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David Zielinski & Reshma Amin on behalf of the CTS Pediatric Home Ventilation Guidelines Panel

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Section 8: Muscular dystrophies and home ventilation

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Introduction and review of the muscular dystrophy types

Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is the most common muscular dystrophy and is present in about 1 in 3600 to 6000 newborn males.\textsuperscript{1}

Respiratory function typically peaks during the pre-adolescent period\textsuperscript{2} and then declines by approximately 5–8% each year in the adolescent.\textsuperscript{5–8} Nocturnal events in patients with DMD initially consist of obstructive events without hypercapnia, followed by central and hypopneic events associated with hypercapnia. These events are first seen during REM sleep but will progress to other sleep states and waking periods as the disease progresses.\textsuperscript{9} Once significant signs of end-stage disease are present, such as a vital capacity less than 1 L, death from respiratory failure typically follows within 3 years (5-year survival of 8%).\textsuperscript{10} Furthermore, when daytime hypercapnia develops, survival without respiratory support decreases to <12 months.\textsuperscript{11} Death usually occurs due to respiratory failure around the age of 20. Respiratory failure and infection are the most common causes of morbidity and mortality in this population, but cardiomyopathy can also be a significant contributor in dystrophinopathies.

Currently, the natural history and progression of DMD has been altered with the advent of respiratory ventilatory support (reviewed in this section), airway clearance supports (reviewed in Section 4) and medical treatments with cardio-support (reviewed in this section), airway clearance supports has been altered with the advent of respiratory ventilatory support decreases to \textless\textsuperscript{12} months.11 Death usually occurs due to respiratory failure around the age of 20. Respiratory failure and infection are the most common causes of morbidity and mortality in this population, but cardiomyopathy can also be a significant contributor in dystrophinopathies.

When should long-term home ventilation be initiated? A total of 2414 citations were found and abstracts were scanned. A total of 153 articles meeting inclusion criteria (Tables 2–4) were reviewed, including articles identified through references in key articles. This section will largely focus on long-term ventilation for children with muscular dystrophies. For a complete review of the pulmonary management of children with neuromuscular disease, please see the American and British Thoracic Societies as well as the DMD Care Considerations Working Group guidelines.\textsuperscript{1,23–25}

Question 1: Is there a benefit from the initiation of ventilatory support in muscular dystrophies?

Survival

The only randomized controlled trial studying preemptive initiation of noninvasive ventilation (NIV) in DMD was stopped prematurely due to increased mortality in the treatment arm. Raphael et al\textsuperscript{26} randomized patients with FVC 20% to 50% predicted, normal arterial oxygenation (paO2 > 60 mm Hg) and ventilation (PaCO2 < 45 mm Hg) to receive NIV or to be followed clinically. The intervention...
group received a median tidal volume of 15 ml/kg with a rate of 17 breaths per minute for a mean of 7 hours/day. Eight of the 35 patients in the NIV group died as compared with 2 out of 35 in the control group. The majority of deaths were due to retained secretions and acute respiratory failure, and occurred in the home setting. The authors suggested that the NIV may have provided a false sense of security and delayed the seeking of medical attention. This study has been criticized for 1) measuring daytime but not nocturnal CO2, suggesting that NIV may not have really been prophylactic; 2) inadequate airway clearance management; 3) suboptimal anticipatory follow-up, all of which could have contributed to the poor outcome.27,28 Overall, this study suggests that initiation of NIV should be done in conjunction with airway clearance techniques and routine respiratory follow-up.

A second randomized controlled trial included a heterogeneous neuromuscular population including DMD, CMD, spinal muscular atrophy 2, and other neuropathies as well as children with chest wall abnormalities with evidence of nocturnal hypoventilation. Children were randomized to the initiation of ventilation versus current clinical care. Although there were no differences in survival, 9 out of 10 individuals in the control group developed daytime hypercapnia during the 24-month follow-up period and were started on NIV.29 This suggests that without ventilatory support after the development of nocturnal hypoventilation, daytime hypercapnia will develop within two years.

