Chapter 33
Neuromuscular Disease

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A 14-year-old girl with juvenile myasthenia gravis has been treated with steroids and pyridostigmine for the past year; she now presents for thymectomy via median sternotomy. BP = 110/72, HR = 100 bpm, RR = 28/min, and Hgb = 12.6.

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Preoperative Evaluation

Questions

1. What is myasthenia gravis? Is this patient at risk of pulmonary aspiration of gastric contents? How would you assess this preoperatively? Should she receive pharmacologic prophylaxis? Which drugs? Are there any interactive effects with her current medications?

2. Is it important to know which steroid she is on? Should she be "covered" for surgery? Should she receive her pyridostigmine preoperatively? Would you base your management on an assessment of her pulmonary function tests?

Preoperative Evaluation

Answers

1. Myasthenia gravis (MG) is a neuromuscular disease that is caused by circulating antibodies that block acetylcholine receptors at the postsynaptic neuromuscular junction, inhibiting the excitatory effects of acetylcholine on nicotinic receptors. The disease leads to fluctuating muscle weakness and fatigue.

   Yes, patients with myasthenia gravis can experience fluctuating weakness including pharyngeal, laryngeal, and respiratory muscles. Swallowing and effective cough effort is impaired. She should be considered at risk.

   Her actual risk could be evaluated by history. How much weakness is she experiencing now? Has she had issues with passive regurgitation or aspiration while sleeping? The patient's ability to protect and maintain a patent airway postoperatively should be assessed. The general muscle strength or weakness is assessed by physical examination including the presence of ptosis, double vision, dysphagia, and rapid fatigue with repetitive movement such as opening and closing her hand. Pulmonary impairment can be defined by vital capacity less than 40 mL/kg, impaired expiratory effort (maximum static expiratory volume), and flow-volume loops showing decreased flow on expiration in the supine and sitting position.

   Yes, a histamine-2 blocker such as ranitidine and an antacid (Bicitra®) are indicated.

   We would not use metoclopramide as the extrapyramidal effects that could occur with that drug would make interpretation of muscle strength and eye findings somewhat difficult.

2. It is important to know what type of steroid she is on and how much she has been taking. The hypothalamic-pituitary-adrenal axis is often suppressed by exogenous administration of a glucocorticosteroid. The effect depends on the maintenance dose of steroid that the patient is on. The patient will need stress dose coverage when the maintenance daily dose is greater than 10 mg of prednisone (or equivalent). There are arguments against the need for stress dose steroids if patients have been on daily maintenance doses of less than 10 mg of prednisone (or equivalent) or if the child has had very minor surgery where the actual stress to the patient is minimal. If one chooses not to give a stress dose, the patient should be carefully monitored for lethargy or hypotension in the postoperative period – both of which could be signs of glucocorticoid deficiency. I will administer steroid coverage for this particular patient because she is scheduled for a sternotomy. Ideally, the patient should not take her pyridostigmine preoperatively. Omitting the morning dose of pyridostigmine will weaken the patient and obviate the need for intraoperative muscle relaxants in most cases. Added weakness may provoke her anxiety so the issue should be carefully discussed prior to

3. She is very anxious; how would you counsel her about preoperative sedation? She wants a mask induction; is that OK? What endpoints would you look for to determine the onset of anesthesia? What if she goes into laryngospasm during induction – how will you manage it?

Intraoperative Course

Questions

1. What are your monitoring considerations? Does this patient need an arterial line? Why? Should the patient have central access? Why? Are there circumstances in which a pulmonary artery catheter would help?

the day of surgery. Yes, if pulmonary function is impaired despite optimal medical therapy, the morning dose of pyridostigmine would be indicated. Standard pulmonary function tests should be normal when the myasthenia is well controlled with medical therapy. If myasthenia is not well controlled, the forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) are decreased due to weakness. If FVC is normal and the FEV_1 is decreased, it may indicate intrathoracic airway obstruction due to an enlarged thymus and may portend difficulty when the patient undergoes positive pressure ventilation.

