DRAFT Care Considerations for DM1

As new therapies for DM enter clinical testing in multi-site trials, there is a need to standardize care for DM to reduce variability in clinical testing and to improve care for DM in areas that lack specialists in this rare disease. Although practice parameters for DM are in development by the American Academy of Neurology, it is not anticipated that many specific recommendations will be made with this methodology. Consensus-based guidelines may serve to fill the gap until evidence-based guidelines are available.

The following draft guidelines were created by combining recommendations from four sources:


A separate, annotated notes version of these guidelines exists with the individual source of each item cited, and contradictions between sources highlighted (these were remarkably few). This document is meant to serve as a “strawman” to guide discussion on consensus in each subject area, using whatever methodology is selected to achieve this end and should not be considered a final draft. Whole subject areas may be added, deleted, changed or expanded based upon the consensus recommendation of this committee.

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Diagnosis

Background

Diagnosing adult-onset type 1 myotonic dystrophy (DM1) is not difficult if the disorder is suspected. However, the path to diagnosis is complicated by the wide range of body systems involved, the number of different practitioners consulted by the patient, and the variability of severity of the signs and symptoms of the disease. It can take more than seven years for a patient to receive a correct DM1 diagnosis.

Recommendations

1. Patients suspected of having DM1 should be referred to a neuromuscular disease specialist as early as possible in the diagnostic process.

2. Diagnosis of DM1 should start with a complete family history and physical examination, with particular emphasis on neuromuscular and ophthalmologic assessments.

3. Neuromuscular aspects of the physical examination should include checking for muscle strength/weakness and checking for myotonia using a grip test or percussion hammer to tap the muscles in the hand or forearm.

4. The presence of distal-predominant myotonic discharges, myopathic motor units and early recruitment seen on electromyography (EMG) is useful to confirm the presence of skeletal muscle myotonia suggestive of DM1.

5. Initial aspects of the ophthalmologic examination should include questioning the patient about difficulties with vision and examining the patient for cataracts; the presence of cataracts before age 55, along with muscle symptoms, is suggestive of DM1 or DM2.

6. Referral to an ophthalmologist for slit-lamp eye examination is recommended to further characterize lens opacities typically seen in DM1 and to diagnose early-stage lens opacities.

7. A serum creatine kinase (CK) level should be checked; in DM1 patients with weakness, it is generally mildly elevated, while in those without weakness, it is generally normal; a very high CK level suggests a muscle disorder other than DM1.
8. Muscle biopsies are less often performed now that genetic testing is widely available for DM1 and are not considered necessary where genetic testing can be employed. However, if muscle biopsy tissue is available, it can help support a DM1 diagnosis if there are increased numbers of centralized muscle fiber nuclei, ring fibers, pyknotic clumps in cell nuclei, and selective atrophy of type 1 fibers.

9. Genetic testing (DNA testing) provides a definitive diagnosis of whether or not a person has DM1; it is performed from a sample of blood or other tissue, from which DNA is analyzed to determine whether or not an expanded number – more than 37 – cytosine-guanine-thymine (CTG) repeats on chromosome 19q13.3 is present.

10. Prenatal testing, where the DNA of the fetus is checked for the presence of a DM mutation, is available, as is preimplantation genetic diagnosis, in which testing of fertilized eggs is performed before eggs are implanted into the uterus.

**Genetic counseling**

*Background*

DM1 is caused by the expansion of an unstable CTG repeat sequence in an untranslated, but transcribed, portion of the 3’ untranslated region of the myotonic dystrophy protein kinase (DMPK) gene located on chromosome 19q13.3. While DNA testing, including prenatal and presymptomatic testing, for DM1 is now widely 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.

The mutation is inherited in an autosomal dominant pattern. As a general guideline, unaffected individuals have between five and 37 CTG repeats at 19q13.3. Those with 38-49 CTG repeats are considered to have a “premutation,” one that is likely to expand into a DM1-causing mutation as it is passed to offspring. Patients with 50-150 repeats generally develop mild DM1; while those with 50-1000 repeats are likely to develop adult-onset (“classical”) DM1. The most severe form of the disease, congenital-onset DM1, generally occurs when there are more than 1000 repeats.

A distinctive feature of DM1 genetics is somatic mosaicism – inconsistency of the DNA in different cells and different tissues, even in the same person at any given time point. In DM1, the CTG repeat size is stable in some postnatal tissues, such as leukocytes, but is not in others, including those of the cardiac
and skeletal muscles. Therefore, the diagnostic test results from leukocyte DNA correlates poorly with the expansion size in affected tissues and organs. In addition, the size of the repeat generally expands with time in many tissues, so the number of repeats reported in a given diagnostic test depends on the age of the patient when the sample was taken, as well as on the particular tissue sampled.

The phenomenon of anticipation – earlier age of onset and increased severity of disease symptoms – from generation to generation is a known feature of DM1. Although appreciation of this phenomenon is important for all families, it is particularly crucial information for women of childbearing potential, who may have a DM1 mutation that causes mild or no DM1 symptoms but give birth to a baby with a mutation that causes the severe, congenital-onset form of the disease.

