A Review of Muscular Dystrophies

Tiffany Hoang;[1] and Regina A. E. Dowdy, DDS[2]

[1]Dental Student, Herman Ostrow School of Dentistry of University of Southern California, Los Angeles, California, [2]Adjunct Assistant Clinical Professor in Anesthesia and Emergency Medicine, Herman Ostrow School of Dentistry of University of Southern California, Los Angeles, California

Muscular dystrophy encompasses a group of genetic conditions with progressive muscle damage and weakness. Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are X-linked recessive disorders that affect the production of the protein dystrophin. Emery-Dreifuss muscular dystrophy (EDMD) is typically an X-linked-recessive disorder involving the gene that codes for emerin. Facioscapulohumeral muscular dystrophy and oculopharyngeal muscular dystrophy (OPMD) are both autosomal dominant disorders. Although commonly mistaken as a condition in which patients are susceptible to malignant hyperthermia with volatile inhalational anesthetics, muscular dystrophy is more closely associated with rhabdomyolysis. Providers developing an anesthetic plan for dental patients with muscular dystrophy must take into consideration the patient's baseline cardiac and pulmonary function as well as the potential for abnormalities. Nondepolarizing neuromuscular blocker use is safe but likely to result in prolonged skeletal muscle relaxation. Succinylcholine and volatile anesthetics are generally contraindicated due to the risks of rhabdomyolysis and hyperkalemia with subsequent ventricular fibrillation, cardiac arrest, and death if left untreated. In-depth understanding of the more commonly encountered forms of muscular dystrophy is vital to providing safe and effective ambulatory anesthesia care for patients undergoing dental treatment outside the traditional hospital operating room setting.

Key Words: Muscular dystrophy; Duchenne muscular dystrophy; Becker muscular dystrophy; Emery-Dreifuss muscular dystrophy; Facioscapulohumeral muscular dystrophy; Oculopharyngeal muscular dystrophy; Sedation; Anesthesia; Rhabdomyolysis; Malignant hyperthermia.

Muscular dystrophy is a group of genetic diseases in which skeletal muscles progressively weaken over time and encompasses more than 30 subcategories Because these diseases are genetic, they can be inherited from 1 autosomal dominant parent or 2 autosomal recessive parents or they can be sex linked. Muscular dystrophy is categorized based on the extent and distribution of weakness, age at onset, progression, symptom severity, and genealogy. This review will focus on several of the most common types of muscular dystrophy and discuss considerations for sedation and general anesthesia along with a brief overview of implications for dental care.

BASIC REVIEW

Striated myocytes are composed of numerous muscle fibers that have even smaller units known as myofibrils. Myofibrils are a parallel stack of thick and thin filaments otherwise known as sarcomeres. The thick filaments are myosin, and the thin filaments are made of actin, tropomyosin, and troponin. A muscle contracts when actin and myosin can bind (creating a cross-bridge), release, and rebind when active. When inactive, tropomyosin serves to block the binding of actin and myosin.

Nerve impulses travel from the brain or spinal cord to the peripheral nervous system, where they synapse with the neuromuscular junction. The nerve terminal releases acetylcholine, which binds to the receptors on the myocytes leading to depolarization, opening of the ryanodine receptors found on the sarcoplasmic reticulum, and an influx of calcium. The calcium causes a confirmational change in tropomyosin, freeing up the actin binding site and resulting in cross-bridging. This cycle continues until intracellular calcium levels normalize. Within the muscle fiber membrane, there are a group of proteins called the dystrophin-glycoprotein complex. These proteins are responsible for preventing damage to the myocytes with contraction and relaxation. Some forms of muscular dystrophy affect the skeletal muscles by damaging this membrane, allowing for increased leakage of creatine kinase (CK) and excess calcium.

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Address correspondence to Dr Regina A. E. Dowdy, 925 W 34th St, Los Angeles, CA 90089; rdowdy@ostrow.usc.edu.