In a non-randomized controlled study, Vianello et al. compared five individuals with DMD and respiratory failure who were initiated on long-term ventilation with five who refused ventilatory support. Four of the 10 individuals were under the age of 18 years, including two in each group. There was a significant improvement in survival at 24 months (all five alive) in the ventilated group, compared to only one survivor in the control group. The groups were similar at the initiation of the study. There was also a suggestion of improved pulmonary function at six months (+0.03 L in the ventilated group vs −0.23 L in the controls).11

At present, the strongest evidence for the benefit of nocturnal ventilation comes from historical cohort comparative studies that have been performed in multiple centers around the world. Eagle et al. described a significant change in the mean survival from 19.29 years (n = 134) to 25.3 years (n = 24) since NIV was offered routinely in the 1990s at their clinic in the United Kingdom. The chances of surviving to 25 years increased from 12% in the 1980s, before ventilation was offered, to 53% in the ventilated group.30 Ishikawa et al. reported on a Japanese cohort of DMD patients treated with NIV and airway clearance techniques. There was a 50% chance of survival to age 39.6 years, as compared to 18.6 years without respiratory management.31 Passamano et al. retrospectively reported an improvement in the mean age of death from respiratory failure from 17.7 years off of ventilation to 27.9 years on ventilation, in a cohort of 516 patients.32 Rall et al. also reported a median survival improvement from 19.0 to 27.0 years with the initiation of ventilation in a German cohort of DMD patients.33