A diagnosis of DM1 in one person in a family has implications for other family members, giving rise to questions about whether or not the affected person should tell family members who show no symptoms and then whether or not those family members should be tested. Diagnosis of DM1 in a presymptomatic person (including a child) can have important implications for health monitoring and family planning, but it can also raise the possibility of difficulty in obtaining insurance or encountering prejudice in the workplace.

Recommendations

1. Referral to genetic counseling is recommended for all DM1 patients, particularly if the patient – male or female – desires to have children.

2. Genetic counseling in DM1-affected families should convey information about the inheritance pattern of the disease (autosomal dominant inheritance); the wide variability in the scope and severity of DM1 symptoms, even within the same family; the possibility of changes in symptom scope and severity over time; the likelihood that the mutation will expand and the disease will become more severe as it is passed from generation to generation, with particular attention to the possibility of a minimally affected mother giving birth to a severely affected child.

3. Genetic counseling should include discussion of whether and how to impart information about DM1 to relatives.
Cardiovascular considerations

Background

Preventing sudden cardiac death is the highest priority in the care of patients with DM1. Such deaths in DM1 are mostly attributable to complete cardiac conduction block or to ventricular fibrillation/tachycardia. Cardiac dysrhythmia, particularly heart block, is the second leading cause of death in DM1, after respiratory failure.

The impact of DM1 on the heart is mainly on the cardiac conduction system. The conduction defects are progressive and may lead to severe bradycardia or even asystole (no heartbeat). While patients with severe cardiac conduction blocks may present with syncope (fainting) or presyncope (feeling faint), patients with milder conduction blocks may be asymptomatic, especially when the block does not cause significant hemodynamic changes. However, conduction delays at the atroventricular (AV) node, the His bundle and the ventricle need careful assessment and potential intervention. A high-degree AV block should be considered as a possible cause of bradycardia in DM1 patients.

Atrial tachycardias are relatively common, and the risk of ventricular tachycardia is elevated. The most common type of arrhythmia in patients with DM1 is atrial fibrillation/flutter, which poses risks for cardiogenic embolism. Various tachyarrhythmias and bradyarrhythmias may cause palpitations, fatigue, chest pressure or pain, dyspnea, syncope, presyncope, lightheadedness or dizziness.

In contrast to cardiac arrhythmias, cardiomyopathy is rarely a significant feature of DM1 until the late stages of the disease, when dilated cardiomyopathy leading to congestive heart failure may occur.

The size of the CTG repeat expansion in DM1 is not particularly useful for stratifying cardiac risk.

Hypotension is often found in patients with DM1; although it has been attributed to autonomic dysfunction, the exact mechanism remains unknown.

Recommendations

1. Patients with DM1 should have an annual 12-lead electrocardiogram (ECG).

2. DM1 patients with the following ECG abnormalities, which are correlated with an increased risk of sudden death, should be referred for further cardiac evaluation: a PR interval of greater than 240 milliseconds, a QRS duration of greater than 120 milliseconds, or an atrial tachyarrhythmia.
3. Holter monitoring is a useful adjunct to detect nocturnal bradycardia or other intermittent arrhythmias in patients with DM1.

4. Because of the possibility of sudden death in DM1, invasive electrophysiology (EP) testing should be performed with relatively liberal indications when there is potential for serious conduction blocks or arrhythmias.

5. Syncope, presyncope, dizziness or lightheadedness should be considered as potential cardiogenic symptoms in patients with DM1.

6. Patients and family members should be educated that symptoms such as palpitations, syncope or near-syncope require prompt attention.

7. Regular exercise for patients with DM1 is likely to help with cardiovascular fitness; however, sudden, vigorous exertions that elevate the heart rate have been associated with sudden death and should be avoided.

8. Patients with DM1 should have an echocardiogram every two to five years.

9. Although some debate exists regarding the use of implantable cardiac devices in DM, arrhythmias in DM1 patients can be treated with the insertion of a pacemaker or implantable cardioverter-defibrillator.

10. Pharmacologic treatment can be used to control atrial fibrillation in DM1, although class I anti-arrhythmic drugs, which act via sodium channels, may have pro-arrhythmic effects and are considered by some to be contraindicated in DM1.

11. Anti-myotonic medications and general anesthetics should be used with caution, as these can elevate the risk of cardiorespiratory complications.

12. Congestive heart failure should be managed with standard treatments, such as dietary modifications, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta blockers or device implantation.

13. Management of hypotension is required only if it becomes symptomatic.
Respiratory considerations

Background

DM1 patients often have significant breathing problems that can result from muscle weakness of the diaphragm, abdominal and intercostal muscles and myotonia of these muscles, leading to poor ventilatory force and resulting in low blood oxygen and elevated blood carbon dioxide levels. Chronic respiratory impairment is the primary cause of mortality and morbidity in patients with DM1.

