Consensus-based Care Recommendations for Pulmonologists Treating Adults with Myotonic Dystrophy Type 1
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Overview

Due to the multisystemic nature of this disease, the studies and rigorous evidence needed to drive the creation of an evidence-based guideline for the clinical care of adult myotonic dystrophy type 1 (DM1) patients are not currently available for all affected body systems and symptoms. In order to improve and standardize care for this disorder now, 12 myotonic dystrophy (DM) clinicians with experience treating DM patients in Western Europe, Canada and the US joined together to create the Consensus-based Care Recommendations for Pulmonologists Treating Adults with Myotonic Dystrophy Type 1. The project was organized and supported by Myotonic.

A complete list of authors and an overview of the process is available in Addendum 1. A complete reading list for each of the study area sections is available in Addendum 2.

An update policy has been adopted for this document and will direct a systematic review of literature and appropriate follow up every three years. Myotonic staff will provide logistical and staff support for the update process.

Background

Myotonic dystrophy type 1 (DM1) is a hereditary autosomal dominant disorder, caused by the multiple repetitions of an unstable trinucleotide (CTG) in the region of the dystrophia myotonica protein kinase (DMPK) gene at chromosome 19q13.3. Population-based (not diagnosed) prevalence is 1:2500. DM1 is a multisystem disorder involving not only skeletal and smooth muscles, but also visual, cardiac, endocrine, central nervous system, digestive and respiratory systems. Respiratory failure is the primary cause of death and typically occurs between 50 and 60 years of age in adult-onset DM1 patients.

Life expectancy is decreased in patients with DM1, with mortality being 7.3 times higher than expected in the age-matched population, particularly in those with early onset of disease. Respiratory failure is the primary cause of death, and occurs between 50 and 60 years of age.

Respiratory involvement is due to a combination of respiratory muscle and diaphragmatic weakness and dysregulation of central ventilatory control, resulting in alveolar hypoventilation, microatelectasis, reduced lung compliance, ineffective coughing, and hypercapnia. In several studies, a reduced ventilatory response to CO2 was also noticed.

Sleep-related breathing disorders (SRBD) are frequently seen in DM1 patients, as well as excessive daytime sleepiness (EDS). EDS may occur secondary to an involvement of the central nervous system or to respiratory muscle weakness. These causes may overlap: insufficient airflow during sleep may contribute to disrupted sleep and excessive daytime fatigue, and central nervous system factors may affect respiratory control, thus promoting SRBD.

Respiratory insufficiency initially manifests as sleep-related hypoventilation that begins during rapid eye movement (REM) sleep, and then progresses to non-REM sleep stages when respiratory muscle strength further declines. Finally, patients often have chronic hypercapnic respiratory failure, where hypercapnia is present while patients are awake. Importantly, SRBD in patients with DM1 comprise hypoventilation, obstructive or central sleep apnea and upper airway flow limitation.
Furthermore, the weakness of inspiratory and expiratory muscles reduces cough effectiveness and impairs clearing of secretions, leading to an increased risk of mucus retention, aspiration, and pulmonary infections. In addition, weakness of the swallowing muscles can increase the risk of aspiration of food and drink, saliva, nasal secretions, and stomach fluids.

General anesthesia and pain medications (intravenous and oral routes), specifically opiates and sedatives, may cause acute respiratory failure in patients who were previously clinically stable but with impaired baseline respiratory muscle function. DM1 patients therefore need careful perioperative management.

