Assisted Ventilation in Children with Neuromuscular Diseases

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Abstract
Noninvasive mechanical ventilation (NIV) has been applied for several decades in patients with neuromuscular diseases (NMDs). Many available reports suggest that benefit of NIV to NMDs including decrease hypoventilation, improve quality of life and prolong survival even for children. Practical guidelines also have been provided for healthcare professionals in delivering good quality patient care1. Here we review the available data including natural history of the evolution of respiratory insufficiency in patients with NMD, the reasons of ventilation support for children with NMD, the symptoms of nocturnal and daytime hypoventilation, the benefit evidences and adverse effects of NIV, the indications and monitor for NIV in NMD children. Tracheostomy should be taken into consideration if NIV is failed to correct hypoventilation. (J Pediatr Resp Dis 2014;10:28-39)

Key words: NIV, NMD, assisted ventilation

INTRODUCTION

Natural history of the evolution of respiratory insufficiency in patients with neuromuscular diseases (NMDs)

Normal breathing depends on the intact function of the ventilator pump, which consists of the central respiratory control centers, the bony rib cage, and the muscles of breathing. In progressive neuromuscular diseases (NMDs), the ventilator pump is often impaired and leads to a predictable pattern of respiratory compromise beginning with normal or near normal unassisted gas exchange early in the disease, adequate daytime gas exchange with nocturnal hypoventilation during mid-stage disease, and chronic and/or acute respiratory failure requiring full-time assisted ventilatory support for survival in late-stage disease. In addition, normal defense of the lung depends on adequate secretion management and the precise timing of and force generated by the activities of the ventilator pump to produce an effective cough. NMDs would lead to alveolar hypoventilation. When the onset is slow and progressive, alveolar hypoventilation typically goes undiagnosed and untreated until an episode of acute respiratory failure occurs. This episode of decompensation is frequently seen during common upper airway infections, and it results from patient incapacity to eliminate secretions. Pneumonia, respiratory failure, and, ultimately, death can all occur as a consequence of ventilator pump dysfunction (Fig 1). Respiratory failure is the most common cause of mortality in patients with neuromuscular disease.2,3 The age of onset of respiratory problems varies with the underlying condition, as indicated in table 1.1 However, appropriate screening with timely intervention and use of assistive respiratory devices can prevent complications and prolong life in those in whom NMD compromises their respiratory system.3-5
### Table 1. Spectrum of diseases with surfactant dysfunction

<table>
<thead>
<tr>
<th>Condition</th>
<th>Respiratory failure</th>
<th>Secretion clearance difficulty</th>
<th>Recurrent pneumonia</th>
<th>Progression</th>
<th>Disease-specific features</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>All by 2 years</td>
<td>Marked</td>
<td>All</td>
<td>Rapid</td>
<td>All require full-time respiratory support</td>
</tr>
<tr>
<td>Type 2</td>
<td>~40% in childhood</td>
<td>Early</td>
<td>~25% in first 5 years</td>
<td>Slow</td>
<td></td>
</tr>
<tr>
<td>Type 3</td>
<td>Rare in childhood</td>
<td>Rare in childhood</td>
<td>Rare in childhood</td>
<td>Slow</td>
<td></td>
</tr>
<tr>
<td>SMA with respiratory distress type 1</td>
<td>All by 6 months</td>
<td>Marked</td>
<td>All</td>
<td>Rapid in first year, then slows.</td>
<td>All require full-time respiratory support</td>
</tr>
<tr>
<td>DMD/severe childhood onset limb-girdle muscular dystrophy</td>
<td>After loss of ambulation</td>
<td>After loss of ambulation</td>
<td>Late</td>
<td>Cardiomyopathy usually occurs after respiratory problems but may precede them</td>
<td></td>
</tr>
<tr>
<td>Facioscapulohumeral muscular dystrophy</td>
<td>When onset &lt;20 years</td>
<td>With infantile onset</td>
<td>With infantile onset</td>
<td>Slow</td>
<td>Severe infantile onset type is frequently associated with sensorineural deafness</td>
</tr>
<tr>
<td>Congenital muscular dystrophy</td>
<td>Any age depending on severity</td>
<td>Any age depending on severity</td>
<td>Any age depending on severity</td>
<td>Slow</td>
<td></td>
</tr>
<tr>
<td>All types</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ullrich</td>
<td>70% in adolescence</td>
<td>Mild</td>
<td>Infrequent</td>
<td></td>
<td>Proximal contractures with marked distal laxity</td>
</tr>
<tr>
<td>Rigid spine muscular dystrophy</td>
<td>Early while ambulation preserved</td>
<td>Mild</td>
<td>Infrequent</td>
<td>Hypoventilation may occur in ambulant children with relatively preserved vital capacity</td>
<td></td>
</tr>
<tr>
<td>Congenital myopathy</td>
<td>Uncommon except in severe recessive type</td>
<td>Uncommon</td>
<td>Uncommon</td>
<td>Slow</td>
<td>Susceptible to malignant hyperthermia</td>
</tr>
<tr>
<td>Central core</td>
<td>Early while ambulation preserved</td>
<td>In severe form</td>
<td>In severe form</td>
<td>Slow</td>
<td></td>
</tr>
<tr>
<td>Minicore</td>
<td>Early while ambulation preserved</td>
<td>In severe form</td>
<td>In severe form</td>
<td>Slow</td>
<td></td>
</tr>
<tr>
<td>Nemaline</td>
<td>Early in severe neonatal form, mild later onset form may develop early while ambulation preserved</td>
<td>In severe form</td>
<td>In severe form</td>
<td>Slow</td>
<td></td>
</tr>
<tr>
<td>Myotubular</td>
<td>85% in severe X-linked form</td>
<td>In severe form</td>
<td>In severe form</td>
<td>Slow</td>
<td>Ophthalmoplegia, rare coagulopathy and liver haemorrhage</td>
</tr>
</tbody>
</table>
The reasons of ventilation support for children with neuromuscular disease

