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What You NEED to Know about Malignant Hyperthermia

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History

The first case of malignant hyperthermia (MH) that can be identified dates back to the 1960s when a patient with a known familial history of anesthesia complications demonstrated tachycardia, increased body temperature and hypotension following induction of anesthesia. After this incident, clinicians described MH as an increased metabolic state that has a range of signs associated with induction of inhaled anesthetics (Seifert, Wahr, Pace, Cochrane, & Bagnola, 2014).

Causes

MH is a serious, life-threatening reaction that occurs after being exposed to certain inhaled and local anesthetics. Some of the inhaled volatile anesthetic agents that can trigger MH include halothane, sevoflurane, desflurane and isoflurane (Genetics Home Reference, 2015). MH is also known to be induced by succinylcholine, a depolarizing muscle relaxant and neuromuscular blocker that is used to protect the airway of those undergoing surgical procedures and can sometimes preserve the respiratory function during disease states. The prevalence of persons that have experienced MH is said to be one in 5,000 to 50,000 individuals, but could be higher since not all is exposed to anesthesia (Rosenberg, Sambuughin, Riazi, & Dirksen, 2003). Ama, T., Bounmythavong, S., Blaze, J., Weismann, M., Marienau, M., & Nicholson, W (2010) state that the prevelance in children can be as high as one in 15,000. Emotional stress, trauma, or extreme heat stressors such as vigorous exercising and high temperatures can also trigger MH (Seifert, Wahr, Pace, Cochrane, & Bagnola, 2014).

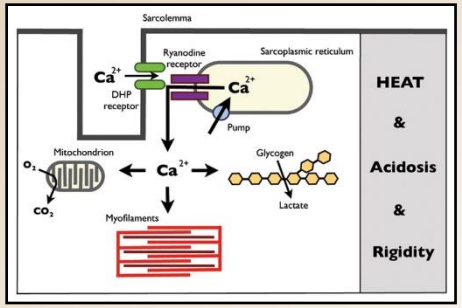
Signs and Symptoms

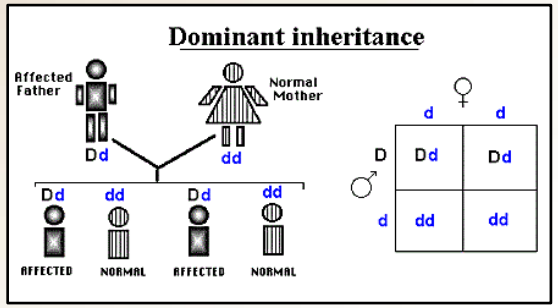
During a MH reaction, a person develops life-threatening skeletal muscle break down (increased metabolism) by elevated intracellular calcium that is rapidly released by the sarcoplasmic reticulum (SR) (Ama, Bounmythavong, Blaze, Weismann, Marienau, & Nicholson, 2010). Rosenberg, Sambuughin, Riazi, and Dirksen (2013) state that "signs and symptoms could include acidosis, hypercapnia, tachycardia, hyperthermia, muscle rigidity, compartment syndrome, rhabdomyolysis with increase in serum creatine kinase concentration, hyperkalemia with risk of heart arrhythmias or even arrest, and myoglobinuria with a risk for renal failure." Early signs of MH are tachycardia and hypercapnia and are usually noticed first in the operating room. The hallmark sign of malignant hyperthermia is increased body temperature, which can exceed 43.3 degrees Celsius, or 109.9 degrees Fahrenheit. This reaction is delayed in part due to hypothermia induced by the surgical room environment and anesthetics. Cardiac arrest, kidney and liver failure, abnormal blood coagulation, internal hemorrhage, neurologic injury, cardiovascular collapse occur in those untreated MH reactions (Seifert, Wahr, Pace, Cochrane, & Bagnola, 2014). The classic triad of late MH can lead to end-organ damage. The triad includes muscle rigidity, usually noticed in the masseter muscles, hyperthermia and metabolic acidosis (Musselman & Saely, 2013).

Greater Anesthesia Solutions. (2015). *Modernizing.jpg*. [photograph]. Retrieved from http://www.greateranesthesiasolutions.com/wp-content/uploads/2015/03/modernizing.jpg. Reprinted with permission.

Pathophysiology

Malignant hyperthermia reactions are associated with over eighty genetic defects (Mitchell-Brown, 2012) with the gene RYR1 on chromosome 19 being the most prevalent. The RYR1 is a ryanodine receptor that mediates calcium release from the sarcoplasmic reticulum, which is essential for muscle contraction. Normal cell energy production and muscle contraction is mediated by calcium, which is an essential ion (Twine, 2014). In MH, the release of calcium supersedes the reuptake of calcium resulting in the inability of muscle contraction termination (Ama, Bounmythavong, Blaze, Weismann, Marienau & Nicholson, 2010). "The excessive calcium leads to sustained muscle contraction and rigidity, increasing metabolism and generating heat. Eventually the overworked cells are depleted of oxygen and adenosine triphosphate (ATP), their energy source" (Mitchell-Brown, 2012). MH is an autosomal dominant inherited disorder, meaning a child or sibling of a susceptible patient has a 50% chance of inheriting a defective gene (Mitchell-Brown, 2012).