**Gas exchange**

Several other non-controlled cohorts give further evidence of improvements in symptoms and gas exchange with the initiation of NIV in DMD and CMD patients (Table 2). Daytime hypercapnia was found to improve with initiation...
<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study type</th>
<th>Intervention</th>
<th>Age at initiation: Years (range)</th>
<th>Sample size</th>
<th>Outcome: Mortality</th>
<th>Outcome: Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raphael (1994)</td>
<td>RCT</td>
<td>Initiation of NIV if: FVC &gt; 20%, pO2 &gt; 60 mmHg, pCO2 &lt; 45 mmHg</td>
<td>15.5 (11–33)</td>
<td>70 DMD</td>
<td>Increased mortality in the treatment arm (8/35 vs 2/35)</td>
<td>No change in pulmonary function or gas exchange</td>
</tr>
<tr>
<td>Ward (2005)</td>
<td>RCT</td>
<td>Initiation of NIV if nocturnal TcCO2 &gt; 6.5 kPa and normal daytime PaCO2</td>
<td>18 (7–51)</td>
<td>25 Various neuromuscular disease</td>
<td>No change in mortality; 9 out of 10 in control group started NIV during follow up</td>
<td>Improved baseline nocturnal saturations and percentage of time with elevated nocturnal CO2 in treatment group</td>
</tr>
<tr>
<td>Vanello (1994)</td>
<td>Case control</td>
<td>Initiation of NIV with evidence of daytime hypercapnia (pCO2 &gt; 45 mmHg)</td>
<td>20.1 (13–27)</td>
<td>10</td>
<td>Decreased mortality in treatment arm (0/5 vs 4/5)</td>
<td>Plateau in FVC decline after 6 months of therapy (&lt;0.03 L vs –0.23 L)</td>
</tr>
<tr>
<td>Rall (2012)</td>
<td>Case control</td>
<td>Ventilation – reasons for offering not specified</td>
<td>N/A</td>
<td>23</td>
<td>Improved survival in group with ventilation: 27.0 vs 19.0 years</td>
<td>Improved baseline nocturnal saturations and percentage of time with elevated nocturnal CO2 in treatment group</td>
</tr>
<tr>
<td>Simonds (1998)</td>
<td>Observational</td>
<td>NIV for symptomatic diurnal hypercapnia</td>
<td>20.0 (13–28)</td>
<td>41</td>
<td>Improved survival compared to historical cohort</td>
<td></td>
</tr>
<tr>
<td>Jeppesen (2003)</td>
<td>Retrospective</td>
<td>NIV and change to tracheostomy when 24/7 need; indication for initiation not clear</td>
<td>12.3 (6–19)</td>
<td>30</td>
<td>100%</td>
<td>Significant improvement in daytime and night time CO2 and O2 measurements; no significant impact on vital capacity</td>
</tr>
<tr>
<td>Mellies (2003)</td>
<td>Observational</td>
<td>NIV for symptomatic SDB (&gt; 10 events/hour) or ventilator insufficiency (&gt; 50 mmHg &gt; 50% of night)</td>
<td>22 (16–27)</td>
<td>8</td>
<td>5/8</td>
<td>Improved daytime CO2 (63 to 45) with 8 hours/night of NIV use</td>
</tr>
<tr>
<td>Mohr (1990)</td>
<td>Observational</td>
<td>NIV for DMD patients with diurnal hypoventilation</td>
<td>15.3 (SD – 5.2)</td>
<td>22 out of 43 started ventilation during follow-up period</td>
<td>Median survival: 35 years</td>
<td></td>
</tr>
<tr>
<td>Kohler (2009)</td>
<td>Observational</td>
<td>Ventilation for DMD Patients – indication not clear (19 NIV and 3 IMV)</td>
<td>15.3 (SD – 5.2)</td>
<td>22 out of 43 started ventilation during follow-up period</td>
<td>Median survival: 35 years</td>
<td></td>
</tr>
<tr>
<td>Eagle (2002)</td>
<td>Historical cohort</td>
<td>NIV routinely offered since 1990s; indication: FVC &lt; 1.25 L with Ab normal oximetry or symptomatic hypoxemia</td>
<td>15.3 (SD – 5.2)</td>
<td>No NIV: n = 134 NIV: n = 24</td>
<td>Improved survival with NIV from 19.29 years (n = 134) to 25.3 year (n = 24)</td>
<td></td>
</tr>
<tr>
<td>Ishikawa (2010)</td>
<td>Historical cohort</td>
<td>Group 1: &lt;1984: no intervention Group 2: 1984–1991: tracheostomy for CO2 narcosis or intubation Group 3: &gt;1992: NIV for symptomatic hypercapnia, MAC for peak flow &lt;270 L/min, cardioprotective</td>
<td>18.9 ± 3.3 years</td>
<td>Group 1: (n = 56) Group 2: (n = 35) Group 3: (n = 96)</td>
<td>Improving 50% mortality</td>
<td>11 patients in group 2 and 8 in group 3 died from predominately cardiac causes before regular ventilation was initiated</td>
</tr>
<tr>
<td>Passamano (2012)</td>
<td>Type of ventilation and indication not clearly indicated</td>
<td>n = 516</td>
<td></td>
<td>Improved respiratory mortality in patients on NIV: 17.7 years (11.6–27.5) vs 27.9 (23.6–38.6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RCT = Randomized controlled trial.
of nocturnal NIV. Mellies et al. demonstrated an improvement in daytime hypercapnia with NIV. However, if NIV was not used for three consecutive nights, the daytime hypercapnia recurred, suggesting the importance of regular use.42

Quality of life
Kohler et al. examined patient-reported health-related quality of life (HRQL) using the Short Form 36 (SF36) and disability scores, comparing individuals with DMD on and off NIV. NIV had been started due to symptoms and/or stabilization of respiratory scores; stabilization of vital capacity decline

Table 3. Modes of ventilation.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study type</th>
<th>Sample size</th>
<th>Age: Years ± SD</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>McKim (2013)41</td>
<td>Cohort retrospective</td>
<td>n = 12 DMD</td>
<td>19.8 ± 3.4</td>
<td>Mean survival of 5.7 years on 24 hour NIV (10/12 still alive)</td>
</tr>
<tr>
<td>Soudon (2005)44</td>
<td>Case control</td>
<td>N = 42 DMD IMV, N = 26 NIV</td>
<td>32.7 ± 5.1, 27.0 ± 5.7</td>
<td>Increased secretions and chest infections in the IMV group. Improved weight in the IMV group. Similar reasons for death.</td>
</tr>
<tr>
<td>Bach (1993)40</td>
<td>Observational</td>
<td>N = 257 (43 DMD)</td>
<td>DMD patients 18.4 ± 4.1</td>
<td>23/43 DMD patients utilized MPV including 10 for &gt;10 years. Death rates were similar to those who converted to IMV</td>
</tr>
<tr>
<td>Toussaint (2006)42</td>
<td>Observational</td>
<td>N = 42 DMD</td>
<td>23.5 ± 4.7 at time of initiation of MPV</td>
<td>50% survival at age 31 with NIV/MPV; stabilization of respiratory scores; stabilization of vital capacity decline</td>
</tr>
</tbody>
</table>