Respiratory muscle weakness is common among patients who have neuromuscular disease. It can be acute (eg, Guillain-Barré syndrome), chronic and relapsing (eg, multiple sclerosis, myasthenia gravis), or relentlessly progressive (eg, amyotrophic lateral sclerosis [ALS]). Regardless of its clinical course, respiratory muscle weakness is a serious problem among patients with neuromuscular disease. Some patients with NMD will die from respiratory failure. Therefore, subjective clinical findings and objective physiologic tests are used together to determine when mechanical ventilation is indicated.

Patients who present with cardiorespiratory arrest, respiratory distress, marked blood gas abnormalities, severe bulbar dysfunction with aspiration, or impaired consciousness need immediate mechanical ventilation. For all other patients, mechanical ventilation should be initiated on the basis of their overall clinical status. Serial measures of pulmonary function (instead of using one measure at one point in time) can be used as rough guidelines, especially when the respiratory decline is acute:

1. Forced vital capacity (FVC) - Ventilatory support is indicated when the FVC is less than 50 percent of predicted in many patients with respiratory muscle weakness.

2. Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) - Ventilatory support is indicated when the MIP is less negative than -30 cm H2O (eg, -20 cm H2O) or the MEP is below 40 cm H2O in many patients with respiratory muscle weakness. The diminished MIP indicates a high risk for hypercapnia, while the low MEP indicates inadequate cough strength and risk for secretion retention.
(3) Vital capacity (VC) - Ventilatory support may be indicated when the VC falls below 15 to 20 mL/kg, 60 percent of predicted, or 1 L. It may also be indicated if the VC falls more than 30 to 50 percent compared to a prior measurement. The normal VC is 60 to 70 mL/kg.\textsuperscript{10-13} These thresholds are derived from studies of patients with Guillain-Barré syndrome. It is uncertain whether the VC is similarly helpful in patients with other peripheral neuromuscular diseases, such as myasthenia gravis.\textsuperscript{14}

Clinical evidence fails to establish any of the measures as being superior to the others. As a result, the measures are generally considered in combination. A “20-30-40 rule” has been proposed.\textsuperscript{5,10} The rule advocates the initiation of ventilatory support when the VC is less than 20 mL/kg, the MIP is less negative than -30 cm H2O (eg, -20 cm H2O), or the MEP is less than 40 cm H2O. More prospective studies are needed to determine if this rule decreases the need for emergent intubation and improves overall outcome.

