Assessment and Management of Patients with NeuromuscularWeakness

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KEY POINTS

- The progressive weakness of respiratory muscles predisposes neuromuscular disease patients to recurrent chest infections, aspiration, sleep-disordered breathing, and ultimately respiratory failure
- Patient may have hypoventilation, disrupted sleep, nocturnal oxyhemoglobin desaturation, and eventually develop hypercapnia
- Muscle weakness may be assessed by spirometry, maximal inspiratory and expiratory pressure, peak cough flow, sniff nasal inspiratory pressure, and assessment of end-tidal CO_2 by capnography
- Respiratory management of patients with neuromuscular weakness consists of airway clearance, management during acute infections, perioperative care, and management of chronic respiratory failure
- Non-invasive positive pressure ventilation at nighttime allows them to rest their fatigued respiratory muscles and improve their lung and chest wall mechanics by reducing microatelectasis and increasing chest wall excursion

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INTRODUCTION

Neuromuscular disorders (congenital and acquired) are common causes of weakness and hypotonia among infants and children. Finding out the specific aspect of the peripheral neuromuscular system (either the motor neuron in the spinal cord, the nerve root or peripheral nerve, the neuromuscular junction or the muscle) that is affected can help to determine the etiology and specific clinical diagnosis. Commonly encountered neuromuscular diseases in childhood include Duchenne muscular dystrophy (DMD), spinal muscular atrophy (SMA), myotonic dystrophy, congenital myopathies, congenital muscular dystrophies (CMDs), and acquired and congenital myasthenic syndromes.

Among all neuromuscular diseases in childhood, DMD is the most common muscular dystrophy followed by SMA.

DUCHENNE MUSCULAR DYSTROPHY

Duchenne muscular dystrophy is an inherited muscle disorder caused by defective expression of the protein dystrophin. The disorder is inherited in an X-linked, recessive pattern and primarily affects boys. Incidence ranges from 1 in 3,600–4,700 live male births[1] making it the most common form of muscular dystrophy in children.[2] It is characterized by progressive symmetric proximal muscle weakness (difficulty climbing stairs) and gait disturbance (waddling, toe walking, and lordotic posture), with onset in early childhood.[3] Majority of DMD patients become wheelchair bound between ages 9 years and 12 years. Cardiorespiratory complications (dilated cardiomyopathy, respiratory failure) appear during the second decade and eventually lead to death.[4] Glucocorticoids such as prednisolone and deflazacort are the first-line therapy in the treatment of DMD.

SPINAL MUSCULAR ATROPHY

Spinal muscular atrophy is an autosomal recessive genetic disorder that occurs due to mutations in the survival motor neuron gene 1 (*SMN1*). It is the second most common pediatric neuromuscular disorder, with an estimated frequency of 8 per 1,00,000 live births.[5] The pathologic hallmark of SMA is the degeneration of the anterior horn cells of the spinal cord, which causes symmetrical muscle weakness and atrophy. It has been classified into four subtypes (I–IV) based on the age of onset of symptoms. With SMA type I (Werdnig-Hoffman disease), the onset of symptoms may occur at birth or in the first few months of life, and there is a rapid, severe, and progressive muscle weakness that results in an inability to sit without support for these infants. The infantile/intermediate form (type II) has onset during the second half of infancy and again has a severe, progressive course where the affected children are able to maintain the ability of sitting without support, but are unable to walk. The course is heterogeneous for type III or juvenile form (Kugelberg-Welander disease) of SMA, which has its onset beyond the second year of life, when the child has generally achieved independent walking. Over time, these affected children may or may not maintain the ability to walk without support. Similar to the pattern of type III SMA, the type IV or adult-onset clinical form of SMA is also clinically

heterogeneous with a much later age of onset. Progressive respiratory muscle weakness associated with a restrictive pattern is the most common and most serious life-limiting complication in SMA.

