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Anesthesia and rare neuromuscular diseases

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Neuromuscular diseases, although rare in the general population, can be present in people who need to undergo surgery and anesthesia. Fortunately, the possibility of early diagnosis, new therapeutic approaches and the application of a multidisciplinary approach have significantly extended the life expectancy of such patients. The presence of such a disorder represents a challenge in anesthesiology practice, both during the preparation for surgery itself, the operative procedure and postoperative recovery in intensive care units. A basic understanding of the main disorders of the disease and their potential interactions with the anesthetic itself and the necessary agents in anesthesiology is necessary in order to reduce the risk of perioperative morbidity and mortality, with the aim of reducing the possibility of complications. Rare muscle diseases are very difficult to classify in a standard way because of the variability of their etiology and pathology. This work focuses on a number of muscle diseases such as Dubowitz syndrome, rhabdomyosarcoma in children, spinal muscular atrophy, Kennedy's disease, Congenital muscular dystrophy of the Ullrich type (UCMD), Sotos syndrome, Polymyositis and Setleis syndrome, Nemaline rod myopathy, Pompe disease, Emery-Dreifuss muscular dystrophy (EDMD). The medical literature on anesthetic techniques and perioperative complications was reviewed. Given that they can have a very unfavorable effect on the course of general anesthesia in particular and that these diseases can cause very serious, even life-threatening complications, an adequate anesthesiological approach is very important to reduce the possibility of the mentioned complications. A multidisciplinary approach is imperative for such patients before and after surgery, whether it is performed under analgosedation, some type of regional or general anesthesia. The operative procedure itself must be performed in institutions that are adequately equipped to treat such patients and by personnel who have experience in treating them.

KEYWORDS

anesthesia, muscle disease, rare neuromuscular diseases, perioperative management, multidisciplinary approach

1. Introduction

Neuromuscular diseases, although rare in the general population, can be present in people who need to undergo surgery and anesthesia, or some diagnostic procedure that require anesthesiological management. With this group of patients, which, although small, must be studied and understood by the anesthesiologist, complications can occur precisely because of muscle disorders. They may experience weakness of the entire musculature with reduced strength of the respiratory muscles and the possibility of increased sensitivity to drugs with a neuromuscular mechanism of action, which predisposes them to complications both during the procedure itself and the recovery period. Complications can be related to the anethesiological treatment itself (drugs which are commonly used

during anesthesia) and most often affect cardiovascular and respiratory system, while after the procedure and anesthesia the difficulty in movement, instability in walking and an increased risk of falling and thus the injury could be present (1, 2).

Considering the seriousness of the complications that can arise perioperatively, the monitoring should be especially focused on the cardiopulmonary system, the possibility of occurrence and degree of muscle paralysis, as well as variations in the body's temperature (2, 3). As there is a high risk of respiratory and other postoperative complications, patients should be carefully monitored in the early postoperative period (3).

Because of all the above, a basic understanding of the main disorders of the disease and their potential interactions with the anesthetic itself and necessary agents in anesthesiology is necessary in order to reduce the risk of perioperative morbidity and mortality and to minimize the possibility of complications (4). Rare muscle diseases that we can encounter in our work are a very heterogeneous group of muscle disorders, and as many of them are not classified due to their specificity and newly discovered, while some are classified in one of the subgroups of muscle diseases, it is necessary for a better understanding of the disorders below to attach a short a reminder of the basics of muscle diseases themselves. We made a systematic review of papers searching the PubMed library.

2. Muscular diseases

Muscle diseases are caused by mutations in the genetic code. Mutations in different genes are associated with different types of muscle diseases; in general, these mutations interfere with the function of genes that are essential for muscle health. For example, Duchenne's and Becker's muscular dystrophies are caused by a mutation in the DMD gene, which codes for dystrophin, a protein that helps protect muscle cells from damage during movement. Mutations that cause muscular dystrophy are most often inherited from the patient's biological parents, and very rarely can arise spontaneously, so called *de novo* mutations (5).

Diseases that affect skeletal muscles can affect any part of the motor unit, so they include primary disorders of the motor neuron or axon, disorders of the neuromuscular connection and a wide range of diseases that primarily affect the skeletal muscles themselves and are called myopathies. This group of diseases can be divided into hereditary and acquired diseases (6). The classification of muscle diseases is shown in **Table 1**.

TABLE 1 Classification of muscle diseases.

