



5-20-2019

Malignant Hyperthermia Precautions in the Pediatric Patient

Amanda Versteeg

Follow this and additional works at: <https://commons.und.edu/nurs-capstones>

Recommended Citation

Versteeg, Amanda, "Malignant Hyperthermia Precautions in the Pediatric Patient" (2019). *Nursing Capstones*. 211.
<https://commons.und.edu/nurs-capstones/211>

This Independent Study is brought to you for free and open access by the Department of Nursing at UND Scholarly Commons. It has been accepted for inclusion in Nursing Capstones by an authorized administrator of UND Scholarly Commons. For more information, please contact zeinebyousif@library.und.edu.

PEDIATRIC MALIGNANT HYPERTHERMIA

MALIGNANT HYPERTHERMIA PRECAUTIONS IN THE PEDIATRIC PATIENT

By

Amanda Versteeg

Bachelor of Science in Nursing, University of South Dakota, 2015

An Independent Study

Submitted to the Graduate Faculty

Of the

University of North Dakota

in partial fulfillment of the requirements

for the degree of

Master of Science

Grand Forks, North Dakota

December 2019

PERMISSION

Title: Malignant Hyperthermia Precautions in the Pediatric Patient

Department: Nursing

Degree: Master of Science

In presenting this independent study in partial fulfillment of the requirements for a graduate degree from the University of North Dakota, I agree that the College of Nursing and Professional Disciplines of this University shall make it freely available for inspection. I further agree that permission for extensive copying or electronic access for scholarly purposes may be granted by the professor who supervised my independent study work or, in his absence, by the chairperson of the department or the dean of the School of Graduate Studies. It is understood that any copying or publication or other use of this independent study or part thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me and to the University of North Dakota in any scholarly use which may be made of any material in my independent study.

Signature _____

Date _____

Abstract

Title: Malignant Hyperthermia Precautions in the Pediatric Patient

Background: An 8-year-old patient presented for a tonsillectomy and adenoidectomy for acute pharyngitis and recurrent strep tonsillitis. The patient had a family history significant for malignant hyperthermia (MH), a hypermetabolic skeletal muscle disorder that is triggered by commonly used anesthetic gases and succinylcholine. If not prepared for, recognized, or swiftly diagnosed, this hypermetabolic reaction can be fatal for the pediatric patient.

Purpose: To review the genetic component of this inherited disorder, as well as the current recommendations for preparation, treatment, and anesthetic management in pediatric patients with a personal or family history of MH.

Process: A systematic literature review was completed utilizing the University of North Dakota's Harley E. French Library. The databases used included CINAHL and PubMed. The search was carried out with the use of controlled vocabulary and limits on the publications to include recent and efficacious data. The information gathered is presented to provide evidence-based recommendations for the care of the pediatric patient presenting for a general anesthetic that has a personal or family history of MH.

Results: Multiple case reports, meta-analyses, and pieces of clinical evidence were reviewed and data gathered for use in the development of a recommendation for the preparation and care of the MH susceptible pediatric patient. Evidence-based preparatory steps are outlined, as well as recognizable manifestations that may be seen. The use of total intravenous anesthesia (TIVA) through the administration of propofol or dexmedetomidine is outlined. Pediatric patients with MH susceptibility should be discharged only after a minimum of a one hour stay in the post anesthesia care unit (PACU) and satisfying the facility-specific predetermined discharge criteria.

Implications: Due to the potential for end-organ complications and fatality, the appropriate precautions should be taken prior to admitting an MH susceptible pediatric patient to the operating room for a safe, nontriggering general anesthetic. In addition to preparatory steps that can be taken to prepare the operative suite, a nontriggering general anesthetic with appropriate monitoring should be implemented. Once the surgery is completed, the pediatric patient should be monitored in the PACU for a minimum of one hour before discharge, assuming the patient meets the appropriate criteria.

Keywords: Malignant Hyperthermia, Pediatric, Anesthesia, Genetics, RYR1 Mutation, Dantrolene, TIVA

Malignant Hyperthermia Precautions in the Pediatric Population

Background

Malignant hyperthermia (MH) is an “uncommon, life-threatening, hypermetabolic disorder of skeletal muscle” (Nagelhout & Elisha, 2018, p. 773). The first reported MH event occurred in 1960 as witnessed by Denborough and Lovell after a patient, concerned about receiving anesthesia, reported that ten of his family members had died while undergoing a general anesthetic (Hopkins, Gupta, & Bilmen, 2018). This initial occurrence of the reaction brings to light the importance of genetics in the recognition and diagnosis of MH, as well as the potential implications for pediatric patients that present for general anesthesia.

The incidence of MH is not exactly known, but is estimated to be a complication in the range of 1 in 3,000 to 1 in 50,000 general anesthetics (Nagelhout & Elisha, 2018). The incidence of an MH crisis was 1 in 62,000 anesthetics when triggering agents were not used and increased to 1 in 4,500 anesthetics when triggering agents were administered during general anesthesia (Miller, 2015). MH is thought to affect males more than females, and is also more common in children under the age of 15. In addition, the incidence of MH is higher in the French, Scandinavian, and Japanese populations, though every ethnicity may be affected (Mullins, 2017). Due to the genetic component of the disorder, clusters of MH susceptible patients exist in the states of Wisconsin, Nebraska, West Virginia, and Michigan in the United States (Mullins, 2017). The prevalence of MH in relatives that are known carriers of an MH mutation is 1 in 2,000 (Miller, 2015).

The mortality of MH was nearly 60% when it was first discovered, and because of the development of protocols and the introduction of dantrolene into practice, the mortality rate has been reduced to less than 5% (Miller, 2015). MH reactions that are not treated promptly can lead

to many end-organ complications. Untreated MH reactions are fatal, illuminating the need for appropriate preparation, swift recognition, and prompt treatment of the reaction by anesthesia professionals (Hopkins et al., 2018).

In addition to the potential for fatality, another alarming statistic is the fact that the pediatric patient population accounts for 52.1% of all MH reactions (Miller, 2015). Pediatric implications of having a personal or family history of MH susceptibility are related to all phases of anesthesia care. It is vital that anesthesia professionals understand preoperative, intraoperative, and postoperative management of pediatric patients who are at risk for MH to prevent a potentially fatal occurrence in the operating room. Appropriate anesthetic plans should be prescribed for the pediatric patient that may be MH susceptible, and preparatory steps should be taken to ensure that the child's anesthetic course proceeds smoothly. The presented case describes an appropriate anesthetic plan for the management of an MH susceptible pediatric patient, followed by a literature review that describes the considerations that should be called to mind when caring for an MH susceptible child.