Excessive daytime sleepiness (EDS) and respiratory failure are both common in DM1 and both significantly reduce quality of life. Their causes may overlap, but it is thought by some authors that EDS in DM1 is mostly due to primary central nervous system 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 excessive daytime fatigue; and central nervous system factors may contribute to the breathing difficulties associated with DM1.

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

General anesthesia often causes respiratory failure in patients who were previously clinically stable, highlighting the need for careful perioperative management of patients with DM1.

Recommendations

1. DM1 patients should be monitored for adequate gas exchange by measurement of respiratory rate, work of breathing and comfort level; assessment of chest wall motion and recruitment of abdominal muscles with breathing; observation for diaphragm paralysis; and monitoring of breath sounds by auscultation to evaluate air entry into the lung bases.

2. Regular screening of DM1 patients should include annual assessment of forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) in the sitting and supine position.

3. In addition to FVC and FEV1, maximal inspiratory force, gas diffusion studies and arterial blood cases can be used as a predictive measure of respiratory failure susceptibility if further investigations are indicated.
4. Imaging studies such as chest X-ray or high-resolution computed tomography (HRCT) scans can help detect silent or asymptomatic respiratory tract changes if these are suspected.

5. Overnight oximetry is indicated in DM1 patient if the vital capacity is less than 1.5 liters or if there are indications of possible hypopnea during sleep.

6. The threshold for obtaining a sleep study (polysomnography) in DM1 patients should be low.

7. Patients with DM1 should be carefully monitored for respiratory infections.

8. DM1 patients should receive vaccinations for influenza and pneumonia.

9. In DM1 patients who have difficulty clearing airway secretions, regular use of manually assisted coughing and/or a cough assist device may help reduce the risk of pneumonia.

10. Use of breathing exercises, such as with an incentive spirometer, may help to clear mucus from the lungs and increase the amount of oxygen that gets deep into the lungs in DM1 patients.

11. Noninvasive positive-pressure ventilation should be tried as a treatment for respiratory insufficiency in patients with DM1 who have hypoventilation-related symptoms and sleep apnea or hypopnea; many DM1 patients will progress to requiring nighttime ventilatory support, and some to needing full-time ventilation.

12. Treatment of respiratory infections should follow standard clinical practice.

13. If a patient with DM1 is scheduled for surgery, all members of the surgical team should be made aware of the potential for respiratory failure in association with general anesthesia, and appropriate precautions should be taken (see Surgery, anesthesia and pain control [to come with 2nd set of guidelines]).
Excessive daytime sleepiness

Background

Excessive daytime sleepiness (EDS) has been estimated to affect at least 39 percent of patients with DM1, and it often has a major impact on quality of life for the patient and family. EDS can even be the primary and presenting symptom in adult-onset DM1.

As opposed to generalized fatigue, which is also common in DM, hypersomnia causes patients to sleep frequently, and often unpredictably, throughout the day, even if sleep duration during the night has been normal or greater than normal.

EDS in DM1 can result from one or more distinct mechanisms, including behavioral abnormalities, with an erratic sleep schedule and poor sleep hygiene; ventilatory muscle weakness resulting in sleep-related hypoventilation and nonrestorative sleep; airway obstruction due to pharyngeal weakness and obstructive sleep apnea; central nervous system (CNS)-caused alveolar hypoventilation; and CNS-caused hypersomnia due to disordered arousal mechanisms. Its positive response to the psychostimulant drug modafinil in a few studies suggests to some experts that impaired arousal may be the most common cause of EDS in DM1.

Recommendations

1. The Epworth Sleepiness Scale or similar scales or sets of questions (such as the questions in the MDF Toolkit) can be used to assess EDS in patients with DM1.

2. Patients should be questioned regarding alcohol and caffeine consumption, medications and sleep habits for their possible contribution to EDS.

3. DM1 patients should be assessed for the possible contribution of respiratory muscle weakness to EDS (see Respiratory considerations).

4. If poor sleep habits, alcohol or caffeine consumption, or medication side effects are suspected causes of EDS, these factors should be addressed and altered if possible.
5. In addition to the questions about sleepiness, the following screening measures can help determine whether intervention or referral to a sleep laboratory is indicated: having the patient keep a sleep diary; actigraphy (noninvasive measurement of gross motor activity); and nocturnal oximetry (noninvasive measurement of overnight blood oxygen levels).

6. In DM1 patients, the threshold for obtaining a sleep study should be low, with the caveat that many sleep laboratories focus only on sleep apnea, being unaware of the complexities of sleep disturbance in DM.

7. Physicians caring for DM1 patients should make certain that the sleep laboratory to which a DM1 patient is referred is informed about the complexities of DM1-related sleep disturbance.

8. If the DM1 patient’s sleepiness is thought to be related to nocturnal or daytime hypoventilation or sleep apnea, positive-pressure ventilation can be tried (see Respiratory considerations).

9. If CNS dysfunction is suspected, the psychostimulant modafinil can be tried as a treatment for EDS in patients with DM1. A suggested regimen is to start with a morning dose of 200 milligrams, increasing to 200 milligrams in the morning and at lunchtime if there is no response to the morning dose alone, and then stopping the drug if there is still no benefit.