The symptoms of nocturnal and daytime hypoventilation

Respiratory muscle weakness due to neuromuscular disease can cause insufficient ventilation, nocturnal hypoventilation, ineffective cough or bulbar dysfunction.\textsuperscript{8}

(1) Insufficient ventilation may induce dyspnea, orthopnea, rapid shallow breathing (tachypnea plus decreased tidal volume), accessory respiratory muscle use, thoraco-abdominal paradox (inward motion of the abdomen during inspiration), hypercapnia, or hypoxemia. The principal cause of insufficient ventilation is weakness of the inspiratory muscles (diaphragm, external intercostal, scalene, sternocleidomastoid, and trapezi). The weak inspiratory muscles cause tidal volume to decrease. Respiratory frequency increases in an effort to compensate for the diminished tidal volume and maintain alveolar ventilation. However, the tidal volume may eventually fall to such a degree that the increased respiratory rate is insufficient to maintain alveolar ventilation and arterial carbon dioxide tension (PaCO2) begins to rise. Early in the course of the disease, the symptoms and signs described above may exist only when carbon dioxide production is elevated (eg, fever, infection). In such patients, ventilation may be adequate to maintain a normal PaCO2 when carbon dioxide production is at its baseline, but cannot be sufficiently increased to maintain a normal PaCO2 when carbon dioxide production is elevated.

(2) Nocturnal hypoventilation may induce choking, insomnia, daytime hypersomnolence, morning headaches, fatigue, or impaired cognition. Inadequate ventilation may first manifest during sleep in patients who have chronic neuromuscular disease. This results from upper airway obstruction due to bulbar dysfunction, as well as decreased accessory respiratory muscle activity during rapid eye movement (REM) sleep.

(3) Bulbar dysfunction may induce difficulty swallowing, dysarthria, dysphagia, weak mastication, facial weakness, nasal speech, or a protruding tongue. Bulbar dysfunction is due to impairment of the upper airway muscles: the lips, tongue, palate, pharynx, and larynx. Patients with bulbar dysfunction have

\begin{figure}[h]
\centering
\begin{tikzpicture}
  \node[coordinate] (start) at (0,0) {Normal breathing};
  \node[coordinate, below of=start] (nocturnal) {Nocturnal hypoventilation};
  \node[coordinate, below of=nocturnal] (chronic) {Chronic and/or acute respiratory failure};
  \node[coordinate, below of=chronic] (death) {Death};
  \node[coordinate, right of=chronic] (chest) {Chest infection};
  \draw[->] (start) -- (nocturnal);
  \draw[->] (nocturnal) -- (chronic);
  \draw[->] (chronic) -- (death);
  \draw[->] (chronic) -- (chest);
\end{tikzpicture}
\caption{Pneumonia, respiratory failure, and, ultimately, death can all occur as a consequence of ventilator pump dysfunction}
\end{figure}
an increased risk of aspiration. In addition, they are predisposed to upper airway obstruction during inspiration, which may induce or exacerbate nocturnal hypoventilation.

4) Ineffective cough predisposes patients to aspiration, retention of secretions, or pneumonia. Poor cough is caused by weakness of the upper airway, inspiratory, and expiratory muscles. Effective cough is a principal defense against aspiration and is necessary for clearance of respiratory secretions.15,16

**NIPPV (non-invasive positive pressure ventilation)**

Once it is determined that mechanical ventilation is necessary, options include noninvasive positive pressure ventilation (NIPPV) or invasive positive pressure ventilation. NIPPV may benefit patients who require (1) continuous mechanical ventilation for a short duration (ie, days), such as patients with an acute neuromuscular disease (eg, Guillain-Barré syndrome) (2) intermittent mechanical ventilation for a long duration (ie, years), such as patients with nocturnal hypoventilation or early chronic respiratory failure.

NIPPV is not used for continuous long-term mechanical ventilation because of the potential for local skin breakdown at the patient-mask interface. The likelihood that NIPPV will be unsuccessful or cause a complication is increased when any of the following exist: severe bulbar dysfunction, upper airway obstruction, retention of respiratory secretions, inability to achieve a satisfactory interface, poor cooperation, or inadequate cough. Clinicians should always weigh the potential benefits and risks before initiating NIPPV.