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TYPES OF MUSCULAR DYSTROPHY

Duchenne and Becker Muscular Dystrophy

Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are X-linked recessive disorders that occur due to a mutation in the *DMD* gene (Xp21), which is most notable for encoding the protein dystrophin.[1–3] The *DMD* gene is composed of 2.4 million nucleotides with 79 exons throughout, and 65% of DMD and BMD mutations occur due to the deletion of 1 or more of these exons.[1] It is important to note that these dystrophinopathies occur on the X chromosome, making them genetically distinct from malignant hyperthermia mutations, which are located on chromosome 19.[2]

Dystrophin is found on the membrane surface of skeletal and cardiac myocytes and is integral to maintaining the sarcolemma. Essentially, it serves to reinforce the sarcolemma by protecting it from contractile stress as sarcolemma damage can be directly linked to the degree of stress.[2] The mutations associated with dysfunctional or absent dystrophin allow for a breakdown of the sarcolemma. This contributes to atrophy of the myofibril contained by the sarcolemma, eventually leading to necrosis and fibrosis.[2] These muscle fibers are also more susceptible to contraction-induced sarcolemmal rupture.[2]

DMD is the most common childhood muscular dystrophy and occurs in approximately 1:3500 births; BMD is one-third as frequent.[1,2] The diagnosis of DMD is often prompted when the child fails to meet gross motor milestones during early childhood development, typically 2 to 3 years of age with diagnosis by 5 years of age.[2,3] In contrast, clinical signs and symptoms of BMD typically manifest by 10 years of age. Children with BMD can ambulate after 15 years of age, unlike DMD, in which affected patients typically cannot ambulate after 12 years of age.[1] After loss of ambulation, the diaphragm then begins to weaken, resulting in a reduction of forced vital capacity. This insufficiency appears in almost all cases of DMD and is the major cause of mortality.[1] Life expectancy for a patient with DMD is 30 years, whereas those with BMD have a life expectancy of 40 to 60 years.

The primary difference between DMD and BMD is the quantity of dystrophin present in skeletal and cardiac muscle. In DMD, dystrophin is almost always absent, while partially functional dystrophin is present with BMD and results in a milder form of the disorder. In the absence of dystrophin, which helps link the sarcolemma cytoskeleton to the extracellular matrix, the sarcolemma is more susceptible to damage. The cyclical nature of muscle fiber degeneration and regeneration results in fibrosis and fatty replacement of the myocytes.[1]

In evaluating patients for appropriateness of care in outpatient settings, providers should note that patients with a history of BMD have an increased risk for significant morbidity and mortality in the perioperative period. As always, careful attention must be paid to the history and physical exam, and particular attention should be focused on the cardiac evaluation, as cardiomyopathy is a common pathology associated with DMD and BMD. Approximately 59% of patients with DMD have cardiomyopathy by 10 years of age.[1] It is recommended that these patients receive an echocardiogram or a cardiac magnetic resonance imaging MRI (CMRI) biannually starting at age 6 years and then annually after age 10 years.[1,3] It is also common practice for DMD and BMD patients to engage in frequent continuous Holter cardiac monitoring to determine severity of conduction disturbances, which may become apparent before systolic dysfunction. CMRI has a diagnostic advantage in that it sensitive for myocardial fibrosis, which is present prior to left ventricular dysfunction.[3]

It is generally recommended that the patient be evaluated by their cardiologist within close proximity to surgery as this can facilitate optimization of the patient.[3] During the preoperative assessment, the resting heart rate should be observed. It is not uncommon for patients in advanced stages of DMD and BMD to have sinus tachycardia in addition to cardiomyopathy. This is due to a complicated relationship between cardiomyopathy and autonomic dysfunction. In addition, such patients are typically hypotensive at baseline, making them further sensitive to decreases in systemic vascular resistance such as during induction of general anesthesia or with significant blood loss.[3] Any signs of heart failure should be noted, such as peripheral edema, hepatosplenomegaly, or audible cardiac murmurs and gallops. Obtaining a recent 12-lead electrocardiogram (ECG) prior to providing any treatment is advised. As patients with DMD and BMD age and the disease progresses, they are more likely to experience cardiac conduction abnormalities as they commonly suffer from ventricular hypertrophies and heart failure. Progressively worsening left ventricular hypertrophy is a common finding and is often manifested as Q waves in leads III and V6.[3] Treatment for cardiomyopathy preferably begins prior to clinical evidence of systolic dysfunction. First-line treatment is initiated with afterload reducers such as angiotensin receptor blockers or angiotensin-converting enzyme inhibitors. Clinical interventions may eventually require placement of a left ventricular assist device.[1]

There are significant airway and musculoskeletal risk factors that are associated with sedation and general anesthesia for patients with DMD and BMD. Nocturnal ventilatory insufficiency is common, and treatment with appropriate ventilation, such as bilevel continuous airway pressure (ie, BiPAP) has been shown to increase the survival age to 25 years in 53% of patients.[1] Once wheelchair dependent, the risk of scoliosis is great and has been found to affect 77% of DMD patients.[1] Often orthopedic intervention is required and ideally would occur prior to any signs and symptoms of

cardiomyopathy. There is anecdotal evidence suggesting that DMD and BMD patients are more susceptible to thrombotic events. Theories include propensity for lower extremity deep vein thrombosis due to muscle inactivity and enhanced thrombosis and fibrinolysis due to acute muscle destruction.[2]