Case Report

An 8-year-old male presented for a tonsillectomy and adenoidectomy for acute pharyngitis and recurrent episodes of strep tonsillitis. The patient was categorized as an American Society of Anesthesiologists classification score of 1. The patient's past medical history included Lyme disease and a left arm fracture. The child had not undergone any prior surgical procedures. The patient was not taking any prescribed medications with the exception of amoxicillin/clavulanic acid (Augmentin) for the treatment of his recent tonsillitis infection. A preoperative assessment revealed vital signs and a review of systems that were all within normal limits for his age. The patient weighed 37.8 kg and was 142.24 cm tall. Laboratory studies were

not indicated, and therefore they were not completed prior to the scheduled surgical procedure. The patient was determined to be a Mallampati airway class I with a full range of motion in his neck and a thyromental distance greater than three fingerbreadths. The patient's family medical history was pertinent for MH reactions related to general anesthesia in both his mother and grandmother.

Because it was known that this child was potentially MH susceptible, preparatory steps were taken to ensure that the operating room environment would be safe for the child to proceed with general anesthesia. The anesthetic gas vaporizers were removed from the anesthesia machine, a new pediatric-sized breathing bag and circuit were attached, a fresh CO₂ absorbent was applied, and charcoal filters were placed on the inspiratory and expiratory limbs of the machine. The anesthesia machine was then flushed for 90 seconds to purge any residual volatile anesthetic gas from the machine per the recommendations of the manufacturer.

The patient received oral midazolam 20 mg in the preoperative area. Upon arrival to the operating room, N₂O 70% and O₂ 30% were administered to the child via facemask to allow for the placement of a 24-gauge intravenous line. The patient was then given lidocaine 30 mg, propofol 100 mg, and fentanyl 20 mcg intravenously for the induction of general anesthesia. After an appropriate anesthetic depth was achieved, the patient's trachea was easily intubated with a 5.0 mm oral RAE endotracheal tube in one attempt using a Miller 2 blade. A leak of less than 20 cm H₂O was noted. The patient's EtCO₂ was noted to be present and bilateral breath sounds were confirmed to assess proper endotracheal tube placement. The patient was then placed on the ventilator in a pressure support mode to achieve a tidal volume of 4-6 mL/kg. The patient's initial temperature was 37°C, and all other vital signs remained stable through the induction of general anesthesia.

The patient's anesthetic depth was maintained with a propofol infusion that was infused at a rate of 140 mcg/kg/min for the duration of the surgical procedure. An additional dose of fentanyl 10 mcg was administered during the procedure, for a total dose of 30 mcg of fentanyl. Antiemetics, including ondansetron 4 mg and dexamethasone 8 mg, were given intravenously. A total of 150 mL of lactated ringer's solution was infused during the case. The patient's vital signs and EtCO₂ remained within normal limits throughout the surgical procedure. The estimated blood loss for this case was 1 mL. The patient was extubated when awake and able to sustain adequate tidal volumes. The patient was subsequently transferred to the post anesthesia care unit (PACU) in a drowsy state with 6 L of O₂ flowing through a simple facemask. The patient's temporal temperature immediately after arriving in the PACU was 36.6°C. Through a chart review, the patient was noted to be monitored in PACU for one hour before being moved to the facility's discharge unit. There he was monitored for one additional hour prior to being discharged home. The patient's temperature remained stable throughout the postoperative course until he was discharged upon reaching the appropriate criteria. The patient had no apparent complications from his general anesthetic, including the lack of postoperative nausea and vomiting, recall, and uncontrolled pain.

Literature Search Methods

Databases

A search in the CINAHL database was completed to obtain literature related to nursing and allied health to determine appropriate recognition, interventions, and management of MH in the pediatric patient population (Stillwell, Fineout-Overholt, Mazurek & Williamson, 2010). The text heading search terms of "malignant hyperthermia," "pediatric," "genetics," "TIVA," and "anesthesia," were utilized for this literature search. The limits of "peer reviewed," "randomized

controlled trials,” “meta-analysis,” and a date range between 2008 and 2018 were first used to obtain the most relevant and recent data related to the identified topic. With these limits, there were no relevant results yielded. The search was then repeated using only the limits of “peer reviewed,” “human,” and the date range for the past 10 years. After the searches were completed, there were fourteen relevant articles found for a review of literature to be completed. Case reports were excluded, leaving nine of the fourteen articles to be utilized for a literature review to maintain a high level of evidence for the articles included.

A search in the PubMed database was then completed to include literature relevant to medical and life sciences pertinent to MH in pediatric patients (Stillwell et al., 2010). MeSH terms were used when available in addition to the text heading search terms which included “malignant hyperthermia,” “pediatric,” “genetics,” and “anesthesia.” The search yielded ten articles of relevance for the identified topic. After duplicate articles were removed, four of these articles were found to have a high level of evidence and they were all included in the literature review that was completed. Again, to ensure the most recent and accurate data was obtained, the limiting factors of “peer-reviewed” and “human” with the date range of the past ten years were utilized.

Once the search in the databases listed above was completed, the reference sections of the relevant articles obtained were reviewed to identify further research that could be of use for the described topic. There was a significant overlap in the review of cited references with that of the articles of relevance obtained from the initial literature search, which was promising for the utility of the literature. A search in the SCOPUS database was completed without finding any additional articles of relevance to be added to the review of literature. A brief literature search within Google Scholar was then completed to round out the collection of data. This search

yielded three relevant article results, in addition to the use of the Malignant Hyperthermia Association of the United States (MHAUS) website. Overall, there is a high level of evidence that was gathered to present evidence-based recommendations in the recognition, treatment, and anesthetic management of MH susceptible pediatric patients.