3. Depending on how weak the patient is, preoperative intravenous anxiolytics may be administered with caution and close monitoring for respiratory depression. Yes, there is no contraindication to an inhalation induction, provided the patient is appropriately NPO and there is no history of reflux-related aspiration pneumonia in the past. Due to weakness of the extraocular muscles, the loss of response to eyelash stimulation is not as helpful as general stimulation to determine the onset of general anesthesia in this particular patient. Similarly, testing of the muscle twitch may be falsely absent or diminished around the eyes as opposed to ulnar nerve stimulation. If the patient develops laryngospasm, it can be overcome with simply applying positive pressure, particularly in the presence of weak pharyngeal muscles. Alternatively, due to the deficiency of acetylcholine receptors, a small dose of nondepolarizing muscle relaxant (or a large dose of succinylcholine) is administered to relax the glottic muscles.

Intraoperative Course

Answers

1. Standard monitors should be placed including ECG, pulse oximeter, blood pressure cuff, end-tidal carbon dioxide, and body temperature. In this case – where muscle strength is a major issue – a neuromuscular monitor is helpful. I would place an arterial line. An arterial catheter is useful for monitoring intraoperative blood pressure, perioperative arterial blood gases, and intravascular volume status (through respiratory variation in systolic pressure analysis). Central access is not necessary because this particular procedure is not associated with significant blood loss or fluid shift and it is not likely that vasoactive infusions will be needed. A pulmonary artery catheter is indicated if cardiac dysfunction is present and monitoring of filling pressures, cardiac output, and systemic vascular resistance was needed.

2. Assuming an intravenous induction, which agents will you choose? Any advantage for propofol? Etomidate? Explain your choice. Should the patient undergo a mask induction with a volatile agent and breath spontaneously? Explain your choice of inhalation agent.

3. Assume that you have administered a dose of propofol and started sevoflurane; the patient is now in laryngospasm and her saturation is 85 %. There is no $ETCO_2$ on the monitor. What would you do? Would succinylcholine be safe to give? How do myasthenic patients respond to succinylcholine? Should the patient receive a nondepolarizing agent? How much should be given? Which nondepolarizer would you choose?

4. The patient was successfully intubated and is oxygenating well. Your blockade monitor indicates no twitches, yet the patient moves when the median sternotomy begins. The surgeon insists that you have to relax the patient. Which relaxant would you give and how much would you give? How will you judge the efficacy of your muscle relaxant? How do you use a blockade monitor for a myasthenic patient?

5. During the thymus dissection, the patient begins wheezing, and you note a prolonged and slow upstroke to the exhalation CO_2 curve on the capnograph. What are your considerations? How do you diagnose the problem? Albuterol inhalation through the endotracheal tube does not help. With an FiO_2 of 1.0, the O_2 saturation is 92 % and the $ETCO_2$ waveform is small and prolonged. What would you do now? The wheezing is better when the surgeons stop operating. Would endobronchial intubation help? Would a double-lumen tube be indicated? What would you tell the surgeons?

2. I would choose propofol over etomidate. Propofol is a longer-acting agent and results in longer respiratory depression than etomidate, but etomidate (even a single induction dose) can potentially suppress adrenal steroid synthesis and may precipitate adrenal crisis (or unpredictably increase the requirement of a steroid stress dose). Propofol also causes less emesis than etomidate. No, because volatile agents produce muscle relaxant effect and spontaneous ventilation is almost certain to be inadequate under anesthesia. I would choose sevoflurane. Sevoflurane has the least respiratory depressant effect compared to other currently used volatile agents, isoflurane and desflurane.

3. Yes, succinylcholine is safe. Because of the paucity of receptors, patients with myasthenia are relatively resistant to succinylcholine; they may require a larger dose than non-myasthenic patients. If a large dose is given, they are at risk for phase II block with prolonged muscle relaxant effect. Yes, nondepolarizing agents can be used with the expectation that the onset action could be delayed and the duration of relaxation could be very prolonged. It is reasonable to start with one half the ED95, which is a much smaller dose than typically required for non-myasthenic patients.

   Any of the nondepolarizing agents could be used, but I will choose cisatracurium because of its generally predictable duration of action.