Emery-Dreifuss Muscular Dystrophy

Emery-Dreifuss muscular dystrophy (EDMD) is most commonly inherited as an X-linked recessive or autosomal dominant disorder with a male predilection.[4] The X-linked form of EDMD occurs due to a mutation of the *EMD* gene in the Xq28 region of the X chromosome, which is the gene locus that encodes for a nuclear membrane protein called emerin.[4,5] An important protein that belongs to a family of lamina-associated structural proteins,[6] emerin localizes to the inner nuclear membrane. It projects into the nucleoplasm and is important in nuclear membrane organization and its attachment to heterochromatin.[6] Muscle biopsy of patients with EDMD shows an absence of emerin but normal levels of dystrophin.[4]

The rare autosomal dominant form of EDMD can be caused by subsequent mutations in lamin A/C when there are mutations on the chromosome 1q21 in the *SYNE1* and *SYNE2* genes that encode for the nuclear envelope proteins, nesprin-1 and nesprin-2, as well as in transmembrane protein 43 (TMEM43) or LUMA.[5,6] The clinical phenotype of muscular dystrophy and cardiac abnormalities seen with emerin and lamin A/C mutations are essentially identical. Therefore, genetic testing is performed to confirm the diagnosis as emerin is present in many tissues, so a skin biopsy with absent protein from the nuclei in the skin confirms an emerin mutation.[6] Other diagnostic tools include muscle biopsy and electromyography, which reveal only nonspecific myopathic features, such as myofiber necrosis and endomysial fibrosis.[5,6] From these tests, the serum CK level is usually only slightly elevated, suggesting muscle damage or degeneration and distinguishing its diagnosis from other X-linked recessive muscular dystrophies.[5,6] Since isolated cardiac involvement may be seen in patients with EDMD, a 12-lead ECG should be performed on these patients at regular intervals.[6]

In the first few years of life, patients with EDMD show muscle weakness of the upper arms, shoulders, and anterior compartment muscles in the legs.[6] Thus, it is very characteristic of EDMD patients to have an awkward gait and a tendency for toe walking.[4] Teenage patients, a time of peak disease presentation, experience fixed equinus deformities of the ankles, flexion contractures of the elbows, extension contracture of the neck, and tightness of the lumbar paravertebral muscles.[4] Most patients are able to ambulate until the fifth or sixth decade of life.[4] EDMD frequently causes cardiac abnormalities consisting of bradycardia and atrial ventricular conduction defects leading to complete heart block.[4] Thus, analysis and treatment of cardiac problems are the most pertinent parts of therapy. Atrial paralysis occurs when the atria are electrically inexcitable and the heart responds only to ventricular pacing.[6] Other cardiac problems include ventricular myocardial disease with failure and stroke, secondary to cardiac arrhythmia.[5,6] These cardiac abnormalities are initially asymptomatic but result in a high incidence of sudden cardiac death if not properly diagnosed and treated with a cardiac pacemaker or intracardiac defibrillator.[4,6] The severity of cardiac abnormalities increases with age in both males and females.[6] Respiratory insufficiency is more prominent in early and severe forms of EDMD and may require mechanical ventilation, especially in severe congenital-onset patients.[5] There is no facial weakness, myotonia, or altered intellectual function.[5]

Orthopedic treatment of EDMD involves surgery to release heel cord contractures and other muscles around the foot.[4] This procedure usually requires Achilles tendon lengthening, posterior ankle capsulotomy, and anterior transfer of the posterior tibial tendon.[4] In addition, in patients with EDMD, elbow flexion contractures do not usually exceed 35° but can also be very severe, as contractures of 90° have been reported.[4] As the arm extends, sudden resistance is met, which feels more like bone than the pressure of a tight tendon.[6] However, there has not been success in surgeries for the release of elbow contractures.[4] The ability for full flexion and normal pronation and supination are not affected in patients with EDMD.[4] Contractures around the neck and back should be treated conservatively with range of motion, although full range of motion after treatment should not be expected.[4] In addition, rigid spine syndrome and scoliosis are other features of EDMD but have a lower incidence of progression.[1,3]

