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Malignant Hyperthermia

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Introduction

Malignant hyperthermia, according to the Orphanet Journal of Rare Diseases, is "pharmacogenetic disorder of skeletal muscle that presents as a hypermetabolic response to potent volatile anesthetic gases" (Rosenberg, Pollock, Shiemann, Bulger, and Stowell, 2015, p. 1). Its incidence in anesthetics is 1 in 10,000 to 1 in 250,000, and the prevalence is increased in an individual with certain genetic abnormalities that may be as common as one in every 400 people. It is caused by the uncontrolled rise in myoplasmic calcium, leading to a cascade of muscle activation. The symptoms of malignant hyperthermia include hyperthermia, tachypnea, tachycardia, increased oxygen consumption and carbon dioxide production, acidosis, hyperkalemia, muscle rigidity, and rhabdomyolysis. It is a condition that is likely to be fatal if untreated (Rosenberg et al., 2015). The specific treatment for this condition is the antagonist dantrolene sodium, which must be readily available whenever general anesthesia is utilized (Eagle Pharmaceuticals, 2016).

As the chief purpose of the certified registered nurse anesthetist is to administer safe and effective anesthesia to patients of many backgrounds and circumstances, intimate knowledge and preparation for malignant hyperthermia is of paramount import to me and my chosen career. I chose this topic because it is one that I had only passing knowledge of. Detailed investigation into the etiology and pathophysiology of the condition, the early warning signs and different manifestations, and identification of effective steps for treatment and crisis management are all important areas of discovery for the CRNA. It is for this reason that malignant hyperthermia is a warranted and prudent topic of study.

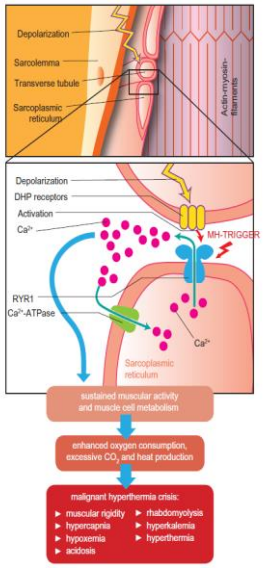
Signs and Symptoms

Early
Masseter Spasm
Generalized Muscular Rigidity
Tachycardia
Hypercapnia
Hypoxia
Combined Metabolic-Respiratory Acidosis

Late
Hyperthermia
Rhabdomyolysis
Acute Renal Failure
Cardiac Arrhythmia
Hypotension
Circulatory Failure

(Schneiderbanger, Johannsen, Roewer, & Schuster, 2014)

Though hyperthermia is in the name of the condition, it is itself often a late sign and is reflective of the metabolic breakdown in the patient. Thus, it is necessary to watch for all early signs, though occasionally the increase in temperature is the only outward sign. (Schuster, Johannsen, Schneiderbanger, & Roewer, 2013).



(Schneiderbanger, et al., 2014)

Underlying Pathophysiology

Malignant hyperthermia is a pharmacogenetic disorder which results in a hypermetabolic state. The signs and symptoms of MH are related to an uncontrolled release of intracellular calcium from skeletal muscle sarcoplasmic reticulum. It occurs as a result of a reaction to inhaled anesthetics or the skeletal muscle relaxant succinylcholine in susceptible people. It is an autosomal dominant inherited disorder, and thus a child of a susceptible patient has a 50% chance of inheriting a defective gene (Mitchell-Brown, 2012). A susceptible individual will possess a defective or disordered calcium channel in their sarcoplasmic reticulum termed the ryanodine receptor (RyR1). As many as 70% of families susceptible to MH possess one of the 34 causal mutations for the disorder (Rosenberg, Pollock, Schiemann, Bulger, & Stowell, 2015). The increase in intracellular calcium results in the muscles metabolizing, contracting, and causing a subsequent increase in oxygen consumption and carbon dioxide production, as well as ATP hydrolysis and heat production.

During the excitation-contraction coupling, acetylcholine causes an action potential at the neuromuscular endplate. This action potential is then propagated to the transverse tubule, causing a displacement of the charge at the dihydropyridine receptor. This voltage-gated receptor directly transmits to the RyR1, opening the channel and leading to the large influx of calcium into the cytosol. This calcium presence causes the muscle contraction by initiation of cross-linking myofilaments. Normally, active reuptake of the calcium would stop the muscle contraction, however in an MH crisis, the defective receptor stays open. This constant activation of aerobic and anaerobic metabolism leads to the increase in oxygen consumption, hypoxia, lactate acidosis, excessive CO_2 production, and increase in bodily temperature. Eventually, as the cellular ATP is depleted, the membrane integrity of the muscle cells will break down and rhabdomyolysis will occur from the potassium, creatine phosphokinase, and myoglobin that are released from the cells (Schneiderbanger, et al., 2014).