Hereditary muscle diseases	Acquired muscle diseases
Duchenne muscular dystrophy (dystrophinopathy)	Idiopathic inflammatory myopathies
Becker muscular dystrophy (dystrophinopathy)	Endocrine myopathies
Hip-girdle muscular dystrophies	Myopathies caused by drugs and toxins
Congenital muscular dystrophies	
Distal muscular dystrophies	
Emery-Drei-fuss muscular dystrophy	
Facio-scapulo-humeral muscular dystrophy	
Oculo-pharyngeal muscular dystrophy	
Myotonic dystrophies	

2.1. Hereditary muscle diseases

In the narrowest sense, hereditary muscle diseases include progressive muscular dystrophies, including congenital myopathies. Progressive muscular dystrophies—genetically determined diseases in which there is progressive degeneration and weakness of skeletal muscles. Progressive muscular dystrophies include: Duchenne muscular dystrophy, Becker muscular dystrophy, Lumbar muscular dystrophy, Congenital muscular dystrophies, Distal muscular dystrophies, Emery-Dreifuss muscular dystrophy, Fascio-scapulo-humeral muscular dystrophy, Oculo-pharyngeal muscular dystrophy, Myotonic dystrophies, Metabolic myopathies, McAdler's disease (7).

Apart from these, there are conditions in which muscle disease is an occasional or permanent clinical sign in the spectrum of hereditary diseases of another organ system, such as disorders of muscle energy metabolism, mitochondrial diseases, disorders of muscle membrane excitability and other metabolic disorders (8). An undiagnosed or unrecognized neuromuscular disease from anesthesiological point of view can be life threatening. Special attention should be on drugs with neuromuscular effect, as well as the possibility of difficult airway management (9).

2.2. Acquired muscle diseases

When it comes to acquired muscle diseases, they are the result of non-hereditary diseases such as myopathies within endocrinological diseases, inflammatory myopathies and other types of myopathies that can accompany various systemic diseases. In addition, various toxins and drugs can cause severe damage to muscle tissue, which is also necessary to pay attention to when taking an anamnesis.

1. Idiopathic inflammatory myopathies can be further divided into:
   - Dermatomyositis
   - Polymyositis
   - Myositis with inclusion bodies
2. Endocrine myopathies—They can be caused by the disorder of numerous glands with internal secretion, most often by dysfunction of the pituitary gland, thyroid and parathyroid glands, adrenal gland and pancreas.
3. Myopathies caused by drugs and toxins—Muscle changes can manifest as focal myopathy, inflammatory myopathy, acute rhabdomyolysis, acute and subacute proximal myopathy, weakness related to hypo- or hyperkalemic states, muscle fibrosis, malignant hyperthermia (10).

2.3. Symptomatology

The primary indicator of muscle diseases is progressive weakening and atrophy of the muscles. Certain muscles that are affected, as well as accompanying symptoms, indicate a specific type of disease. Many forms of muscle disease cause weakness in the muscles necessary for movement, thus causing fatigue and impaired mobility. Many patients are confined to wheelchairs or use other mobility aids. Also, muscle contractures are often present (11).

In certain diseases, the heart muscle can also be affected, leading to heart problems. Also, problems with breathing may occur as a result of weakness of the muscles responsible for breathing. If the muscles of the trunk are affected, deformities of the spine (scoliosis) occur, which makes it difficult to position patients on the operating table. Some types of muscle diseases affect the eye muscles, causing various visual problems. Neurological abnormalities and intellectual instability occur in some types of muscle disease (1).

3. Anesthesia and muscle diseases

3.1. Preoperative management

Anesthesia must be carefully administered in patients with muscular dystrophy, since most anesthetic agents act directly on the muscles, which are weakened and damaged in these patients. The need for special care, including alerting the anesthesiologist that the patient has muscular dystrophy, is very important for anesthesia, whether local, regional, or general (2).

Physicians should thoroughly examine a patient diagnosed with muscular dystrophy before administering any anesthetic. Special care is focused on the anesthetics themselves and their effects on the skeletal and cardiac muscles. Patients with muscular dystrophy may respond differently to anesthetics than patients without muscular dystrophy. The stage of the patient's illness should also be considered (12).