Facioscapulohumeral Muscular Dystrophy

Facioscapulohumeral muscular dystrophy (FSH) is an autosomal dominant disorder with high penetrance and variable expression.[7] The prevalence is about 3.95 per 100,000.[7] There is also high variability of signs and symptoms as between 10% and 30% of cases show new mutations.[7] Clinical signs and symptoms usually manifest before the age of 20 years and normally constitute weakness of the facial muscles, fixators of the scapula, and dorsiflexors of the ankle.[7] Although the skeletal muscles are the most effected, other systems may also be involved if the disease becomes more developmental and degenerative.[7]

The genetic basis of FSH involves deletions of a 3.3-kb tandem repeat (D4Z4) in the subtelomeric region at the 4q35 locus.[8] D4Z4 acts as a lamins-dependent insulator, exhibiting both enhancer-blocking and barrier activities, and displaces the telomere toward the nuclear periphery.[8] In a normal patient, there are 11 to 100 D4Z4 repeats.[8]

When there are fewer repeats (eg, <10 repeat units), this allows for chromatin remodeling and leads to decreased methylation, thus turning on DUX4 expression (which is typically dormant in normal patients).[3] In addition, the disease will occur only in chromosomes that carry a pLAM1 polyadenylate site distal to the last D4Z4 repeat.[8] When all of these factors are present, this creates a "permissive" haplotype or state that allows for the expression of DUX4, which is normally repressed.[8] In the 5% to 10% of patients who do not have a mutated 4q3 locus, there is typically a mutation in the *SMCHD1* gene (on chromosome 18p) that can lead to hypomethylation of D4Z4, causing FSH type 2.[3] When these mutations are present in the setting of a "permissive" haplotype and the polyadenylation signal, DUX4 is expressed, causing FSH.[8] The prevalence varies geographically but ranges from 1:8000 to 20,000.[3]

Weakness is first found in the facial muscles and may be asymmetric.[7] Patients with FSH have difficulty with lip puckering, whistling, sipping through a straw, and blowing up balloons due to the weakness of the orbicularis oris muscle, leading to limited facial expression and a transverse smile.[7] Weakness of the orbicularis oculi is usually asymptomatic, but it may be observed by the incomplete burying of the eyelashes with forced eyelid closure and easy ability to pry apart closed eyelids.[7] The scapulae sit high on the back, and weakness of scapular fixation is shown by scapular winging.[7] The ability of FSH patients to abduct their arms is impaired, and there is wasting of the biceps and triceps with the preservation of the deltoid and forearm muscles.[7] There is also wasting of the clavicular head of the pectoral muscles and the lower abdominal muscles while standing.[7] Ankle dorsiflexor weakness is typically the first sign of lower extremity weakness with compromised heel walking or overt footdrop.[7] Muscle atrophy is most severe in the tibialis anterior muscle.[7]

The motor deficits that patients with FSH experience are slowly progressive.[7] Some patients report long periods of stability in terms of their symptoms, followed by abrupt stepwise loss of power in some restricted muscle groups.[7] Although this muscle weakness and atrophy may be asymmetric and striking, most patients remain functionally independent throughout their lives.[7] Sensorineural hearing loss is identified in 18.6% of FSH patients, even in young children under the age of 7 years.[7] Hearing loss is typically bilateral, progressive, and associated with the size of the D4Z4 contraction.[7] Retinal vasculopathy (Coats disease) may be idiopathic or associated with FSH.[7] If idiopathic, it is usually identified in males by age 20 and unilateral.[7] FSH-related Coats disease may present with retinal detachment and blindness at about 10 years of age, with boys and girls equally affected.[7] Patients with large D4Z4 contractions are at higher risk of this complication.[7]

Symptomatic cardiac disease is not frequently seen in patients with FSH.[7] Restrictive lung disease may be seen in patients with more severe, nonambulatory FSH and should be assessed regularly with pulmonary function tests and sleep studies.[7] Congenital onset of FSH has been associated with intellectual disability and epilepsy in children with large D4Z4 deletions (eg, <4 repeats).[7] Patients with infant-onset FSH usually present with significant facial weakness from early childhood, and the acquisition of motor milestones may be delayed.[7] They tend to show a progressive limb-girdle pattern of weakness with marked muscle wasting and hyperlordosis as well as loss of ambulation between 9 and 31 years of age.[7] Atypical features in patients with FSH include ptosis, head drop, joint contractures, cardiomyopathy, and respiratory insufficiency.[7]