Discussion

Pathophysiology

In an individual that does not have a history of MH or of being MH susceptible, the neurotransmitter acetylcholine initiates an action potential that moves along the sarcolemma of a muscle fiber to ultimately affect the RYR1 receptor. Once an action potential reaches the RYR1 receptor, a channel is opened and calcium is released from the sarcoplasmic reticulum (SR) into the cytosol to result in the contraction of skeletal muscle. As the muscle fiber relaxes, calcium is returned to the SR by sarco/endoplasmic reticulum calcium ATPase (SERCA) pumps (Nagelhout & Elisha, 2018). Though the cause of MH is not fully understood, the widely accepted opinion is that MH is a disorder of skeletal muscle function that is inherited and results in an abnormal calcium regulation following the body's exposure to a triggering agent (Nagelhout & Elisha, 2018). Acute episodes of MH are dependent upon four variables according to Miller (2015): "a genetic predisposition, the absence of inhibiting factors, the presence of an anesthetic or nonanesthetic trigger, and the presence of environmental factors that could potentiate the action of one or more of the other three variables" (p. 1294).

Alterations in both the RYR1 and CACNA1S genes have been noted to be associated with MH reactions, although the predominant genetic mutation responsible for MH involves the RYR1 gene with a resultant defect in the ryanodine channel (Smith et al., 2018). The RYR1 receptor is the predominant receptor found in skeletal muscle that is necessary in the regulation

of calcium. In patients that have an MH reaction, the accelerated release of calcium from the SR into the cytosol progresses to a point that the SERCA pumps are unable to compensate; these factors result in uninhibited muscular activity (Smith et al., 2018). Regardless of the genetic component behind the disorder, an MH reaction is the result of an abnormally high calcium release from the SR through the RYR1 channel causing dysregulation of excitation-contraction coupling in the skeletal muscle (Hopkins et al., 2018). This alteration in calcium regulation results in a rise in myoplasmic calcium levels that leads to the clinical manifestations that are witnessed during an MH reaction. The increase in myoplasmic calcium levels leads to the resultant sustained skeletal muscle contraction, as well as the loss in cellular membrane integrity that causes hyperkalemia and rhabdomyolysis to be present (Schuster, 2013). The increased activity of the SERCA pumps trying to correct calcium levels increases the cells' need for ATP. The result of these reactions is the production of heat, manifesting as the presence of hyperthermia (Miller, 2015). Cell death ultimately occurs as a result of heat production and the continual rise in calcium levels (Hopkins et al., 2018).

Morbidity and Mortality of MH

The mortality of MH was nearly 60% when it was first discovered, and because of the development of protocols and the introduction of dantrolene into practice as a treatment modality, the mortality rate has been reduced to less than 5% (Miller, 2015). Untreated MH reactions will always be fatal due to cellular and end-organ complications (Hopkins et al., 2018). The complications of MH can include acute renal failure, compartment syndrome, cardiac dysfunction, disseminated intravascular coagulation (DIC), multiorgan failure, and death (Nagelhout & Elisha, 2018).

Contributing factors to increases in mortality rates can include a delay in the appropriate treatment of the reaction and the failure to control the patient's core temperature. Mortality rates have been noted to increase 2.9 times per 2°C increase in maximum core temperature, and 1.6 times per 30-minute delay in the administration of dantrolene (Rosenberg, Sambuughin, Riazi, & Dirksen, 2013). Mortality has also been noted to increase when the initial presentation of an MH reaction occurs in an ambulatory surgery setting due to the potential lack in preparation and education of personnel. For this reason, any facility that utilizes triggering agents should have mock MH drills and formal education on a regular basis (Rosenberg et al., 2013).

In-Depth Epidemiology

The prevalence of MH in the pediatric patient population is about 1 in 10,000 general anesthetics, which is greatly increased from the adult patient population prevalence rates of 1 in 50,000 general anesthetics (Rosenberg et al., 2013). The prevalence of MH in relatives that are known carriers of an MH genetic mutation is 1 in 2,000 (Miller, 2015). MH reactions are thought to affect males more than females, and are also more common in children under the age of 15. The pediatric population accounts for 52.1% of all MH reactions (Miller, 2015).

The incidence of MH is not exactly known, but is estimated to be a complication that occurs in the range of 1 in 3,000 to 1 in 50,000 general anesthesia cases (Nagelhout & Elisha, 2018). The incidence of an MH crisis is 1 in 4,500 general anesthetics when triggering agents are utilized and decreases to 1 in 62,000 general anesthetics when triggering agents were not used (Miller, 2015). The incidence of MH is also higher in the French, Scandinavian, and Japanese populations, though every ethnicity may be affected (Mullins, 2017). Due to the genetic component, clusters of MH susceptible patients exist in the states of Wisconsin, Nebraska, West Virginia, and Michigan in the United States (Mullins, 2017).

Genetic Considerations

MH is an inherited disorder through an autosomal dominant pattern with incomplete penetrance, which accounts for the relatives of carriers that do not develop MH susceptibility (Nagelhout & Elisha, 2018). Each child of a parent with MH susceptibility has a 50% chance of also being MH susceptible, and each grandchild of an MH susceptible adult has a 25% chance of also being MH susceptible until the parents' MH susceptibility status is known (Rosenberg et al., 2013). Genetic or nongenetic factors may be responsible for the incomplete penetrance of this genetic mutation, with a genetic factor being the degree of the anomaly noted in the gene (Hopkins et al., 2018).

There have been six different forms of MH documented by researchers, with the most common form being MHS1. This form of MH susceptibility occurs as the result of an alteration in the RYR1 gene, which is responsible for 70% of the occurrences of the disorder (Rosenberg et al., 2013). As previously mentioned, alterations in the RYR1 and CACNA1S genes have been found to be associated with MH reactions, although the predominant genetic mutation responsible for MH involves the RYR1 gene that leads to the subsequent defect in the ryanodine channel (Smith et al., 2018).

Triggering Agents

Medications that are commonly given in the perioperative setting can be divided into triggering agents and nontriggering agents. Triggering agents include all of the volatile inhalational anesthetics (ether, halothane, enflurane, isoflurane, desflurane, and sevoflurane) and the depolarizing muscle relaxant succinylcholine (Miller, 2015). Nondepolarizing muscle relaxants, N₂O, and other commonly used intraoperative medications are all considered nontriggering anesthetics that are safe to use in known MH and possible MH susceptible

patients. An episode of MH may be more pronounced in patients that receive both succinylcholine and a volatile anesthetic (Miller, 2015). In contrast, an MH crisis can be delayed in the presence of “mild hypothermia and the proadministration of barbiturates, tranquilizers, propofol or nondepolarizing neuromuscular blockers” (Miller, 2015, p. 1294). In addition to anesthetic triggering agents, there are also nonanesthetic triggers of MH that can include environmental stressors. These stressors include, but are not limited to, heat exposure, exercise, anoxia and/or excitement (Miller, 2015). The presence of a personal or family history of events related to these nonanesthetic triggers should also be included in the preoperative patient assessment.