3.1.1. Neurological evaluation

A detailed neurological diagnosis is necessary in order to better assess the risk during surgery and anesthesia. It is necessary to confirm the diagnosis, if possible, as well as to determine the degree of disease progression in each patient (12). However, the diagnostic procedure can be complex, and in some patients there is the impossibility of making a definitive diagnosis, especially since they only present with isolated elevation of creatine kinase levels with or without minor signs. These patients are at risk of life-threatening anesthesia-related complications and should be treated as the highest-risk patients (13–15).

3.1.2. Respiratory evaluation

Involvement of the respiratory system can vary between different neuromuscular diseases. Decreased inspiratory muscle strength results in restrictive pulmonary deterioration with a progressive decrease in forced vital capacity (FVC). Subsequently, as a result of poor alveolar ventilation, nocturnal hypercapnia can occur, and possibly also during the day (16). And weakness of the expiratory muscles leads to inadequate clearance of airway secretions.

Hypoventilation, associated with weakened cough, can lead to atelectasis and respiratory failure. Patients with neuromuscular diseases often have mild to moderate bulbar dysfunction, affecting their ability to swallow. Patients with type 1 spinal muscular atrophy, amyotrophic lateral sclerosis, myasthenia gravis and other rapidly progressive neuromuscular diseases may develop more severe forms of bulbar dysfunction with an increased likelihood of aspiration (17, 18). Drugs such as benzodiazepines and opiates, which cause some degree of respiratory depression, should be given carefully and their doses selected carefully.

Eventually, sleep apnea, nutritional problems, gastroesophageal reflux, or progressive scoliosis may occur. All this can lead to nosocomial infection, prolonged intubation, tracheotomy, and possibly death. Therefore, a strict respiratory evaluation is necessary in these patients to assess the risk of respiratory complications and the need for specific preoperative and postoperative management (15, 19, 20). Patients should be continuously monitored during surgery in case of signs of rhabdomyolysis, malignant hyperthermia, respiratory insufficiency and cardiac arrest. Patients with muscular dystrophy have an increased risk of apnea after extubation and in the first 24 h after surgery.

Assessment of respiratory function should include accurate medical documentation, physical examination, lung radiography, as well as evaluation of sleep-disordered breathing, as well as measurement of respiratory function and cough efficiency (15, 17, 20).

3.1.3. Cardiovascular evaluation

Several neuromuscular diseases are associated with cardiac dysfunction (cardiomyopathies and/or conduction system disorders). However, clinical manifestations of heart failure are often revealed late due to musculoskeletal limitations (21, 22).

Assessment of cardiac function before surgery can help the anesthesiologist in the decision to use inhalational anesthetics. Gases, such as ethane and halothane, can reduce the contractility of the heart muscle and thereby further worsen conduction.

All patients with relevant cardiac dysfunctions have a limited ability to increase cardiac output in response to stress. These patients are at high risk of perioperative cardiac side effects, due to the negative inotropic effect of volatile and intravenous anesthetics, positive ventilatory pressure, hypoxemia, and acute anemia (23).

In all patients, it is necessary to have an electrocardiogram and an echocardiogram performed before anesthesia or sedation, if this has not been done in the previous 12 months (21, 22). An electrocardiogram should be performed in all patients with periodic paralysis in order to rule out long QT intervals that precede Andersen's syndrome with the risk of ventricular arrhythmias, therefore it is necessary to perform Holter tests (21, 22).

Additionally, in patients with a high degree of AV block, it is necessary to place a pacemaker before general anesthesia.

In all patients with significant cardiac dysfunctions, it is necessary to monitor invasive arterial pressure during general anesthesia, as well as in the postoperative period (24). And in patients without primary myocardial dysfunction, preoperative cardiac evaluation is recommended only if pulmonary hypertension is suspected (25).

3.2. Intraoperative management

3.2.1. Succinylcholine and halogen anesthetics

In the case of motor neuron and peripheral nerve diseases, the use of halogens is permitted, while the use of succinylcholine is contraindicated (12, 25). In patients with a disorder of the neuromuscular junction general anesthesia with halogens is considered safe (12, 26).

In myopathic patients, the use of inhaled anesthetics and succinylcholine can be highly risky for malignant hyperthermia or acute rhabdomyolysis (27). It is recommended to avoid the use of succinylcholine and halogenated anesthetics in these patients (12, 26, 27).