Need to specify that results are presented as mean ± SD; IMV — invasive mechanical ventilation via tracheostomy; MPV — mouth piece ventilation.

Table 4. Predictors of nocturnal hypoventilation/SDB.

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Population</th>
<th>Outcome</th>
<th>Predictive measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lyager (1995)49</td>
<td>DMD n = 14; age: 19.2 (15.4–30.4)</td>
<td>Ventilation need (Daytime symptoms and daytime hypercapnia)</td>
<td>For DMD: FVC &lt;30%</td>
</tr>
<tr>
<td>Mellies (2003)51</td>
<td>Total n = 49; SMA, other dystrophies/myopathies; age: 11.3 ± 4.4 DMD n = 7; age: 14.6 ± 4.0</td>
<td>SDB (polysomnography) Nocturnal hypercapnia</td>
<td>Inspiratory VC &lt;60% had 97% sensitivity Peak Inspiratory (PIP) Pressure &lt;41 cm H2O sensitivity of 87% Nocturnal Hypercapnia: Inspiratory VC &lt;40%, 96% sensitivity for PIP &lt;25 cm H2O 72% predicted</td>
</tr>
<tr>
<td>Hukins (2000)54</td>
<td>DMD n = 19; 18.6 ± 3.9 years TST &lt;90% (proportion of total sleep time &lt;90% SaO2)</td>
<td>Nocturnal hypoventilation Diurnal hypercapnia</td>
<td>Vital capacity of &lt;1820 mL sensitivity/specificity: 97%/51% MIP &lt;39 cm H2O; sensitivity/specificity: 71%/54%</td>
</tr>
<tr>
<td>Toussaint (2007)47</td>
<td>DMD n = 114</td>
<td>Nocturnal hypoventilation Diurnal hypercapnia</td>
<td>Vital Capacity of &lt;680 mL sensitivity/specificity of 90%/95%</td>
</tr>
<tr>
<td>Ragette (2002)52</td>
<td>N = 42; 10 DMD, 10 CMD, 7 limb girdle dystrophy; mean age: 28.7 (14–63)</td>
<td>Sleep disordered breath (Polysomnography – REM related hypopneas) Continuous nocturnal hypoventilation</td>
<td>Vital Capacity &lt;60%; sensitivity/specificity: 91%/89% MIP &lt;45 cmH2O; sensitivity/specificity: 82%/89%</td>
</tr>
<tr>
<td>Canny (1989)50</td>
<td>DMD n = 143</td>
<td>Daytime hypercapnia</td>
<td>Vital Capacity &lt;40%; sensitivity/Specificity: 94%/79% MIP cmH2O; sensitivity/specificity: 95%/65%</td>
</tr>
<tr>
<td>Bersanini (2012)51</td>
<td>N = 52 (20 DMD); age: 14.9 (10.1–16.1)</td>
<td>Nocturnal hypoxemia (&gt;2% of night with &lt;90% saturation) and nocturnal hypercapnia (PCO2 &gt; 50 mmHg for &gt;2% of night) Polysomnography in 27 patients</td>
<td>No correlation with pulmonary function or blood gas anomalies. No PFT/blood gas marker predicted Apnea Hypopnea Index &gt;5</td>
</tr>
<tr>
<td>Katz (2010)56</td>
<td>n = 39; congenital muscular dystrophy n = 6</td>
<td>Nocturnal hypoventilation on polysomnography: Elevation of CO2 by 10 mmHg and/or drop in saturation by at least 5% for 10 minutes</td>
<td>FVC &lt;70% predicted; sensitivity/specificity of 71.5%/64.1% FEV1 &lt;65% predicted; sensitivity/specificity of 71.4%/79.5% Scoliosis correlated with nocturnal hypoventilation: sensitivity/specificity of 88.9%/80.4%</td>
</tr>
</tbody>
</table>