MYOTONIC DYSTROPHY

The autosomal dominant myotonic dystrophy (Steinert disease) is the most common form of muscular dystrophy in adults. The amplification of a trinucleotide repeat—CTG—is the genetic defect that causes the disease. Clinical severity depends on the number of repeats. The congenital form of myotonic dystrophy is classically related to a maternal transmission and shows the greatest number of repeats. Myotonic dystrophy is characterized by progressive muscle wasting and weakness. Patients with this disorder often have prolonged muscle contractions (myotonia) and are not able to relax certain muscles after use. Also, affected patients may have slurred speech or temporary locking of jaw. In the congenital form, polyhydramnios and reduced fetal movements are often reported. Facial diplegia and dysmorphic craniomandibular structures contribute to increase in the respiratory difficulty. More than 50% of the babies who survive have speech difficulties, learning disabilities, or mental retardation. Characteristic myotonia and systemic organ involvement typically develops by the second decade of life.

CONGENITAL MYOPATHIES

Congenital myopathies are rare genetic neuromuscular disorders affecting infants and young children. Common congenital myopathies include central core disease (RYR1 mutations), nemaline rod myopathy (NEB, ACTA mutations), and centronuclear myopathy [myotubular myopathy (MTM), dynamin 2, BIN1 mutations]. Children with X-linked MTM are very weak at birth and have myopathic facies, high arched palate, lack of antigravity muscle strength, and need breathing and feeding assistance. Majority of these babies die in first year of life without respiratory and pulmonary support. Central core and nemaline myopathies have spectrum of muscle weakness with mild-to-severe myopathy. The diagnosis of congenital myopathies is suspected in infants with weakness of the face and proximal muscles with failure to thrive and recurrent pneumonias due to bulbar and respiratory muscle weakness. Muscle biopsy is done to confirm the diagnosis, and genetic testing is available.

CONGENITAL MUSCULAR DYSTROPHIES

Congenital muscular dystrophies refer to a genetically and clinically heterogeneous group of autosomal recessive disorders that begin in the perinatal period or during the first year of life. Proteins commonly responsible for CMDs are either involved in glycosylation processes or are structural components of the extracellular matrix.[6] It is characterized by congenital hypotonia and slowly progressive muscle weakness. The muscular involvement may be isolated or included within a spectrum of central nervous system and eye involvement.[7] The most common forms of CMD are collagen VI-deficient CMD, laminin α2 deficiency, and secondary dystroglycanopathies, followed by forms with rigid spine and early respiratory involvement, such as *SEPN1*-related CMD

(previously known as rigid spine syndrome) and *LMNA*-related CMD.[6] Multidisciplinary care by experienced teams is important for diagnosing and promoting the health of children with CMD. Accurate assessment of clinical presentations and genetic data help in identifying the correct subtype-specific diagnosis. Multiorgan system complications occur frequently; surveillance and prompt interventions are likely to be beneficial for affected children.

MYASTHENIC SYNDROMES

Congenital myasthenic syndromes are genetic disorders present in infancy and childhood with breathing difficulty, ptosis, stridor, and failure to thrive.[8] These babies are often misdiagnosed and myopathies, however, the muscle enzymes and muscle histology is normal or nonspecific. Electrodiagnostic testing in the form of electromyography (EMG) or nerve conduction study and specialized genetic testing is required to confirm the diagnosis. Depending on the level of defect in the neuromuscular junction (presynaptic, synaptic, and postsynaptic), the treatment is tailored although respiratory and gastrointestinal support is a norm in all congenital myasthenic syndrome kids.

Acquired myasthenia gravis is autoimmune in nature and range from mild ocular myasthenia gravis to generalized myasthenia gravis. Children can have bulbar symptoms and breathing difficulty especially during myasthenia gravis crisis or exacerbations. Close respiratory monitoring with simple spirometry and overnight sleep study to evaluate for hypoventilation is helpful in preventing respiratory compromise. Symptoms of weakness can be well controlled in myasthenia gravis kids with pyridostigmine, steroids, intravenous immunoglobulin, and/or plasma exchange/thymectomy.