3.2.2. Total intravenous anesthesia (TIVA)

If halogens are contraindicated, general anesthesia can be performed as total intravenous anesthesia (26, 28, 29). It should be taken into account that the use of intravenous anesthetics and opioids can lead to respiratory and cardiac depression. Therefore, it is necessary to carefully titrate the doses of these drugs.

3.2.3. Non-depolarizing neuromuscular relaxants

In all patients with neuromuscular dystrophy, nondepolarizing neuromuscular relaxants can show a prolonged effect of neuromuscular block, even though they are short-acting. There are several reports that recommend avoiding these relaxants whenever possible (24, 26, 30). If their use is necessary, then it is preferable to reduce the doses and use TOF (train-of-four) monitoring (15, 19, 31). Anticholinesterase drugs are not recommended because they can lead to hyperkalemia (12). The use of sugammadex as an antidote to rocuronium or vecuronium may be beneficial in these patients as it reduces the risk of postoperative residual muscle paralysis.

The combination of rocuronium and sugammadex can replace the use of succinylcholine in rapid sequence intubation of patients with neuromuscular dystrophies (32, 33).

3.2.4. Regional anesthesia

There are potential risks with regional anesthesia in patients with pre-existing diseases of the peripheral nervous system. Although, on the other hand, the use of regional or local anesthesia showed a significant advantage in terms of avoiding anesthetics and reducing postoperative respiratory complications in all patients with neuromuscular diseases, especially in those with reduced lung function (26, 34). The use of ultrasound during regional anesthesia can reduce the amount of local anesthetic and the incidence of hematomaif a blood vessel is injured (35). Therefore, regional anesthesia can be used, even in patients with disorders of the peripheral nervous system (18, 26, 36).

4. Rare muscle diseases

As previously mentioned, we cannot classify rare muscle diseases in a standard way due to the variability of their etiology and pathology, so they will further be described individually with an anesthesiological approach for each of them. Given that they can have a very unfavorable effect on the course of general anesthesia in particular, sometimes causing very serious, even life-threatening complications, an adequate approach is very important to reduce the possibility of the previously mentioned complications (15).

4.1. Dubowitz syndrome

This represents a rare autosomal recessive genetic disorder. Since its discovery in 1965, only 141 cases of this rare syndrome have been reported (37). It is characterized by stunted growth, characteristic triangular face shape, microcephaly, intellectual disability and behavioral disorders (38). According to known data, this syndrome manifests itself through cardiovascular, urogenital, endocrinological, immunological, hematological, neurological, and skeletal muscle disorders (38).

In the case report by Lee et al. (39) the patient underwent a total hysterectomy in order to stop bleeding. The patient had mildly pronounced muscular retardation with pronounced intellectual disability that corresponds to the cognitive function of a 1-year-old baby. The patient had a characteristic facial appearance, with microcephaly, scanty hair, sloping forehead, scanty eyebrows and eyelashes, blepharophimosis, low-set ears, phiroca and flat nasal septum, micrognathia and dental malocclusion, in addition to eczema all over the body and limbs, which are common symptoms of this syndrome. General anesthesia was inducted by thiopental, while rocuronium was used for muscle relaxation.

In addition to difficult intubation and poor visibility due to malformations present in the oral cavity or upper respiratory tract, there is also the possibility of muscle hypotonia in patients with Dubowitz syndrome (38). For patients with suspected hypotonia, it is necessary to conduct a preoperative assessment of neuromuscular tone and provide neuromuscular monitoring during surgery (39).

4.2. Spinal muscular atrophy

Spinal muscle atrophy is a muscle disease with neuromuscular etiology and occurs rarely. It is classified into four groups and can

affect children of different age, but it mainly occurs in newborns or in early childhood. Degeneration of anterior horn neurons of spinal cord and occasionally brainstem nuclei correspond to a range of clinical features including global hypotonia, pulmonary insufficiency, autonomic and bulbar dysfunction. In type I (Werdnig–Hoffmann), these symptoms are expressed in childhood and rapidly evolve in the first year of life. Myopathic changes occur later in type II and III (Kugelberg–Welander), and minimal disability in old age is experienced by those with type IV (40, 41).

According to a retrospective study performed in Boston in the period from 1981 to 2008, forty-five children with SMA were discovered, and twenty-five children with spinal muscular atrophy were clinically monitored, of which ten with type I, eight with type II and seven with type III spinal muscular atrophy. A total of 56 procedures were performed on these children, some under general and some under regional anesthesia. In 38% of cases, children were already dependent on mechanical ventilation due to weakened muscles and inability to breathe spontaneously. General anesthesia using nitrous oxide was performed in 14 patients, and balanced anesthesia using inhalation anesthetics and epidural anesthesia or systemic opioids was performed in 41 patients. In one newborn, the procedure was performed under spinal anesthesia (41).

