MYOTONIC DYSTROPHY FOUNDATION

Care and a Cure

Consensus-based Care Recommendations for Children with Myotonic Dystrophy Type 1

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Overview

Recommendations for the health care of children with myotonic dystrophy are crucial to assure that all clinicians and professionals encountering children and their families with this complex disorder have a guidance document endorsed by experienced clinicians that encompasses pathways for health care delivery. While the studies and rigorous evidence needed to drive the creation of an evidence-based guideline for the clinical care of children with myotonic dystrophy type 1 (DM1) are not currently available for all affected body systems and symptoms, this document functions as a first step. The recommendations were built via a consensus-based process informed by the literature and clinical experience.

Myotonic dystrophy is a multi-systemic disorder, and these care guidelines are therefore divided into two main sections: a. general care considerations and b. a system-based approach to care. Each section includes a brief background section outlining critical information, followed by a set of consensus-based recommendations.

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General care considerations

Diagnosis and classification

Background

Making a diagnosis of congenital or childhood onset myotonic dystrophy type 1 (DM1) can be extremely difficult unless a clinician is familiar with the condition. The path to diagnosis is often complicated by the wide range of body systems involved, the number of different practitioners consulted, and the wide variability in severity of the signs and symptoms of disease. It can take years for a patient to receive a correct diagnosis of CDM and childhood-onset DM1.

The diagnosis of congenital and childhood-onset DM1 should be suspected in any juvenile with a family history of DM1 and/or presenting with one or more of the following features:

- Eyelid ptosis
- Distal weakness, primarily of the finger and wrist flexors, without contractures
- Myotonia or "stiffness" of muscles
- Autistic features or social communication difficulties
- Attention deficit disorder, anxiety and other behavioral problems
- Developmental delay and/or intellectual disability
- Learning disabilities (eg. dyslexia, dyscalculia)
- Excessive daytime sleepiness
- Gastrointestinal issues: constipation or diarrhea
- Scoliosis
- Arrhythmia
- Prolonged recovery or respiratory arrest following anesthesia
- Neonatal features of hypotonia, weakness, club foot, respiratory distress or feeding problems

If DM1 is suspected clinically, a definitive diagnosis can be made via a genetic test. A family history and a single symptom or sign consistent with DM1 should prompt genetic testing. In the absence of a known family history, a detailed family history from the parents often reveals a sub-clinical case of DM1 in a parent. In the case of no family history, a constellation of signs or symptoms, rather than just one, should prompt genetic testing. Arriving at a definite genetic diagnosis of DM1 in children and adolescents is very important in managing the presenting problem and to ensure proper monitoring and precautionary measures. In particular, cardiac monitoring by annual ECG should be done to identify potentially problematic arrhythmias.

The DM1 genetic test measures the number of CTG repeats in the 3" untranslated portion of the dystrophia myotonica protein kinase (DMPK) gene on chromosome 19. CTG repeat numbers between 37 and 50 are considered premutations and repeat expansions greater than 50 are associated with disease. (see **Genetic counseling**).

Recommendations

a. Refer to genetic counseling (see **Genetic counseling**) if patients or at-risk family members exhibit clinical signs indicative of DM1, to enable them to make an informed decision about whether to proceed to genetic testing. Such testing should be done through an accredited laboratory experienced in providing DM1 diagnoses (see myotonic.org). Individuals with 37 to 49 CTG repeats are deemed very unlikely to develop detectable DM1 symptoms. However, such "premutations" can expand into the disease range in subsequent generations. Individuals thus identified should be offered genetic counseling (see **Genetic counseling**) to discuss their risk for transmitting DM1

   Once the diagnosis is confirmed, refer to an expert multi-disciplinary myotonic dystrophy team to coordinate care, prioritize symptom management and make appropriate additional referrals.

Focus on CDM

- Congenital DM1 (CDM) is defined in a child who has one or more of the following features:

  a. Physical signs or symptoms attributable to DM1 at birth, or in the first month of life, including one or more of the following features: respiratory failure, feeding problems, weakness and hypotonia, clubfoot, polyhydramnios, and/or reduced fetal movement

  b. Genetic confirmation of expanded CTG repeat size

  c. Need for medical intervention or hospitalization in the first month of life for medical issues specific to myotonic dystrophy

  Diagnosis may not necessarily be made in the neonatal period but could be made later in life if the above criteria a. through c. were demonstrably present.

- All other DM1 patients presenting in the pediatric age range (that do not meet the congenital criteria) are herein referred to as childhood-onset DM1. The diagnosis of childhood-onset DM1 can be made at any age if features of DM1 were demonstrably present during the childhood years but were not medically identified or diagnosed. There are other classification systems in the literature that further subdivide patients by age of symptom onset, such as the following: mild and severe congenital (age 0-1 years), childhood (1-10 years), and juvenile (10-18 years). However, at this time we do not have the evidence necessary to clearly prognosticate or change management based on these age ranges. Much of the current childhood-onset DM1 medical literature does not clearly define the classification system used

General care considerations

Genetic counseling

Background

DM1 is caused by the expansion of an unstable CTG repeat sequence in an untranslated, but transcribed, portion of the 3' region of the dystrophia myotonica protein kinase (DMPK) gene located on chromosome 19q13.3. While DNA testing, including prenatal and presymptomatic testing for DM1 is now available there are many potential pitfalls in interpreting the results for the patient and family, making genetic counseling a useful part of the diagnostic process.