Ages given in years ± SD or (range).
hypercapnia. There was no significant difference in HRQL between those on NIV and those not, despite the fact that the ventilated cohort was older and had more significant physical disabilities. Therefore the initiation of NIV appears to preserve HRQL. Similar findings of maintenance of quality of life have been reported by others. Qualitatively, invasive ventilation has also been reported to facilitate breathing and prolong life.

Conclusion

Based mainly on data from historical controls, initiation of long-term home mechanical ventilation (HMV) can lead to a prolongation of life in DMD, while maintaining QoL. There is also evidence that nocturnal long-term ventilation improves nocturnal hypercapnia and can prolong time to onset of diurnal hypercapnia. There is insufficient evidence to explore these questions in the other CMDs; based on the limited studies available, however, it appears to have similar benefits.

Question 2: What modes of ventilation should be considered in muscular dystrophies?

The majority of the publications described in Question 1 report on ventilatory support with NIV. Few studies have compared the relative efficacies of pressure versus volume NIV, and additional research is needed. One of the benefits of using a volume-controlled mode of NIV over pressure-controlled ventilation is the ability for the patient to use the ventilator in volume-control mode for breath stacking (e.g., LVR and MI-E). In the past, if daytime hypercapnia developed despite nocturnal NIV, patients would have been transitioned to invasive ventilation via tracheostomy. However, there is emerging evidence that daytime hypercapnia can still be managed effectively noninvasively. This would involve nocturnal NIV in addition to daytime ventilation administered intermittently using a mouthpiece for on-demand ventilatory support. The latter, however, requires adequate oral and neck control, for using the mouthpiece.

A comparison of DMD patients requiring 24-hour support via tracheostomy vs. NIV showed that those with NIV had fewer airway secretions and pulmonary exacerbations, and spent less time in hospital. Invasively ventilated patients had better weight percentiles. Death (eight of 16 in tracheostomy group and 10 of 24 in noninvasive group) occurred from similar reasons in both groups. The tracheostomy group, however, was older (32.7 vs 27.0). Within the historical cohorts described in the previous section, Ishikawa showed improved survival with NIV (50% survival to 39.6 years) and mechanical airway clearance compared to those treated with tracheostomy (50% survival to 28.1 years). However, NIV appeared to be initiated earlier in the course of disease and was done in association with early aggressive airway clearance and initiation of cardiac protective medications as necessary. Therefore it is difficult to directly compare the outcomes in terms of life expectancy between tracheostomy and NIV.

There are no HRQL studies directly comparing invasive and noninvasive ventilation. The study by Dreyer did show that in a subset of DMD patients with tracheostomies who had been on NIV previously, there was a preference for invasive ventilation. Therefore, in at least a subset of patients, tracheostomy may be the preferred option.

Conclusion

Ventilatory support up to 24 hours a day can be provided by both invasive and noninvasive methods. NIV may provide the advantage of decreased secretions and hospitalizations. Especially in the DMD population, candidacy for NIV plus mouthpiece ventilation to manage diurnal hypercapnia should be evaluated prior to tracheostomy insertion. Tracheostomy, however, may be the preferred option in some individuals.

Question 3: When should long-term home ventilation be initiated?

As hypoventilation at night precedes daytime hypoventilation and is often not associated with symptoms, recognizing its onset to help determine when ventilation should be initiated is an important aspect of DMD and CMD care.