1) Desirable characteristics of an NIPPV interface

The patient interface has a major impact on comfort during NIPPV. The interface is often the weak link in the application of NIPPV. A poorly-fitting interface decreases clinical effectiveness and patient adherence to therapy. Desirable characteristics of an NIPPV interface including:

- Low dead space
- Transparent
- Lightweight
- Easy to secure
- Adequate seal with low facial pressure
- Disposable or easy to clean
- Nonirritating (non-allergenic)
- Inexpensive
- Variety of sizes; adult and pediatric
- Adaptable to variations in facial anatomy
- Quickly removable
- Anti-asphyxia mechanism
- Compatible with a wide range of ventilators

2) Types of NIPPV interface

The most commonly used interfaces are nasal masks (Fig.2A) and oronasal (face) masks (Fig.2B). Other interfaces include nasal pillows (Fig.2C), total face masks (Fig.2D), helmets (Fig.2E), and mouthpieces (Fig.2F).17

3) Advantages and dis-advantages of different NIPPV interface

The advantages and dis-advantages of different NIPPV interface had been well reviewed and summarized in Table 2.17

4) How to choose an interface

Selection of the type and size of the mask and securing the mask are critical to successful NIPPV. To optimize the fit and comfort, the type of mask (nasal or full face mask) that is used depends on the patient’s facial features. A mask that fits properly is crucial in minimizing air leaks and maximizing noninvasive ventilation efficiency. Recommendations for evaluating different sizes and types of masks at the bedside are important to select the best fit for each patient. When the nasal mask is used, the chinstrap decreases air leakage from around the mouth. An ill-fitting mask may cause breakdown of facial skin and skin ulcers around the nasal bridge. In patients who require prolonged intermittent mechanical ventilation for ventilator support, rotating the use of different types of mask may decrease these problems. In patients requiring long-term ventilator support, custom-fitted masks that conform to the patient’s facial features ensure proper fit and comfort.

5) Adverse effects of NIV – The most common side effects of NIV including skin breakdown and mid-face hypoplasia.

- Skin breakdown - Break down of the skin, usually on the bridge of the nose or forehead, can occur when using nasal or face-mask ventilation. Prevention is better than cure, and careful attention to mask fitting, and avoidance of over-tight straps is usually sufficient to keep the contact areas healthy. It is better to allow
a small leak around the mask, than to have it overly tight. When red patches are seen after mask use, these should be dealt with promptly before the skin breaks down. Use of wound care tape, particularly those made of duoderm or hydrocolloid material, is often helpful. Forehead spacers can also reduce the pressure of the mask on the nasal bridge. A wide range of commercial masks are now available for older children and changing the mask to one which avoids the area of skin damage is usually possible. This is more difficult for infants in whom there is a much more limited choice of interfaces. Custom-made masks are associated with a lower incidence of skin injury.18

- Mid-face hypoplasia - Pressure from the nasal or face mask used for NIV on the growing face can result in under-development of the maxilla, leading to mid-face flattening and mal-occlusion of the teeth. There are no large studies indicating the incidence of this problem, nor how it should be managed.

Assessment for skin injury and facial flattening should be carried out regularly in children using NIV and the mask interface adjusted as necessary to minimize these complications.

**The benefit evidences of NIV for patients with NMD**

Noninvasive ventilation is now commonly used to assist ventilation in patient with a variety of neuromuscular disease.19 NIV can be used to support breathing in children at home and in hospital easily. Nasal masks or pillows and face masks are commercially

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*Figure 2. Types of NIPPV interface*

A

B

C

D

E

F
available for all except the smallest infants. Nearly all children can be persuaded to wear a nasal or face mask at night for the purposes of ventilation. There are some reasons for using assisted ventilation in children with NMD, including to treat the symptoms of nocturnal or/and daytime hypoventilation, to reduce the frequency of hospital admission due to pulmonary infections, to prevent chest wall deformity in young children with the expectation of improved long-term outcome, and to prolong life and improve quality of life.\(^1,20-22\) The exact mechanism by which nocturnal noninvasive ventilation can improve daytime spontaneous ventilation in patients with NMD has not been fully understood. Hill has suggested that NIV may work by (1) improving ventilatory mechanics, (2) resting fatigued respiratory muscles thereby improving strength and endurance, or (3) enhancing ventilatory sensitivity to CO\(_2\).\(^23\)