RESPIRATORY ISSUES IN CHILDREN WITH NEUROMUSCULAR WEAKNESS

Respiratory muscle weakness is common in above-mentioned neuromuscular diseases. The progressive weakness of respiratory muscles exposes these patients to recurrent chest infections, sleep-disordered breathing, and ultimately respiratory failure. In addition, neuromuscular patients have hypoventilation, disrupted sleep, nocturnal oxygen desaturation, and eventually develop hypercapnia. The introduction of non-invasive ventilation, assisted cough methods, nutritional support, and coordinated multidisciplinary care has led to improved survival outcomes in neuromuscular patients in recent decades.[9-11]

The following discussion focuses on detailed respiratory management of neuromuscular disorders:

Assessment of Respiratory Muscle Strength

With progression of the neuromuscular weakness, there is increasing incidence of respiratory complications, which can be monitored and treated appropriately in consultation with a pulmonologist. This requires periodic assessment of respiratory status and objective measurement of respiratory muscle strength that can be done through several testing methods. The general indications for respiratory muscle strength testing include patients with neuromuscular disorders, patients with unexplained respiratory failure, those with chronic lung

disorders or restrictive defect noted on pulmonary function testing. The techniques for assessment of respiratory muscle strength are as discussed below:

Spirometry

This is one of the most widely available measures of lung function, and can be easily performed in most clinics. Patients with neuromuscular weakness demonstrate a restrictive pattern [low forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) with a normal FEV_1/FVC ratio; small flow volume loop] on spirometry, and their FVC is generally maintained until they remain ambulatory. As they lose ambulation, there is a steady decline in FVC but the rate of decline may vary between individuals and depending on the underlying disorder. Performing spirometry in sitting position is recommended annually to track changes over time. For patients with FVC less than 80% predicted, a measurement should also be performed in supine position. A drop in FVC by more than 20% in supine position indicates diaphragmatic weakness, and these patients may also exhibit dyspnea in the supine position as well as paradoxical breathing. As the primary disease progresses and their FVC falls below 50%, there is risk of development of nocturnal hypoventilation—this risk is higher for patients that have FVC less than 40% and coexisting diaphragm weakness as well. Additional tests to measure lung volumes by body plethysmography may be performed to measure static lung volumes, which can help confirm the restrictive pattern seen on spirometry. Since assessment of lung function requires accurate height measurement, it may not be feasible for patients that are nonambulatory or those who have significant joint contractures or scoliosis. Use of forearm length or ulnar length can be used to estimate their standing height using the following equations:

$$\text{Standing height} = 3.497 \times \text{forearm length} + 9.595$$
$$= 6.332 \times \text{ulna length} + 1.157$$

Ulnar length is measured by placing the left forearm across the patient's chest with left hand touching/pointing towards the right shoulder. The distance between the bony point of the elbow and the bony point at the wrist on the lateral aspect is measured with a tape measure to calculate ulnar length. Arm span can also be measured as an alternative but may sometimes be limited by contractures and the need for two people for accurate measurement.

Maximal Inspiratory and Expiratory Pressures

Measurement of maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) can be performed using simple equipment that can be useful for serial assessment of the strength of inspiratory and expiratory muscles over time. It is important to use a rubber mouthpiece (Fig. 1) with flanges to allow the patient to form a tight seal with their lips and prevent leaks. To prevent artifacts from use of cheek muscles during testing, there is usually a small opening in the tubing. For MIPs, the patient takes a deep inspiration from residual volume and is asked to sustain the inspiratory effort for at least 1–1.5 seconds. The measurement is recorded for each effort and it is recommended to wait for one minute between efforts. Similarly, for MEPs, the patient is asked to inhale to total lung capacity and then forcefully exhale into the mouthpiece
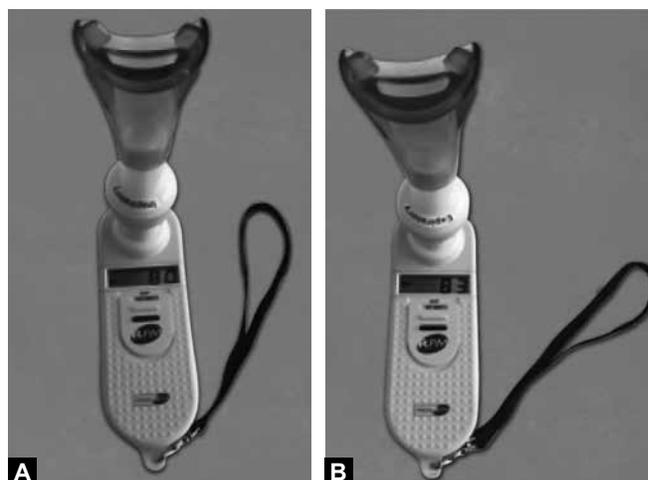

Fig. 1: Equipment for measurement of maximal inspiratory pressure and maximal expiratory pressure

while sustaining expiratory effort for at least 1.5 seconds. The maximum-recorded value is reported and the goal is to have variability of less than 10 cmH_2O between individual measurements. It is important to remember that MIPs and MEPs are dependent on lung volumes due to the length-tension relationships of the respiratory muscles. Any rib cage deformities (such as scoliosis) can affect the performance and results of these tests.