Top left: *Figure 1.* Representing excitation-contraction mechanism of muscles. The action potential is initiated along the sacrolemmal membrane into the transverse tubule, where the dihdropyridine receptors (DHP receptor) senses the action potential voltage change and opens up. This activates the ryanodine receptors, which release calcium from the sarcoplasmic reticulum (SR). In malignant hyperthermia, an uncontrolled release of calcium from the SR overwhelms the compensatory mechanisms within the skeletal muscle cell. This leads to increased muscle contraction and metabolic stimulation follows. Reprinted from Malignant Hyperthermia. O. Brandschapp & T. Girard, 2012, *Swiss Medical Weekly, Volume* (142): w13652. Copyright 2012 by Swiss Medical Weekly. Reprinted with permission. doi:10.4414/smw.2012.13652

Top Right: *Figure 2.* Representing dominant inheritance with malignant hyperthermia. Adapted from *Recessive and Dominant Inheritance*, n.d., Retrieved July 27, 2015, from http://www.accessexcellence.org/RC/VL/GG/recessive.php. Copyright 1999-2009 Access Excellence @ the National Health Museum. Adapted with permission.

Treatment

Once MH is suspected, it is extremely important to take prompt action to "discontinue the inhaled agent, hyperventilating the patient with 100% oxygen, administering intravenous dantrolene, cool the patient and treat the symptoms" (Ama, Bounmythavong, Blaze, Weismann, Marienau, & Nicholson, 2010) . Without prompt treatment of dantrolene sodium, mortality is extremely high in persons with MH (Malignant Hyperthermia Association of the United States, 2015). It is estimated that dantrolene can reduce the mortality rate of MH reactions from 40% to 1.4% (Denholm & Spruce, 2015). Researchers estimate that 44 MH events occur every year in acute surgery centers and 33 lives were saved when using dantrolene sodium rather than only supportive measures (Aderibigbe, Lang, Rosenberg, Chen & Li, 2014). Dantrolene decreases the release of calcium from the SR, which restores balance between the release and reuptake of calcium (Ama, Bounmythavong, Blaze, Weismann, Marienau, & Nicholson, 2010).

Although the only chemical treatment for MH is dantrolene, it is important to be familiar with the potential side effects of this drug. Side effects include muscle weakness, dizziness, dysarthia, drowsiness, and pulmonary edema. Calcium channel blockers should be avoided with administration of dantrolene; this combination can lead to hyperkalemia and myocardial depression (Twine, 2014).

Testing

The most common diagnostic test for MH susceptibility is the caffeine halothane contracture test (CHCT). This test requires a muscle biopsy and measure the contracture in response to halothane and caffeine. Most people at risk and at increased susceptibility for MH will be identified with this test due to its high sensitivity. Unfortunately, this test provides risk associated to biopsy sampling, invasiveness, expense and limited biopsy centers. Genetic testing is also available in the United States for persons with a positive caffeine halothane contracture result. Mitchell-Brown (2012) states that "the CHCT is performed only in specialized centers, thirty centers worldwide and only six in North America. Because the CHCT test must be performed on a fresh muscle specimen, the patient must travel to one of these centers for testing." This genetic test screens for the 17 most common RYR1 mutations, but also has its limitations. Only 25% of the persons at risk for MH are detected because of the multitude of mutations associated with MH (Ama, Bounmythavong, Blaze, Weismann, Marienau, & Nicholson, 2010).

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Nursing Implications

The amount of procedures in the US alone top over 50 million, with many of them being done with local anesthesia (CDC, 2015). With such a high number of cases in the continental United States, it is important to be aware of possible life-threatening side effects of anesthesia, such as MH. Professional health care workers, such as anesthesiologists, nurse anesthetists, critical care physicians, perioperative personal and registered nurses are the first line responders to recognizing the signs and symptoms of MH as well as prompt and proper treatment.

It is extremely important to obtain a thorough anesthetic history before providing anesthesia for possible suspicions of MH reactions. Once the person is identified as being at an increased risk, avoidance of the triggering agents is key. It is not recommended or necessary to pretreat these patients with dantrolene, but having it available is crucial (Ama, Bounmythavong, Blaze, Weismann, Marienau, & Nicholson, 2010).

Mortality has decreased 80% from the 1980s to less than 5% today (Ama, Bounmythavong, Blaze, Weismann, Marienau, & Nicholson, 2010). Research has proven that stocking dantrolene and providing adequate education of MH and how to recognize and treat this condition has prevented mortality. Nurses who care for patients during or after surgery must be knowledgeable of MH and since susceptibility to this reaction is inherited, nurses must educate patients and their families about the risk involved (Mitchell-Brown, 2012).

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