(1) Correction of nocturnal hypoventilation and improve quality of life - One randomized trial of NIV for nocturnal hypoventilation performed by Ward S et al,\(^22\) included several school age children (mean age of 18 years, range 7-51 years). The subjects were identified from a clinic population of patients with congenital neuromuscular or chest wall disease. Those with the combination of nocturnal hypoventilation and daytime normocapnia were randomized to either nocturnal NIV or standard care and followed for 2 years. NIV was effective at correcting nocturnal hypoventilation and led to an improvement in QOL scores. In other four observational studies a total of 91 children were commenced on NIV because of symptoms of hypoventilation, the presence of daytime hypercapnia, or following an episode of respiratory failure.\(^24-27\) All these 4 studies showed improvement in oxygenation and carbon dioxide levels during sleep and markedly improved respiratory disturbance index. Symptom scores were also significantly improved.

(2) Reduce the frequency of hospital admission

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Table 2. Advantages and dis-advantages of different NIPPV interface

<table>
<thead>
<tr>
<th>Interface</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| Nasal           | • Less risk of aspiration  
• Easier secretion clearance  
• Less claustrophobia  
• Easier speech  
• Patient may be able to eat  
• Easy to fit and secure  
• Less dead space | • Mouth leak  
• Higher resistance through nasal passages  
• Less effective with nasal obstruction  
• Nasal irritation and rhinorrhea  
• Mouth dryness |
| Oronasal (face) | • Better oral leak control  
• More effective in mouth breathers | • Increased dead space  
• Claustrophobia  
• Increased aspiration risk  
• Increased difficulty speaking and eating  
• Asphyxiation with ventilator malfunction |
| Mouthpiece      | • Less interference with speech  
• Very little dead space  
• May not require headgear | • Less effective if patient cannot maintain mouth seal  
• Usually requires nasal or oronasal interface at night  
• Nasal leak  
• Potential for orthodontic injury |
| Total face mask | • May be more comfortable for some patients  
• Easier to fit (one size fits all)  
• Less facial-skin breakdown | • Potentially greater dead space  
• Potential for drying of the eyes  
• Cannot deliver aerosolized medications |
| Helmet          | • May be more comfortable for some patients  
• Easier to fit  
• No facial-skin breakdown | • Rebreathing  
• Poorer patient-ventilator synchrony  
• Less respiratory muscle unloading  
• Risk of asphyxiation if ventilator malfunctions  
• Cannot deliver aerosolized medications |
NIV is effective in reducing hospital admissions for respiratory exacerbations in children with either symptomatic sleep-related hypoventilation or daytime hypercapnia. In one retrospective study of 24 patients with regular use of NIV and 11 patients without NIV with neuromuscular disorders. In the first year of NIV consultations of a general practitioner due to respiratory tract infection decreased from 9.2±20.8 to 3.2±5.3 per year and the number of hospital admissions due to respiratory tract infection decreased from 1.6±1.7 to 0.7±1.3 per year. In 12 patients using NIV for more than 5 years the incidence of respiratory tract infection requiring hospital admission decreased from 0.54±0.41/year in the pre-ventilation period to 0.12±0.09/year in the NIV period. Katz S, et al also demonstrated the similar finding. Fifteen children (mean age 11.7, range 3.4-17.8 years) diagnosed with NMD who had been started on nocturnal NPPV and had at least one year of follow up. Children spent 85% fewer days in hospital (mean pre-NPPV 48.0 days, mean post-NPPV 7.0 days) and 68% less days in intensive care after initiation of NPPV (mean pre-NPPV 12.0 days, mean post-NPPV 3.9 days).

(3) Prevention of chest wall deformity - NIV may be effective in preventing chest wall deformity, typically pectus excavatum, which is common in children with severe forms of SMA. The patients with paradoxical breathing seem to develop pectus excavatum if untreated. This is caused by the action of the diaphragm that is not modulated by the intercostal muscles. As the diaphragm contracts, the abdomen expands, and the “bucket-handle” effect of its insertion on the lower ribs causes their outward expansion, and the upper chest wall paradoxically sinks in. This results in a funnel-shaped chest with the xiphoid process retracted and in underdevelopment of the lungs as well. Avoidance of chest wall deformity may preserve larger passive lung volumes in later life. The NIV not only corrects nocturnal hypoventilation, but also corrects asynchronous chest and abdominal movements, preventing longer-term chest wall deformity.