In many cases, a child with DM1 will be the first person in the family diagnosed with DM1, due to genetic anticipation. A diagnosis of DM1 in one person in a family has implications for other family members, raising questions about whether other family members who show no symptoms should be informed of the diagnosis and whether those family members should be tested. Diagnosis of DM1 in a presymptomatic person, especially if that person is a child, can have important implications for self-perception, health monitoring and future work and school functioning. DM is multisystemic disorder and many manifestations are not pathognomonic. Children especially have complex issues such as learning disabilities, physical fitness problems, etc. which are not uncommon among children without DM. However, the genetic diagnosis of DM may result in significant differences in the therapeutic approach, such as potentially preventable sudden deaths. As a result, there is significant debate about whether or not to test asymptomatic children. Certain countries have established legal precedent regarding this question, and it is therefore advisable to confer with a local genetic counselor before testing.

Recommendations

1. Refer all patients with congenital and childhood myotonic dystrophy and their parents to a genetic counselor (see nsgc.org for referrals in the United States) and to assess the parents for the diagnosis of DM1

2. Review pedigree annually. Genetic counseling should be repeated when new information or circumstances change the risks for family members

3. Ensure that genetic counseling for affected families conveys information about:

    a. The inheritance pattern of disease (autosomal dominant inheritance)

    b. The wide variability in the scope and severity of DM1 symptoms, even within the same family

    c. The possibility of changes in symptom scope and severity over time

    d. The likelihood that the mutation will expand and the disease will become more severe as it is passed from generation to generation (anticipation) and as patients age

    e. The possibility of a minimally-affected mother giving birth to a severely affected child-important

    f. Options for family planning

4. Help mutation carriers inform their close relatives of the possibility that they may also have inherited the risks and repercussions of DM1, even if they or their children are currently asymptomatic

5. Do not use CTG repeat numbers, if available, for genetic advice or prognostication; these need to be discussed with a genetic counselor

6. Advise parents who have a child with myotonic dystrophy that they have a 50% risk of having another child with DM1, and clinical experience suggests that they are likely to have congenital or childhood-onset in future births as well

7. Suggest that parents consider in vitro fertilization with pre-implantation diagnosis to prevent DM1 transmission, or other alternatives for expanding their family

8. If the family and physician are considering testing an asymptomatic child, recommend that all parties take part in a counseling session before testing, and at the time of the disclosure of the result. The counseling should involve the child, parents, child's physician, a genetic counselor, and if necessary, a psychologist. This may be cumbersome and deter casual testing; at least consider this approach for critical cases

Focus on CDM

- Repeat size is often large (typically >1000 repeats) but as mentioned above (point 5) the repeat size cannot absolutely in isolation be used to determine whether a child will have CDM or how severe his/her symptoms will be

- Once a family has had a child with CDM, there is an increased risk that the next child with DM1 will have congenital form as well

General care considerations

Neonatal care

Background

Women with DM1 can have a complicated pregnancy, labor, and delivery, including premature delivery or prolonged labor that can have impact on the newborn. In addition, the baby may be born with congenital-onset DM1, with severe neonatal complications, including respiratory and swallowing abnormalities. (see **Diagnosis and classification**, and **Genetic counseling**).

Prenatal and preimplantation genetic diagnosis (PGD) may be options for parents seeking to avoid transmitting the genetic mutation to their children. Knowing if a pre-neonate has a risk of CDM also enables the parents and the obstetric team to prepare for the birth of a DM1-affected baby.

Babies with congenital-onset DM1 may have the following prenatal and neonatal signs of varying severity:

- Polyhydramnios due to in utero swallowing difficulties
- Reduced fetal movement
- Poor feeding at birth, possibly requiring enteral feeding
- Respiratory muscle abnormalities, possibly requiring mechanical ventilation at birth
- Poor muscle tone and lack of fetal movement, often referred to as hypotonia or floppy infant syndrome
- Club foot and other joint problems such as arthrogryposis (multiple joint contractures)
- Abnormal accumulation of fluid in the body
- Enlarged ventricles in the brain (ventriculomegaly or even hydrocephalus)

Recommendations

1. A high-risk obstetrician should provide prenatal obstetric care for mothers known or suspected to be carrying a child with DM1
2. A pediatric or neonatal specialist should be present at delivery if a mother is known to have DM1, or if the child is known or suspected to have DM1
3. Neonatal intensive care consultation is recommended for neonates known to have, or suspected to have, DM1

Focus on CDM

- Children with CDM will often need management in a NICU that can provide breathing and feeding support, and a range of neonatal and consulting specialists who can manage genetic, respiratory, GI, orthopedic, neuromuscular, neurosurgical, and cardiac issues
- Breathing support should be managed by endotracheal intubation or supplemented with non-invasive maneuvers as dictated by the severity of the respiratory failure. As most CDM infants will improve in their breathing function as they age, an adequate trial of ventilation should be given
- Weaning from ventilatory support can be much slower than would be the case for other disorders such as prematurity and pneumonia. Using a respiratory muscle aid protocol with manually and mechanically assisted coughing (to reverse airway mucus-associated decreases in oxyhemoglobin saturation) and non-invasive positive pressure ventilation if needed, with gradual weaning of support, is therefore recommended over a conventional weaning management strategy
- Feeding support should be managed by nasogastric tube initially, as many children with CDM will improve in feeding function over time. Placement of a gastrostomy-tube for longer term feeding is warranted for those who do not show improvement by one month of age, corrected for prematurity if needed
- Conduct monitoring for joint contractures and other orthopedic complications, and refer to orthopedics and/or physiotherapy
- Prevent skin pressure injuries by frequent repositioning and avoidance of pressure points in cribs or car seats for infants with reduced movement resulting from severe weakness
- Optimize social and cognitive development using age-appropriate developmental care and infant stimulation programs
- Monitor head circumference to identify hydrocephalus
- Refer parents to genetic counseling and family planning services for future child-bearing decisions and subsequent pregnancies
- Implement comprehensive discharge planning to ensure that all necessary services (e.g. infant development services) and equipment (e.g. proper car seats) are in place and follow up appointments are scheduled
- Refer to pediatric neuromuscular multidisciplinary clinic on discharge from the neonatal unit to manage the many issues that children with CDM will encounter