Skeletal muscle weakness

Background

Skeletal muscle weakness is a major feature of DM1. The weakness, which is characterized by a dystrophic process, is bilateral and progresses slowly over several years. In general, flexors are weaker than extensors, and distal muscles weaken before proximal muscles. Substantial proximal weakness is usually a late feature of DM1, although some patients develop shoulder- and hip-girdle weakness early.

Typical effects of adult-onset DM1 on skeletal muscle include weakness and atrophy of the jaw and facial muscles, leading to thinning of the facial contour and reduced facial expression; weakness of the facial, tongue and palatal muscles, leading to indistinct speech; weakness of the eyelid muscles, leading to drooping of the eyelids (eyelid ptosis); weakness of the ocular muscles, causing limitation of lateral and vertical eye movements; distal muscle weakness, interfering with dexterity, handwriting and mobility; weakness of the foot dorsiflexor muscles, leading to foot drop and a high-stepping, toe-
dragging or shuffling gait; calf muscle weakness, causing difficulty jumping or rising up on the toes; neck flexor weakness, causing difficulty raising the head from a surface; neck extensor weakness, leading to a dropped head posture and difficulty holding the head upright; and weakness of the diaphragm and other breathing muscles, causing shortness of breath.

The combination of weak calf muscles and foot drop can lead to instability of the ankles, difficulty standing still and frequent falls.

Regular exercise may help with stamina, cardiovascular fitness and weight control. Moderate-intensity strength training appears not to cause harm in DM1, although evidence of benefit is lacking.

Recommendations

1. Patients with DM1 should be monitored for foot drop, finger grip weakness, head drop, eyelid ptosis and falls, and walking and other aspects of mobility should be evaluated to see whether assistive devices may be indicated.

2. There are currently no medications available that address DM1 weakness, and none can be recommended.

3. Although dysarthria often develops in DM1, no effective intervention has yet been identified, and none can be recommended.

4. Symptomatic treatments to address skeletal muscle weakness in DM1 include occupational and physical therapy; molded ankle supports and leg braces to reduce foot drop and enhance gait stability; a fitted collar to reduce the effects of neck muscle weakness; and low-intensity exercise strength training, to the extent that individuals are capable of it without undue physical or cardiac stress.

5. Low- or moderate-intensity exercise can be recommended for its likely beneficial effects on stamina, cardiovascular fitness and weight control in DM1; however, sudden, vigorous exertions should be avoided, as sudden death has been associated with rapidly elevated heart rate.

6. Mechanical ventilation, manually assisted cough or cough assist devices, and incentive spirometry exercises can be considered to treat respiratory muscle weakness in DM1.
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 nearly 100 percent of patients with adult-onset DM1, but it is not the most disabling aspect of the disease.

Myotonia in DM stems from an abnormality of the muscle fiber membrane (sarcolemma), which results in an extended delay before muscles relax after a contraction. A muscle starts its contraction on cue, but the electrical activity continues after the nerve signal has ended, causing a stiffness or “locking up” of the muscle. Research suggests that the DM-associated myotonia is related to decreased chloride ion conduction across the sarcolemma.

Myotonia in DM1 is most prominent in the forearm and finger muscles, where it causes 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, esophagus and throat muscles, and myotonia of the respiratory muscles can lead to poor breathing force and low blood oxygen levels.

Myotonia of the ocular muscles is not characteristic of DM-related myotonia, although it is present in other forms of genetic myotonia.

Myotonia can be observed by having a DM patient grip tightly with the fingers. It may take the hand muscles 20 seconds or more to fully relax after a sustained grip (grip myotonia). It can also be demonstrated by sustained contraction after tapping a muscle with a reflex hammer (percussion myotonia) and by electromyography (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. Myotonia in adult-onset DM1 generally declines as weakness increases.

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

Recommendations
1. Patients with DM1 should be monitored for prolonged hand grip and for speech and swallowing difficulties.

2. Physical examination of the DM1 patients should include checking for myotonia by having the patient make a tight grip or using a percussion hammer to tap the muscles of the hand or forearm; sustained contraction and delayed relaxation indicate myotonia.

3. Physicians should be aware that myotonia of the ocular muscles suggests a diagnosis other than DM.

4. A needle electrode placed in the muscle (EMG) can record myotonic discharges and can be used to confirm the presence of myotonia.

5. Patients should be told that warmth, such as that provided by heated gloves, can help relieve myotonia in cold temperatures.

6. Patients and physicians should be aware that myotonic spasms can occur after the use of depolarizing muscle relaxants used in association with anesthesia; these agents should be avoided (see Surgery, anesthesia and pain control [to come in second group of guidelines]).

7. If myotonia seriously interferes with daily life, anti-myotonia drugs such as mexiletine can be considered, although their potentially adverse effects on the heart (induction or worsening of arrhythmias) must be weighed against their potential benefit.

8. Before prescribing anti-myotonia drugs that act on ion channels (mexiletine, phenytoin and others), the DM1 patient’s ECG should be evaluated.