See Myotonic’s Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient and Anesthesia Quick Reference Guide here https://www.myotonic.org/toolkits-publications

**Recommendations**

**Look for:**

a. Respiratory symptoms that may indicate:
   1. Nocturnal hypoventilation (poor sleep, morning headaches, orthopnea, excessive daytime sleepiness)
   2. Obstructive sleep apnea (snoring, apnea, poor sleep, excessive daytime sleepiness)
   3. Decreased respiratory reserve or decreasing respiratory muscle function (dyspnea, orthopnea, tachypnea, fatigue, shortness of breath, decreased exercise tolerance)
   4. Ineffective cough (decreased ability to cough, coughing when eating or drinking, choking, history of excessive frequency and duration of chest infections, including hospitalizations)

b. Physical examination results indicative of respiratory muscle weakness and/or increased risk of obstructive sleep apnea. Important aspects to assess include at minimum resting respiratory rate, pulse oximetry, auscultation, assessment of chest wall motion, evaluation of accessory and abdominal muscle recruitment and breathing pattern. Signs of diaphragmatic paralysis should be evaluated, particularly whether there is orthopnea and/or tachypnea or paradoxical breathing when lying flat.

c. Results from questionnaires covering symptoms of respiratory muscle weakness or sleep-disordered breathing (Epworth Sleepiness Scale - ESS, Fatigue and Daytime Sleepiness Scale - FDSS).

d. The single breath count may also be used to evaluate pulmonary function.

e. Assessment of cough strength is recommended. Consider that patients with DM1 may not complain of respiratory symptoms and may not be aware that they are experiencing key symptoms until specifically questioned about them. Schedule more time with these patients to go over symptoms than would be typically allotted to patients with more common respiratory problems.
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Test for:

a. Forced vital capacity (FVC) in the sitting and supine position if possible, every 6 months. Spirometry tests should be performed using either a mouthpiece along with a nasal clip or a mask (if weakness of orbicularis oris muscle is present). In either instance, the device that provides the better fit should enable a more precise measurement. FVC is considered abnormal if less than 80% of the predicted normal value, or if it falls by more than 20% or 500 ml from sitting to supine.

b. Maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) in the upright position, every 6 months. MIP value is considered abnormal if less than -60 cmH2O, MEP if less than 40 cmH2O. A nasal clip should be used. Sniff nasal inspiratory pressure (SNIP) can substitute for MIP if significant buccal weakness is present or if the patient is unable to tolerate the MIP test due to myotonia or other mitigating symptoms.

c. Cough peak flows (CPF), every 6 months. If CPF is less than 270 liters/minute in adult patients, then cough is relatively ineffective, and manual and/or mechanical cough assistance techniques should be implemented. If CPF is less than 160 liters/minute, the risk of pneumonia and respiratory failure is considered high, especially during intercurrent respiratory tract infections.

d. Nocturnal oximetry/capnography or polysomnography every 6 months. This test is considered abnormal if the Apnea Hypopnea Index (AHI) exceeds 5 per hour. The Oxygen Desaturation Index (ODI) is greater than 15 events/hour in adults. Sleep studies are recommended in patients with suspected sleep-disordered breathing (SDB), especially in the absence of nocturnal or daytime hypercapnia. Polysomnography is superior to polygraphy since it allows for assignment of respiratory events to sleep stages. Oximetry alone is not suitable to identify patients with nocturnal hypoventilation, and overnight carbon dioxide monitoring is advisable. Transcutaneous capnometry most accurately reflects nocturnal CO2 changes. Blood gas analysis during the night or immediately after waking may show either hypercapnia or an elevated base excess reflecting renal bicarbonate retention.

e. Daytime blood gas analysis, or end-tidal and/or transcutaneous CO2 analysis to evaluate for hypercapnia in patients with more advanced respiratory muscle weakness. Daytime hypercapnia is defined as PaCO2 >45 mm Hg or >6.0 kPa, respectively.

f. Indicators of sleep-disordered breathing including snoring, witnessed apneas, gasping/choking from sleep, nightly interrupted or fragmented sleep, a MIP value of less than 60 or an FVC of less than 50 percent of predicted. If DM1 patients have sleep-related symptoms such as excessive daytime sleepiness, fatigue, morning headaches or poor sleep, a full night polysomnography is recommended.

g. Airway clearance capacity and other respiratory assessments prior to surgery. If needed, adaptation to nocturnal noninvasive ventilation or to mechanical insufflation-exsufflation devices should occur prior to surgery. See “Treat with” recommendation d below for treatment parameters.

h. Patients should be referred to a specialist in dysphagia evaluation if swallowing problems are suspected (cough before, during or after meals, food stagnation in the oral cavity, drooling, regurgitation of undigested food, aspiration, gurgling in the throat, dysphonia, malnutrition).
i. Consider that patients with DM1 may need additional time to understand test procedures because of some degree of visual-spatial and executive problems that may be present as part of their brain disease burden. Give examples to ensure proper execution during test procedures and to allocate more time than usual to allow extra time to assist these patients in providing reliable test results.