Oculopharyngeal Muscular Dystrophy

Oculopharyngeal muscular dystrophy (OPMD) is an autosomal dominant disorder with near complete penetrance.[9] The geographical distribution of this disorder is quite uneven, and most cases are found in in Quebec, Germany, and Uruguay (Montevideo) as well as the Spanish-American populations of Colorado, New Mexico, and Arizona, Ashkenazi Jews, and those of French-Canadian descent.[9,10] OPMD is caused by a mutation and expansion of GCG repeats on chromosome 14q11.2-13 in the gene that encodes for polyadenylate-binding protein nuclear 1 (*PABPN1*, formerly known as *PABP2*).[9] Mutations can contain between 8 and 13 repeats.[10] The role of this nuclear protein is in mRNA polyadenylation. The gene repeats result in the presence of intranuclear inclusions in muscle fibers as a result of abnormal protein clumping, which diminishes the membrane's integrity.[9,10] The onset of OPMD can start in the fourth decade of life, but the disease usually begins in the fifth or sixth decade of life.[9] The longer the *PABPN1* expansion repeat, the earlier the age of onset. Homozygotes for the mutation show a more severe form of OPMD.[9,10]

OPMD is a progressive form of muscle wasting and atrophy of the myocytes, affecting the eye and periocular muscles.[10] Patients with OPMD present with extraocular muscle weakness and mild ptosis.[9] Initially, the ptosis is usually asymmetrical, but as the muscles weaken over time, both eyelids become severely ptotic, and eye movements gradually diminish in all directions.[9] The severity of the extraocular palsies often varies, but the ptosis is constant in all patients with OPMD.[9] Either during or shortly after the development of ocular symptoms, patients with OPMD begin noticing dysphagia due to impaired function of the oropharyngeal musculature.[9,11] The impaired swallow efficiency can be due to reduced pharyngeal constriction, speed of hyoid movement, and degree of airway closure and can lead to oral and nasal regurgitation, aspiration, postswallow pharyngeal residue, and esophageal retention.[11] Difficult swallowing can lead to weight loss, malnutrition, and aspiration, and at more severe stages of the disease, complete dysphagia

may occur.[9,11] Some patients may also experience facial weakness as well as hip and shoulder weakness in the later stages.[9] Other symptoms that patients may experience include changes in voice quality, excessive fatigue, and impaired cognitive function.[11] Extreme emaciation and starvation may result in death.[9] The terminal event is often pneumonia caused by aspiration of secretions.[9] Although the symptoms associated with OPMD may be extremely severe, patients' life spans may be unaffected, making management of their nutritional status all the more important.[9]

Diagnosis usually involves genetic testing, making muscle biopsy unnecessary.[9] However, biopsy of weak muscles may be able to show dystrophic findings, random variation in fiber size, necrotic fibers, some fibrosis, and occasional internal nuclei.[9] In addition, biopsies can reveal the presence of fibers that may contain autophagic (rimmed) vacuoles, a feature common to OPMD.[9] A hallmark of OPMD is the presence of small 8- to 10-nm intranuclear tubulofilaments that occur as palisading filamentous inclusions.[9] The filaments are unbranched and may be stacked side by side or occur in tangles.[9] Biopsy can also show the presence of abnormal mitochondria as well as nemaline rods, particularly in pharyngeal muscles.[1] PABPN1 is an important part of the muscle OPMD inclusions.[9] The inclusions also contain parts of the ubiquitin-proteasome pathway, transcription factors, and mRNA-binding proteins.[9]

The treatment of OPMD is usually supportive.[9] Patients with dysphagia should be advised to have a soft diet, including pureed foods.[9] Both cricopharyngeal myotomy and botulinum toxin injection into the cricopharyngeal muscle are effective in diminishing dysphagia.[11] A temporary solution may be feeding with a nasogastric tube, but eventually, gastrostomy tube placement will be required.[9] Surgery to correct ptosis in patients with OPMD may be very successful, unlike in other diseases such as myasthenia gravis or Kearns-Sayre syndrome.[9] Normal levator action is 15 mm, and frontalis sling surgery is the ideal intervention if levator action is limited to 4 mm.[10]

SEDATION AND GENERAL ANESTHESIA CONSIDERATIONS

For patients with any muscular dystrophy undergoing sedation or general anesthesia, there is a need for a thorough preoperative evaluation to determine the exact genetic diagnosis, extent of muscle weakness, and specific assessment of cardiorespiratory/musculoskeletal involvement depending on the specific genetic background.[12] For DMD and BMD, a great degree of attention must be paid to the airway exam; progressive fibrosis of the skeletal muscles can lead to limited mouth opening due to masseter involvement or diminished flexion and extension of the neck.[3] If these issues are encountered, it is imperative that alternative plans for sedation and general anesthesia as well as intubation be discussed with the patient and surgical team. Intravenous (IV) access can be difficult to attain in these patients; however, if there is a chance of significant blood loss, it is imperative that 2 large-bore IV catheters be placed for emergent administration of blood products or volume resuscitation during extensive surgeries. Use of invasive monitoring is dependent on the patient and surgical intervention to be performed and is unlikely to be used in outpatient ambulatory dental settings.