General care considerations

Palliative care counseling and management

Background

Caregivers of neonates with CDM may be faced with major medical care decisions, including life-sustaining choices. Children with CDM can make a surprisingly strong recovery after a prolonged critical period in the neonatal stage, and that information should be conveyed to the family. It is important to offer families anticipatory guidance to review the natural history of CDM, what choices and options are available for medical management, as well as the complications that arise during a NICU admission. Options for maintaining nutrition via enteral tube feeding, assisting respiratory function via assisted ventilation, and treating progressive hydrocephalus should be discussed.

Have these discussions as early as possible to promote better awareness among caregivers and the medical team of the choices available and their effects on each person involved. Recognizing the potential for significant caregiver burden is an open discussion that will also help guide decision making.

Recommendations

Physicians and other health professionals caring for CDM patients that require significant life sustaining therapies such as invasive ventilation should take the following steps toward providing palliative care and encouraging advance directives:

1. Recommend the introduction of palliative care at the time of diagnosis and at regular intervals thereafter. When a formal pediatric palliative care team is available, it should be consulted
2. Recognize and address caregiver burden, whether or not the caregiver has DM1, offering respite care or equivalent measures to improve family support. Address grieving patients and family members and offer counseling as appropriate
3. Establish an emergency health care plan and advance directives with the family

Focus on CDM

- Introduce the concept that the natural history of CDM is one of childhood progressive muscle strength improvement, but that the complications of CDM can be critical and have a high risk of mortality, particularly in the first year of life
- Create a shared decision-making environment with families so that they develop their own prognostic awareness and can accept difficult decisions
- Advise families or caregivers that invasive and noninvasive ventilation, and nutrition via gastrostomy tube, are acceptable elements of care for patients with CDM

General care considerations

Surgery and anesthesia

Background

DM1 patients, including children with DM1, are far more likely than the general population to have adverse reactions to medications used for anesthesia and analgesia. Children may undergo sedation for a wider range of medical issues than adults, and deep sedation for such procedures as dental examinations, MRIs and other diagnostics tests, eye examinations, etc. General pediatricians should therefore advise patients and their families that any sedation should be treated carefully and anyone administering anesthetic or sedation should be aware of the diagnosis of DM1, including subspecialists such as dentists, radiologists, etc.

Interactions of the cardiac, respiratory, muscle and central nervous systems in DM1 patients can lead to a variety of untoward responses before, during and after surgery. Serious adverse events have been reported even in patients whose overall DM1 symptoms were mild. A guide for peri-surgical management has been produced for adults by the Myotonic Dystrophy Foundation. See *Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient and Anesthesia Quick Reference Guide* http://www.myotonic.org/clinical-resources

Anesthetic risks of concern for children with DM1 include the following:

- Cardiac conduction defects and potentially fatal arrhythmias
- Ventilatory insufficiency and poor airway protection
- Gastrointestinal dysmotility that frequently results in pseudo-obstruction and can lead to aspiration
- Erratic responses to succinylcholine (although DM1 does not increase true malignant hyperthermia reactions, this drug should not be used in DM1 patients because of the risk of masseter spasm and hyperkalemia)
- Prolonged and heightened sensitivity to sedatives and analgesics, resulting in serious complications in the post-anesthesia period. After-anesthesia risk of aspiration and other complications is increased due to the following drug-induced effects:

    a. Reduction in level of consciousness

    b. Exaggerated ventilatory weakness

    c. Pharyngeal dysfunction with reduced airway protection

    d. Gastrointestinal dysmotility and potential pseudo-obstruction

Recommendations

1. Before any surgeries or procedures requiring anesthesia, see Myotonic Dystrophy Foundation *Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient* for anesthesia risks and recommendations and the *Anesthesia Quick Reference Guide* http://myotonic.org/clinical-resources
2. Inform all caregivers that any clinicians administering or prescribing an anesthetic should be aware of the DM1 diagnosis and impact of sedation on DM1 patients
3. When possible combine procedures under a single sedation
4. Arrange for a pre-anesthetic visit for all children planning to have deep sedation for a diagnostic test, procedure or surgery. If possible, include a pulmonologist with expertise in neuromuscular diseases during this visit
5. Consider referral to a Child Life Specialist or a similar program that specializes in reducing the anxiety for children undergoing a surgical procedure
6. Monitor during anesthetization for untoward responses and interactions of the cardiac, respiratory, muscle and central nervous system before, during and after surgery
7. Monitor for a longer than typical period of time after sedation, even in mild DM1 cases, in order to detect any serious adverse events in the hospital setting
8. Provide patients with a DM1 wallet card or bracelets

Focus on CDM

- Children with CDM are at a higher risk of anesthetic complications when compared to individuals with childhood or adult-onset, given the underlying respiratory involvement

Systems-based approach to management

Respiratory management

Background

Most children with childhood-onset myotonic dystrophy have normal breathing function and few respiratory issues. However, the spectrum of severity is wide, and some children with DM1 may have significant breathing problems resulting from muscle weakness of the diaphragm, abdominal and intercostal muscles. The weakness and myotonia of these muscles may lead to poor ventilatory force and result in low blood oxygen and elevated blood carbon dioxide levels. Patients with CDM are typically very weak, and respiratory failure in the neonatal period is often a presenting feature and a significant cause of morbidity. See **Neonatal care** regarding issues of ventilation in the newborn.

