Pro-Con: Anesthesia and the Patient with Neuromuscular Disease

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Anesthetic management of pediatric patients with neuromuscular disease can be complicated. It is useful to consider pre-operative planning, complications that arise in the course of anesthetic administration, and post-operative complications.

Pre-Operative Planning
It is a useful endeavor to learn about the most common neuromuscular diseases in pediatric patients, because when we anesthetize a young patient for corrective orthopedic surgery or any other procedure, it may be the case that there is no diagnosis of muscular disease when a sub-clinical myopathy is indeed present. Symptoms may have been ignored. A neurologist, even after detailed medical history and careful physical exam, may decide that time should be the first test of the natural history of the disease.1 Alternatively, when diagnostic procedures are indicated, planning for anesthesia may be facilitated because muscle biopsy is more often the second or third diagnostic choice rather than the first. Analysis of DNA is now the first diagnostic step when the suspected diagnosis is dystrophinopathy, limb-girdle, Emery-Dreifuss, fascioscapulohumeral, or myotonic dystrophy, or other myotonias, periodic paralysis or spinal muscular atrophy.2 If we are aware of the most likely diagnosis, then we can look for the likely concomitant systemic impairments.

A relevant example is the cardiac disease that occurs in patients with dystrophinopathy in skeletal muscle. There are commonly intra-atrial conduction abnormalities in patients with dystrophinopathy and 90% have abnormal electrocardiograms.3 Furthermore, by the age of 14 years one third of the patients with Duchenne muscular dystrophy have cardiomyopathy.4 Peri-operative cardiac arrest is more frequent when dystrophinopathy has not been identified pre-operatively.5

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[1] Chapter 1, Introduction: Historical Perspectives, by DC De Vivo, BT Darras, HR Jones, page 3 in Neuromuscular Disorders of Infancy, Childhood, and Adolescence: A Clinician's Approach, ed. Jones, HR, De Vivo, DC, Darras, BT, Butterworth Heinemann, Elsevier Science, Philadelphia, USA, 2003.

[2] Ibid. page 4, Table 1-1.

[3] Farah MG, Evans EB, Vignos PJ: Echocardiographic evaluation of left ventricular function in Duchenne's muscular dystrophy. Am J Med 1980; 69:248-254.

[4] Nigro G, Comi LI, Politano L, Bain RJ: The incidence and evolution of cardiomyopathy in Duchenne muscular dystrophy. Int J Cardiol 1990; 26:271-277.

5 Breucking E, Reimnitz P, Schara U, Mortier W: Anesthetic complications. The incidence of severe anesthetic complications in patients and families with

Cardiac disease is also frequent in myotonic dystrophy, Emery-Dreifuss dystrophy, limb-girdle dystrophies 1B and 1D, Anderson's syndrome, mitochondrial diseases, some glycogen storage diseases, carnitine deficiency, and inflammatory myopathies. Pre-operative recognition of conduction abnormalities and limited cardiac reserve may alter anesthetic plans. Pre-operative treatment may be necessary. There are pediatric patients, with Pompe's disease for example, whose cardiovascular reserve will not tolerate general anesthesia. Pre-operative history and physical exam should look for evidence of cardiac failure. Individualized plans for appropriate cardiovascular support should be prepared.

The possible diagnosis of myotonia should be evaluated and appropriate treatment instituted pre-operatively. Diet generous in complex carbohydrates and serum potassium levels close to 4.0 mEq/L may lessen stiffness. Mexiletene or tocainide have been useful in several forms of sodium and chloride channel myotonia.6 Thiazides, acetazolamide and sodium restriction are therapeutic in hyperkalemic periodic paralysis with myotonia.

Anesthetic Concerns

In general a "stress free" anesthetic is beneficial because increased neuromuscular activity may demonstrate the limited respiratory and cardiovascular reserve of the myopathic patient. Some patients, in particular those with myotonic dystrophy, are extremely sensitive to the respiratory depressant effects of drugs.7 This is due to neurologic abnormalities associated with this disease.8 If regional anesthesia can be applied, it may produce the desired result without the side effects of inhalation and intravenous anesthetics.

Evaluation of individual patients is necessary to assess potential difficulty with airway management. Dysmorphic features and inability to co-operate with pre-operative oral examination suggest that airway management may be difficult. Choice of anesthetic induction method, inhalation or intravenous, should be made with consideration of the potential airway and cardiovascular problems.

Neuromuscular blockers can have unpredictable effects. Succinylcholine may produce hyperkalemia sufficient to produce cardiac arrest.9 Succinylcholine increases resting

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progressive muscular dystrophy of the Duchenne and Becker types. Anaesthesist 2000; 49:187-95.

[6] Moxley RT III: Channelopathies. Current Treatment Options in Neurology 2000; 2:31-47.

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[9] Larach MG, Rosenberg H, Gronert GA, Allen GC: Hyperkalemic cardiac arrest during anesthesia in infants and children with occult myopathies. Clin Pediatri (Phila) 1997; 36:9-16.

tension of normal muscle10,11 and can produce severe contractures in some patients with myotonia.12 Nondepolarizing blockers will have unpredictably prolonged effects. These drugs will not alter the increased muscle tension produced by the hyperexcitability of the muscle membrane in myotonia or by the metabolic exhaustion of malignant hyperthermia. It is uncertain whether or not administration of anticholinesterase will induce a myotonic episode.

