Summer 7-26-2022

Malignant Hyperthermia

Christina Bensley
bensley1@otterbein.edu

Malignant Hyperthermia

Christina Bensley BSN, RN, CCRN
Otterbein University, Westerville, Ohio

Topic

- Malignant Hyperthermia (MH) is a rare genetic mutation of the skeletal muscle that induces a hypermetabolic response when patients are exposed to volatile inhaled anesthetics or depolarizing neuromuscular blockers (Weant & Gregory, 2021).

Signs & Symptoms

Symptoms of MH are:

- Increased carbon dioxide production
- Hyperthermia
- Muscle rigidity
- Tachypnea
- Acidosis
- Hyperkalemia
- Rhabdomyolysis

(Weant & Gregory, 2021).

Significance

- Incidence of MH ranges from 1:5,000 to 1:10,000 with a mortality rate of 70%-80% without treatment (Min et al., 2021).
- Early recognition and treatment with dantrolene and cooling reduces the mortality rate to 5% (Gallegos & Hennen, 2022).
- There is no specific age or ethnicity MH tends to develop affect (Amare & Wilson, 2020).
- Most reactions were in children and young adults (Amare & Wilson, 2020).
- Higher prevalence is seen in males (Amare & Wilson, 2020).

Why MH?

- MH is a pharmacogenetic disorder that is an uncommon but frequently fatal reaction to inhaled anesthetics (Zhao et al., 2019).
- It causes a rapid rise in body temperature that is fatal if left untreated (Zhao et al., 2019).
- MH leads to death in 3 out of 4 cases (Zhao et al., 2019).
- For every 20 minutes that dantrolene administration is delayed in an MH crisis, mortality increases by >1% (Gallegos & Hennen, 2022).

Triggering Agents

Volatile anesthetic gases:
- Desflurane
- Sevoflurane
- Isoflurane
- Halothane
- Methoxyflurane.

Depolarizing muscle relaxant:
- Succinylcholine

(Min et al., 2021)

Initial Nursing Care

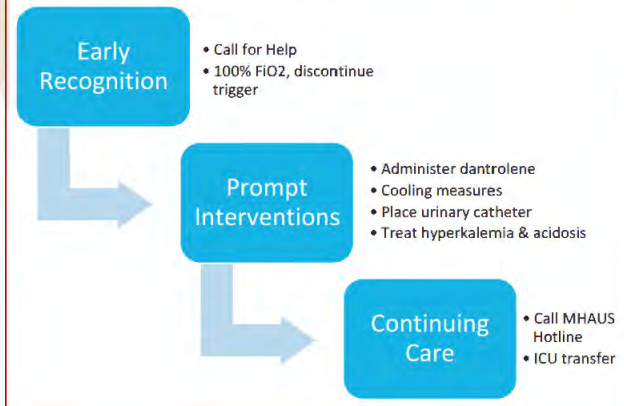
- Nursing education regarding MH is critical. Delay in treatment of MH is associated with increased mortality and more severe complications (Hopkins et al., 2021)
- Priority of treatment is to reverse the reaction and treat the consequences of the reaction (Hopkins et al., 2021).

3 ways to reverse the MH process

1. Eliminate the triggering agent
2. Administer intravenous Dantrolene
3. Start body cooling

(Hopkins et al., 2021)

- The perioperative team must be aware of the tasks that are required to manage MH (Kleidon, 2020).
- Dantrolene acts as an antagonist, binding to a specific region in the ryanodine receptor 1 (RYR-1) channel. It reduces the uncontrolled release of intracellular calcium (Ravaei et al., 2020).
- Treatment should be aimed at prompt administration of dantrolene, cooling to a target core temperature of no more than 38.5C, hyperventilation, and supportive measures (Ravaei et al., 2020).



The picture above can be used as a quick reference guide for the recognition and treatment of MH (Gallegos & Hennen, 2022).

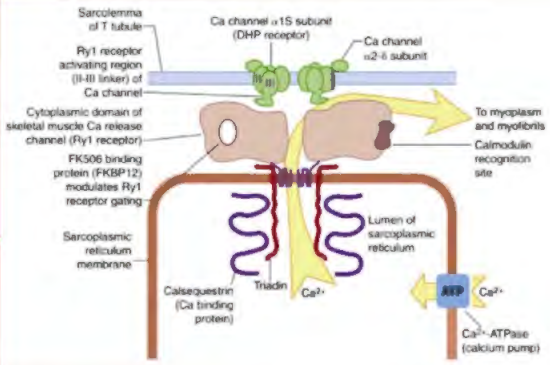
Malignant Hyperthermia Pathophysiology

- A pharmacogenetic disorder of skeletal muscle triggered in susceptible individuals by volatile anesthetics and/or succinylcholine (Riazi et al., 2018).