Intraoperative care is dependent on the type of surgical procedure as well as the status of the patient. For minor procedures, if possible, it may be ideal to avoid general anesthesia and endotracheal intubation to decrease the chance of respiratory complications.[3] The use of volatile anesthetics is controversial due to the possibility of rhabdomyolysis and hyperkalemia during a prolonged exposure. One theory is that the exposure to volatile agents causes destabilization of the sarcolemma, leaving it susceptible to further insults commonly encountered in the postoperative period such as shivering, hypothermia, and emergence agitation.[2] However, there appears to be limited risk when undergoing a brief inhalation induction for IV catheter placement.[3] For IV induction of general anesthesia, etomidate is typically the most appropriate choice as DMD and BMD patients often suffer from diminished myocardial function. Patients can with DMD and BMD receive nondepolarizing neuromuscular blockers (NDNMBs), but it is important to note that the duration of action will likely be prolonged. While NDNMBs are well tolerated in patients with muscular dystrophies, there is controversy regarding the use of cholinesterase inhibitors, as antagonism of acetylcholinesterase has been postulated as a potential mechanism of rhabdomyolysis.[3] Succinylcholine is absolutely contraindicated.[3] Alternatively, suitable intubation conditions often can be attained via propofol and remifentanil, barring any hemodynamic contraindications.

Meticulous attention to cardiac function is imperative as the change from spontaneous to positive pressure ventilation can result in significant fluctuations in hemodynamics, specifically decreases in preload. Positioning such as Fowlers (reclined seated position), beach chair, or prone position can further reduce cardiac function and output; these positions should be used with caution.[3]

Maintenance of anesthesia is generally achieved with total intravenous anesthesia (TIVA). This technique is beneficial as it helps to limit the risk of rhabdomyolysis and is useful for facilitation of neurological monitoring with motor and sensory evoked potentials.[3] The most common TIVA combination is propofol with a synthetic opioid (eg, remifentanil), although occasionally dexmedetomidine or ketamine are incorporated to decrease propofol requirements.

Postoperatively, DMD and BMD patients must be monitored until cardiorespiratory function returns to baseline. Telemetry should be observed as rhythm abnormalities can be indicative of electrolyte disturbances requiring treatment.[3]

For patients with a functional residual capacity less than 30% undergoing long procedures, it may be wise to provide noninvasive respiratory support postoperatively. Postoperative analgesia is ideally mitigated with intraoral local and regional anesthesia and adjunct agents to prevent decreases in ventilation. Some adjuncts of note include preoperative gabapentin and postoperative dexmedetomidine and IV acetaminophen.[3]

There is a known link between the administration of succinylcholine and hyperkalemic cardiac arrest in patients with muscular dystrophies. In 1992, the US Food and Drug Administration placed a warning on the use of succinylcholine in young children. Nicotinic acetylcholine receptors (AChRs) are found postsynaptically within the neuromuscular junction. Patients with DMD and BMD may have an upregulation of the neuronal isoform nicotinic AChRs (7AChRs).[13] These receptors are more sensitive to succinylcholine and its metabolite than normal AChRs, and the response correlates to the degree of upregulation. This sensitivity has been linked to the risk of hyperkalemia and cardiac arrest after administration of succinylcholine.[13]

Patients with EDMD undergoing surgery should have a recent echocardiogram performed to assess cardiac function and any arrhythmias to determine if surgery under general anesthesia is safe.[14] However, preoperative echocardiography may not always reflect how the diseased myocardium will respond to perioperative stress.[14] Heart failure and sudden death can occur during anesthesia for any major surgery, even with a normal preoperative echocardiogram and ECG.[14] Because atrial and atrioventricular conduction defects with bradycardia are common in patients with EDMD, anesthesiologists recommend preoperative prophylactic cardiac pacing as well as having emergency pacing available when any anesthesia is performed.[14] In several studies, sudden cardiac arrests have occurred in patients with EDMD when they received general anesthesia with an inhalational agent and/or succinylcholine.[14] Thus, anesthesiologists recommend avoiding triggering agents such as succinylcholine and volatile anesthetics to decrease the risk of severe anesthetic complications.[14] In addition, life-threatening complications, such as dysrhythmias, cardiac arrest, and rhabdomyolysis, have occurred after anesthesia with the depolarizing muscle relaxant succinylcholine and inhalational agents.[14]