Treat with:

a. Vaccinations for influenza and pneumonia (pneumococci, haemophilus) if no contraindications.

b. Standard medical therapy, as well as cough assistance and mechanical ventilation (as needed) for respiratory support.

c. Manual and/or mechanical cough assistance techniques (e.g., breath stacking, abdominal thrust, mechanical insufflator/exsufflator) for adult DM1 patients with ineffective cough (cough peak flow of less than 270 liters/minute), and during chest infections and perioperative periods. An intrapulmonary percussive or high frequency chest wall oscillation device can be used as a supplement to the above cough assistance techniques but is insufficient if used without effective expectoration of mucus.

1. A manually assisted cough (MAC) uses either, or a combination of, a manual Heimlich/abdominal thrust maneuver and a manual costophrenic compression to increase expiratory airflow. Limits of effectiveness for the use of MAC in neuromuscular disorders have been reported when unassisted peak cough flow is ≥ 140 L/min.

2. Insufflation techniques when FVC is ≤ 2L or ≤ 50% predicted or if there is evidence of weak cough.

3. Air-stacking techniques if CPF are between 160 and 270 liters/minute in order to increase cough efficacy (if the patient has glottic competence) or if there is evidence of weak cough.

4. Resuscitator bag with a one-way valve (AMBU) if patient can operate with hands, knees, or foot. Otherwise a caregiver is needed in order to help the patient perform the technique.

5. Intermittent Positive Pressure Ventilation (IPPV), since these devices can be used by the patient alone, even with hand weakness. These devices require good lip strength to correctly hold the mouthpiece.

6. For patient's already using volume cycled ventilators, mouthpiece ventilation (MPV) can be implemented for lung volume management and secretion clearance. The correct execution of the technique should be evaluated by measuring Peak Cough Flow (PCF) with air-stacking maneuver; if results are >270 liters/minute, the technique can be considered efficient for secretion management. Otherwise, mechanical cough assistance is the best strategy to increase cough efficacy (see Cough Management Guide).

7. Devices for secretion mobilization such as Intrapulmonary Percussive (IPV) and High Frequency Chest Wall Oscillation (HFCWO) devices should be considered in excessivesecretion encumbrance situations. IPV is an adaptation of high frequency percussive ventilation, which promotes airway vibrations by injecting rapid bursts of air into the lung via the mouth. IPV may be delivered via a face mask, a mouthpiece, an endotracheal tube, or a tracheostomy and it facilitates airway clearance and improves homogeneity of ventilation in patients with neuromuscular disorders with retention of mucus. HFCWO devices
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generate either positive or negative trans-respiratory pressure excursions to produce high-frequency, small-volume oscillations in the airways. HFCWO can lead to changes in volume of 15–57 ml and in flow up to 1.6 L/s, which generate minimal coughing to mobilize secretions. The typical treatment lasts 20–30 minutes, and consists of short periods of compression at different frequencies, separated by coughing. Coughing should always be assisted with cough assistance techniques if ineffective. Patients and caregivers (if needed) should be taught how and when to perform the above techniques at home.

d. Noninvasive Positive-Pressure Ventilation (NIV) for respiratory insufficiency in patients who have respiratory muscle weakness and sleep-related breathing disorders. According to the 207th ENMC [European Neuromuscular Centre] Workshop (2014-07-21), NIV should commence when there is at least one or more daytime or nighttime symptoms suggestive of chronic respiratory insufficiency in combination with:

- Daytime hypercapnia, PaCO2 ≥ 45 mmHg (6.0 kPa) or
- FVC < 50% of predicted based on the best of 3 measures and MIP < 60 cmH2O or
- Evidence of nocturnal hypoventilation, such as:

1. A rise in PaCO2 of ≥ 10 mmHg (1 kPa) between evening and morning arterial blood gas measurements or other accurate CO2 surrogates.