Weakness of the inspiratory and expiratory muscles and the facial muscles often reduces cough effectiveness and impairs clearing of secretions, leading to an increased risk of pulmonary infections and to aspiration of material into the lungs. Weakness of the swallowing muscles can add to the risk of aspiration of food and drink, saliva, nasal secretions and stomach fluids.

Excessive daytime sleepiness (EDS) and respiratory failure are common in DM1 and both significantly reduce quality of life. Their causes may overlap, but some sources believe that EDS in DM1 is mostly due to primary central nervous system involvement and that respiratory insufficiency or failure is mostly due to respiratory muscle weakness. That said, insufficient air flow during sleep may contribute to disrupted sleep and to excessive daytime fatigue. Restless leg syndrome is also very common in children with DM1 and should be considered during evaluation.

Recommendations

Look for:

a. Signs of respiratory problems in children with myotonic dystrophy, including ineffective cough, recurrent pulmonary infections, orthopnea, dyspnea, poor sleep, morning headaches, apnea, fatigue and snoring

Test for:

a. Forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) in the sitting and supine positions, when the child is old enough to cooperate for an accurate study (typically around 5 years). Consider using a mask if lip seal is not ideal or the child lacks muscle control

b. Sniff nasal inspiratory pressure (SNIP) test when an FVC is difficult to obtain

c. Nocturnal oximetry if snoring, nightly interrupted sleep, morning headaches or excessive daytime sleepiness are present

d. Peak expiratory flow during cough

e. A polysomnogram (sleep study) if symptoms of snoring, nightly interrupted sleep, morning headaches or excessive daytime sleepiness are present

f. Clearance capacity and other respiratory assessments prior to surgery; if needed, adaptation to nocturnal noninvasive ventilation or to cough-assist devices should also occur prior to surgery (see **Surgery and anesthesia**)

Treat with:

a. Vaccinations for influenza and pneumococcus pneumonia. For infants RSV prophylaxis is also suggested

b. Standard medical therapy as soon as possible for patients with respiratory infections, including respiratory cough assistance and mechanical ventilation as needed. Obtain consultations from respiratory therapy and pulmonary medicine groups

c. Cough assistance techniques (e.g., air stacking, abdominal thrust and cough machine) for DM1 patients with ineffective cough and during chest infections and perioperative periods

d. Noninvasive positive-pressure ventilation (NIV) for respiratory insufficiency in patients who have respiratory muscle weakness and sleep-related breathing disorders. Noninvasive positive-pressure ventilation should be launched according to the criteria defined in the respiratory consensus ENMC (European Neuromuscular Centre) Workshop (2014-07-21). In this case, NIV is specifically referring to a BiPAP machine, but a CPAP is an adequate alternative if necessary

e. Supplemental oxygen with caution and only in conjunction with noninvasive ventilation (see **Surgery and anesthesia**)

f. Emergency medical alert devices or wallet cards

Focus on CDM

- CDM children who remain on longer-term trach ventilation often improve in respiratory strength over time and consideration to decannulate a tracheostomy should be made after careful consideration with the multidisciplinary team including neurology, respirology, ENT and the family. Airway control, respiratory infection frequency, ability to tolerate a facial or nasal mask for NIV and compliance and cooperation with maintenance pulmonary therapy such as cough assist, breath stacking etc. should be considered. Testing for hypoventilation in sleep should be done prior to decannulation
- For children with CDM who remain on invasive or non-invasive ventilation, ongoing management by a pediatric respirologist and otolaryngologist is recommended

Systems-based approach to management

Cardiovascular management

Background

DM1-related cardiac pathology manifests predominantly as arrhythmias due to progressive abnormalities in the conduction system of the heart. Clinical presentations may include: pre-syncope, syncope, palpitations, dyspnea and, rarely, chest pain or sudden death from cardiac arrest. Sudden cardiac death is one of the most common causes of death in adult DM1. Bradyarrhythmias (arrhythmias that cause a slowing of the heart rate) are not reported in literature under the age of ten years. Rarely, life-threatening tachyarrhythmias have been reported in patients as young as ten. Although exact numbers of sudden cardiac death in children with DM1 or CDM are not known, they are thought to be very low.

It is important to evaluate the severity of cardiac rhythm disturbance via a 12-lead electrocardiogram (ECG), and long-term ambulatory ECG monitoring. Serial ECG studies are useful to follow progression of conduction system abnormalities over time, as they are often asymptomatic. Recommendations for preventative pacemaker implant may be based on serial changes. Although children are at a very small risk of sudden death due to tachyarrhythmia, there is not necessarily a consistent ECG abnormality or bradyarrhythmia that has been linked to cardiac events. ECG results may therefore be normal preceding sudden death by tachyarrhythmia. Sudden death in children has been described following surgical procedures and severe illness, and monitoring in hospital may therefore be appropriate in these situations.