Peak Cough Flow

Cough is an important protective reflex that is essential for airway clearance and comprises of three phases:
1. Inspiratory phase: Where a large, rapid inspiration helps to stretch out the expiratory muscles and expand the rib cage
2. Compressive phase: Where the glottis is closed and expiratory muscles start contracting to increase intrathoracic pressure
3. Expiratory phase: Where sudden glottic opening is accompanied by high expiratory flow rates that mobilize airway secretions by shear force to more proximal segments.

Children with neuromuscular weakness have limited ability to inhale deeply (due to inspiratory muscle weakness), have reduced ability to generate enough expulsive expiratory force to clear their own secretions and thus remain at risk for atelectasis. Measurement of peak cough flow is, therefore, a measure of both inspiratory and expiratory muscle strength and can be used in conjunction with pulmonary function tests to decide when patients might need assistance with airway clearance and the rate at which their disease is progressing. Generally, a peak cough flow measurement can be done in clinic with a peak expiratory flow meter with a filter attached, along with nose clips to block flow of air through the nostrils. There are some commercially available devices that can record the flow signal digitally, but the simple set up described above (as shown in Fig. 2) can be alternative as well. Values of peak cough flow less than 270 L/min signify the need for airway clearance therapies in postoperative period or during an acute respiratory illnesses. However, as the disease progresses and the peak cough flow drops below 160 L/min, most patients need daily airway clearance to maintain patency of their airways and prevent atelectasis.
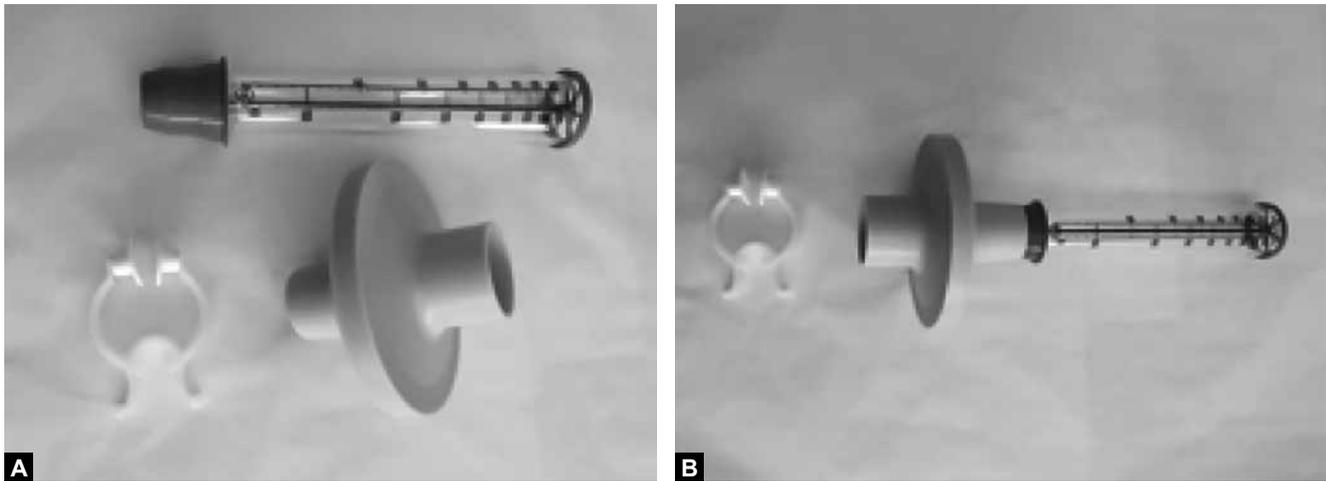
Fig. 2: Assembly of equipment for measurement of peak cough flow