Signs and Symptoms

The clinical manifestations of an MH crisis may include multiple clinical events and changes in laboratory findings that can range in time of onset and severity. These clinical manifestations may occur immediately after the induction of general anesthesia or could have a delay in presentation. As aforementioned, the signs and symptoms are the result of the presence of increased intracellular calcium concentrations and increased body metabolism. Early signs that a patient may be having an MH event will include tachycardia, an increase in EtCO₂ levels, and masseter spasm (Nagelhout & Elisha, 2018). Tachypnea, skin mottling, generalized muscle rigidity, profuse sweating, cardiac arrhythmias, and unstable blood pressure may also be present during the early phase of an MH reaction. Late signs of an MH episode may include hyperkalemia, a rapid increase in core body temperature, elevated CK levels, gross myoglobinemia and myoglobinuria, cardiac arrest, and DIC (Miller, 2015).

Metabolic features. Due to the presence of sustained skeletal muscle activity in the patient having an MH reaction, O₂ consumption and CO₂ production are severely increased as

the body's metabolic rate rises (Hopkins et al., 2018). These metabolic reactions result in the increase in EtCO₂ that is characteristic during the early phase of an MH reaction. An important aspect to this rise in EtCO₂ that is vital to the professionals' differential diagnosis, is that it will be refractory to an increase in minute ventilation. The peak level of EtCO₂ and the time that it takes to reach its peak are going to vary from case to case (Hopkins et al., 2018).

Cardiac symptoms are related to the adverse consequences of the ongoing hypermetabolic state which includes acidosis, hyperthermia, and hyperkalemia. Tachycardias develop in a compensatory effort of the heart to increase cardiac output as the O₂ consumption of the tissue continues to rise during the progression of the MH reaction (Hopkins et al., 2018). Arrhythmias that may be seen during an MH reaction could include atrial and ventricular ectopy, nodal tachycardias, bigeminal arrhythmias, and least common, ventricular tachycardia. The presence of cardiac arrhythmias may be more common in the pediatric patient, making electrocardiography an important monitoring tool in pediatric patients undergoing a general anesthetic (Hopkins et al., 2018). Cardiac arrhythmias are also more common when using halothane as an inhalational anesthetic gas (Chan et al., 2017).

In addition to the increase in EtCO₂ and cardiac symptoms that are displayed, the anesthesia professional may also notice an increase in the core temperature of the pediatric patient. Pediatric patients, especially infants and neonates, are normally predisposed to a drop in their core body temperature while in the operating room; this is due to a larger body surface area and a reduced amount of subcutaneous and heat producing brown fats (Hines & Marschall, 2018). However, the sustained skeletal muscle contraction that occurs during an MH reaction as a result of elevated calcium levels produces heat and a subsequent rise in core body temperature (Hopkins et al., 2018). A significant temperature rise may be more evident as the reaction

progresses, but will not be an early indicator of MH. If the MH reaction progresses to a point where hyperthermia is a concern, a very rapid temperature increase will be noted by the anesthesia practitioner, increasing the suspicion of MH in the differential diagnosis. When hyperthermia is present, the patient's temperature may be noted to precipitously rise at a rate of 1 to 2°C every five minutes (Mullins, 2017).

Muscle features. Masseter spasm is a common clinical manifestation that may be noted during an MH reaction. Interestingly, masseter spasm can also be a side effect of succinylcholine administration that is not related to an MH reaction. The differentiating factor anesthesia professionals should consider when an MH reaction is suspected is the length of time that the masseter spasm has been present. If the masseter spasm is occurring as a side effect of the succinylcholine administration, it should subside in 60-90 seconds according to Hopkins et al. (2018). Conversely, a masseter spasm occurring as a clinical manifestation of MH may last for up to 5 minutes. If present, there is a 24-50% chance that a masseter spasm is related to an MH event if it continues for longer than 2 minutes, and at this point alternate means of obtaining a patent airway need to be explored (Hopkins et al., 2018). In addition to the spasm of the jaw muscles, the presence of generalized muscle rigidity may also be noted after the administration of a triggering agent to an MH susceptible patient (Hopkins et al., 2018). Due to the fact that masseter spasm can be common after the administration of succinylcholine both as a side effect and as a manifestation of MH, it should not be used as a sole diagnostic manifestation.

Rhabdomyolysis is another clinical manifestation that may be noted as an MH reaction progresses. Continual muscle activity and heat production will result in the death of the muscle cells, causing the release of potassium (Hopkins et al., 2018). As the muscle cells continue to die, creatine kinase (CK) levels begin to rise and protein begins to be cleared in the urine, causing a

dark-colored appearance. CK levels may continue to rise for up to 12-24 hours after the MH reaction (Hopkins et al., 2018).

Laboratory findings. Laboratory findings that are consistent with an MH reaction will include the presence of a mixed acidosis, hyperkalemia, elevated CK, elevated serum myoglobin, and elevated urine myoglobin. Acidosis is a result of the increased CO₂ production by skeletal muscle cells and the alteration in the patient's respiratory efforts. Metabolic features of acidosis are the result of lactate production as the muscular metabolic rate is sustained at an abnormally high level (Miller, 2015). As aforementioned, elevated potassium and CK levels, as well as the signs of muscle breakdown are the result of rhabdomyolysis.

Diagnosis

The current gold standard for the diagnosis of MH include the halothane and caffeine muscle contracture test or the caffeine halothane contracture test (Miller, 2015). To complete the halothane and caffeine muscle contracture test, a biopsy of the quadriceps muscle is taken and a series of studies are performed. As the study progresses, the muscle biopsy is assessed for the threshold at which muscle tension is sustained. The caffeine halothane contracture test also takes a muscle biopsy from one of a variety of sites and studies can then be undertaken. The patient will be determined to be MH susceptible with a positive halothane or caffeine test and MH negative when both of the test results are negative (Miller, 2015). The limitations to contracture testing include that they must be completed at a qualified center, and they cannot be completed on infant and pediatric patients under the age of 5 or patients that weigh less than 20 kg (Rosenberg et al., 2013) (Smith et al., 2018). DNA testing that can be completed on patients of any age is in the process of being developed, though it is likely that this testing may be somewhat inaccurate in the diagnosis of MH susceptible patients.