Ocular considerations

Background

Visual impairments in patients with DM1 and DM2 are most often caused by cataracts. Posterior, subcapsular, iridescent lens opacities are highly suggestive of DM1 or DM2, although they are not diagnostic. Cataracts in DM1 and DM2 may progress faster than usual cataracts, and thus patients with
DM1 and DM2 may present with early-onset cataracts. (Cataracts before the age of 55 or a family history of premature cataracts suggest a diagnosis of DM1 or DM2 in patients with muscle symptoms.)

By direct ophthalmoscopy, the cataracts associated with DM are nonspecific and appear as punctate (dotlike) opacities. By slit-lamp examination, they have a multicolored, iridescent appearance and are located in the posterior lens capsule. Posterior, subcapsular, iridescent lens opacities represent an initial phase of cataract formation in DM. They are detectable only with slit-lamp examination and are usually found in patients who have not developed visual symptoms.

Glare and blurriness of vision develop as lens opacities progress to stellate (starlike) cataracts and eventually to mature cataracts, which may be indistinguishable from more common types of cataracts. Surgery to remove cataracts in DM1 patients can be performed, but local anesthesia is preferred so that complications associated with general anesthesia in these patients can be avoided (see Surgery, anesthesia and pain control [to come in second group of guidelines]).

Bilateral eyelid ptosis is a frequent feature of DM1. In severe cases, it can obstruct vision and may require surgical or nonsurgical intervention.

**Recommendations**

1. DM1 patients should have an annual eye examination, including a slit-lamp examination if cataracts have not already been detected.

2. Surgical removal of the opaque lens with intraocular lens implantation is indicated in DM1 when cataracts interfere with the ability to meet the needs of daily living.

3. Surgical techniques that allow local, rather than general, anesthesia should be used to remove DM1-associated cataracts where possible, because of the risks associated with general anesthesia in DM1 patients.

4. If general anesthesia is contemplated for cataract surgery in DM1, anesthesia risks should be reviewed with the patient and the surgical team.

5. DM1 patients should be monitored for eyelid ptosis that interferes with vision.

6. If eyelid ptosis becomes severe and interferes with vision, intervention may be warranted.
7. Eyelid “crutches” that can be inserted into glasses should be tried as a remedy for ptosis before eyelid surgery is considered.

8. Surgical correction, such as frontalis suspension, may be warranted, although anesthesia risks need to be made clear to the DM1 patient and surgical team, and the risks of an eye that does not completely close (such as corneal damage) following surgery should be communicated to the patient.

9. Surgery for eyelid ptosis should be delayed as long as possible; otherwise, multiple surgeries may be needed as the disease and eyelid muscle weakness progress.

Gastrointestinal considerations

Background

Because the smooth, as well as the skeletal, muscles are involved in DM1, dysfunction along the entire gastrointestinal (GI) tract is common in this disorder. Weakness and myotonia of the smooth muscles occurs. Among the common problems are dysphagia; aspiration; abdominal pain and bloating, especially after eating; constipation, diarrhea and “irritable bowel” symptoms; gallstones; dilated colon, which can result in fecal impaction, megacolon and even perforation of the bowel; and anal incontinence. GI symptoms are not only surprisingly common in DM1 but can also be the initial or dominant clinical characteristic. However, these symptoms may be underestimated or ignored.

Recommendations

1. DM1 patients should be asked about problems with chewing or swallowing, gastroesophageal reflux, bloating of abdominal pain, frequency and characteristics of bowel movements and fecal incontinence.

2. Routine physical exams for DM1 patients should include special attention to the GI tract, noting involuntary weight loss, dysphonia that may indicate pharyngeal muscle weakness, frequent cough that may indicate aspiration, abdominal pain on palpation (generally or in the area of the gall bladder), and abdominal bloating.
3. Care should be taken that DM1-associated pseudo-obstruction of the bowel not be mistakenly diagnosed as mechanical obstruction, which would subject the patient to unnecessary surgical risks.

4. Detailed evaluation of the GI tract in DM1 patients may include the following:
   
a. abdominal X-ray to evaluate abnormal bowel gas or stool, or free abdominal air
   
b. swallow study to characterize dysynergic movements, pharyngeal weakness, pharyngeal or esophageal construction, or aspiration
   
c. abdominal ultrasound or magnetic resonance imaging (MRI) to detail stomach, small bowel, large bowel or gall bladder anatomy
   
d. barium upper GI radiographic evaluation to assess lower esophageal function and reflux, gastric emptying, and small bowel anatomy and function; if acute bowel obstruction is considered, a barium radiographic investigation with small-bowel follow-through can distinguish pseudo-obstruction from the surgical emergency of true obstruction
   
e. manometry to demonstrate weakness or disordered contraction of esophagus, gastroesophageal sphincter, stomach, small bowel, rectum or anal sphincter
   
f. endoscopy to define abnormal structure or function of pharynx, esophagus, stomach, small intestine or large intestines
   
g. blood tests to investigate cholestasis or hepatic involvement (serum alkaline phosphatase and bilirubin elevation correlate with cholestasis in DM)

5. Dysphagia can be treated with dietary modifications and with behavioral and postural modifications related to eating and swallowing.