Recommendations

General:

a. Encourage use of emergency medical alert devices to identify DM1 diagnosis and risk of arrhythmia

b. Inform families of the risks of arrhythmias and cardiac dysfunction and the importance of prompt medical attention if symptoms are observed (i.e. palpitations, pre-syncope, syncope, dyspnea, chest pain, unexplained fatigue)

Look for:

a. Symptoms representing arrhythmias. Assess for sinus bradycardia, heart block, atrial fibrillation and flutter, orventricular tachycardia on ECG and systolic dysfunction on echocardiogram

b. Symptom change, abnormal cardiac imaging, abnormal ECG in any DM1 patient. This should prompt referral to a cardiologist or electrophysiologist knowledgeable about cardiac manifestations in DM1

c. DM patients with palpitations, dizziness, syncope, non–sinus rhythm, PR interval >240 ms, QRS duration >120 ms, or second- or third-degree atrioventricular block in order to be evaluated at least annually and also considered for invasive electrophysiology study for possible pacemaker or ICD placement

Test for:

a. Cardiac involvement; a 12-lead ECG should be performed at DM1 diagnosis. If normal and the patient remains asymptomatic, ECG should be performed annually. Investigate further if the patient is symptomatic

b. Transient arrhythmia via 24-48 hour ambulatory holter ECG monitoring. Longer monitoring if the 12-lead ECG is abnormal or if the patient has symptoms which are suggestive of an arrhythmia

c. Cardiology evaluation with examination, ECG, echocardiogram, and ambulatory electrocardiographic monitoring should occur at the time of DM diagnosis, regardless of symptoms

d. For DM patients with normal LV ejection fraction and no evidence of the symptoms described prior, it is reasonable to reassess by examination, ECG, and ambulatory electrocardiographic monitoring annually and by echocardiogram every 2 to 4 years

e. For young DM1 patients, serial exercise stress testing and signal-averaged ECGs may be considered

An ECG should always be performed prior to commencing any medication that can cause or exacerbate cardiac conduction disorders (i.e. antiarrhythmic agents or medications for treatment of ADHD). ECGs should be performed subsequently every six months after an initiation of therapy. Clinical judgment may warrant holter monitoring or cardiology referral in this setting.

Treat with:

a. Serial periodic clinical cardiology evaluation; specialist cardiology consultations are essential in patients with abnormal electrocardiograms or cardiac symptoms

Refer to:

a. In-hospital cardiac monitoring to detect arrhythmias if admitted for longer duration than typical following surgical procedures

b. In-hospital cardiac monitoring if admitted due to severe illness or infection

c. American Heart Association (AHA) Management of Cardiac Involvement Associated With Neuromuscular Diseases: A Scientific Statement From the American Heart Association 2017 and ACC (American College of Cardiology)/AHA (American Heart Association))/ESC (European Society of Cardiology) Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death section on pediatric issues 13.4.

Systems-based approach to management

Skeletal muscle weakness, orthopedic complications, and rehabilitation

Background

Skeletal muscle weakness is not usually a major feature of childhood-onset DM1 but can be functionally limiting in those with CDM. Children with CDM have delayed gross motor skills, but almost all obtain independent ambulation. Children with CDM have improving motor function during the first few years of life, even those with profound hypotonia at birth. They benefit from promotion of motor function through therapy and other activities.

Weakness and atrophy of the jaw and facial muscles has the greatest functional impact and results in a number of manifestations:

- Reduced facial expression
- Weakness of the facial, tongue and palatal muscles, leading to dysarthria, dysphagia, and jaw tightness
- Weakness of the eyelid muscles, leading to drooping of the eyelids (eyelid ptosis)

Orthopedic complications may occur in children with CDM. The most common complication is talipes equinovarus, though children may develop knee or hip contractures and scoliosis.

Recommendations

Look for:

a. Physical, occupational, and speech therapy needs early and often with specific attention to:

   i. Feeding concerns and dysphagia

   ii. Gross motor delay

   iii. Gross and fine motor weakness

   iv. Dysarthria and potential augmentative and alternative communication (AAC) needs

   v. Language acquisition delays

b. Scoliosis; if necessary, consider bracing or referral to orthopedic surgeon

c. Crowded teeth that benefit from orthodontic treatment. The goal of such treatment is to facilitate oral hygiene. Caregivers should be counseled to proactively maintain oral hygiene

Treat with:

a. Surgical correction of talipes equinovarus or other contractures early in evaluation if these changes prevent appropriate biomechanical alignment for mobility, cause pain, or limit functional mobility

b. Speech therapy targeting speech, language, and communication from a very early age

c. Augmentative and alternative communication (AAC) therapy individualized for their linguistic and cognitive abilities if appropriate or necessary

Focus on CDM

- Newborns with CDM often have difficulty feeding and alternative nutrition should be considered. After about a year of actively working with a speech therapist or OT, most children can generally start on PO feeding
- Children with CDM experience progressive improvement in their proximal strength until adolescence, at a minimum. Children should therefore be encouraged to participate in physical activity
- Assessment of joint arthokinematics and range of motion should be observed to manage development of joint contracture
- Prevention of joint contractures is key to management and should be closely monitored with early initiation of stretching. Treatment of talipes equinovarus and other joint contractures should include initial stretching regiment and appropriate ankle bracing (for talipes equinovarus). Serial casting may be considered

Systems-based approach to management

Skeletal muscle myotonia

Background

Myotonia – sustained muscle contraction and difficulty relaxing muscles – is a hallmark of DM1 and is an aspect of the disease that distinguishes it from other forms of muscular dystrophy. It affects many patients with adult-onset DM1 but is uncommon in young individuals with DM1. In some late childhood or adolescent patients, myotonia can become problematic. Myotonia can contribute to muscle stiffness, pain, prolonged hand grip, speech and swallowing difficulties, and GI issues.