2. A rise in transcutaneous CO2 to > 50 mmHg (6.7 kPa) for more than 50% of total sleep time.

3. While not ideal, when a measurement of CO2 is not available, continuous nocturnal oximetry demonstrating sustained oxygen desaturation (SpO2) ≤ 88% for 5 consecutive minutes or SpO2 < 90% for > 10% of total sleep time.

4. An attended polysomnogram showing evidence of sleep-disordered breathing with an Apnea Hypopnea Index (AHI) >5 events per hour and transcutaneous CO2/end tidal CO2 changes as above.

5. Some patients will progress from requiring nocturnal ventilatory support to daytime ventilatory support. With daytime ventilation, different mask interfaces or mouth piece ventilation are options.

6. Facial morphology should be considered in the choice of mask interface. In case of facial muscle weakness with difficulties in mouth closure, oronasal masks or nasal interfaces in association with chinstraps can be the best option in order to avoid excessive leaks (providing aspiration is not a significant concern). If NIV is also used during the daytime, mask rotation strategies and/or mouthpiece ventilation should be adopted to offload skin pressure points.

7. Adherence should be monitored and is usually based on a minimum threshold of 4 hours/day. It is preferable to use NIV at night for sleep. Initially, some individuals may require desensitization to NIV during the day. Adherence to NIV has been reported to be lower specifically in patients with no subjective symptoms of respiratory insufficiency, with high body mass index or most frequently in presence of excessive leaks, so special attention should be paid in these cases.
8. In the United States and other countries, recommendations for insurance reimbursement are contingent upon adherence review by the treating physician. Individuals must demonstrate NIV adherence by daily use of a minimum of 4 hours, greater than 70% of the time during adherence review, within a 90 day period from the day the device is set up. The majority of insurance companies follow the U.S. Centers for Medicare and Medicaid guidelines for adherence and reimbursement. At each follow up visit after NIV adaptation, or if the patient complains of subjective symptoms of respiratory compromise, patients should be tested with overnight cardiorespiratory polygraphy and carbon dioxide monitoring (either with NIV and/or arterial blood gas analysis, end tidal CO2 or transcutaneous CO2, if indicated). Symptoms of nocturnal hypoventilation should also be asked for. Downloaded data from NIV devices may also provide additional information about adequacy of ventilator support.

9. Supplemental oxygen should not be used alone or in conjunction with noninvasive ventilation unless there is specific lung pathology baseline O2 saturation that cannot be normalized by airway clearance techniques or ventilatory setting adjustments. In this case individuals must be evaluated for specific lung pathology that would explain the hypoxemia. Supplemental oxygen may need to be used with extreme caution without NIV in specific rare cases.

10. Start Modafinil for excessive daytime sleepiness for the central component but look for the respiratory component, if any, which might improve with NIV.

11. Check overweight and aim to lose weight which may reduce lung volumes.

e. Emergency medical alert card or bracelet.

f. Whereas “NIV” has come to mean Continuous Positive Airway Pressure (CPAP) and/or low spans of bi-level PAP used to titrate away obstructive apnea and hypopneas, many myotonic dystrophy patients’ vital capacities diminish to under 100 ml and require either high pressure support bi-level PAP (IPAP – EPAP difference >15 cm H2O) with back up respiratory rate modality, or volume cycled ventilation at full ventilator delivered volumes called noninvasive ventilatory support or “NVS.” Therefore, tracheostomy should only be considered for patients who are dependent on noninvasive ventilatory support 24 hours/day and are not suitable candidates for daytime ventilation either with mask interface or mouth piece ventilation (i.e. sip ventilation). Tracheostomies must be managed in order to maintain swallowing and speech.