Significance of Pathophysiology

Malignant hyperthermia is rare and life threatening. Early recognition, diagnosis, and treatment with dantrolene sodium have reduced the mortality rate from MH from 80% in the 1970s to less than 5% by 2006 (Rosenberg, et al., 2015). Many clinicians may be unprepared for a crisis, failing to acknowledge the early signs and symptoms of the condition until it has progressed to a dangerous level. The prognosis for a patient suffering from a MH crisis is based on how soon MH is suspected and how quickly the appropriate treatments are performed.

- Stop the trigger agent immediately
- Continue anesthesia using intravenous opioids, sedatives, or nondepolarizing muscle relaxants if necessary
- Initiate Malignant Hyperthermia Response Team
- Give Dantrolene 2.5mg/kg and repeat as needed every 5 minutes until cardiac and respiratory stabilization
- Removal of the vaporizer used for volatile anesthesia administration
- Hyperventilation of the patient with 100% oxygen at maximum fresh gas flow
- Increasing minute volume by approximately 2-3 times, aiming for end-tidal pCO2 within normal limits
- Cool patient if core temperature greater than 39˚C using cold infusions or ice packs in the axilla or groin

(Schneiderbanger, et al., 2014), (Eagle Pharmaceuticals, 2016).

Following these steps, it may be necessary to utilize volume resuscitation, vasopressor administration for hemodynamic instability, blood gas analysis and lab draws, treatment of acidosis, or administration of beta blockers or amiodarone for arrhythmia.

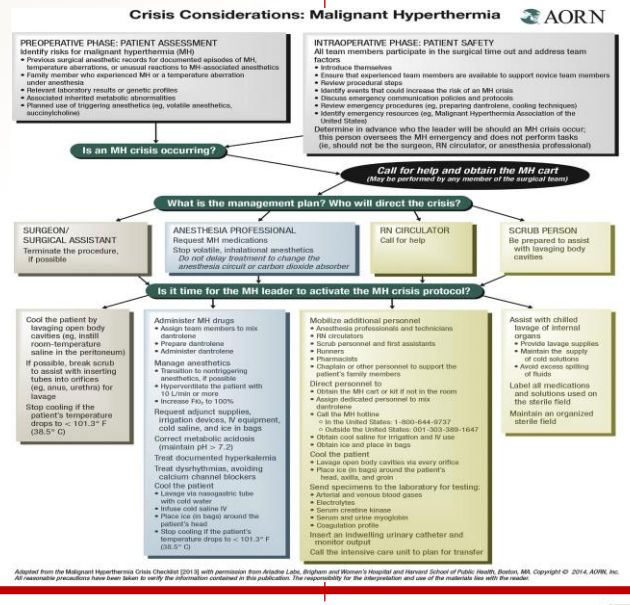
Identification for at-risk patients is of key import, as one can suspect a reaction from the start. The definitive standard for diagnosis is an in vitro contracture test (IVCT), which is based on contracture of muscle fibers in the presence of halothane or caffeine. This method has more than 97% specificity, though it is expensive, only available at certain testing centers, requires a surgical procedure to obtain the tissue sample, and has the possibility of yielding a false positive or negative result. Alternatively, susceptibility can also be tested by DNA analysis. 50-70% of susceptibility is linked to the defective RyR1 with over 400 variants noted to have MH association (Rosenberg, et al., 2015).

Known Drug Triggers:

Inhalation Anesthetic Agents:
- Desflurane
- Enflurane
- Halothane
- Isoflurane
- Methoxyflurane
- Sevoflurane
- Ether

Depolarizing Muscle Relaxant:
- Succinylcholine

(Schuster, et al., 2014)



Implications for Nursing Care

Given the gravity of the condition and its potential for devastating consequences, a prudent nurse or CRNA will do well to be mindful of the drugs that can cause the crisis, the early warning signs of a reaction, and the correct steps for treatment to ensure rapid, effective intervention. Knowing a patient's preoperative condition, be it through familial history or through genetic testing, can allow a practitioner to be ready for all eventualities during a case. To improve skills, identification, and proper reactions, literature suggests the validity of simulation and team-based practice drills. These exercises, ideally performed at least once per year, will keep staff updated, alert, and improve collaboration. This education is potentially life-saving. Knowing protocols, guidelines, and how to prepare and administer dantrolene sodium are of chief importance. Nurses are also responsible for the education of their patients. When a patient who has had MH is to be discharged, it is imperative to teach these individuals so that their children and siblings realize their susceptibility, as well. This knowledge could potentially save a life in the future (Theofanis, 2015). The American Association of Nurse Anesthetists, in their crisis, preparedness, and treatment publication (2015), suggest all anesthesia professionals delivering MH trigger agents have all requisite drugs, supplies, and emergency equipment readily available. This includes stocking dantrolene sodium at all ambulatory surgical centers and offices. Effective drills for the management of MH include the following:

- Visual aids to illustrate dantrolene preparation and administration
- Cognitive aids and written Instructions for management/treatment steps
- "Reader" who is responsible to read the cognitive aids aloud, which is shown to help with all actions being performed properly
- Checklists, shown to result in six-fold reduction in failure to perform all critical steps
- Rotation of personnel responsibilities for MH cart helps to familiarize all team members with cart contents and identify out of date or out of stock items
- Use of emergency whiteboard for designating team assignments illustrates clear roles
- MH Hotline Contact Information: 1-800-644-9737 (1-800-MH-HYPER)

(Cain, Reiss, Gettrust, & Novalija, 2014).

Conclusion

Malignant hyperthermia is a rare, life-threatening, autosomal-dominant inherited disorder that may lead to a metabolic crisis of skeletal muscle in susceptible individuals following exposure to triggering agents, such as volatile anesthetics or depolarizing muscle relaxants. Functionally altered calcium release channels cause influx of intracellular calcium from the sarcoplasmic reticulum, which may lead rapidly to a fatal hypermetabolic state known as MH crisis. Because of the variable clinical presentation of MH, ranging from only mild or moderate symptoms to complete MH crises, patient survival depends on early recognition of symptoms and prompt action with appropriate treatments. In clinics that use known MH-triggering agents for induction and maintenance of general anesthesia, dantrolene must be available for immediate treatment, and those practitioners present must be trained in its use so that in the time of need the reaction is swift and effective (Schneiderbanger, et al., 2014).

References

American Association of Nurse Anesthetists. (2015). Malignant hyperthermia crisis preparedness and treatment. Retrieved June 26 from http://www.aana.com/resources2/professionalpractice/Pages/Malignant-Hyperthermia-Crisis-Preparedness-and-Treatment.aspx

Cain, C., Riess, M., Gettrust, L., & Novalija, J. (2014). Malignant hyperthermia crisis: Optimizing patient outcomes through simulation and interdisciplinary collaboration. *Association of Perioperative Registered Nurses Journal, 99*(2), 300-311. https://doi.org/10.1016/j.aorn.2013.06.012

Dirksen, S., Wicklin, S., Mashman, D., Neiderer, P., & Merritt, D. (2013). Developing effective drills in preparation for a malignant hyperthermia crisis. *Association of Perioperative Registered Nurses Journal, 97*(3), 329-353. https://doi.org/10.1016/j.aorn.2012.12.009

Eagle Pharmaceuticals. (2016). Innovative Option for the Treatment of Malignant Hyperthermia [Brochure]. Retrieved May 31, 2017, from www.ryanodex.com/wp-content/uploads/2014/09/ryanodex-mh-white-paper.pdf

Mitchell-Brown, F. (2012). Malignant hyperthermia: Turn down the heat. Nursing, 42(5). https://doi.org/10.1097/01.nurse.0000414679.93741.6c

Rosenberg, H., Pollock, N., Schiemann, A., Bulger, T., & Stowell, K. (2015). Malignant hyperthermia: A review. *Orphanet Journal of Rare Diseases, 10*(1). https://doi.org/10.1186/s13023-015-0310-1

Schneiderbanger, D., Johannsen, S., Roewer, N., & Schuster, F. (2014). Management of malignant hyperthermia: Diagnosis and treatment. Therapeutics and Clinical Risk Management, 10. https://doi.org/10.2147/TCRM.S47632

Schuster, F., Johannsen, S., Schneiderbanger, D., & Roewer, N. (2013). Evaluation of suspected malignant hyperthermia events during anesthesia. *BMC Anesthesiology, 13*(1). https://doi.org/10.1186/1471-2253-13-24

Seifert, P., Wahr, J., Pace, M., Cochrane, A., & Bagnola, A. (2014). Crisis management of malignant hyperthermia in the OR. *AORN Journal, 100*(2). https://doi.org/10.1016/j.aorn.2014.06.014

Theofanis, F. (2015). Malignant hyperthermia: Nursing implications for care. *British Journal of Anaesthetic & Recovery Nursing, 15*(4). Retrieved June 16, 2017, from http://eprints.brighton.ac.uk/id/eprint/14549

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