For more than 20 years there has been debate about the risk of uncontrolled metabolism of muscle and severe rhabdomyolysis in myopathic patients exposed to inhalation anesthetics. Are all forms of myopathy associated with increased risk of malignant hyperthermia (MH)? In 2004 it is recognized that about 50% of patients identified as MH susceptible by muscle contracture testing have mutations in the ryanodine receptor that are responsible for this disorder.13 What causes the other 50% of patients to have abnormal contracture tests? Will hyperexcitability of the sarcolemma or structural abnormalities of the muscle cell compromise intracellular control of calcium sufficiently to produce an episode of MH? Does anesthetic technique make a difference to this risk?

Some conclude that all myopathic patients are at increased risk of MH because in one group of 25 consecutive patients, there were positive contracture tests in 7 of 18 with myopathic disorders and 3 of 7 with neurogenic disorders. Two of these patients had anesthetic events suggesting MH.14 Others state that predisposition to true MH has been established only for 3 myopathies15: Evans myopathy, King Denborough syndrome16 and central core disease.17 Another group studied 44 myotonic patients, and found four positive, 10 equivocal and 30 negative results of the caffeine-halothane contracture test. The results for 27 control muscles from normal subjects all had negative results on this test. When the test was performed with less than normal concentrations of contracture-triggering substances (caffeine less than or equal to 2 mmol litre-1, less than or equal to 2% halothane), 70% of the muscles from the

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[17] Shuaib A, Paasuke RT, Brownell KW: Central core disease: clinical features in 13 patients. Medicine 1987; 66:389-396.

patients and 15% of the controls responded with small contractures (less than 0.2 g). Their conclusions were that these results should not be taken to indicate that the patients have the genetic trait for MH. The positive and equivocal test results, in addition to the slight contractures, may be accounted for by the electrical after-activity in the cases of pure myotonia, and by increased resting myoplasmic [Ca2+] in myotonic dystrophy.18

Nevertheless there have been rare cases of increasing metabolism and muscle injury in patients with myopathy after minutes19,20 to hours21 of inhalation anesthesia. For example, a patient with fascioscapulohumeral dystrophy had this complication reported through the MH Hotline. Total intravenous anesthesia may not avoid this problem. A patient with merosin deficient dystrophy experienced signs of MH during “trigger free” anesthesia.22 Dantrolene can be useful in restoring normal muscle metabolic rate in such cases. One presumes, although this is difficult to prove, that dantrolene administration can also decrease rhabdomyolysis in such cases and so speed recovery.

Postop

Problems in systems other than skeletal muscle or the heart may be the limiting factor in anesthetic management. For example, the gastrointestinal dysfunction and greatly increased risk of post-operative respiratory depression in myotonic dystrophy patients mandates close observation after general anesthesia.23

There are patients that have had cardiac arrests in the recovery room after unremarkable anesthetics. Often these are hyperkalemic episodes associated with apparent anesthetic induced rhabdomyolysis.24 Sometimes there is progressive hypotension without electrolyte imbalance. There should be a low threshold for continued electrocardiogram and invasive blood pressure monitoring in patients with myopathy. A dipstick screen of urine can rule out myoglobinuria. Post-operative creatine kinase can be compared with pre-operative values to demonstrate that there was no major increase.

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Myopathic patients have several reasons why they may need intensive care after general anesthesia.

Conundrums and Conclusion

Much has been learned about the genetics and pathophysiology of neuromuscular disorders. Some terminology that is decades old does not easily reflect recent distinctions. Because many observations have associated congenital defects and corrective musculoskeletal surgery with MH25, we continue to worry that any patient with a musculoskeletal disorder may be at increased risk of this anesthetic complication.

Infants undergoing clubfoot repair have a high incidence of myopathic changes on muscle biopsy.26 Does this imply that all infants with arthrogyposis are at increased risk of MH? There are many different causes of multiple congenital contractures. The only common factor is that decreased fetal movement for any reason can result in multiple contractures. Among the possible diagnoses are some syndromes that have been said to be associated with MH.27 One of these is the Schwartz-Jampel syndrome. This syndrome is distinctive phenotypically with short stature, bone and joint deformities, chondrodystrophy, hypertrichosis, blepharophimosis and stiffness of muscle. Electromyography shows continuous high-frequency electrical discharges and delayed muscle relaxation. There is marked action myotonia on movement and percussion myotonia. Affected patients are prone to episodic hyperthermia. Therefore the label MH susceptible has been applied. But this syndrome is a myotonic disorder of unknown mechanism. Two of the three types of Schwartz-Jampel syndrome are associated with mutations in a major proteoglycan of basement membranes and cartilage. Carbemazepine can be helpful. Some cases show disappearance of muscle discharges after curare. No doubt much care and vigilance is indicated during anesthesia administration, but it is unfair to restrict the anesthetic choices without more understanding of pahtophysiology. Perhaps the excessive muscle activity of a patient with Schwartz-Jampel syndrome can lead to increased metabolism, rigidity and injured muscle. But these facts do not imply that inhalation anesthetics are necessarily more dangerous than other anesthetics for the Schwartz-Jampel patient.

In all pediatric anesthetics, especially when the patient has signs of a neuromuscular disorder, capnography and minute ventilation and core temperature should be documented. There should be means to check serum electrolytes and urine screen for myoglobin. When all these are normal, there will be documentation that this myopathic individual has not suffered complications of anesthesia.

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