Differential diagnosis. Due to the broad spectrum of manifestations that may be seen during the presentation of MH, there are a wide variety of conditions that need to be promptly ruled out prior to the treatment of MH to ensure that the patient is receiving treatment for the correct condition. It is important for the anesthesia professional to work through each differential diagnosis thoroughly, but efficiently, to ensure a high-quality patient outcome. As an example, tachycardia could be the result of hypoxia, hypercarbia, insufficient anesthetic depth, as a side effect from an administered medication, or as the result of another hypermetabolic state. Similarly, the increase in core body temperature could be due to a blood transfusion or drug reaction, infection, neuroleptic malignant syndrome, serotonin syndrome, and other hypermetabolic states (Hopkins et al., 2018). Masseter muscle rigidity may be the result of an insufficient neuromuscular blockade, temporomandibular syndrome, neuroleptic malignant syndrome, or myotonia. Also, as aforementioned, masseter spasm can be a side effect after the administration of succinylcholine and should not be relied upon solely as a clinical indicator of an MH reaction. After the administration of succinylcholine, it is common to have muscle discomfort in the neck, shoulder and upper abdominal muscles that occurs as a result of muscle fasciculations after its administration. Conversely, muscle rigidity and discomfort as the result of an MH reaction may be more common in the calf muscles (Chan et al., 2017).

Syndromes that may develop a clinical presentation that is similar in presentation to that of MH could include anaphylactic reactions, Freeman-Sheldon syndrome, malignant neuroleptic syndrome, muscular dystrophies (i.e Duchenne and Becker), osteogenesis imperfecta, Prader-Willi syndrome, thyroid storm, or Wolf-Hirschhorn syndrome (Miller, 2015). It is important to note that because these reactions are not true MH reactions, these conditions and disorders will not be responsive to standard MH treatments. If any of the early clinical manifestations

mentioned above (i.e. tachycardia and/or an unexplained increase in EtCO₂) are present after the use of succinylcholine or volatile anesthetics, MH should be included in the differential diagnosis and treatment should be initiated promptly if confirmed.

As can be seen, there are many conditions that must be considered and ruled out prior to moving forward with the treatment of MH. An MH clinical grading scale was developed to aid anesthesia professionals in the swift recognition and diagnosis of a possible MH event. This tool aids the anesthesia professional in working through a differential diagnosis with rankings that identify the probability of an MH event as a patient presents with clinical manifestations that make the anesthesia practitioner question whether or not they may be having an MH reaction. The clinical indicators including rigidity, muscle breakdown, respiratory acidosis, temperature increase, cardiac involvement, and “other” are assigned points that can then applied to this ranking tool (Chan et al., 2017). Based on the score that is achieved, the probability of an MH reaction can be assumed.

Treatment

Acute treatment. Once a patient is suspected of having an MH reaction in the operating room, the appropriate MH hotline should be notified for expert guidance in the treatment of an MH crisis. The treatment of MH or suspected MH should be prompt and efficient for an optimal patient outcome to be achieved. The triggering anesthetic should be discontinued immediately and help should be summoned when MH is suspected. The surgeon should be made aware of the concern of an MH reaction, and surgery should be stopped as soon as possible. If the surgery needs to be continued, a nontriggering anesthetic should be utilized to continue with general anesthesia. The patient should then be hyperventilated with 100% FiO₂ with a fresh gas flow rate of at least 10 L/min in an attempt to decrease EtCO₂ levels. The breathing circuit should be

changed and activated charcoal filters should be added to the inspiratory and expiratory limbs of the circuit to remove residual volatile agent from the anesthesia machine (MHAUS, 2019).

Dantrolene is the only medication that has been shown to be effective in reversing the MH reaction, making this a vital component of MH treatment protocol. Dantrolene works by antagonizing the RYR1 receptor, ceasing the abnormal release of calcium from the SR of the skeletal muscle cell (Nagelhout & Elisha, 2018). Dantrolene should be reconstituted with sterile water and administered at a dose of 2.5 mg/kg intravenously every 5 to 10 minutes until the initial symptoms of the MH episode are controlled (Miller, 2015). Because dantrolene is preserved with mannitol, diuresis will be noted after its administration (Hall, 2001). This will aid in the treatment of any rhabdomyolysis that may be present.

In the acute phase of an MH event, symptom management should be directed at the treatment of hyperthermia, hyperkalemia, acidosis, oliguria, and cardiac arrhythmias (Mullins, 2017). If hyperthermia is present, the patient's core body temperature should be actively cooled to 38°C and should then continue to be monitored for subsequent improvement. Cardiac arrhythmias should be treated as though they are being caused by hyperkalemia through the administration of the treatments of calcium chloride, insulin and dextrose, and sodium bicarbonate (MHAUS, 2019). Calcium channel blockers should not be used during an MH event because of the risks of worsening hyperkalemia and severe hypotension (Rosenberg et al., 2013). The anesthesia professional should ensure that urine output is at least 1 ml/kg/h through the administration of diuretics and crystalloid fluids intravenously as indicated by the patient's presentation. Standard and invasive monitoring should be implemented as warranted by the severity of the clinical manifestations during the MH event. When the patient is stable, they should be transferred to a PACU or to an appropriate intensive care unit (ICU) for at least 24

hours after the MH event to ensure the patient has stabilized. Signs that the patient is stabilizing will include a decrease in EtCO₂, a stable heart rate with a normal rhythm, and the resolution of hyperthermia and muscular rigidity (MHAUS, 2019).

Prolonged treatment. Once the patient has been initially stabilized in the operating room, the patient can then be moved to a PACU or an ICU for further monitoring and treatment if indicated. Vital signs and laboratory studies including arterial blood gases, electrolytes, CK, coagulation studies, and urine studies should be evaluated frequently to ensure effective treatment has been provided. If clinical manifestations are refractory to the initial dose of dantrolene, the medication can be repeated in the postoperative period based on the patient's clinical presentation every 10 to 15 minutes up to a maximum dose of 30 mg/kg. If the MHAUS hotline had not already been notified, this should occur so appropriate treatment modalities can continue to be implemented for the patient.

Recrudescence of MH may be possible after the initial event, even when the event has been properly treated. This has been evidenced in 20 to 25% of MH episodes, and may be more common in those that have a muscular body habitus, those that have a higher temperature increase, or those that have a delay in onset of the MH reaction after induction (Smith et al., 2018). For these reasons, it is recommended that patients that have had an MH reaction be monitored in an appropriate ICU for a minimum of 36 hours (Rosenberg et al., 2013).