Sniff Nasal Inspiratory Pressure

The sniff maneuver can be used as an adjunctive measure of inspiratory muscle strength, particularly for children with significant facial muscle weakness that does not allow them to hold the mouthpiece used for MIPs and MEPs with a good seal. The child is asked to occlude one nostril and sniff with maximal effort from the open nostril from functional residual capacity. The best of three measurements is generally reported and normal values for children between the ages of 6 years and 17 years range from 104 ± 26 cmH$_2$O in boys, and 93 ± 23 cmH$_2$O in girls. For patients with motor neuron disease, sniff nasal inspiratory pressure values of less than 40 cmH$_2$O are predictive of nocturnal hypoventilation. However, it can sometimes underestimate the true inspiratory muscle strength, as it is a voluntary maneuver, and there can be some dampening of the transmission of pressure to the upper airway. Nevertheless, it remains a useful adjunctive measure, as it is a short maneuver and can be easily performed in outpatient setting with minimal equipment.

Assessment of End-tidal Carbon Dioxide by Capnography

This assessment is important for detection of daytime hypoventilation leading to persistently elevated partial pressure of carbon dioxide (pCO$_2$) and may signify the need for step-up of respiratory support. The measurement can be done in clinic with the help of a portable device (Fig. 3) that can be used with nasal cannula interface or with an inline connector for patients with tracheostomy with or without mechanical ventilatory support. The measured values are generally closely correlated with blood gas values of pCO$_2$, with a variation of ± 5 mmHg, depending on the device. For any abnormal values that are greater than 45 mmHg, it is always useful to obtain a simultaneous blood gas to confirm the results.

Less Commonly used Invasive Tests

In some instances, additional testing can be performed for assessment of respiratory muscle strength of patients (e.g., those in intensive care unit setting) that are unable to perform some of the tests listed above. Measurement of transdiaphragmatic pressure using a nasogastric catheter with

Fig. 3: Portable device for measurement of end-tidal CO$_2$

esophageal and gastric pressure transducers or surface EMG of respiratory muscles can be used to monitor the activity of the diaphragm or intercostal muscles. Phrenic nerve conduction may be tested by electrical or magnetic stimulation to calculate latency time that can be useful to measure for patients with diaphragm weakness.

Assessment of Nocturnal Hypoventilation

With progression of respiratory muscle weakness, the patients may start to report early morning headaches, daytime sleepiness, fatigue, or decreased activity level. These may be signs of nocturnal hypoventilation that may not be clinically noticeable in clinic but can be predicted on the basis of lung function and other measures listed above. The initial changes occur in rapid eye movement (REM) sleep where the drops in oxyhemoglobin saturations cause arousal from sleep to limit the extent of desaturation or cause a rise in pCO$_2$. Over time, progressive loss of REM sleep occurs which causes daytime somnolence and the body begins to tolerate more extreme changes in blood gases. As periods of hypoventilation become longer, the rise of bicarbonate in cerebrospinal fluid in compensation for elevated pCO$_2$

cause further suppression of the respiratory drive. This may be undetected for some time until the patient gets an intercurrent viral illness that precipitates acute respiratory failure and is found to have abnormal blood gases. Once nocturnal hypoventilation is suspected or when FVC drops below 50% predicted, it is useful to get a polysomnography (sleep study) with measurement of end-tidal CO_2 levels to document the presence of elevated pCO_2 during sleep. Thereafter, it should be repeated at least annually to continue to monitor the progression of the primary neuromuscular disease or to assess the effectiveness of noninvasive ventilatory support, if needed. Generally, an increase in partial pressures of carbon dioxide levels by more than or equal to 10 mmHg during sleep when compared to daytime pCO_2 or supine levels signifies nocturnal hypoventilation. End-tidal CO_2 levels measured during a sleep study that remain more than 45 mmHg for more than 25% of total sleep time also suggest nocturnal hypoventilation.

Follow-up Assessment

The use of a proactive approach in monitoring and treating patients with neuromuscular weakness using a structured multidisciplinary program in consultation with a pulmonologist can help prevent and manage respiratory complications in a timely manner. The traditional reactive approach does not allow timely detection of respiratory failure in these patients and can cause significant morbidity that can be prevented. Using DMD as a template, the follow-up assessment and management of patients with various causes of neuromuscular weakness can be done along the same lines.