This study concluded that it is possible to provide perioperative anesthetic care to children with spinal muscular atrophy safely and effectively with intravenous general anesthesia or inhalation anesthesia together with careful use of opioids to increase comfort in this patient group without increasing morbidity (42).

Buettner reported a case of a female patient diagnosed with spinal muscular atrophy type III who underwent spinal anesthesia for caesarian section. Spirometry was performed preoperatively and diagnosed restrictive lung disease in this patient, therefore, general anesthesia was contraindicated. A spinal block was performed with hyperbaric bupivacaine and fentanyl. The procedure was successful for both mother and child (43).

Another reason why general anesthesia should be avoided in such patients is increased sensitivity to non-depolarizing muscle relaxants, potential hyperkalemia during the administration of suxamethonium, and the possibility of difficult intubation in this case. Regional anesthesia may be technically unfeasible. Epidural anesthesia may prove to be a bad choice due to inadequate spread of local anesthetic, especially if a patient with spinal muscular atrophy has undergone corrective spinal surgery. Adequate doses for performing spinal anesthesia have proven to be difficult to calculate, with the risk of the block not being present or being too high. Combining spinal and epidural anesthesia or performing continuous spinal anesthesia may be convenient due to the possibility of titrating the block and bringing it to the ideal level. In the end, it was concluded that in such a rare case, patients should be observed in a multidisciplinary environment with early referral to an anesthesiologist. Respiratory function tests should be repeated after the second trimester because muscle strength may weaken even more in patients with spinal muscular atrophy (43).

4.3. Kennedy's disease

Kennedy's disease is a rare, genetically predisposed disease that is recessively linked to the X chromosome. It is characterized by a neurodegenerative disorder that leads to progressive limb atrophy and bulbar muscle atrophy with laryngospasm that can pose a great risk in anesthesia (44–46).

At the Mayo Clinic, Rochester, Minnesota, an examination of clinical data was performed in the period from January 1996 to May 2008 related to patients with this disease who underwent total anesthesia (47). Six patients were identified, with a total of 13 total anesthesia performed.

Most patients received the regular doses of benzodiazepines and opioids, without side effects. Succinylcholine was used in two cases, while non-depolarizing muscle relaxants were used in seven patients. Although laryngospasm did not occur in any of these cases during anesthesia, in one patient, postoperatively, glottis edema developed, which led to worsening of respiratory distress, bulbar dysfunction, and the development of the patient's condition which required tracheostomy and prolonged support of mechanical ventilation. One of these patients developed a pneumothorax.

Because of possibility for developing bulbar dysfunction and muscle weakness anesthesiologists must be aware of the potential risks after anesthetic administration (48).

4.4. Ullrich congenital muscular dystrophy (UCMD)

This type of congenital muscular dystrophy is very rare; so far only 50 cases have been registered so far. The consequences of these disorders include weakness of trunk and limb muscles, hyperflexibility of distal and proximal joint contractures, which necessitates the use of a wheelchair, as well as stiffness and scoliosis of the spine and progressive restrictive ventilation disorder. About 50% of cases of sick children between 10 and 11 years of age due to impaired diaphragm function and other disorders also require non-invasive ventilation (NIV) (31).

In the latest case report from 2022, intravenous anesthetics (propofol) and opioids (sufentanil, remifentanil) showed safe effect, and the administration of muscle relaxants was omitted due to the lack of data on their effect in patients with UCMD (49).

From the anesthesiology point of view, it is necessary to look at the problem from several aspects when it comes to congenital muscular dystrophy of the Ullrich type. Scoliosis and limb contractures as well as the general poor physical condition of these patients require careful handling on the operating table to avoid pressure ulcers or nerve lesions. Given that the opening of the mouth is limited, that there are anatomical changes in the face as well as laryngeal and pharyngeal changes, contractures of the cervical spine and other deformities, anesthesiologists must count on reduced airway patency in such patients (50, 51). There

is a recommendation for these patients that breathing should remain spontaneous as much as possible during anesthesia (52, 53).