In patients with EDMD, respiratory complications are a major concern when administering any level of sedation or general anesthesia.[14] In adolescence, patients with EDMD show reductions in inspiration, expiration, vital capacity, and total lung capacity due to weakness of the respiratory muscles.[14] Preoperative pulmonary function studies should be done to determine the postoperative course for these patients.[14] Even if the skeletal muscle strength returns to preoperative levels, delayed pulmonary insufficiency may occur up to 36 hours postoperatively.[14] To decrease the incidence of respiratory complications during and after surgery, patients with EDMD should undergo chest physiotherapy and nasal continuous positive airway pressure in recovery.[14] Opioids or anxiolytic drugs, such as fentanyl or benzodiazepines, pose a risk for respiratory depression and further muscle relaxation resulting in a potentially difficult airway.[15]

Airway management is extremely difficult but very important to consider in patients with EDMD undergoing surgery.[16] Laryngeal mask insertion (LMA) may be done to provide an excellent airway during the procedure,[16] although LMAs may be problematic for restorative dentistry. In addition, laryngoscopy can be done after induction to determine how difficult tracheal intubation would be if required.[16] If the patient is considered at high risk for aspiration pneumonia, awake intubation with a flexible fiber-optic scope should be considered.[16] Because it may be difficult to intubate patients with EDMD, it is important to assess with a cervical radiograph or lateral cephalogram prior to the proposed procedure.[16]

TIVA is often chosen over inhalational anesthesia for a few reasons.[16] First, volatile agents are best avoided due to the possibility of rhabdomyolysis.[16] Second, TIVA allows for a rapid onset and offset of anesthesia, allowing any problems with recovery of consciousness to be assessed quickly. It may also decrease the possibility of postoperative nausea and vomiting.[16] In addition, succinylcholine is contraindicated in patients with EDMD since it may cause an exaggerated hyperkalemic response. NDNMBs are best avoided due to possibly causing delays in muscle function recovery; however, in the event of an airway emergency (i.e., laryngospasm), NDNMBs, with close monitoring, would be the paralytic of choice if positive pressure or deepening of the anesthetic are insufficient.[16] Regional anesthetic techniques may be chosen over deep sedation or general anesthesia as there is a lower likelihood of complications from airway management and invasive ventilation, such as hypoventilation, atelectasis, and hypoxia.[15] If the duration of surgery is more than 2 hours, epidural anesthesia may be favorable over spinal anesthesia due to the need to avoid sudden and unpredictable hemodynamic changes.[15] Overall, the anesthesia technique must be customized and adjusted to each patient.

FSH is one of the most common and benign muscular dystrophies and typically has little respiratory involvement.[17] The affected muscles usually include those of the neck, face, and scapular stabilizing muscles, which tend to become weak.[17] Autonomous airway support upon recovery from sedation or general anesthesia may be compromised. However, it is important to understand that there are still anesthetic considerations for FSH.[17] Most of the complications usually result from acute hyperkalemia, which may cause sudden cardiac arrest.[17] These events can occur in patients who are still in the subclinical stage of their disease and may be the first manifestation.[17] Because of this, many clinicians may choose to avoid or minimize exposure to volatile anesthetics and omit succinylcholine completely in patients with FSH.[17]

Other anesthetic considerations in FSH include monitoring for skeletal muscle weakness, decreased cardiopulmonary reserve, and increased risk of aspiration pneumonia.[18] The pharmacologic response to NDNMBs is normal in FSH.[18] However, disease-induced muscle weakness may call for the use of NDNMBs and may compound any pharmacologic residual muscle weakness during recovery from anesthesia.[18] In addition, patients with FSH may experience pharyngeal and respiratory muscle weakness as well as gastrointestinal hypomotility, ultimately decreasing their ability to clear airway secretions and increasing the risk of pulmonary aspiration of gastric contents during induction and emergence. A longer fasting time for solid foods may be required in these patients. Delayed pulmonary insufficiency may occur up to 36 hours after surgery, even after skeletal muscle strength has returned to normal.[18] Myocardial depression, cardiac arrhythmias, and conduction abnormalities can be triggered by anesthetic agents or perioperative stress.[18]