Inhalation agents and the depolarizing muscle relaxants trigger:

- Calcium stores to be released from the sarcoplasmic reticulum
- Uncontrolled entry of calcium from the myoplasm
- Activation of biochemical routes related to muscle activation causing the contracture of skeletal muscles
- Glycogenolysis
- Increased cellular metabolism

--all of which result in the production of heat, increased lactate level, and acidosis (Ravaei et al., 2020).



The picture above represents the triadic junction of the skeletal muscle and the ryanodine [Ry1] receptor with its associated proteins (Mullins, 2017).

Complications

Complications of MH include:
- Cardiac arrhythmia or arrest (from acidosis and hyperkalemia)
- Renal failure
- Compartment syndrome
- Disseminated intravascular coagulation (DIC)
- Pulmonary edema
- Central nervous system injury

(Riazi et al., 2018).

Post-Reaction Management

- Observe the patient in an intensive care unit for at least 24 hours (Riazi et al., 2018).
- Reoccurrence of reaction may occur in 25% of patients requiring further intervention (Riazi et al., 2018).
- MHAUS suggests administering bolus doses of dantrolene sodium 1 mg/kg IV every six hours for at least 24 hours or longer as clinically indicated (Riazi et al., 2018).
- Dantrolene can be discontinued or the interval between doses increased to every eight or twelve hours if the core temperature is less than 38C, CK is declining,, muscle is not rigid, there is no evidence of myoglobinuria, and there is metabolic stability for 24 hours (Riazi et al., 2018).
- Monitor arterial blood gases, serum CK, potassium and calcium, urine and serum myoglobin, and clotting factors every six hours until they return to normal (Riazi et al., 2018).
- Core temperature should be continuously monitored until stable (Riazi et al., 2018).
- Counsel the patient and family regarding MH and the possibility of MH susceptibility in other family members (Riazi et al., 2018).
- Refer family members to the nearest MH diagnostic testing center for testing (Riazi et al., 2018).
- Individuals who experienced an MH episode should have blood sent for genetic screening of the three implicated genes (Riazi et al., 2018).

Genetics

- The phenotype is inherited as an autosomal dominant trait with incomplete penetrance and variable expression (Amare & Wilson, 2020).
- The gene can be inherited from either parent or can be the result of a new mutation in the affected individual (Amare & Wilson, 2020).
- Affected individuals have a 50% risk of passing the abnormal gene to their children (Amare & Wilson, 2020).
- The risk of inheritance is the same for males and females (Amare & Wilson, 2020).
- Molecular genetic studies have established the subtype 1 ryanodine receptor (RYR1) calcium release channel gene on chromosome 19 as the primary locus for MH (Amare & Wilson, 2020).
- Mutations in the RYR1 gene account for most MH cases (Amare & Wilson, 2020).
- Another known causative gene is the CACNA1S gene located on chromosome 1. This gene encodes the alpha-1 subunit of the voltage-gated dihydropyridine receptor (DHPR) (Amare & Wilson, 2020).
- Many different variants causing MH have been identified in the RYR1 gene but only a fraction of these meet the requirements for the causing MH. (Amare & Wilson, 2020)

Diagnostic Testing

- A molecular genetic blood test can identify MH susceptible individuals
- The caffeine-halothane muscle contracture test remains the gold standard (Mullins, 2017).
- Test results depend on the in vitro muscle contracture response of biopsied muscle to graded concentrations of the calcium releasing agents of caffeine and halothane (Mullins, 2017).

Conclusion & Implications

- Episodes of MH are very rare. However, early recognition and treatment are required to prevent death or other serious complications.
- It is crucial that perioperative staff understand MH and how it is treated to prevent delays in treatment.
- Dantrolene should be kept in stock in all facilities that utilize volatile inhalants or depolarizing muscle relaxants (Kleidon, 2020).
- All patients undergoing general surgery should complete a pre-admission screening regarding MH history or familial history.
- The Malignant Hyperthermia Association of the U.S. (MHAUS) has a hotline that should be utilized as a resource as soon as MH is identified.

MHAUS Hotline

In the United States a "hotline" was created to provide emergency assistance (1-800-644-9737) in the management of MH. The web site of the MHAUS provides helpful resources (www.mhaus.org) (Riazi et al., 2018).

Resources

OTTERBEIN UNIVERSITY