For prevention of recurrent respiratory illnesses, yearly immunization with influenza vaccine is recommended for all patients, and one dose of the 23-valent-pneumococcal vaccine should be given to all patients above the age of 2 years. For patients that are on long-term steroid therapy, it is important to recognize that these vaccines can be given (as they are not live vaccines) but their effectiveness may be slightly reduced. Most nonambulatory patients should be seen by a pulmonologist every 3–6 months depending upon the severity of their respiratory muscle weakness and the need for monitoring of respiratory muscle strength. Regular testing of lung function and respiratory muscle strength can be done as per the timeline in table 1.

RESPIRATORY MANAGEMENT OF PATIENTS WITH NEUROMUSCULAR WEAKNESS

Several key aspects in the long-term respiratory care of patients with neuromuscular weakness are addressed by a pulmonologist working as part of a multidisciplinary team that is involved in the care of these patients.

Airway Clearance

Airway clearance is of paramount importance for preventing both acute and chronic respiratory complications in patients with neuromuscular weakness. Manually assisted cough is a technique that can be performed by giving an abdominal thrust into the upper abdomen of the patient in coordination with patient's own expiratory phase of coughing. However, it may not be very effective for patients with inspiratory muscle weakness as they may not be able to generate enough lung volumes after inspiration to provide effective airway clearance with the use of this technique alone. It can be combined with hyperinflation maneuvers (such as breath stacking, glossopharyngeal breathing) that help to increase inspiratory tidal volume. Breath stacking occurs when the next inspiration is provided with a ventilator or resuscitation bag before the expiratory phase has completely ended. Glossopharyngeal breathing involves taking gulps of air into the airways to allow patients to achieve breath stacking on their own.

Most patients will benefit from the use of mechanical insufflator-exsufflator device (also known as CoughAssist), which is a mechanical device for airway clearance (Fig. 4). It delivers a breath at a preset pressure, followed by a brief pause (for allowing recruitment of distal airways) and then a rapid exsufflation (sucking out of air) at a preset negative pressure to allow the secretions from the airways to be mobilized by shear force. This device mimics the action of a natural cough, but augments the patient's own weak coughing efforts and helps overcome their inability to clear their secretions. It is generally used on a daily basis for patients with neuromuscular weakness, but can be used as frequently as desired if the patient has an acute respiratory tract infection or increased secretions. For patients with a tracheostomy, this device can still be used with an adapter that attaches its tubing to the opening of the tracheostomy tube. Other secretion mobilization devices such as high frequency chest wall oscillation or intrapulmonary percussive ventilation can also be used in the hospital during

TABLE 1: Timeline for follow-up of patients with Duchenne muscular dystrophy		
Patient status	**Measurements performed**	**Frequency**
Ambulatory patient 6 years of age and older	• Sitting forced vital capacity (Spirometry)	At least annually
Nonambulatory patients	• Oxyhemoglobin saturation • Sitting forced vital capacity • Peak cough flow • Maximal inspiratory and expiratory pressures	At least every 6 months
Nonambulatory and any of the following: • Suspected hypoventilation • Forced vital capacity <50% predicted • Current use of assisted ventilation	• Awake end-tidal carbon dioxide level by capnography	At least annually

Fig. 4: CoughAssist device (mechanical insufflator-exsufflator)

an acute illness or atelectasis. Postural drainage can also be utilized for non-ambulatory patients to improve drainage of secretions by gravity in conjunction with the above-mentioned techniques.

Management during Acute Infections

During any acute respiratory infection, most children with neuromuscular weakness have excessive buildup of secretions in their airways and will need additional interventions to manage them. Some patients may develop acute respiratory acidosis and may benefit from short-term use of non-invasive ventilatory support, such as bilevel positive airway pressure (BiPAP). For patients that are already receiving nocturnal BiPAP support, their respiratory support may have to be extended to the daytime as well, either with continued noninvasive support, or in more severe cases, with intubation and mechanical ventilatory support. However, decisions to escalate respiratory support should be made with careful considerations of the patient's underlying diagnosis, prognosis, parental wishes regarding level of interventions to be performed and the likelihood of successful weaning off the escalated level of support once the acute respiratory illness is resolved. Supplemental oxygen should be used with caution in the setting of an acute respiratory illness as it may help correct the hypoxemia but may not provide relief for hypoventilation or atelectasis, which may have caused the hypoxemia. Provision of positive pressure support will help ensure adequate gas exchange, thereby reducing hypercarbia and respiratory acidosis. Monitoring of blood gases or end-tidal CO_2 is helpful in guiding respiratory support during acute illnesses. Many patients with significant muscle weakness may fail extubation after recovery as their respiratory muscles may be further weakened during their critical illness. In those patients, extubation to BiPAP or continuous positive airway pressure (CPAP) can help them transition to their previous baseline state as they improve and recover some of their strength.