4. I will administer cisatracurium, 0.1 mg/kg, in a stepwise fashion, to the desired clinical effect after ensuring an adequate depth of anesthesia. Myasthenic patients have variable involvement of different body muscles, and monitoring multiple sites may be useful to monitor a nondepolarizing agent's effect. Sites might include facial muscles or posterior tibial nerve stimulation. I will obtain a baseline T1/T4 ratio before the administration of a nondepolarizing agent and titrate the dose of the selected agent to maintain a visible T1 response. There are many surgical cases where muscle relaxation is not necessary, and this issue should be discussed with the surgeon prior to surgery.

5. The wheezing could be due to airway obstruction by surgical manipulation. I will ask the surgeon to stop manipulation of the thymus and the airways and remove any retractors. If the obstruction does not resolve, it may indicate bronchospasm due to light general anesthesia. I will prefer placement of a double-lumen tube to unilateral endobronchial intubation to bypass the surgical obstruction and allow ventilation of both lungs because unilateral ventilation can produce unacceptable shunting and ventilation-perfusion inhomogeneity.

Postoperative Care

Questions

1. Should you reverse the neuromuscular blockade? Why? What is a cholinergic crisis? What are the symptoms and signs of cholinergic crisis? How is it treated?

2. Are pulmonary function criteria helpful for deciding about extubation? Which ones? What would you do if PFTs are OK but there is a weak gag reflex while the patient is still intubated? Would you extubate?

3. How should pain relief be managed? With a thoracic epidural or a morphine PCA? Why? What are the advantages and disadvantages of each?

Postoperative Care

Answers

1. I would not reverse the neuromuscular blockade. It is advisable not to administer anticholinesterase drugs to reverse the neuromuscular blockade as this may precipitate a cholinergic crisis. It is fatal if not treated in a timely fashion. A cholinergic crisis is defined as excessive accumulation of acetylcholine at the nicotinic and muscarinic cholinergic receptors in the CNS and in the periphery. The symptoms are salivation, lacrimation, nausea, vomiting, urinary incontinence, diaphoresis, rhinorrhea, bronchorrhea, muscle fasciculation, weakness and paralysis, laryngospasm, bronchospasm, respiratory failure, miosis, agitation, convulsion, and coma. Treatment is to support the respiratory and cardiovascular systems and offer symptomatic treatment. Benzodiazepines will control seizures and atropine will treat the bradycardia.

2. Pulmonary function criteria are helpful; pulmonary function parameters that are useful to guide extubation of the trachea are a vital capacity greater than 10 mL/kg, maximum negative inspiratory pressure greater than −25 cm of water, a respiratory rate below 20 breaths/minute, an inspired oxygen requirement less than 50 %, and PEEP of 5 cm of water or less. Clinically, the patient's bulbar strength (gag and cough reflexes) should be normal. No, I would not extubate until reflexes were present.

3. The pain control is best managed with thoracic epidural analgesia. The use of thoracic epidural analgesia may minimize the PCA morphine-induced depression of central respiratory drive. The advantage of epidural analgesia with local anesthetic alone is to avoid central respiratory depression caused by neuraxial and systemic opioids. The disadvantage of epidural analgesia with local anesthetics is the potential for intercostal muscle weakness that can impair ventilation and may be confused with inadequate treatment of myasthenia or myasthenic crisis.

Additional Questions

Questions

1. A child was playing in a commercial tomato-growing field. She is brought to the ED where she is weak, breathing quickly, delirious, and smells of stool. You are asked to help with intubation and management. What do you think is the diagnosis? Are there specific pharmacologic agents you should use? Is there anything other than atropine? How much atropine should be used?

2. A 13-year-old boy with Duchenne muscular dystrophy (DMD) comes to the operating room emergently for an incarcerated umbilical hernia. What are your considerations for induction? Do these patients have difficult airways? What are your considerations for performing an awake intubation in a DMD patient? Is this stressful? Does it matter? If the patient cannot be intubated and he must have general anesthesia for the procedure, is a mask anesthetic reasonable? Is a laryngeal mask airway with spontaneous breathing a reasonable alternative?

Additional Questions

Answers

1. My preliminary diagnosis is pesticide toxicity as the child was likely present when spraying of the field took place. The pesticides are acetylcholinesterase enzymes that have two components. An acetylcholine molecule, bound at both ends to both sites of the enzyme, is cleaved in two to form acetic acid and choline. In organophosphate poisoning, an organophosphate binds to just one end of the acetylcholinesterase enzyme (the esteric site), blocking its activity and causing an overabundance of acetylcholine. I would offer cardiorespiratory support and symptomatic treatment.