Myotonia in DM1 is most prominent in the forearm and finger muscles, where it causes locking of the grip ("grip lock"). It sometimes affects tongue and jaw muscles, leading to difficulty with speech and chewing. Difficulty swallowing can be caused by myotonia of the face, tongue, jaw, pharyngeal and esophageal muscles, and myotonia of the respiratory muscles can lead to poor breathing force and low blood oxygen levels.

Grip myotonia can be observed by having a DM1 patient tightly grip the clinician's fingers, and then asking the patient to relax his hand after a sustained grip; the hand muscles will typically take 20 seconds or more to fully relax. Percussion myotonia can be demonstrated by a sustained contraction after the patient's muscle is tapped with a reflex hammer. Electrical myotonia can also be demonstrated by abnormal, spontaneous muscle fiber discharges seen on a needle electromyogram (EMG).

DM1-associated myotonia is commonly worse in cold weather and is more pronounced after rest. Its improvement with muscle activity is known as the "warm-up" phenomenon.

Drugs affecting ion channels, such as mexiletine (Mexitil), can improve myotonia, although their potential for causing cardiac arrhythmias must be weighed against their possible benefits.

Recommendations

Look for:

a. Delayed relaxation after grip or percussion, difficulty related to activities of daily life, progressive speech impairment, or profound irritable bowel symptoms

Treat with:

a. Mexiletine (Mexitil) if myotonia is demonstrated and is distressing to the patient. As mexiletine is an antiarrhythmic, conduct an electrocardiogram (ECG) prior to use, again within three months of starting therapy, and then at serial intervals. Instruct the patient to avoid dyspepsia and transient 'dizzy feelings' associated with mexiletine treatment by taking it with food to extend absorption and lower peak level in blood

Systems-based approach to management

Ocular and hearing management

Background

Major and clinically relevant eye manifestations in congenital and childhood-onset DM1 can include hyperopia, eyelid ptosis, incomplete eyelid closure, strabismus, and other eye movement abnormalities. Cataracts, while a common concern in adults, are almost never seen in children.

Bilateral eyelid ptosis is a frequent feature of DM1. In severe cases, it can obstruct vision and may require surgical or nonsurgical intervention. Weakness of eyelid closure muscles is also a common problem and can cause corneal damage.

Otic infections during infancy manifested as an infection of the upper respiratory tract are frequent, and patients typically require surgical interventions, such as uni or bilateral tympanostomy.

As described in the literature, adult patients can have "early presbycusis", high frequency hearing loss and vestibular dysfunction as a manifestation of cochlear/vestibular dysfunction, however none of these have been shown in childhood-onset DM1 or CDM.

Recommendations

Look for:

a. LETTERS Baseline audiometry, especially at school age

b. Signs of upper respiratory tract infections, especially when manifesting as an otitis media, and give proper treatment as needed. Advise parents to be aware of and look for symptoms

Test for:

a. Signs of strabismus or other ocular misalignment using a cover/uncover test. Persistent dysconjugate gaze in childhood can result in amblyopia

b. Eyelid ptosis; if ptosis becomes severe and interferes with vision, intervention such as eyelid "crutches" that can be inserted into glasses may be warranted. Try crutches as a remedy for ptosis before eyelid surgery is considered, due to anesthesia risks

Refer to:

a. An optometrist for examination at diagnosis and thereafter at least annually to identify hyperopia, astigmatism, strabismus

b. An ENT If the patient presents with frequent ear infections

c. An ophthalmologist for regular follow-up if eye movement abnormalities or weakness of eyelid closure are putting vision at risk. Ophthalmic lubricants for dry eye can be considered

Systems-based approach to management

Gastrointestinal and genitourinary management

Background

Because both the smooth and skeletal muscles are involved in DM1, dysfunction along the entire gastrointestinal (GI) tract is common in this disorder. Children with CDM may have profound oral facial weakness that prevents oral intake and requires a gastrostomy tube. This will improve with age, though not completely. Other gastrointestinal symptoms include aspiration, abdominal pain and bloating. Intractable constipation and diarrhea may occur, as well as fecal incontinence. These may result in fecal impaction and megacolon. While children with childhood-onset DM1 do not have neonatal feeding problems, they may have any of the other symptoms.

Children may have urinary incontinence and difficulty toilet training. This may resolve, or partially resolve, with age.