Acute respiratory illnesses due to common viruses tend to cause respiratory muscle weakness, and most studies have shown benefits of use of noninvasive respiratory support in the short term. Combined with aggressive use of airway clearance therapies, most patients can be managed at home during minor acute illnesses, but more severe infections or patients with profound respiratory muscle weakness may require hospitalization for the management of these episodes. Prevention of infections by ensuring adequate immunizations (yearly influenza vaccinations, 23-valent pneumococcal vaccination after age of 2 years for all patients) and preventing contact with other household members with an acute respiratory illness can help reduce the number of such illnesses in patients with neuromuscular disease.

Perioperative Management

Children with neuromuscular weakness are especially vulnerable to the physiologic changes in lung ventilation and perfusion and other adverse effects of sedation and general anesthesia. Preoperative assessment of their respiratory status (including assessment of lung function, respiratory muscle strength, and adequacy of gas exchange) may have to be done in consultation with a pulmonologist to prevent any intra- and postoperative complications. It is preferable to use total IV anesthesia technique for induction and maintenance of general anesthesia (using propofol and short-acting opioids). The use of depolarizing muscle relaxants such as succinylcholine is contraindicated for patients with DMD due to the risk of development of fatal reactions. Patients with FVC less than 50% predicted will generally require assisted or controlled modes of ventilation during induction and recovery and also during procedural sedation. Intraoperative monitoring of oxygenation and end-tidal CO_2 levels can help guide their respiratory support. During the recovery phase, most patients (especially those with FVC less than 50% predicted) will benefit from short-term use of noninvasive ventilatory support (such as BiPAP) until the effect of the anesthesia wears off and the patient is back to baseline respiratory status. Postoperative airway clearance and suctioning should be continued with CoughAssist device or other airway clearance techniques to prevent atelectasis. For those patients with significant postoperative pain, adequate pain control, and extension of respiratory support (invasive or non-invasive) for another 24–48 hours after the procedure will help ensure safe recovery. The use of opioids may predispose these patients to constipation and it is important to provide an appropriate bowel regimen to prevent and treat constipation. Placement of a nasogastric tube for gastric decompression and to initiate small volume enteral feeding may be necessary, unless contraindicated due to the procedure or patient's status (in which case parenteral nutritional support should be initiated if feeding is delayed for >24–48 hours postoperatively).

Chronic Respiratory Failure and Its Management

For patients with pump failure as in the case of neuromuscular weakness causing hypoventilation and chronic respiratory failure, the use of noninvasive positive pressure ventilation (NIPPV) at night-time allows them to rest their fatigued respiratory muscles and improves their lung and chest wall mechanics by reducing microatelectasis and increasing chest wall excursion; and also helps to reset their central chemoreceptor sensitivity to the chronically elevated pCO_2. The decision to initiate night-time NIPPV support is based upon significant reduction of respiratory muscle strength (FVC

<30% predicted), baseline oxyhemoglobin saturation <95% or awake pCO_2/end-tidal CO_2 >45 mmHg; or if a sleep study shows an apnea-hypopnea index >10/hour, four or more episodes of oxyhemoglobin saturation <92%, or drops in oxyhemoglobin saturation of at least 4% per hour of sleep.

A wide variety of oronasal interfaces (nasal prongs, nasal masks, oronasal masks, and total face mask), circuits (single limb or double limb for inhalation and exhalation), and devices with a variety of modes are now available. Continuous positive airway pressure may be used for patients with acute illness who have not been on prior respiratory support as it helps to stent open their airways with the continuous positive pressure and maintains adequate airflow. However, BiPAP may be preferable in patients with significant hypoventilation where the higher inspiratory positive airway pressure (IPAP) ensures adequate lung expansion and air entry, and the subsequent lower expiratory positive airway pressure (EPAP) ensures adequate exhalation at a lower pressure. There are three different modes that are commonly used with BiPAP, which include:

Spontaneous (S): Where the patient's own inspiratory effort triggers the device and cycles it to EPAP.