6. Gastrostomy tube feeding can be used to maintain nutrition and protect the airway in DM patients with dysphagia, but nasogastric tubes are typically contraindicated in these patients because they increase the risk of aspiration.

7. Mexiletine can be considered to reduce myotonia of the chewing or swallowing muscles.
8. Friends and family members of DM1 patients should be taught the Heimlich maneuver to dislodge “stuck” food particles in the upper GI tract.

9. Dilation of the esophagus and cricopharyngeal myotomy can be considered to improve esophageal function.

10. Prokinetic medications, such as metoclopramide, can be used intermittently to reduce symptoms of GI hypomotility.

11. Cholestyramine (which sequesters bile acids in the GI tract and increases their elimination) can be tried to treat diarrhea, incontinence and pain.

12. Antibiotic medications can be considered to treat bacterial overgrowth in the GI tract.

13. Dietary modifications to increase fiber and fluids can be tried to treat DM1-associated constipation.

14. Emollients, osmotic laxatives, irritant laxatives and bowel cleansing can be considered for the treatment of constipation in DM1.

**Pregnancy and obstetrics**

*Background*

The deleterious effects of DM1 on both smooth and striated muscle can complicate pregnancy, labor and delivery. Added to these maternal complications is the possibility that the baby may have congenital-onset DM1, with severe neonatal complications, including respiratory and swallowing abnormalities.

Mothers with DM1 are more likely than the general population to experience ectopic pregnancy; premature delivery; prolonged labor and delivery related to both uterine muscle dysfunction and skeletal muscle weakness; postpartum hemorrhage due to inadequate uterine contractions or retained placenta; uterine overdistention with polyhydramnios (because of impaired swallowing of amniotic fluid by a fetus with congenital DM1), which can lead to preterm labor, inadequate uterine contractions during labor, or premature rupture of the membranes; and untoward reactions to analgesia or
anesthesia during labor and delivery. Women with DM1 have a higher than average rate of spontaneous abortion and stillbirth, although most can expect to have a normal vaginal delivery.

Babies with congenital-onset DM1 may have swallowing difficulties, leading to polyhydramnios during pregnancy and poor feeding at birth, possibly requiring tube feeding; respiratory muscle abnormalities, possibly requiring mechanical ventilation at birth; poor muscle tone and lack of fetal movement; abnormal positioning; club foot; abnormal accumulation of fluid in the body; and enlarged ventricles in the brain.

Prenatal and preimplantation genetic diagnosis can allow for termination of the pregnancy or selective implantation of unaffected embryos; it can also prepare the obstetric team for the birth of a DM1-affected baby.

Recommendations

1. Intensive prenatal care/counseling and intensive obstetric care are recommended for women with DM1.

2. Intensive neonatal care is recommended for neonates known to have or suspected to have DM1; newborns with congenital DM1 may require tube feeding and/or ventilatory support.

3. Prenatal genetic diagnosis or preimplantation genetic diagnosis may be performed to determine whether the embryo or fetus has the DM1 genetic expansion.

4. Extreme care must be taken with analgesic or anesthetic drugs given to a DM1-affected mother during labor or delivery; e.g., depolarizing agents can cause myotonic spasms, and barbiturates can cause respiratory depression (see Surgery, anesthesia and pain control).

5. During pregnancy, amniotic fluid volume reduction can be considered if there is preterm labor or significant maternal discomfort.

6. Management of excess fluid in DM1-affected neonates may include support for respiratory distress with supplemental oxygen or mechanical ventilation; removal of excess fluid from around the lungs and abdomen; or diuretic medications.
Surgery, anesthesia and pain control

Background

DM1 patients are far more likely than the general population to have adverse reactions to medications used for anesthesia and analgesia, and a combination of the cardiac, respiratory, muscle and central nervous system aspects of DM1 can lead to a variety of untoward responses before, during and after surgery. Serious adverse event have been reported even in patients whose overall DM1 symptoms were mild.

DM1 patients are extremely sensitive to the respiratory depressant effects of anesthetic, sedating and analgesic medications, and weakness of the pharyngeal muscles and delayed gastric emptying predispose them to aspiration. The depolarizing muscle relaxant succinylcholine can cause myotonia, making intubation difficult or impossible. In addition, various other medications, as well as hypothermia, potassium, and electrical or mechanical stimuli, can cause dangerous myotonia during surgery.

DM1 patients are at increased risk for pneumonia and other perioperative respiratory complications, and cardiac conduction delays and other dysrhythmias can lead to sudden death in the DM1 surgical patient. Behavioral and cognitive abnormalities can complicate the DM1 patient’s course, as can hypersomnia and preoperative sleep deprivation.

Recommendations

1. Physicians should consider whether, given the risks, an operation for a DM1 patient is really necessary; and if so, whether regional anesthesia rather than general anesthesia can be employed.

