord injury in the acute phase
Severe hypercapnia with respiratory acidosis
Concomitant acute brain disease causing coma
Severe agitation requiring sedation
Excessive respiratory secretions
Severe acute systemic complications (shock, unstable arrhythmias, myocardial ischemia, ileus)
Anticipated procedures requiring sedation

ALS, amyotrophic lateral sclerosis; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease.

fatigability. Rest makes the weakness better. Thus, when the respiratory muscles start to fatigue, prompt support with NIV can reverse the worsening weakness and prevent complete muscle failure [5▪,6▪▪].

Prompt support with BiPAP has been shown not only to avert the need for tracheal intubation [5▪] but also to shorten the length of ICU and hospital stay in patients with myasthenic crisis [6▪▪]. This is achieved by reducing the rate of pulmonary complications (atelectasis and especially pneumonia) compared with patients who are intubated [6▪▪]. However, the timing of initiation of NIV is crucial to its success. The chances of BiPAP failure increase significantly once the myasthenic patient has developed hypercapnia [5▪,6▪▪]. Thus, NIV with BiPAP should be started as soon as possible when a patient with myasthenia gravis presents with a severe exacerbation involving respiratory muscles. In patients with myasthenia gravis, the value of bedside pulmonary function tests is not well elucidated, but in practice it is not infrequent to note that they are not very reliable because of the fluctuating nature of the weakness in these patients. The decision to start NIV in myasthenia gravis should, therefore, be based on clinical judgment and the treating clinician should have a low threshold to initiate this therapy [2].

NIV ventilation can also be quite helpful after extubating patients who are recovering from a myasthenic crisis [17]. It is important to keep in mind that the risk of extubation failure in myasthenia gravis is quite high, with approximately one in four patients having this complication especially if atelectasis is visible radiologically [18,19▪]. Consequently, this potential problem should be anticipated. When patients start getting fatigue after being extubated, NIV should be provided without delay. In patients who are doing well after extubation but are still weak (a very common scenario), it is also a reasonable practice to put the patient on NIV overnight to prevent the occurrence of ventilator failure and alveolar collapse during rapid eye movement sleep (when muscle tone is absent) [20].

NIV can also be used to support patients with GBS in the recovery phase after extubation. By then, these patients no longer have labile dysautonomia and progressive recovery of muscle strength can be expected. A similar consideration can probably be applied to other less common causes of neuromuscular failure, such as inflammatory myopathies. NIV with mechanically assisted coughing can also make extubation possible in patients with critical illness neuromyopathy (ICU-acquired weakness) [21▪]. Another reasonable indication for NIV is to treat neuromuscular disorders decompensated by chronic obstructive pulmonary disease or heart failure with pulmonary edema, conditions that are known to be successfully managed with NIV [13].

NIV is the preferred form of respiratory support in patients with irreversible chronic progressive neuromuscular diseases. ALS and muscular dystrophies (such as Duchenne or myotonic muscular dystrophies) are prime examples [3▪,4]. Although NIV is generally started in these patients in the ambulatory setting as they slowly decline, there are instances when a concurrent disease causes an acute worsening of the respiratory function on patients who were able to cope with their respiratory muscle weakness until then. In such cases NIV, especially when combined with mechanically assisted coughing (insufflation–exsufflation with exsufflation-timed abdominal thrust), can be very effective in avoiding intubation and tracheostomy (generally not desired by these patients) [21▪]. When NIV is tried for the first time in the ICU on these patients, it is essential to clarify with the patient if intubation would be an acceptable option should NIV fail to provide sufficient support.

When not to try noninvasive ventilation in a patient with neuromuscular disease

GBS is an autoimmune polyradiculoneuropathy (generally demyelinating, more severe when axonal) that can progress quickly toward respiratory

failure from severe diaphragmatic weakness and bulbar muscle weakness [22]. It is also associated with dysautonomia, which can produce labile blood pressure and cardiac arrhythmias (notably including severe bradyarrhythmias and conduction blocks in response to various medications, such as β-blockers, stimulants of peristalsis, and antiemetics) [23]. Because of this dysautonomia, emergency intubation in GBS can result in life-threatening complications and should definitely be avoided as much as possible [24]. By the time a patient with GBS develops respiratory muscle weakness, the clinical course will be persistently declined followed by a prolonged nadir. Thus, trying to temporize with NIV is not going to be effective. Moreover, it is not well tolerated because as the patient continues to worsen, intubation is often needed as an emergency [25]. Instead, patients with GBS should be intubated electively when weakness is severe or progressing fast, bulbar weakness is pronounced, or there is evidence of ventilatory muscle insufficiency. The latter can be reliably tested with bedside respiratory function tests: a FVC less than 20 mmHg, a maximal inspiratory pressure below $-30\,cmH_2O$, a maximal expiratory pressure less than 40 mmHg, or a worsening of FVC greater than 30% over 24 h are reliable predictors of the need for invasive mechanical ventilation [26].

Patients with upper cervical spinal cord injury should be expected to have long-term neuromuscular respiratory failure and should, therefore, be intubated and then undergo tracheostomy. Patients with concomitant cerebral disease resulting in coma should be intubated for airway protection. In addition to trauma, West Nile virus encephalomyelitis can present with a combination of depressed level of consciousness and neuromuscular respiratory failure [27]. Intubation is also necessary when the need for sedation can be anticipated and in patients who are systemically unstable such as those in septic shock. Extreme agitation, pooling of abundant oral and respiratory secretions, and severe respiratory or mixed acidosis are additional contraindications for NIV in neuromuscular patients.

CONCLUSION

NIV can be a valuable treatment for select patients with acute or acute on chronic neuromuscular respiratory failure. However, the key to NIV success is in understanding which patients can benefit from this type of ventilatory support and which ones can actually be harmed by it. Among the two most common causes of primary neuromuscular respiratory failure presenting to the ICU, NIV applied early can be extremely useful in myasthenia gravis and, conversely, it can be a dangerous choice in GBS. Recognizing the specific neuromuscular disorder and having sufficient understanding of its pathophysiology and predicted clinical course can allow the clinician to make the right choice.

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There are no conflicts of interest.

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