Recommendations

Treat with:

a. Fiber supplementation (more than 8 grams daily) for children with constipation or diarrhea

b. Gentle laxatives for constipation:

   i. First-line therapy recommendations: polyethylene glycol (Miralax), senna (Ex-Lax, Senokot), docusate (Colace) or lactulose (Cholac)

   ii. Second-line therapy recommendations: bisacodyl (Dulcolax, Correctol), lubiprostone (Amitiza) or linaclotide (Linzess)

   iii. Metoclopramide (Reglan) to reduce the symptoms of gastroparesis, pseudo-obstruction and gastric reflux. Long-term use is not recommended because this drug can cause tardive dyskinesia

   iv. Antibiotics to reduce diarrhea if bacterial overgrowth is found on breath testing

   v. Referral to a gastrointestinal specialist for anal manometry should be considered if a patient does not respond to the first- or second-line recommendations above

   vi. Oils should be avoided

c. Mexiletine may be considered for refractory diarrhea or constipation (see **Cardiovascular management** for mexiletine advisory)

Focus on CDM

- As mentioned in **Neonatal care**, children with CDM may require a temporary feeding tube. If dysphagia persists, consider enteral nutrition. Refer to speech therapy. Children should be periodically re-assessed for improving dysphagia
- Children with CDM often benefit from dysphagia therapy. With aggressive dysphagia therapy, children with CDM often are able to PO feed within the first year of life

Systems-based approach to management

Neurodevelopmental management

Background

Cognitive impairment can be a major problem in children and adolescents with DM1, while muscle symptoms may be relatively discrete or absent within the childhood-onset form. Moderate to severe intellectual disability (ID), severe problems regarding adaptive skills and profound dysarthria are frequently associated with CDM. In the childhood-onset phenotype, ID ranges from moderate to subnormal IQ with higher verbal comprehension abilities, but reduced perceptive organization skills and slowed speed of processing. Deficits in visual attention, visual constructive abilities, as well as working memory, planning and cognitive flexibility have also been reported.

The principal behavioral manifestations found in patients with CDM are the Autism Spectrum Disorders (ASD). Most patients present with communication issues. Patients are often described as kind, calm, passive, with a low pace, but easily fatigued and sometimes with social anxiety.

Childhood-onset DM1 patients are commonly described with attention deficit disorders without hyperactivity, anxiety and alexithymia. ASD can be present but with less involvement than in CDM. Parents commonly describe symptoms of fatigue and excessive daytime sleepiness, which may be principal causes affecting the quality of life in childhood-onset DM1 patients.

Family members and caregivers of CDM and childhood-onset DM1 patients, as well as patients themselves, should be made aware that DM1 is also a "brain disorder" and that cognition and behavior are often affected. Cognitive and personality aspects of CDM and childhood-onset DM1 overlap considerably with deficits in psychosocial functioning (see **Psychosocial considerations**).

It is important to accurately assess and follow up on cognition, emotional and adaptive skills in children with CDM and childhood-onset DM1, due to the large impact these deficits can have on the daily lives of patients and their families.

Recommendations

Test for:

a. Cognitive strengths and weaknesses in patients with CDM and childhood-onset DM1 via neuropsychological tests:

   i. Psychometric assessment of global intellectual ability and adaptive functioning

   ii. Assessment of executive functions

   iii. Assessment of social cognition

   iv. Assessment of visuomotor integration and visuospatial ability

   v. Assessment of receptive and expressive language ability

   vi. Assessment of excessive daytime sleepiness (EDS)

   vii. Assessment of learning disabilities (specific tests for dyscalculia, dyslexia and dyspraxia)

viii. The assessments should be performed at diagnosis, in preschool if applicable, and should be repeated, depending on the level of functioning, 2-3 times before adulthood

ix. Psychiatric or behavioral issues; refer patients to a mental health care professional for assessment of Autism Spectrum Disorders, attention deficit disorders with or without hyperactivity and other behavioral problems

Communication between the health care professional and the school should be encouraged to develop educational strategies and individualized educational programs.

Treat with:

b. Psychostimulants if attention deficits are associated with an impairing level of fatigue or excessive daytime sleepiness (see **Excessive daytime sleepiness**)

c. Serotonin-enhancing antidepressants if excessive anxiety or other treatable psychiatric symptoms are present

d. Specific cognitive remediation programs to enhance social abilities (visual contact, joint attention, emotional regulation) or executive functions efficiency (impulsivity, attention, working memory, and mental flexibility) using dedicated software (e.g., Cogmed®)

e. Language remediation and reading therapy in the presence of cognitive deficits, even in children with normal intelligence. These deficits, including attention deficit, fatigability, and visual–spatial construction disability, can result in reading and spelling difficulties as well as mathematical impairment

Systems-based approach to management

Psychosocial management

Background

Children diagnosed with myotonic dystrophy type 1 (DM1) can present with a range of complex physical, cognitive, behavioral and personality features that can have a substantial impact upon development and quality of life status in childhood and during transition to adulthood.

DM1 can seriously hinder a child's developmental stages at home, school and within community settings. Important relationships with peers, family members and others around the child can be at risk of significant breakdown. A child with DM1 may become increasingly stressed, isolated and vulnerable as s/he attempts to progress through early years and beyond.

Children living with DM1 are likely to be part of a family affected by the same diagnosis. Children with an affected DM parent may not receive optimal emotional or intellectual support and guidance, and may lack routine care and nurturing, all of which can destabilizing.

Children with DM1 may struggle to meet milestones in physical and psychological development. Poor social and communication skills may be a cause for concern, along with below-average educational attainment. Due to facial weakness, children can experience speech difficulties ranging from mild to profound and some children's speech may not be understood at all. Communication restrictions can affect social relationships and education.

Educational institutions are likely to have limited knowledge of the condition and will consequently lack the competencies needed to deal with patients' issues. Educators play a pivotal role in a child's life, but they may fail children with DM1 due to a distinct lack of resources and information, and children with DM1 can fail to thrive in education systems.