(4) Improve survival - Several studies demonstrate that use of NIV can result in prolongation of life in children with life-limiting NMD. One study described the clinical course of 10 patients with DMD with daytime hypercapnia. Five patients were treated with NIV while the other five not. At the end of 2-year follow up, 4 of the 5 patients who refused the use of NIV had died of respiratory failure, while all 5 of the NIV group were still alive. Two studies described the outcome of children with SMA type 1, all showed improved survival was associated with use of mechanical ventilation. A non-randomized study of 244 patients with kyphoscoliosis reported improved survival with home noninvasive mechanical ventilation compared to long-term oxygen therapy alone, with a hazard ratio of 0.30 (95% confidence interval, 0.18 to 0.51).

The indications for NIV in NMD patients

The child’s clinical condition usually guides the need for institution of intubation and intensive care, but objective tests such as continuous measurement of arterial oxygen saturation and CO2 may help identify the progression of respiratory failure and allow for earlier intervention with NIV. Subjective clinical findings and objective physiologic test are used to determine when NIV is indicated in the management of patients with NMD. Clinical assessment of respiratory health and early recognition of chronic respiratory failure should be part of routine medical consultation for children with NMD, so that intervention can be instituted before a crisis develops. An increase in frequency and severity of respiratory infections is likely to occur with deteriorating muscle strength and careful attention should be given to establishing how these have been managed and whether they have required hospital admission for intensive treatment. The symptoms of nocturnal hypoventilation include disturbed sleep, morning headache, morning anorexia or nausea, daytime sleepiness, fatigue and poor concentration. These symptoms are non-specific and do not reliably predict the presence of nocturnal hypoventilation. Symptoms relating to obstructive sleep apnea may include snoring, and variable patterns of snoring, breathing effort and arousal. When weakness is severe, daytime hypoventilation may occur. The symptoms of daytime hypoventilation are headache, nausea, dyspnea, tachycardia, sweating, peripheral
vasoconstriction or vasodilation, fatigue and anxiety. Once again these are nonspecific. Clinical assessment of respiratory health should be directed towards identifying progressive muscle weakness, ability to cope with respiratory infection, aspiration, progression of scoliosis and sleep-disordered breathing. Once the symptoms of hypoventilation are more and more severe, NIV should be considered to be used.\(^1\)

Using the spirometry to assess the pulmonary function is generally achievable from 6 years of age. The vital capacity, which is determined by inspiratory muscle strength and lung and chest wall compliance, can be reliably measured in almost all weak subjects by using a slow manoeuvre whereby the child is asked to breathe in as deeply as possible and then to breathe out for as long as possible through the spirometer. In one study that included patients aged 8-16 years with a mixed group of muscle disease, vital capacity had the strongest correlation with the number of chest infections and days of antibiotic treatment in the preceding year.\(^39\) The vital capacity can also predict sleep-disordered breathing, nocturnal hypoventilation, daytime respiratory failure (hypercapnia) in patients with neuromuscular disease.\(^40\)-\(^42\) In addition, the vital capacity can predict survival in patients with neuromuscular disease. The maximum vital capacity, rate of decline in vital capacity and current vital capacity all correlated with survival in non-ventilated patients.\(^43\)-\(^45\) The progression of nocturnal hypercapnia and finally daytime hypercapnia usually follows the loss of ambulation, with vital capacity falling by about 180-200ml per year.\(^44\),\(^45\) A vital capacity fell below 1 liter is a predictor of poor outcome, with a 5-year survival rate of only 8% if assisted ventilation is not provided.\(^44\) Vital capacity should be measured in all patients with neuromuscular disease who are capable of performing spirometry as part of the respiratory assessment. Once the decline of vital capacity is found during the spirometry examination, intervention with NIV is needed.