2. DM1 patients requiring surgery with general anesthesia should have a comprehensive preoperative evaluation by the primary care physician and should undergo a pre-anesthetic assessment by an anesthesiologist one to four weeks prior to surgery.

3. Before any anesthetic care is given, DM1 patients should have a thorough evaluation of the cardiac system, including an echocardiogram, 12-lead CG, and interrogation of any internal cardiac rhythm devices that may be present.

4. DM1 patients should have a preoperative chest X-ray.
5. Pulmonary function tests, including supine and sitting vital capacities, and preoperative arterial blood gases, should be considered for DM1 patients prior to surgery.

6. Before preoperative anesthetics or sedatives (e.g., opioids or benzodiazepines) are administered to DM1 patients, the surgical team should be sure that there is appropriate equipment available for monitoring and for performing urgent intubation.

7. The team should avoid triggers for myotonia in DM1 patients, such as hypothermia, shivering, potassium, certain medications, and mechanical or electrical stimuli.

8. The team should be prepared for the possibility that regional anesthesia may trigger shivering and myotonia in DM1 patients.

9. The DM1 patient’s operating room and table should be kept warm, and warmed intravenous fluids and forced-air blankets should be used to maintain normal body temperature and avoid myotonia.

10. The team caring for a DM1 patient during surgery should consider attaching an external pacemaker/defibrillator; placing an arterial line for monitoring of blood gases and blood pressure; and employing invasive cardiac monitoring in DM1 patients who have significant cardiopulmonary dysfunction.

11. During surgery on a DM1 patient, the team should monitor neuromuscular blockade with a peripheral nerve stimulator, with the caveat that the stimulator could induce myotonia that could be misread as reversal of neuromuscular blockade.

12. During anesthesia induction in the DM1 patient, the team should ensure adequate pre-oxygenation; consider administering medications to counteract altered gastric motility; use rapid sequence induction; and avoid succinylcholine in favor of a non-depolarizing agent if a muscle relaxant is required.

13. The surgical team should have appropriate airway and monitoring equipment available when using anesthetic medications in DM1 patients and be prepared for the likely need for postoperative ventilation until strict extubation criteria are met.
14. Volatile agents can be used to maintain anesthesia in DM1 patients, but the team should consider an agent, such as desflurane, that allows for fast emergence upon completion of surgery.

15. While maintaining anesthesia for DM1 patients, the team should avoid muscle relaxants entirely if possible; if muscle relaxation is required, consideration should be given to infiltrating the muscle with a local anesthetic and/or using a non-depolarizing agent.

16. The team should consider using total intravenous anesthesia for DM1 patients.

17. Intravenous fluids that do not have added potassium should be considered for DM1 patients.

18. During emergence from anesthesia, the DM1 patients should not receive neostigmine, which may induce myotonia; non-depolarizing muscle relaxants should be allowed to wear off without it.

19. Strict extubation criteria should be used for DM1 patients emerging from anesthesia.

20. Postoperatively, DM1 patients should have close and continuous monitoring of cardiopulmonary function (oxygen saturation and ECG) for at least 24 hours.

21. Intensive care unit (ICU) admission for DM1 patients emerging from anesthesia should be considered if there is an anticipated need for mechanical ventilation or other critical care management or for significant opioid analgesia.

22. Postoperative pain control in DM1 patients should be managed without opioids if possible; nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, regional techniques and local anesthetics are preferable.

23. If postoperative pain requires opioids in DM1 patients, close monitoring, preferably in an ICU, is recommended.

24. Postoperatively, DM1 patients should receive close monitoring of pulmonary function, with protection of the upper airways, chest physiotherapy and incentive spirometry.

25. Postoperatively, DM1 patients must be monitored for hypoxia and aspiration for several days.
Endocrine and metabolic considerations

Background

The most common endocrine abnormalities in DM1 are testicular atrophy and insulin resistance, although other metabolic and endocrine abnormalities, such as disturbances of the thyroid, pancreas, hypothalamus and parathyroids, have been reported.

Testicular atrophy in adult males with DM can cause small testes, with decreased or absent sperm production and decreased fertility; weak secondary sex characteristics; low serum testosterone; elevated serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH); and gynecomastia. Women with DM1 do not appear to have gonadal dysfunction or hypogonadism. However, they can experience reduced fertility, spontaneous abortion and stillbirth, and they may have a somewhat higher rate of excessively painful menstruations and irregular menstruations than the general population. Balding is seen in men and women with DM1.

Insulin resistance, secondary to abnormal splicing of the insulin receptor, is common in DM1 patients, although true diabetes mellitus rarely develops.

Abnormal liver function tests are common in DM1. However, they are generally not progressive, and it is not known whether they represent a primary effect of DM on liver cells or are a consequence of metabolic derangements, biliary stasis or fatty liver.

Recommendations

1. DM1 patients should be informed of the symptoms of diabetes and what to do about them.

2. DM1 patients should undergo a fasting glucose tolerance test at baseline and then every three years.

3. Annual glycosylated hemoglobin (HbA1c) estimation may be appropriate for DM1 patients.

4. Treatment of insulin resistance, if required, can be with lifestyle changes (diet and exercise) and/or medications to normalize blood glucose and insulin levels.