At present, there is no international consensus as to when to screen for sleep-disordered breathing (SDB) in children with neuromuscular disease. The published recommendations in the field include the American Thoracic Society consensus statement, which recommends that, where available, annual polysomnography testing would be ideal for surveillance. Alternatively overnight oximetry and capnography can be performed. However, the statement does acknowledge that the ideal timing for the initiation of surveillance monitoring has not been determined. Other statements include:

- The DMD Care Considerations working group recommends nighttime evaluation of gas exchange when there are signs and/or symptoms of hypoventilation, a baseline FVC <40% predicted and/or daytime hypercapnia with pCO2 > 45 mmHg or with a room air oxygen saturation <95%.
- The Canadian Thoracic Society Adult Home Ventilation Guidelines for the same population suggest performing an evaluation for nocturnal ventilation if there are clinical signs of hypoventilation and/or if the FEV1 or FVC <40% predicted.
- The British Thoracic Society Neuromuscular Guidelines recommends annual nighttime assessment with polysomnography or oximetry when there is a vital capacity <60% predicted or a loss of ambulation. It also suggests considering annual testing in infants with neuromuscular weakness, children with diaphragmatic dysfunction, Rigid Spine Syndrome and/or when there are symptoms of hypoventilation.

Little attention has been paid in the literature to the patient and/or family input regarding their perceived clinical status or HRQL as an aid in deciding upon the initiation of home ventilation.
Results

Forced vital capacity (FVC)

A decrease in forced vital capacity (FVC) correlates with an increased risk of hypoventilation and need for ventilatory support. However, a VC cutoff below which nocturnal hypoventilation will develop has not been clearly established to date. In one large study of 115 adolescents and young adults with DMD, VC correlated well with nocturnal hypercapnia. A VC of 1,820 mL (~37% predicted) had a sensitivity of 87% and a specificity of 51% for nocturnal hypercapnia. A VC <680 mL was 90% sensitive and 95% specific for daytime hypercapnia.47 Several other studies of adolescents and young adults have also demonstrated that low VC <35–40% are very sensitive for the need of nocturnal ventilation; however patients are often quite symptomatic and may have daytime hypercapnia.48,49

In at least one study, however, several patients with DMD already had daytime hypercapnia with an FVC in the 40–50% predicted range.50 Out of seven DMD patients with daytime hypercapnia, two had VC of 40% predicted and one had a VC of 47% predicted. A study in children and adolescents with a mixed group of children that included DMD (20 out of 52 children) also showed no correlation between daytime lung function parameters and signs of nocturnal hypoventilation/SDB. However, all of the children with DMD had a FVC of 42% predicted or less (range of 28.0–42.3).51

While a VC of <40% appears to be a useful marker for need for nocturnal ventilation, the use of a higher VC cutoff appears to be more sensitive to capture early onset of SDB. In a study of a mixed group of adolescents and adults with neuromuscular myopathies, an FVC <60% was approximately 90% sensitive and specific for the onset of sleep-disordered hypopneas (REM-related hypopneas) whereas an FVC <40% was 94% sensitive (79% specific) for continuous nocturnal hypoventilation.52 A subsequent study from the same group of investigators with a larger pediatric population of neuromuscular diseases showed very similar results.53 In a Canadian study in children with a heterogenous group of children with a variety of neuromuscular disease, Katz et al. found that FVC of less than 70% predicted had a sensitivity of 71.4% for nocturnal hypoventilation.46

Maximal respiratory pressures

In studies that have compared the relative abilities of FVC and Maximal Inspiratory Pressures (MIP) to predict sleep-disordered breathing (SDB), FVC was found to be a better predictor.46,47,52–54 Within the same studies, Maximal Expiratory Pressures generally had a weaker correlation than MIP. In another study, although sniff nasal inspiratory pressures correlated with VC, they were not predictive of SDB.55

Daytime blood gas measurement

A few studies have looked at daytime blood gas measurements as a predictor of nocturnal hypoventilation. In one study, daytime PaCO2 > 40 mmHg was 92% sensitive and 76% specific for identifying SDB. However, a decreased inspiratory vital capacity was a better predictor of SDB (sensitivity and specificity of 97% and 87%).53 Of note, it is not known if the reliance solely on inspiratory rather than both inspiratory and expiratory muscles to generate the results is significant, as conventionally vital capacity is reported. Another study suggested a base excess of >4 was very specific for nocturnal hypoventilation, as defined by ≥2% of night with SaO2 < 90%. It was 100% specific, though only 55% sensitive as a marker. The base excess was not predictive of an abnormal Apnea Hypopnea Index (AHI).54 While an abnormal base excess should warrant further investigations, a normal value is not sensitive enough to rule out significant hypoventilation.