1. If possible, a tube with deflatable cuff can be used to permit speech.

2. Speaking valves can also be used to improve speech during spontaneous breathing but this may be dangerous in the home setting without appropriate education and monitoring.

g. Progressive weaning after acute respiratory distress:

After acute respiratory distress:

1. Weaning must be progressive.

2. Spontaneous breathing trials may be considered (depending on patient’s respiratory status prior to surgery or acute event) for evaluation of the patient’s weaning capacity, however patients do not need to be weaned from the ventilator to be successfully extubated, as extubation directly to noninvasive ventilation with aggressive use of mechanically assisted cough is recommended. Patients can wean to “baseline” by taking fewer and fewer “sip ventilations” or stay on shorter periods of nasal NIV.
3. Do not use noninvasive ventilation with pressure support in a spontaneous mode (i.e. without back up rate) due to the importance of backup respiratory rate in case of central apnea or respiratory drive impairment.

4. Consider airway clearance techniques such as mechanical insufflation-exsufflation as a lung volume recruitment strategy in addition to airway clearance in preparation for extubation, and to prevent re-intubation.

5. Patients should be extubated to their own ventilatory devices at their usual settings.

After surgery:

1. Extubation should not be done on the operation table immediately after anesthesia.

2. Extubation should be done in a recovery room or intensive care unit due to side effects of anesthetics and morphinics in DM1 (see Myotonic’s Anesthesia Guidelines, https://www.myotonic.org/toolkits-publications)

3. Consider airway clearance maneuvers before and after extubation.

4. Patient can be extubated to their own ventilatory device if the patient was previously using ventilatory support.
Cough Management Guide

- If PCEF > 270 L/min
  - Monitor PCEF every 6 months

- If PCEF 160 - 270 L/min
  - Initiate air-stacking techniques
    - Sufficient glottic closure required
    - Caution if patient has gastric reflux
  - IPPB
    - Hand weakness
    - No caregiver
    - Requires good lip strength (mouthpiece)
  - Ambu bag
    - Good hand grip
    - Caregiver needed

- If after treatment PCEF is > 270 L/min
  - Satisfactory management of secretions

- If after treatment PCEF is 160 - 270 L/min

- PCEF < 160 L/min
  - Mouthpiece ventilation
    - Pts on NIV using volumetric ventilators

- Mechanical in-exsufflation
  - Twice daily, before bedtime and on awakening
  - 6 to 8 in-exsufflations each time
  - Distant from meals (1.5 hours before/after a meal)
  - Caution if gastric reflux
  - As needed during exacerbations or during acute dysphagia

Respiratory Care Flow Sheet - From Diagnosis

- @ Diagnosis

  - Detailed respiratory history
    - *Refer to symptoms in point 1a, pages 3 and 4
  - Laboratory tests, such as blood gasses and polysomnography, sitting and supine SVC, nocturnal oximetry, PCF

  - If FVC is >75% and other tests normal
    - * Refer to text for details
  - If FVC < 75% but > 50% and other tests normal
    - * Refer to text for details
  - If FVC is <50% or other tests abnormal
    - * Refer to text for details

  - Symptom management
    - Reassessment of laboratory tests
    - Symptom checklist every 6 months if symptomatic, or yearly if asymptomatic

  - Symptom management
    - Reassessment of laboratory tests
    - Symptom checklist every 6 months

  - NIV indication
    - *Refer to point iii, treat with d, page 6

(According to 207th ENMC Workshop 2014-07-21)
Addendum 1:
Project overview and list of authors

The Consensus-based Clinical Care Recommendations for Pulmonologists Treating Adults with Myotonic Dystrophy Type 1 was created by a group of 12 international clinicians with expertise in the care and treatment of adults living with myotonic dystrophy type 1. They included:

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Myotonic designed and initiated the consensus-based process and provided project management and document preparation services. Myotonic team members included Paul Formaker, Leah Hellerstein and Molly White.
Addendum 2:

References


Myotonic’s mission is to enhance the quality of life of people living with myotonic dystrophy and accelerate research focused on treatments and a cure.