5. DM1 patients should have a thyroid stimulating hormone (TSH) level measured at baseline and every three years.
6. DM1 patients should undergo testing for serum levels of blood lipids at baseline and then every three years.

7. Liver enzymes and bilirubin levels should be measured at baseline.

8. Patients with DM1 should be asked about infertility and referred for evaluation and treatment if they so desire.

9. Females with DM1 should be asked about painful or irregular menses and reproductive history and referred for further evaluation and treatment if indicated.

10. Males with DM1 should be asked about erectile dysfunction; medications to treat erectile dysfunction in males with DM1 can be considered.

11. Treatment of DM1-associated hair loss, such as with minoxidil, can be considered.

**Neuropsychiatric considerations**

*Background*

Specific cognitive deficits are frequently seen in adult-onset DM1, but they are milder than those seen in congenital-onset and childhood-onset DM1. In addition to the primary alteration in brain function thought to be caused by the DM1 genetic mutation, there may be contributions from the disordered sleep patterns or the hormonal or other systemic abnormalities seen in the disorder.

In adult-onset DM1, cognitive and behavioral abnormalities can involve deficits in intelligence, executive function, visual-spatial construction, arithmetic ability, and attention, although the scope and degree of the involvement vary among patients. Lack of executive function can lead to great difficulty planning and organizing one’s life, affecting areas such as paying bills, keeping appointments and arranging schedules.

In addition to the cognitive deficits, personality features such as anxiety, avoidant behavior, apathy, lack of initiative and inactivity have been used to describe DM1 patients. Some studies report high scores on
depression scales in DM1. However, depression and apathy may be confused with other aspects of DM1, such as somnolence and an inexpressive facial appearance due to facial muscle weakness.

Reduced blood flow in the frontal and temporal lobes of the brain, reduced cerebral volume compared to age-matched controls, and high T2 signal abnormalities in cerebral white matter have been found in patients with DM1, although their relationship to cognitive and behavioral abnormalities is not clear. In addition, studies have shown a unique, abnormal pattern of tau isoform expression in DM1-affected human brains.

The cognitive and personality aspects of DM1 remain relatively uncharacterized, but they can have a significant impact on quality of life for the patient and his or her family. They overlap considerably with deficits in psychosocial functioning (see Psychosocial considerations).

Recommendations

1. Physicians caring for DM1 patients should consider referring them for neuropsychological testing to evaluate cognitive strengths and weaknesses.

2. DM1 patients with depressive symptoms should be referred to a psychologist or other professional for confirmation of the diagnostic impression and for possible treatment.

Psychosocial considerations

Background

The complex physical, cognitive and personality aspects of DM1 can seriously interfere with work, schooling, recreation and family life. The socioeconomic conditions of DM1-affected patients and families are often compromised because of poor education (related to cognitive impairment), limited employment opportunities, low energy levels, daytime sleepiness, impaired vision, muscle weakness, the likelihood that more than one person in the family may have special needs due to DM1, and the use of alcohol or drugs to manage stress and insomnia.

DM1 patients can have difficulty with many activities of daily living, including those related to personal hygiene, housekeeping, organizing and scheduling, and driving a car. Children of DM1-affected parents
may not receive optimal emotional or intellectual support and may sometimes lack even routine care, all of which can be particularly serious if the children themselves have DM1.

**Recommendations**

1. Physicians and other professionals caring for DM1 patients should be alert to the social circumstances of the patient and household, with special attention to the possibility of substance abuse, child neglect, acute financial need, unsafe driving, or an unsafe or unsanitary home; referrals to appropriate social services should be made.

2. Physicians and other professionals caring for DM1 patients should be aware of and refer patients and families to local support groups and organizations.

**Tumors**

Studies about the incidence of malignancies in DM1 patients compared to the general population have shown conflicting results. Some have shown that DM1 patients have a higher than average risk of cancer, especially of the thyroid gland, ovary, colon, endometrium, brain and eye. Others have found no clear evidence to support this idea.

However, it is generally agreed that DM1 patients have a higher than average chance of developing a pilomatrixoma, a skin tumor associated with hair follicles that is usually benign but can sometimes be malignant. A pilomatrixoma feels like a small, hard lump under the skin. It’s often found in the head and neck region but can appear in other locations. They can be surgically removed.

**Recommendations**

1. Physicians caring for DM1 patients should routinely look for evidence of pilomatrixomas and refer patients to surgeons who can safely remove them (see Surgery, anesthesia and pain control).

2. Physicians caring for DM1 patients should recommend that patients follow cancer screening guidelines that apply to the general population.
3. If surgery or other cancer treatment is recommended for a DM1 patient, the neuromuscular disease specialist should be involved and ensure that other professionals are aware of aspects of DM1, such as a high risk of untoward events associated with anesthetics and analgesics, which may influence treatment decisions (see Surgery, anesthesia and pain control).