Daytime hypercapnia is predictive of nocturnal hypoventilation.54 However this is a late sign, as once there is evidence of daytime hypercapnia, life expectancy in DMD may be less than 12–24 months.51 Even in patients with the mildest hypercapnia (PaCO2 45–50) the deaths occurred at 10–16 months.51

Conclusion

The heterogeneous neuromuscular diagnoses in many of the pediatric studies, a lack of standard definitions for SDB or nocturnal and diurnal hypoventilation, as well as differences in assessment tools (polysomnography, oximetry, etc.) make it challenging to directly compare the results of different studies. Nevertheless, there is an apparent correlation with decreasing vital capacity and increasing risk of nocturnal hypoventilation and the need for ventilatory support. The evidence supports that those with a FVC (or FEV1) <40% predicted and/or those who have daytime symptoms of hypoventilation should be screened for signs of nocturnal SDB, ideally with polysomnography, as they are at the highest risk of hypoventilation and hypercapnia. It is also evident that this approach will likely miss individuals with early and milder SDB. A FVC <60% predicted cutoff is likely to be a better threshold for the initiation of screening for early onset of SDB.

However, regular screening of all patients meeting the above mentioned criteria may not be feasible in Canada given the limited access to pediatric polysomnograms.56 In a recent survey of pediatric practices in Canada, there are differences in screening for SDB in children with DMD across Canada. Regional differences in access to polysomnograms accounted for some of the practice variation.57 There is a paucity of data regarding the patient’s or family’s assessment of the patient in helping to evaluate the possible need for further evaluation and/or intervention.

Research questions

1. What is the ideal timing of initiation of NIV in individuals with DMD/CMD?
2. Would early initiation of NIV decrease lung function decline?
3. What are the ideal mode and parameters of ventilatory support in DMD?
4. Can DMD experience be extrapolated to rarer CMD diagnoses?
5. What is the ideal screening test for nocturnal hypoventilation in Canada given the limited access to polysomnograms and what is the timing and frequency of monitoring needed for NIV?
6. What impact does systemic corticosteroid use have on lung function parameters and predictors of NIV need?

**Recommendations**

1. Assessment for sleep-disordered breathing, ideally with a polysomnogram, should be carried out not less than annually for children with an FVC <60% predicted and/or who have symptoms of sleep-disordered breathing. (Grade 1C)
2. Assessments for sleep-disordered breathing, ideally with a polysomnogram, should be considered annually in:
   a. Infants with congenital muscular dystrophies demonstrating weakness.
   b. Infants with congenital muscular dystrophies that may develop hypoventilation <5 years of age (including severe forms of MDC1A and A-Dystroglycan deficiency CMD).
   c. Children with congenital muscular dystrophies who never attain the ability to walk or become nonambulatory. (Consensus)
3. If a polysomnogram is not available for annual surveillance, oximetry and capnography (etCO2 and/or teCO2) are recommended. (Grade 1C)
4. Children who have shown a clinical deterioration, who are having recurring pulmonary exacerbations, and/or who develop symptoms of sleep-disordered breathing may require sleep assessment more often than annually. (Consensus)
5. Initiation of NIV should be considered when there is evidence of diurnal hypventilation (daytime pCO2 ≥ 45 mmHg) and/or nocturnal hypventilation (teCO2 ≥ 50 mmHg for >25% of the total sleep time) with symptoms. (Grade 1B)
6. Initiation of NIV should be considered in patients with evidence of SDB (hypventilation, obstructive sleep apnea, and/or central sleep apnea) even if asymptomatic. (Grade 1C)
7. For patients who require >12 hours of ventilation a day, noninvasive supports with mouth piece ventilation should be considered as a possible alternative to tracheostomy, and continuous mask HIV, factoring in individual circumstances and preferences. (Grade 1C)

**References**