Children with DM1 may have reduced physical capabilities including poor stamina, low energy levels and high levels of fatigue. These symptoms may be interpreted as general laziness or lack of motivation in activity performance. Children with DM1 may demonstrate physical distress via inappropriate behaviors, social withdrawal and/or poor social skills.

Children with DM1 can have problems with skills attainment in a number of activities of daily living, including continence management (toileting and hygiene skills), dressing/undressing and other important personal care domains. If not addressed, these skill delays can exacerbate with age and lead to untoward events with peers, family and staff.

Recommendations

General:

a. Healthcare professionals have a responsibility to coordinate specialist care and support services for children with DM1, monitoring the psychological and social dysfunctions and monitoring the home and educational environment. Coordination between health and social service agencies is essential to ensure a consistent approach to care

Refer to:

a. Speech and language therapy from an early age to manage swallowing issues, deficits in expressive and receptive language, and communication problems

b. Appropriate psychological and therapy services at an early age to ensure that children with DM1 achieve their maximum potential and learn coping strategies for later life. Social engagement strategies can assist children with DM1 to develop confidence and self-esteem

c. Family care and support services throughout childhood with social care assistance where required. Schools should be provided with specialist information about the care and management of a child with DM1. A social work consult or a referral to nursing case management can also be beneficial for patients

d. Agencies that provide access to disability benefits, adequate housing, and adaptive devices and strategies as the disease progresses

e. Special support groups nationally and locally to foster social engagement for children and families, and to provide guidance, advice and community engagement

Systems-based approach to management

Excessive daytime sleepiness

Background

Excessive daytime sleepiness (EDS) and fatigue can significantly impact the quality of life in children with DM1. These symptoms typically develop after age 10 and become progressively worse over time. Children may have difficulty paying attention in school and the need for afternoon naps may restrict their ability to participate in extracurricular activities.

Recommendations

General:

a. Educate family members and teachers about signs and impacts of EDS, including prolonged naps or falling asleep in school

Test for:

a. Sleep apnea via overnight oximetry or polysomnogram

Treat with:

a. Positive-pressure ventilation if a DM1 patient's sleepiness is thought to be related to nocturnal or daytime hypoventilation or sleep apnea. Patients should be referred to pulmonologists who have experience in neuromuscular diseases for consideration of assisted ventilation

b. Stimulant therapy with a psychostimulant such as modafinil (Provigil), methylphenidate, or other if central hypersomnia is suspected (often difficulty staying awake in school is an indicator). Special care should be taken in children with previously-detected cardiac arrhythmias. (See **Cardiovascular management** re: stimulant management)

c. Restless leg syndrome, if present, with pramipexole, gabapentin, or other common medications, though benzodiazepines should be avoided because of their sedating effect

Systems-based approach to management

Endocrine and metabolic

Background

Endocrinological manifestations (estradiol insufficiency and insulin resistance) of the disease are well described in adults with DM1, but have rarely been rarely reported in children.

Cryptorchidism presenting in neonatal hypotonia is frequently reported during the first years of life of male CDM patients, and may be the prenatal manifestation of a low serum testosterone.

Reports describing the presence of thyroid dysfunction in childhood exist, but not as a common co-morbidity in CDM or childhood-onset DM1 patients. CDM and childhood-onset patients may develop insulin resistance, hypothyroidism, hyperparathyroidism, hypogonadotropic hypogonadism and other adult-onset endocrine and metabolic symptoms as they age.

Recommendations

Look for:

a. Gonadal insufficiency and complications of the reproductive system via a detailed physical exam

b. Amenorrhea or dysmenorrhea in female patients; and erectile dysfunction in male patients

Test for:

a. HbA1c and thyroid stimulating hormone (TSH) and Free T4 level at baseline and every 3 years, or if there is a clinical suspicion or symptom development

b. Fasting blood lipids, plasma glucose, liver enzymes, bilirubin levels, and Gamma Glutamyl Transpeptidase (GGT) at baseline

General recommendations

Patient and disease registry referral

General neuromuscular and DM1-specific registries serve a number of purposes that can be helpful to the patient and the wider community. Although individual registries have discrete purposes, the following may be achieved by a well-implemented registry:

- Education and communication across a community or region
- Information dispersal about research studies for which patients may be eligible
- Facilitation of research projects and planning for clinical trials
- Capturing clinically-important natural history data about the disease
- Improvement of clinical care

When referring to a registry, consider the following:

- Patient privacy protections, mechanisms and policies
- Registry ownership, governance and oversight
- Registry objectives

For a list of DM1 registries refer to MDF (www.myotonic.org) or TREAT-NMD (http://www.treat-nmd.eu/resources/patient-registries/list/) or the regional DM1 patient advocacy group.

Alert cards and bracelets

Because DM1 is multisystemic and carries the risk of sudden cardiac death, all patients should use a medical alert bracelet or card. These are generally available through local patient advocacy organizations and online.

Addendum 1:

Project overview and list of authors

The Consensus-based Care Recommendations for Children with Myotonic Dystrophy Type 1 was created by a group of 11 international clinicians with knowledge or experience in the care and treatment of children living with myotonic dystrophy type 1. They included:

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The Myotonic Dystrophy Foundation (MDF) designed and initiated the consensus-based process and provided project management and document preparation services. MDF team members included Paul Formaker, Leah Hellerstein and Molly White.

Addendum 2:

Reading list

Diagnosis and classification

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