Patients with OPMD undergoing sedation or general anesthesia should have their airway closely monitored at all times.[19] OPMD is not known to affect the cardiopulmonary systems.[12] Some complications during surgery include aspiration pneumonitis and airway obstruction due to the presence of profuse pharyngeal and tracheal secretions.[19] Therefore, the anesthesia provider should aspirate pharyngeal secretions before and potentially during induction. Indications for rapid sequence induction are the same as for the nonaffected population.[19] Studies have shown that the extrapharyngeal secretions may cause difficulty during extubation and in some extreme scenarios may require a tracheostomy.[19] Deep extubation would not be advisable due to the inability for the patient to clear their own secretions during emergence from the anesthesia. Postoperatively, patients with OPMD should be carefully monitored, especially if they have severe dysphagia or history of significant weight loss.[19] Patients who receive rocuronium during general anesthesia may have residual airway obstruction and should therefore be monitored closely in the PACU, even after full reversal.[19]

DENTAL CONSIDERATIONS

It is no wonder that medical conditions involving progressive facial muscle dysfunction would affect dental morphology. Egli et al studied dental arch morphological changes over the progression of DMD and found that there was a significantly higher prevalence of anterior and lateral open bite and posterior crossbite when compared with patients without muscular dystrophy.[20,21] Bite forces and labial forces were less when compared with nonaffected patients. Patients with DMD had deterioration of the study's dentofacial parameters over a 2-year period, including widening of the posterior region in the mandibular arch and significant shift to a skeletal sagittal class III.[20] It is assumed that these changes are due to the laxity and subsequent increased volume of the tongue as it hypertrophies.[20,21] There were no reported changes in facial height. Quality of life may be improved if these patients could maintain proper occlusal contacts and have mastication training to aid in sufficient muscular function.[20]

Patients with DMD may be taking oral bisphosphonates to offset glucocorticoid-induced osteoporosis.[22] It is advisable to contact the patient's physician if there is a need to perform a procedure that may result in osteonecrosis. Local anesthesia with epinephrine can be used safely in these patients in the usual and standard fashion. If the disease progression has cardiac involvement, consideration should be given to limiting the amount of epinephrine to only what is required to keep the patient comfortable for the procedure. Nitrous oxide is safe for these patients in the early disease states. At later stages with pulmonary involvement, these patients may be on oxygen at baseline, and the use of nitrous oxide would need to be strongly weighed.

CONCLUSIONS

The cornerstones to muscular dystrophy pathologies are cytoskeletal disruptions, instability of the sarcolemma, and an inability to maintain the equilibrium of calcium ions intracellularly. A multitude of factors must be taken into consideration for patients with DMD or BMD due to inadequate dystrophin. In EDMD, emerin, which is part of the nuclear membrane of the muscle cell, is lacking. FSH has a high degree of variability but typically affects the facial muscles, scapula, and ankle; however, cardiac and respiratory muscles can be affected and may impact ventilation during deep sedation and general anesthesia. In OPMD, abnormal protein clumping occurs within the sarcolemma, and subsequent dysphagia and macroglossia can result in higher risk of aspiration and upper airway obstruction with all forms of sedation. Some of the anesthetic considerations for patients with muscular dystrophies include a need for more extensive preoperative pulmonary and cardiac evaluations, a potential for prolonged NDNMB effects, avoiding succinylcholine and volatile anesthetics, and the need for close monitoring postoperatively. These conditions are all progressive in nature, meaning that a safe prior anesthetic does not negate the need for new and exhaustive evaluation and proper planning prior to these patients receiving sedation or general anesthesia of any form.

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1) Both Duchenne and Becker muscular dystrophies are associated with which of the following complications during general anesthesia using succinylcholine as a skeletal muscle relaxant?

   a. Hyperkalemia-induced cardiac arrest
   b. Malignant hyperthermia
   c. Myasthenia gravis
   d. Rhabdomyolysis

2) During development and as they age, patients with Emery-Dreifuss muscular dystrophy exhibit decreasing:

   a. flexion contractures of the neck region.
   b. prevalence of cardiac conduction abnormalities.
   c. pulmonary function (tidal volume, total lung capacity, inspiratory/expiratory volumes).
   d. risk of stroke associated with cardiac arrhythmias.

3) Patients with oculopharyngeal muscular dystrophy are particularly susceptible to which of the following complications of sedation or general anesthesia?

   a. Abbreviated paralysis with nondepolarizing neuromuscular blockers
   b. Life-threatening cardiac depression
   c. Malignant hyperthermia
   d. Pulmonary aspiration and upper airway obstruction

4) Patients with facioscapulohumeral muscular dystrophy generally exhibit phenotypic traits of weakened facial muscles, scapular winging, and footdrop after the age of 30 years.

   a. True
   b. False