The choice of anesthetic is a special problem due to contraindications and side effects (54). It has already been mentioned that succinylcholine is contraindicated in patients with muscle diseases. In mitochondrial myopathies and myotonic syndromes, the use of propofol is considered contraindicated due to the serious complications, but it showed safe in the case report described above. Volatile anesthetics can lead to rhabdomyolysis, hyperkalemia and asystole in patients with muscular dystrophies (55, 56). There is no available literature about non-depolarizing muscle relaxants effect in this disorder. Postoperative pain therapy could include intravenous administration of opioid anesthetics while monitoring the patient's respiratory function.

4.5. Sotos syndrome

It is a rare genetic disorder characterized by pathological facial anomalies, disorders of motor development induced by muscle hypotonia, cognitive disorders as well as heart and kidney disorders. It is also known as cerebral gigantism (57).

A case report from Chung et al. (58) described the safe use of thiopental in combination with sevoflurane in a patient suffering from Sotos syndrome. Muscle relaxation was achieved with rocuronium, while neuromuscular monitoring was performed using TOF. Also, fentanyl was applied without side effects. In conclusion, muscle relaxants and opioids have been shown to be safe in these patients.

4.6. Polymyositis and Setleis syndrome

Polymyositis is a systemic disease characterized by inflammation and muscle degeneration (59). Symptoms often include muscle weakness, muscle pain, dysphagia, dyspnea, and hand tremors (60, 61). Heart muscle problems as well as joint pain can also occur along with skeletal muscle disorders (62). Respiratory musculature weakness can also be pronounced and lead to carbon dioxide retention. Due to the weakness of the abdominal and neck muscles, the development of GERD and aspiration of acidic stomach contents can occur.

After literature research, we suggest following recommendations in patients with polymyositis:

- Be aware of enhanced or delayed response to administration of neuromuscular blocking agents.
- Pulmonary complications such as pneumonia and pulmonary fibrosis and cardiac complications such as cardiomyopathy and arrhythmias and even cardiac arrest may occur.
- Suppression of the pituitary-adrenal axis and previous steroid therapy that may lead to increased sensitivity to neuromuscular blocking agents may occur.
- There is a risk of skeletal deformities with reduced joint mobility and disorders of the cervical spine.
- Hyperkalemia and disturbed temperature regulation may occur.
- There is a possibility of interaction between non-depolarizing muscle relaxants and immunosuppressants if they exist in the therapy of the primary disease because they can lead to resistance and reduced effect of this group of muscle relaxants.
- Succinylcholine should be avoided because it can be a trigger for malignant hyperthermia and lead to hyperkalemia.
- In such disorders, the use of neuromuscular blockers with a shorter half-life is recommended. Atracurium has been shown to be safe in muscle paralysis, although it leads to slightly increased sensitivity.
- Neuromuscular blockade must be monitored with the use of peripheral nerve stimulators.
- Opioids can lead to postoperative respiratory depression.
- Volatile anesthetics should also be avoided due to the increased risk of malignant hyperthermia as well as the possibility of potentiating the effect of muscle relaxants. It is generally recommended to avoid all agents that can be triggers for malignant hyperthermia in patients with elevated plasma levels of creatine phosphokinase.
- If cardiopulmonary function is normal, epidural anesthesia can be performed in patients with polymyositis.

4.7. Nemaline genus myopathy

Nemaline myopathy is a rare hereditary disease that occurs due to heterogeneous gene mutations and includes several subcategories according to the severity of the disease, from those with mild symptoms to those with a very severe condition with profound hypotonia and no spontaneous movements and with respiratory insufficiency leading to a fatal outcome in in the first year of life. Clinically, what most patients present with is non-progressive myopathy, feeding problems and proximal muscle weakness. When it comes to pediatric patients, physical underdevelopment with atrophic muscles and thin limbs can occur (63). The bulbar muscles are also affected by the disease so dysphagia and the risk of aspiration can occur. The state of the respiratory muscles can be variable from mild difficulty in breathing to complete dependence on mechanical ventilation in some patients who are not capable of breathing independently.

Five different papers related to nemaline myopathies pointed out that muscle relaxants can be used including suncinylcholine, pancuronium, vecuronium and atracurium (61, 64–66). Only in the case of succinylcholine, special attention is needed to avoid the development of hyperkalemia. When succinylcholine was used, there was a delay in the response to a dose of 1 mg/kg, where the latent period was 6 min in this case compared to the normal response up to 25–45 s (66). Also, in four different cases, potent inhalational anesthetics such as halothane, enflurane and isoflurane were used to maintain general anesthesia after induction (67).