Anesthesia Considerations for MH Susceptible Pediatric Patients

Preoperative Considerations. Because many pediatric patients have not had a surgical encounter prior to the scheduled procedure, the reliance on the family history that is obtained by the anesthesia professional is of utmost importance. It is important to note that even if a pediatric patient has had an uneventful prior exposure to a triggering agent, there is a chance that the

patient may develop an MH reaction to a subsequent triggering anesthetic (Bassi & Smith, 2017). Pediatric patients should be given oral anxiolytics in the preoperative area consisting of midazolam and/or ketamine to aid in their transition to the intraoperative phase of care. Topical anesthetics can also be applied during this phase of care to aid in the placement of a peripheral intravenous line if it is needed promptly (Hines & Marschall, 2018).

Preoperative assessment. A thorough preoperative assessment should be completed for each pediatric patient that will be undergoing general anesthesia that includes a family history of complications related to general anesthesia. As aforementioned, because many pediatric patients have not had a surgical encounter prior to the one that they are presenting for, obtaining an accurate family history is of the utmost importance. If prior anesthetic records are available for the child, they should be reviewed, keeping in mind that MH reactions may not occur with the first exposure to a triggering anesthetic. Chan et al. (2017) stated that “On average, MH susceptible patients have two uneventful anaesthetics before triggering with a third” (p. 712). A family history of anesthesia related complications that would make anesthesia professionals suspicious of an MH event could include an unanticipated death or intraoperative complication, having a high fever, or the presence of muscle rigidity during or after surgery. There is also supporting evidence that MH reactions can be precipitated by nonanesthetic triggers such as extreme heat and rigorous exercise. Due to these factors, the personal and family history should include an inquiry of the presence of cola-colored urine, high temperatures, or unanticipated death after exposure to these nonanesthetic triggers.

Associated conditions. There are a group of neuromuscular diseases that have a higher incidence of having a genetic and clinical link to MH susceptibility. Assessments for the presence of these disorders should be included in the anesthesia professional’s preoperative

assessment. These disorders include Central Core Disease, including the subsets of multiminicore myopathy and minicore myopathy, as well as King-Denborough syndrome. It is important to note that there is not an increased risk of MH in patients that have Duchenne or Becker muscular dystrophy, neuroleptic malignant syndrome, myotonia congenita, and myotonic dystrophy. Patients that have these conditions may develop a syndrome in relation to anesthetic medications and gases that is similar in presentation to MH (Nagelhout & Elisha, 2018).

Preparation. If it is known that a patient with a history of MH or an MH susceptible history will be presenting for surgery, a nontriggering anesthetic should be prescribed and the appropriate precautions should be taken prior to the patient coming back to the operating room. The anesthetic machine should be appropriately prepared to ensure that a triggering agent is not inadvertently delivered to the pediatric patient during their intraoperative course. Preparatory steps should include removal of anesthetic vaporizers from the machine; attaching a new, appropriately-sized breathing circuit and breathing bag; placing a fresh CO₂ absorbent; and applying charcoal filters to ensure that the machine does not contain any residual volatile anesthetic that could be delivered to the child to trigger an MH reaction (MHAUS, 2019). MHAUS (2019) states that “These [charcoal] filters are effective in keeping gas concentration below 5 ppm for up to 12 hours with fresh gas flows of at least 3 L/min.” If charcoal filters are not readily available to the anesthesia professional, manufacturer recommendations should be followed for flushing the anesthetic machine. This could mean flushing the anesthesia machine for up to 20 minutes with 10 L/min of fresh gas. If charcoal filters are available to the facility, the anesthetic machine should still be flushed, but the time is decreased to only 90 seconds (MHAUS, 2019). The use of preoperative dantrolene for prophylaxis is not recommended when

the patient is prescribed a nontriggering anesthetic, because the use of a nontriggering anesthetic will not result in the occurrence of an MH reaction (Miller, 2015).

Intraoperative Considerations. The presentation of a fulminant MH crisis may manifest as muscular rigidity after the administration of succinylcholine with induction followed by other clinical manifestations that may include an unexplained increase in EtCO₂, a decrease in SpO₂, or an increase in core body temperature. Because of this, it is the recommendation of MHAUS that core temperature monitoring is used for each patient that will be undergoing general anesthesia, especially when using a triggering anesthetic, to aid in the early detection of temperature changes (Mullins, 2017). As should also be noted, anesthesia professionals often avoid the use of succinylcholine in the pediatric population due to the unknown outcomes that may occur related to undiagnosed MH susceptibility and muscular dystrophies of various types.

The clinical manifestations directly related to the presentation of MH can also be delayed in onset, appearing after a normal induction and endotracheal intubation, but progressing to the otherwise unexplained clinical manifestations that were described above (Miller, 2015). MH that is delayed in onset can often be diagnosed promptly with the identification of an unexplained increase in EtCO₂, tachycardia, and muscle rigidity. Presentation of MH in the pediatric patient can often be mistaken for a state of hypovolemia, allergic reactions, anticholinergic treatments, and disturbances to the CNS (Smith, Tranovich, & Ebraheim, 2018). Specific to the pediatric male, cardiac arrest due to hyperkalemia can be mistaken for MH. All of these factors complicate the already difficult differential diagnosis even further.

Due to the concerns of potential complications related to the administration of triggering agents in pediatric patients that may be unknown to be MH susceptible or that have undiagnosed myotonic dystrophy, the use of total intravenous anesthesia (TIVA) for an anesthetic plan has

been on the rise. There are many advantages to a TIVA in pediatric patients including decreased airway reactivity, less incidence of emergence delirium, and neuroprotection (Lauder, 2014). The disadvantages noted when a pediatric patient is prescribed a TIVA include the need for an intravenous line prior to the initiation of their anesthetic, pain on injection of the medication, and less predictable responses to the medications (Lauder, 2014).