   If organophosphate toxicity is suspected, decontamination is initiated. The patient is stripped and the intact skin cleansed gently with soap and water and ethyl alcohol (for intact skin), eyes are irrigated with saline, and clothing is disposed as hazardous waste. Medical personnel decontaminating the patient should self-protect against accidental exposure to the pesticide dust by wearing protective gear (waterproof gowns, gloves such as neoprene, and eye wear protection). Yes, pralidoxime is a specific antidote to organophosphates. Pralidoxime is able to attach to the other half (the unblocked, anionic site) of the acetylcholinesterase enzyme. It then binds to the organophosphate, changes its conformation, and loses its binding to the acetylcholinesterase enzyme. The conjoined poison/antidote then unbinds from the site and thus regenerates the enzyme, which is now able to function again. It is effective when administered within 48 h of exposure. Diazepam is used to control CNS excitation and seizures. CNS outcomes are improved if seizures and excitation are controlled. If a plan is made to administer pralidoxime, the patient should receive atropine by repeated administration of 50 mcg/kg q 10–30 min to maintain a heart rate above 100 beats/minute.

2. A major concern in adolescents with DMD is difficulty swallowing which may predispose them to aspiration during induction. Some patients may develop an enlarged and stiff tongue as a result of tongue muscle degeneration and replacement with fibro-fatty tissue. Awake tracheal intubation is not a preferable strategy for several reasons: (1) most children at this age are anxious and will not be cooperative; (2) stress-induced tachycardia and hypertension could be detrimental in DMD adolescents since cardiomyopathy is common and tachycardia may lead to decreased cardiac output or ischemia; and (3) gagging and coughing induced by awake intubation is likely to cause respiratory decompensation. No, a mask anesthetic is not indicated because a mask airway may be very difficult to maintain for the duration of surgery. Laryngeal mask airway should be used to secure ventilation, and I would attempt tracheal intubation via the LMA with a fiber-optic scope. Patients with DMD are at risk for acute rhabdomyolysis in response to succinylcholine and (occasionally) with exposure to vapor inhalation anesthetics. It is wise to absolutely avoid any exposure to succinylcholine and

3. A patient is scheduled for a muscle biopsy to confirm suspicion of "central core disease" (CCD). What is this disease? What are the anesthetic concerns? Is a spinal anesthetic likely to aggravate the condition? Why? Is this similar to multiple sclerosis? Are these children developmentally delayed?

4. An infant with a familial history of familial periodic paralysis is scheduled for a hernia repair.

   Why is this family history important? How should this patient be evaluated preoperatively? Would an ECG help? How about serum electrolytes? What if the potassium is normal? Should you include glucose in the IV? What kind of IV fluid would you use? What about muscle relaxants? Does the muscle relaxant effect of volatile agents potentiate the weakness of familial periodic paralysis?

5. You are asked to sedate a patient with spinal muscular atrophy for a spinal tap. What is SMA?

vapor agents. Adequate depth of anesthesia should be maintained throughout the procedure to avoid myocardial decompensation and cardiac arrhythmias. No, laryngeal mask airway with spontaneous breathing is not a reasonable plan because the patient will likely not be able to maintain adequate tidal exchange due to severe restrictive chest wall disorder. This is particularly true with the use of IV anesthetics.

3. CCD is a myopathy, inherited as an autosomal dominant disease. It is a congenital myopathy, often with a mild presentation early in life with variable severity. It arises from defects in the calcium channel that results in release of calcium in to the myoplasm leading to muscle damage and weakness. Many patients with CCD may also carry the defective gene of the malignant hyperthermia syndrome (ryanodine allele on chromosome 19q13.1) on the same locus as the CCD gene. CCD is associated with congenital muscle weakness that causes scoliosis and spontaneous hip dislocation. Spinal anesthesia may aggravate an existing muscle weakness and hip dislocation. Yes, like multiple sclerosis, adult onset CCD may experience transient worsening with intense activity. However, unlike other myopathies, exercise improves muscle strength. In general, these children have normal intelligence.

