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Malignant Hyperthermia

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Introduction

Providing patient care in the operating room as a nurse anesthetist is rewarding and challenging. There is a paramount level of responsibility that lies on certified registered nurse anesthetist (CRNA). Recognition of serious life threatening conditions by CRNA must be prompt and treated urgently. As a student registered nurse anesthetist and future CRNA, knowing how to recognize and treat developed emergency conditions while patient is under anesthesia or recovering from anesthesia is an absolute requirement. Malignant hyperthermia (MH), is a rare autosomal dominant hypermetabolic "potentially fatal disorder of skeletal muscles" (Riazi, & Brandom, 2015). Malignant hyperthermia is caused by volatile anesthetics (desflurane, sevoflurane, isoflurane) or depolarizing muscle relaxant (succinylcholine).

Incidence of MH varies between 1/50,000 to 1/250,000 and highest in young population with average age of 18.3 years upon exposure to volatile anesthetics or succinylcholine and is associated with 23 genetic mutations (Nagelhout & Plaus, 2014).

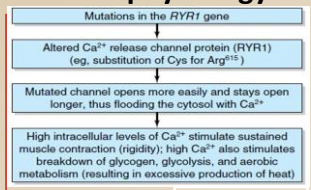
In contrast, according to Malignant Hyperthermia Association of United States (MHAUS, 2015) MH arises 1/100,000 in adults and 1/30,000 in children during exposure to triggering agent. Mitchell-Brown (2012) reports that there are more than 80 genetic defects associated with MH. The two gene mutations directly associated with MH susceptibility are RYR1 and CACNA1S (Rosenberg, Pollock, Schiemann, Bulger, & Stowell, 2015). However, another study states that only 1% of MH cases due to CACNA1S gene on chromosome 1q32, and MH susceptibility due to mutation of the RYR1 gene found on chromosome 19q13.1 (Salazar, Yang, Shen, Abdullah, & Kim, 2014). Wisconsin, Nebraska, West Virginia, and Michigan are states with most MH occurrences. MH has higher prevalence among men versus women, even though it is autosomal dominant disorder.

Upon exposure, MH susceptible individuals could progress to potentially fatal hypermetabolic crisis which occurs shortly after induction of anesthesia (Cain, Riess, Gettrust, & Novalija, 2014). MH is known to happen in post anesthesia care unit (PACU) or any location where patient is recovering from general anesthesia during which volatile anesthetics or succinylcholine were used (Cain et al., 2014). MH could also be triggered by stressors alone such as excessive exercise and heat (Rosenberg et al., 2015). In order to provide lifesaving intervention for patient who is experiencing MH, it is imperative to understand pathophysiology, signs and symptoms, management and treatment, and the importance of thorough preoperative patient assessment for prevention of MH occurrence (Nagelhout & Plaus, 2014). Untreated MH could lead to multiple organ failure and death (Seifert, Wahr, Pace, Cochrane, & Bagnola, 2014).

Signs and Symptoms

-Variable onset of one to 36 hours of administration of volatile anesthetic or succinylcholine (Mitchell-Brown, 2012).
-Early clinical signs:
Hypercapnia, with rise in EtCO2 with normal patient ventilation (indicating underlying hypermetabolism) and increased end-tidal carbon dioxide (ETCO2) refractory to increased ventilation or additional administration of anesthetic
Masseter muscle spasm
Tachycardia without explanation (Seifert et al., 2014).
-Cardinal symptoms: rigidity, muscle breakdown (rhabdomyolysis; causing increase CK and myoglobin), respiratory acidosis, temperature increase, cardiac involvement, and "other indicators of metabolic derangement not part of a single process" (Heytens, Forget, Scholtès, & Veyckemans, 2015).
Labile blood pressures, skim mottling, cyanosis.
-Late clinical signs: Hyperthermia body core temperature may rise at a rate of 1ºC to 2ºC every 5 minutes with average of 39.3ºC or 102.7ºF, with temperature rising above 43.3 ºC (110ºF).
Acidosis, hyperkalemia and hyperthermia causes cardiac irritability, arrhythmias and could lead to cardiac arrest. Death from MH is typically due to cardiovascular collapse (Mitchell-Brown, 2012).
Laboratory results typically show byproducts of muscle breakdown such as myoglobinuria (dark colored urine), hyperkalemia, and elevated creatinine kinase level. Arterial blood gas shows mixed metabolic and respiratory acidosis.