Daytime hypercapnia indicates hypoventilation during wakefulness; children with daytime hypercapnia will also have nocturnal hypoventilation. A daytime blood gas sample showing a raised plasma bicarbonate level may indicate the presence of nocturnal hypercapnia. The daytime PaCO\(_2\) correlated strongly with total sleep time with oxygen saturations below 90% and a daytime PaCO\(_2\) >45 mmHg predicted nocturnal hypoventilation with a 91% sensitivity and 75% specificity.\(^46\) Once daytime hypercapnia develops, life expectancy without ventilatory support is approximately 9-10 months.\(^33\) Having demonstrated the benefits, subjective clinical findings, and objective physiologic test, the indications of NIV support for patients with NMD are as follow:

1. Prevent respiratory decompensation and rest respiratory muscle
2. Alter chest wall or lung growth characteristics
3. Severe or frequent lower respiratory infection
4. Control nocturnal hypoventilation
5. Nocturnal hypercapnia, high PaCO\(_2\) (>45 mmHg)
6. Decline of the vital capacity (VC decrease 180-200ml/year or VC< 1L)
7. Palliate symptoms or end-of-life care

### Monitoring NMD children using NIV

Initial monitoring should focus on patient acceptance of the device, problems encountered, number of hours of use, and symptoms of hypoventilation. The primary purpose of NIV is to correct hypoventilation, hypercapnic respiratory failure and the associated symptoms, so measurement of CO\(_2\) is important to the recognition of respiratory failure and adequacy of intervention. Once the child is able to tolerate NIV throughout the night, monitoring should be carried out to check that hypoventilation has been abolished. It is unrealistic to expect improvements in symptoms or gas exchange until the patient is using the device at least four to five hours nightly, so initial monitoring of gas exchange is performed primarily to assure stability. It is advisable to measure SaO\(_2\) and either transcutaneous PCO\(_2\) or end-tidal CO\(_2\) in the presence of moderate or severe progressive respiratory failure. The minimum requirement is a sleep study recording continuous oximetry and capnography.\(^1\) The ventilator settings should also be adjusted and rechecked as necessary. The frequency at which further monitoring should be carried out depends on the clinical condition. Newly diagnosed patients or those with profound muscle weakness should be seen initially every few weeks for assessment of symptoms, and for measurement of vital signs and daytime arterial blood gases. In stable
children with slowly progressive or non-progressive disease, annual assessment is sufficient.

Air leaks are found in all patients when delivering ventilation via mask and are a common reason for NIV to be ineffective and to be poorly tolerated.\textsuperscript{47,48} The air leak can be minimized by careful mask selection. Mouth leaks when using a nasal mask can be reduced either by a chin strap or by switching to a full face mask.

\textbf{When should tracheostomy be considered?}

With currently available ventilators and mask interfaces, NIV is the mode of choice for the vast majority of children with NMD needing respiratory support during sleep. In patients whose respiratory insufficiency is not adequately addressed by noninvasive ventilation, the decision of receiving tracheostomy should be taken into consideration. The indications for tracheostomy in NMD patients include:\textsuperscript{1}

1. Severe bulbar dysfunction
2. Failure to extubation
3. Require ventilation more than 16 hrs. per day
4. Failure to correct hypoxemia or hypercapnia with NIV
5. Severe mid-face hypoplasia.

When there is severe bulbar dysfunction resulting in frequent aspiration, tracheostomy may be necessary to allow more effective airway clearance. After an acute exacerbation has led to a period of invasive ventilation and extubation has failed despite optimal management for 2 weeks or more, tracheostomy is indicated for further respiratory support and to reduce complication of prolong intubation. Once the NIV cannot correct the nocturnal hypoventilation nor improve oxygenation, the tracheostomy should also be considered.

The preference of the care givers and patients and the experience of the clinical team needs to be taken into account when considering tracheostomy. Tracheostomy has the advantage of leaving the face free, making eating easier and providing direct access for suction. It also provides a more secure interface for patients who are ventilator dependent. However, adverse effects of tracheostomy include increased respiratory secretions and respiration infections, dysphagia, granuloma formation and tracheo-arterial fistulas with catastrophic hemorrhage.\textsuperscript{49,50} Most of these problems can be minimized by using a well-fitting flexible tracheostomy tube and centering in the tracheal lumen.

\textbf{CONCLUSION}

Neuromuscular disease may lead to respiratory compromised and failure and it also causes multiple complication. Once the symptoms are severe or the progression of respiratory insufficiency is identified, noninvasive ventilation is indicated to improve symptoms, to reduce frequency of admission, and to prolong survival. While NIV cannot correct the nocturnal hypoventilation nor improve oxygenation, the tracheostomy should be considered after fully discussion with family and patient.

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