The data listed in the literature are diverse with the possible application of different anesthetics and techniques, but all sources agree that patients with this type of myopathy are at high risk and susceptible to complications, that the approach must be individual because some may also experience disturbances in other organ systems, like cardiovascular and renal system. Finally, in most patients with this disease, a longer period of convalescence is expected after the procedure, with the possibility of developing postoperative respiratory complications, for which we must be prepared (68).

4.8. Pompe disease

Pompe disease is a glycogen storage disorder II characterized by abnormal glycogen deposition primarily in the heart and skeletal muscles leading to progressive loss of muscle function. The juvenile form of this disease is particularly progressive with more severe muscle weakness followed by respiratory failure, bleeding, hemodynamic instability, as well as metabolic imbalance (69).

Clinical experience showed that ketamine and dexmedetomidine are safe in these patients, while muscle relaxants should be avoided (70). Ketamine increases systemic vascular resistance and cardiac muscle contractility so it is considered beneficial (71, 72). Hyperthermia and nondiabetic ketoacidosis have been reported after administration of enflurane and succinylcholine in children with Pompe disease (70). Propofol should be avoided because it can lead to hypotension and cardiac ischemia, especially in patients with myocardial hypertrophy (69, 72).

According to recent research, dexmedetomidine has been used successfully in spinal interventions. It has been shown to induce analgesia, anesthesia, and sedation, providing good hemodynamic stability and reducing the need for other anesthetic agents (73).

4.9. Emery-Dreifuss muscular dystrophy (EDMD)

In 1961, Dreifuss and Hogan published a paper on a rare, benign variant of Duchenne muscular dystrophy (74). In 1966, Emery and Dreifuss defined unique features that differed from those of Duchenne and Becker muscular dystrophies (75). It is characterized by a triad of symptoms: early contractures of elbows, Achilles tendon and posterior cervical muscles; slow progression of muscle wasting and weakening with humero-peroneal distribution at an earlier stage; cardiomyopathy, which often presents as heart block.

After a comprehensive review of the collected data, the conclusion is that there is no ideal anesthesia for patients with Emery-Dreifuss muscular dystrophy. Careful evaluation of the severity of the myopathy and the degree of heart muscle strength impairment can reduce the risk of unwanted events. Local anesthesia has proven to be the safest option. Total intravenous anesthesia or inhalation may be considered appropriate if general anesthesia cannot be avoided (76).

5. Conclusion

At the end of the research on rare muscle diseases, taking into account the study of data from the latest literature, we can conclude that there is a great correlation and the importance of the knowledge that anesthesiologists possess as health professionals responsible both for keeping the patient alive during the state of anesthesia, and for his safe awakening and recovery without consequence.

In the diseases where motor neuron or peripheral nerves are affected the use of halogen anesthetics is safe and use of succinylcholine is forbidden, while in patients with a disorder of the neuromuscular junction the use of volatile anesthetics is considered safe.

In myopathic patients, the use of inhaled anesthetics and succinylcholine carries a risk for malignant hyperthermia or acute rhabdomyolysis. So the recommendation is to avoid their use in these patients. Intravenous anesthetics and opioids can lead to respiratory and cardiac depression, so it is necessary to carefully titrate the doses of these drugs in patients with neuromuscular disorders. According to nondepolarizing neuromuscular relaxants, the general recommendation is that whenever possible, they should be avoided. If their use is necessary, then it is preferable to reduce the doses and use the neuromuscular monitoring. Anticholinesterase drugs are not recommended because they can lead to hyperkalemia. Whenever muscle relaxation is needed during the surgical intervention the safest recommendation is to use of sugammadex as an antidote to rocuronium or vecuronium.

As previously supported by many evidences and clinical cases, patients with rare muscle diseases can be very demanding when it comes to anesthesiological approach precisely because of their often difficult general condition of the body, altered response to anesthetics and a more difficult and longer recovery period. What we all have to work on is adequate and complete taking of a detailed medical history in such patients, as this can greatly influence the decisions we will make during the operation.

There remains the further task of examining this area because it has been covered very little in the literature, and all with the aim of providing the best possible care to this small group of patients.

Author contributions

All the authors did the research and were included in the writing of the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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