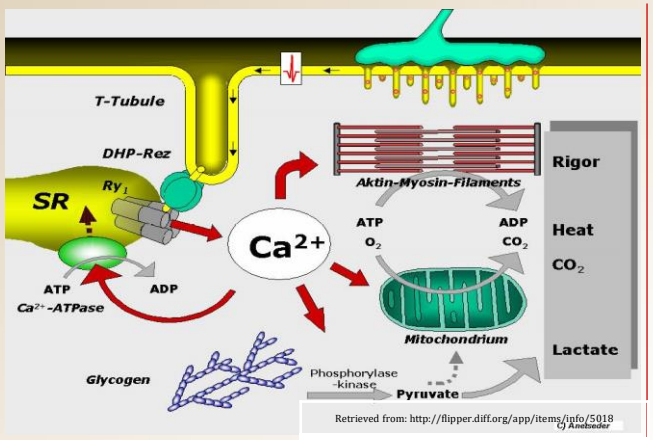
Pathophysiology



Shresta, 2013

The RYR1-ryanodine receptor controls calcium release from sarcoplasmic reticulum (skeletal muscle) and is one of the main defects for MH susceptible individuals, however 40-50% of MH susceptible individuals have no associated defect in RYR1 receptor (Riazi, & Brandom, 2015). MH susceptibility linked to calcium release defect in skeletal muscle; no established linkage to calcium release flaw in cardiac or smooth muscle cells (Mitchell-Brown, 2012).

In MH susceptible patients, volatile anesthetics and/or depolarizing muscle relaxant causes a defect in calcium regulation, leading to increased myoplasmic calcium levels. Excess calcium release causes uncoupling of oxidative phosphorylation and increased metabolic rate (Marino & Sutin, 2014). Excess myoplasmic calcium levels cause sustained actin-myosin interaction (muscle contraction) which causes muscle rigidity, increased body temperature, increased production of carbon dioxide, and increased oxygen consumption (Riazi, & Brandom, 2015). ATP dependent calcium reuptake mechanism attempts to stabilize calcium levels in myoplasm, thus increasing muscle metabolism. Accelerated cellular metabolism requires increased oxygen uptake and causes increased carbon dioxide level, heat production while using all available ATP, causing elevated lactic acid. Acidosis, hypethermia and ATP depletion leads to sarcolemma damage. Elevated levels of potassium (due to cell death and released potassium from the cell into blood stream), myoglobin (rhabdomyolysis, due to death of muscle cells), and creatinine kinase secreted into extracellular fluid (Nagelhout & Plaus, 2014). Elevated potassium levels, above 6 meq/L may lead to fatal dysrhythmias; myglobin released into bloodstream causes precipitate formation in renal tubules, leading to acute kidney injury (Mitchell-Brown, 2012). If no intervention implemented to stop excess calcium release, MH progression leads to left ventricular dysfunction due to hypertension, pulmonary edema and disseminated intravascular coagulation (DIC) (Mitchell-Brown, 2012).



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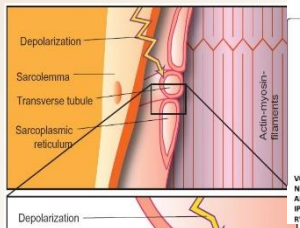