Considerations for induction. It is ordinary to initiate general anesthesia with the use of inhalational anesthetic agents in the pediatric patient population. It is after the patient has reached an appropriate anesthetic depth that an intravenous line can then be placed for the child so adjunct medications can be administered as needed. In the pediatric patient that has a personal or familial history of MH, this is not possible, so the anesthetic management for this phase of care changes. A nontriggering anesthetic should be prescribed, as presented in the case report above. Preoperative oral midazolam in a dose of 0.5-0.7 mg/kg up to a maximum dose of 20 mg can also be utilized to provide anxiolysis and some amnesia for the child prior to being brought back to the operating room. N₂O can then be utilized to provide further anxiolysis to the pediatric patient for the placement of an intravenous catheter so a TIVA can be initiated. If the pediatric patient is cooperative, or part of an age group that is able to appropriately follow directions, EMLA cream can be applied and an intravenous line can be placed in the preoperative area so general anesthesia can be initiated in a timelier manner upon the child's arrival to the operating room.

Considerations for maintenance. A pediatric TIVA can be completed with the use of propofol, ketamine, or dexmedetomidine infusions with or without the use of adjunct medications that are appropriately dosed for the pediatric patient. Examples of adjunct medications that can be used may include fentanyl, morphine, hydromorphone, remifentanyl, or

ketamine. Also, the use of N₂O can be an appropriate addition to the anesthetic plan when indicated for the child. A propofol infusion will most commonly be utilized for a TIVA. For pediatric patients in the age range of 3 to 11 years old, an initial bolus of 2-3 mg/kg can be used for induction, followed by an infusion that will be titrated for an appropriate anesthetic depth as determined by the procedure. A typical propofol infusion may be infused at a rate of 100-200 mcg/kg/min while being titrated for the desired effect (Jaffe, Schmiesing, & Golianu, 2014). The concomitant use of a remifentanyl infusion or the use of N₂O can aid in achieving an appropriate anesthetic depth for the surgical procedure that will be completed (Jaffe et al., 2014).

Another approach to the administration of a propofol infusion involves a stepwise fashion to titrations that will be made. Lauder (2014) recommends an induction dose of 2.5 mg/kg of propofol followed by an initial infusion rate of 15 mg/kg/h for 15 minutes. The infusion can then be titrated down to 13 mg/kg/h for the next 15 minutes of the procedure, followed by 11 mg/kg/h for 30-60 minutes, 10 mg/kg/h for the next 1-2 hours, and 9mg/kg/h for the remainder of the case (p. 53). This infusion delivery model is described to maintain an appropriate plasma concentration of propofol while not overmedicating the pediatric patient, which aids in the expeditious emergence of the child. Lauder (2014) also notes that the requirement for propofol will be increased in the pediatric patient less than three years of age and conversely may be decreased when the anesthesia professional is utilizing adjunct medications such as fentanyl or dexmedetomidine.

Although dexmedetomidine is not currently approved by the United States Food and Drug Administration (FDA) for use in the pediatric patient population, there has been a rise in its off-label use for TIVA and in the prevention of emergence delirium upon wakeup for children. The properties of dexmedetomidine make the medication appealing for use in pediatric TIVAs,

as respirations can be maintained while also providing a sedated state. A standard loading dose can be utilized in the pediatric population at a dose of 1.0 mcg/kg over ten minutes prior to the initiation of a continuous infusion. It is important to mention that one of the most common side effects of dexmedetomidine is bradycardia, and therefore the bolus may be foregone by some practitioners; decreased by other practitioners; or given over an even longer period of time by others to help avoid this unwanted complication for the pediatric patient (Tobias, 2007). Tobias (2007) describes the use of dexmedetomidine in an infusion dose of 0.2–0.7 mcg/kg/h with the same pharmacokinetic profile as that which is displayed in the adult population, making its actions predictable for the pediatric population. Another source described the successful use of dexmedetomidine at an infusion rate of 0.5-2.0 mcg/kg/h without the use of a loading dose (Jaffe et al., 2014). Due to the lack of approval from the FDA, the use of dexmedetomidine for pediatric TIVAs should be assessed for risks and benefits by the anesthesia professional based on each individual case. Anesthesia professionals should proceed with the use of dexmedetomidine, based upon their assessment, utilizing vigilant monitoring for any subsequent adverse effects in the pediatric patient.

If a nontriggering TIVA is going to be utilized in the pediatric patient, it may be prudent for the anesthesia professional to implement the use of bispectral index (BIS) monitoring. This monitoring modality may guide the anesthesia professional in providing a level of anesthesia that both prevent the awareness of the child and also speeds their emergence when general anesthesia is ceased (Rosenberg, Pollock, Schiemann, Bulger, & Stowell, 2015). It should be noted that BIS monitoring may not be reliable in the pediatric patient less than five years old nor those that are not paralyzed (Lerman & Johr, 2009).

Considerations for emergence. Another concern in the pediatric patient population, especially those presenting for a surgery involving the oropharynx, includes the potential for a laryngospasm. It should be noted that there is evidence supporting the decreased incidence of laryngospasm in pediatric patients that receive a TIVA for their general anesthetic in comparison to an inhalational general anesthetic due to the decreased amount of airway irritation (Lauder, 2014). In the event of a laryngospasm, an intravenous or intramuscular dose of succinylcholine may typically be utilized to break the spasm that is refractory to other initial treatments. Because succinylcholine is a triggering agent, it cannot be used in this event for the MH susceptible pediatric patient. In the event of a laryngospasm that cannot be broken with positive pressure ventilation and other initial treatments, a dose of rocuronium 0.9-1.2 mg/kg should be used (Orliaguet, Gall, Savoldelli, & Couloigner, 2012). If there is no intravenous access present in the child, rocuronium is the only paralytic aside from succinylcholine that can be administered via the intramuscular route for the treatment of a laryngospasm (Orliaguet et al., 2012).

Should the use of rocuronium be warranted for the child having a laryngospasm, sugammadex or neostigmine may need to be used to reverse the resultant neuromuscular blockade. Though there is still not FDA approval for its use in children, new research has shown benefits for the use of sugammadex in infants, children and adolescents with various neuromuscular diseases that need a full and adequate reversal prior to extubation (Tobias, 2017). These studies have shown successful reversal and subsequent extubation after the administration of the appropriate dose of sugammadex. Complications identified in early clinical trials of the drug may include severe anaphylactic reactions and bradycardia after administration of sugammadex (Tobias, 2017). Anesthesia professionals should be cognizant of the lack of FDA approval for infants, children, and adolescents, again weighing risks and benefits for the pediatric

patient prior to the administration of sugammadex. Neostigmine with the concomitant use of glycopyrrolate will also give the patient an adequate reversal of neuromuscular blockade, with the difference existing in the amount of time that it takes for the patient to reach total reversal from their neuromuscular blockade (Tobias, 2017). Therefore, if a rapid reversal of neuromuscular blockade is necessary, the anesthesia professional may choose to use sugammadex as the reversal agent of choice for the child.