4. Familial periodic paralysis is an autosomal dominant inheritable disorder. Preoperative evaluation includes a family history of the disorder and symptoms the infant may have that would indicate symptomatic familial periodic paralysis. Usually the onset of the disorder is in the second decade of life. Symptoms include periodic swallowing, breathing, and limb weakness. ECG can be helpful during the acute episodes of the disorder and may change because of hypokalemia, prolonged PR interval >0.32 s, ST-segment depression, T-wave inversion, and a prominent U wave. Serum electrolytes are helpful during the acute episode and may show a low serum potassium. There are cases of normokalemic periodic paralysis. Normal serum potassium does not exclude the disorder because it is a self-limited disorder. Probably, glucose administrated should be limited because glycemic stimulation produces an insulin surge, with intracellular shifting of glucose and potassium, resulting in hypokalemia. I will use a nonglucose-containing solution such as normal saline or lactated Ringer's solution for maintenance fluid therapy. It is advisable to avoid muscle relaxants unless necessary for the optimizing surgical exposure. Yes, volatile agents can potentiate skeletal muscle weakness.

5. The disease is caused by degeneration of the anterior horn cells. The infantile form manifests within the first 3 months of life and is usually a severe form of the disease. Severe muscle weakness is associated with difficulty swallowing, secretion handling, and breathing. These infants are at risk for aspiration and may require postoperative ventilatory support. The Kugelberg-Welander disease is a milder form of the disease and progresses slower than the infantile form. Yes, this syndrome is associated with hypoplasia or agenesis of the cranial nerve

6. You are called to intubate an 18-year-old in the ICU. He has been in the ICU for a week following a flu shot, which resulted in progressive weakness – beginning with walking and now progressive respiratory failure. What is your diagnosis? NG tube feedings were stopped 1 h ago. Should he be intubated awake? Would you perform?

nuclei in the brain stem. The cranial nerves are primarily motor nerves, and hence this syndrome is analogous to SMA syndrome because it involves lower motor neuron degeneration. Both conditions affect motor neurons. Amyotrophic lateral sclerosis specifically affects the motor cortex, spinal motor neurons or both. Unlike SMA, amyotrophic lateral sclerosis affects both the upper and lower motor neurons. It may manifest as spastic weakness as opposed to flaccid weakness in SMA syndrome. These patients have weak and atrophic muscles of respiration and may require ventilatory support postoperatively. They are at risk for aspiration pneumonitis and postoperative pneumonia due to inability to cough effectively from weakened bulbar reflexes. In addition, these patients are intolerant to sedatives, hypnotics, and opioids due to reduced respiratory muscle reserve. Genetic counseling of the family is important to determine whether the disorder is a result of mutation or genetic deletion of survival motor neuron (SMN), which occurs in approximately 90–94 % of SMA patients. Counseling is also necessary for prenatal screening with subsequent pregnancy; the screening test has 98 % reliability. Anesthetic agent choices are made bearing in mind that patients with generalized muscle wasting are unable to protect airways and have limited respiratory system reserve. Therefore, these patients have increased sensitivity to nondepolarizing muscle relaxants and are unable to compensate for hypoventilation and decreased central respiratory drive following administration of CNS depressants such opioids for postoperative pain control.

6. Possible etiologies include post-viral syndromes and metabolic or autoimmune disorders. Following a flu shot, the most likely etiology for this adolescent is Guillain-Barre syndrome. No, the patient should be anesthetized with ketamine or propofol if hemodynamically stable. If hemodynamically unstable, intubation can be achieved with IV midazolam and a low dose of etomidate. Yes, rapid sequence induction can be performed without the use of a muscle relaxant because the bulbar muscles are either paralyzed or weak enough from the disease to allow adequate rapid intubation condition. Succinylcholine should be avoided because in the acute phase of Guillain-Barre disease because there is an active demyelination process that likely predisposes to serious hyperkalemia.

Suggested Readings

1. Abel M. Eisenkraf JB. Anesthetic Implications of Myasthenia Gravis. The Mount Sinai Journal of Medicine 2002;69(1,2):31–37.
2. Dillon FX. Anesthesia issues in the perioperative management of myasthenia gravis. Semin Neurol 2004;24(1):83–94.
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