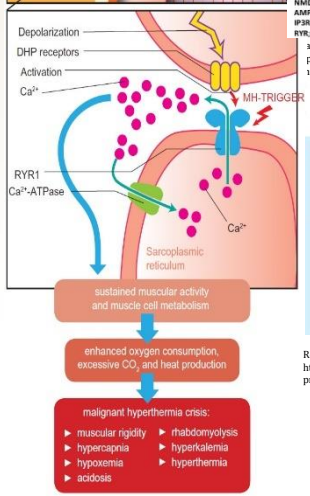

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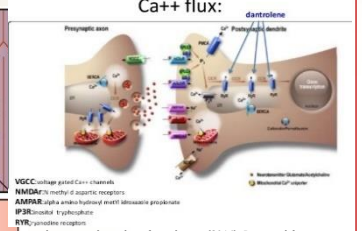
Ca++ flux:



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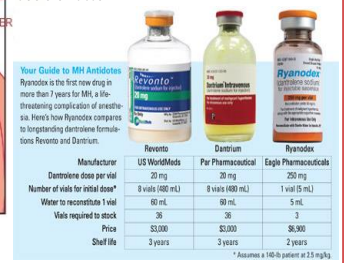

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Significance of Pathophysiology

MH is rare but potentially fatal skeletal muscle disorder which requires prompt intervention to decrease mortality rate. In the initial years of MH discovery, mortality rate due to MH disorder was 80%. In recent years, this number has changed to approximately 5%, and is contributed to increased education and awareness among healthcare providers, early recognition and prompt administration of dantrolene sodium to stop MH crisis (Mitchell-Brown, 2012). Dantrolene inhibits calcium release by inhibiting RYR receptor at postsynaptic dendrite (Bandschapp & Gerard, 2012). Multiple shared signs and symptoms with other disorders, variable penetrance and absence of phenotypical characteristics in the absence of triggering agent and variable onset after administration of triggering agent makes it difficult to timely identify MH crisis and implement timely intervention. Understanding pathophysiology of MH could lead to early recognition and intervention and better outcomes for patients experiencing MH crisis.

Implications for Nursing Care

-At first suspicion of MH, discontinue inhalation agent, call MH hotline

Please Call MH Hotline at:
1-800-644-9737
Be prepared to give your name, number, facility and email, in the event the call is dropped
(outside of the US: 209-417-3722) and
view our Managing an MH Crisis Page. (MHAUS, 2015)

-Hyperventilate with 100% oxygen at high flows (10L/min) to improve tissue oxygenation, eliminate CO2.
-Administer dantrolene 2.5mg/kg IV bolus and repeat as necessary every 5-10 minutes until symptoms subside. If total dose greater than 20 mg/kg of dantrolene administered without improvement, reconsider diagnosis. 20 -mg vial of dantrolene must be reconstituted with 60 ml of sterile water for injection. Additional medical personnel must be utilized to reconstitute dantrolene with sterile water, since it is time consuming.
-Initiate cooling by lavage, chilled IV normal saline, surface cooling. Patient's temperature should be kept under 38.5ºC (Bandschapp & Girard, 2012)
-Do not administer calcium channel blockers with dantrolene.
-Obtain ABG, electrolytes, glucose every 15 minutes. Correct metabolic acidosis with sodium bicarbonate 1-2 meq/kg, based on pH and base deficit. -Obtaine coagulation profile, CK, blood and urine myoglobin, liver enzyme levels.
-Treat hyperkalemia with hyperventilation, bicarbonate and intravenous insulin and glucose.
-Maintain urine output greater than 2ml/kg/hr with hydration, lasix (0.5-1 mg/kg) and mannitol as needed. Invasive hemodynamic monitoring should be established (Nagelhout & Plaus, 2014).

Conclusion

Malignant hyperthermia is a rare, autosomal dominant disorder and medical emergency that requires immediate recognition and treatment in order to increase patient's chances of survival. It has variable penetrance and is typically triggered by volatile anesthetics and/or depolarizing muscle relaxant (succinylcholine). CRNAs must perform a very thorough pre-operative assessment to detect any indications of patient's MH susceptibility. Operating room personnel must be familiar with signs and symptoms of MH, especially early signs of MH in order to implement timely MH protocol treatment. CRNAs, operating room nurses and ICU nurses must be educated on MH treatment and management for best possible patient outcome.

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