Timed (T): The cycling between IPAP and EPAP is timed by the machine based on the rate of breaths/min set up on the machine.

Spontaneous/timed (S/T): Similar to the spontaneous mode, the device is triggered by the patient's inspiratory effort. However, there is a back-up rate that is set to ensure that if the patient does not take enough spontaneous breaths/min, then the machine provides the minimum back-up rate that has been set.

Complications from NIPPV include facial skin breakdown or necrosis due to repeated pressure (especially on bridge of nose), gastric insufflation (especially in patients with esophageal reflux), sinus problems, drying and thickening of oral secretions, and eye irritation from airflow leaks from mask. Barotrauma from NIPPV is less likely as the peak pressures usually never go beyond 25 cmH$_2$O and over distension generally activates the Hering-Breuer inflation reflex. Aspiration from vomiting while wearing a pressurized face mask can be avoided with careful selection of patients for NIPPV (avoiding use in patients with abdominal disorders and those who are obtunded/unable to protect their airways).

As their disease and muscle weakness progresses, most patients with chronic respiratory failure will require continuous positive pressure ventilation. This may become apparent when the patient either self-extends their night-time support into daytime, has persistently elevated end-tidal CO_2/pCO_2 during the daytime, is unable to speak in sentences when off support, or has abnormal swallowing due to dyspnea that is relieved by ventilatory assistance. At that time, placement of a tracheostomy tube may sometimes become necessary to provide a secure, long-term access to the airway. The decision for a tracheostomy is based on need for ventilatory support round the clock, especially if they are not suitable candidates for or have failed non-invasive ventilatory support, or have had three or more extubation failures despite use of noninvasive ventilation and CoughAssist in

the postextubation phase. It may be acceptable to use round-the-clock noninvasive support for short periods of time after extubation, if it is expected that the patient's recovery from acute illness will allow them to resume night-time support only. However, treatment planning in such instances has to be individualized based on several factors such as patient and parental preferences, availability of infrastructure and personnel to support noninvasive ventilatory support, and/or clinician preferences.

OTHER CLINICAL PROBLEMS IN CHILDREN WITH NEUROMUSCULAR WEAKNESS THAT HAS AN IMPACT ON THEIR RESPIRATORY STATUS

Kyphoscoliosis

Most non-ambulatory patients with neuromuscular weakness develop progressive curvature of the spine due to their low truncal muscle tone and gravity. Involvement of the thoracic spine in the curvature causes deformity of the chest wall and reduces chest wall compliance. This restrictive defect adds an extra load on the respiratory muscles that progresses as the degree of curvature worsens over time. The unequal lung expansion because of this deformity can predispose to the development of atelectasis on the concave side, and overexpansion of the lung on the convex side, leading to ventilation-perfusion mismatch. Use of a brace should be considered for most nonambulatory patients with milder degrees of kyphoscoliosis, but for those with more advanced curvature, surgical interventions (such as posterior spinal fusion) may have to be considered. However, it is important to consider the significant risk of any such major surgical procedure versus the benefit in terms of improving their respiratory status before planning such an intervention.

Recurrent Aspiration

Patients with neuromuscular weakness who have bulbar involvement or have developed severe gastroesophageal reflux may be prone to recurrent episodes of aspiration that could further compromise their respiratory status. Periodic assessment of swallowing function may be necessary for patients with neuromuscular weakness that continue to develop recurrent atelectasis or pneumonias despite optimal use of airway clearance techniques and respiratory support.

Poor Nutritional Status

Many patients with neuromuscular weakness tend to have poor nutritional status, which further compromises their respiratory muscle strength. This can be especially important during an acute illness when they are on invasive mechanical ventilatory support or have prolonged stays in the intensive care unit. It is important to pay close attention to optimizing their nutritional status (both for acute illnesses and long-term management) as it can impact their rate of recovery of muscle strength. Patients with DMD who are on long-term steroid therapy may show excessive weight gain which can further impact their mobility, and chronic steroid use may also have an effect on their muscle mass.

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