Postoperative Considerations. Pediatric patients are often discharged home in an expedited manner due to the incidence of emergence delirium that is present upon their arrival to PACU. The question can then be raised: Should a pediatric patient that has undergone a nontriggering general anesthetic be monitored in the PACU for a longer period of time if they have a personal or familial history of MH? Research completed by Barnes, et al. (2015) concluded that pediatric patients that have received a nontriggering general anesthetic can safely be discharged home in the same time frame as a patient that has no personal or familial history of MH. Therefore, standard discharge protocols may be followed for the discharge of pediatrics after their surgical procedure. Hines and Marschall (2018) recommended that pediatric patients be monitored for a minimum of one hour, up to four hours, after a nontriggering anesthetic, though if symptoms of MH have not occurred within one hour postoperatively, they are likely to not occur. Pediatric patients can then be discharged home once the predetermined, facility-specific discharge criteria have been met.

Local Anesthesia Considerations

Local anesthetics are known to be nontriggering anesthetic agents, so their use is acceptable for patients that have a history of MH or are MH susceptible. The use of local anesthesia may be beneficial to aid in the prevention of postoperative pain, but because the

pediatric patient population is often uncooperative and unable to follow commands, regional anesthesia may not be a good option for a sole anesthetic. However, topical anesthetics with the addition of N₂O may be useful in the placement of a peripheral intravenous line in the preoperative or intraoperative phase of care (Hines & Marschall, 2018). This will increase patient satisfaction with IV placement while also assuring that the general anesthetic can be initiated promptly for the child.

Conclusions and Recommendations

In the previously discussed case, an in-depth preoperative assessment revealed the concern of potential MH susceptibility in a pediatric patient presenting for an adenotonsillectomy. The genetic considerations related to the disorder lead to the appropriate management of a potentially MH susceptible pediatric patient. Through the implementation of the appropriate preparatory steps, the use of a TIVA for general anesthesia, and the appropriate postoperative management, the child had a safe and uneventful surgical encounter.

The genetic component of MH reinforces the fact that thorough family histories should be taken for each pediatric patient that presents for a surgical procedure requiring general anesthesia. Should the personal or family history reveal that the child presenting for a general anesthetic is potentially MH susceptible, preparatory steps should be taken by anesthesia practitioners to ensure that the patient will have a safe, but also effective, general anesthetic. The anesthesia professional should take the steps aforementioned to prepare the anesthetic machine for the patient, as well as develop an appropriately tailored anesthetic plan for the MH susceptible pediatric patient.

If an MH susceptible pediatric patient presents for surgery, a TIVA can be performed utilizing propofol or dexmedetomidine, along with other adjunct medications. This approach will

ensure that an efficacious, multimodal general anesthetic is provided to the child. The addition of BIS monitoring can be considered to be used to verify that an adequate depth of anesthesia is being achieved. With the use of N₂O for anxiolysis and/or EMLA cream, an intravenous line can be successfully placed for the child that will be receiving a TIVA prior to coming back to the operative suite to ensure the prompt initiation of the child's general anesthetic.

Because of the implications that an unrecognized MH crisis can have, it is important for the operating room staff and anesthesia professionals to be familiar with the presentation and treatment of MH. Many sources suggest the implementation of annual MH mock drills to ensure that staff are able to work as a team to find the resources that they will need if an MH crisis would happen to occur in their operating room (Mullins, 2017). Mock drills make certain that staff are aware of where to find the appropriate medications, protocols, and resources to provide rapid treatment in a potentially fatal situation. If the clinical manifestations mentioned above are noticed by the anesthesia professional, a quick, but thorough, differential diagnosis should be commenced to ensure that the patient is treated properly according to the underlying condition.

The pediatric patient with a history of MH or who is potentially MH susceptible should be monitored in the PACU for at least one hour after they have received a nontriggering anesthetic. Generally, if symptoms of MH have not occurred within one hour of their general anesthetic, they are likely to not occur. Patients should be discharged home only after the anesthesia professional is certain that the pediatric patient has not suffered any complications from their anesthetic, and once they have met the appropriate discharge criteria. If the anesthesia professional verifies that the aforementioned steps are taken, the administration of a safe and efficacious general anesthetic for the MH susceptible pediatric patient is achievable, as is the swift recognition and treatment of an unexpected MH event.

References


- Barnes, C., Stowell, K. M., Bulger, T., Langton, E., & Pollock, N. (2015). Safe duration of postoperative monitoring for malignant hyperthermia patients administered non-triggering anaesthesia: An update. *Anaesthesia and Intensive Care Journal*, 43(1), 98-104.
doi:10.1177/0310057X1504300115
- Bassi, S., & Smith, C. (2017). Two occurrences of malignant hyperthermia in a pediatric patient following adenotonsillectomy and subsequent control of tonsillar bleed. *Middle East Journal of Anesthesiology*, 24(2), 143-145.
- Butterworth, J. F., Mackey, D. C., & Wasnick, J. D. (2013). Thermoregulation, hypothermia, & malignant hyperthermia. In *Morgan & Mikhail's clinical anesthesiology* (5th ed., pp. 1183-1191) New York, NY: McGraw Hill.
- Chan, T. Y., Bulger, T. F., Stowell, K. M., Gillies, R. L., Langton, E. E., Street, N. E., & Pollock, N. A. (2017). Evidence of malignant hyperthermia in patients administered triggering agents before malignant hyperthermia susceptibility identified: Missed opportunities prior to diagnosis. *Anaesthesia and Intensive Care Journal*, 45(6), 707-713.
doi:10.1177/0310057X1704500610
- Hall, S. C. (2001). General pediatric emergencies malignant hyperthermia syndrome. *Anesthesiology Clinics of North America*, 19(2), 367-382.
[https://doi.org/10.1016/S0889-8537\(05\)70233-9](https://doi.org/10.1016/S0889-8537(05)70233-9)
- Hines, R. L., & Marschall, K. E. (2018). Pediatric diseases. In Diu, M. W., & Mancuso, T. J. (Eds.), *Stoelting's anesthesia and co-existing disease* (7th ed., pp. 666-669). Philadelphia, PA: Elsevier.

- Hopkins, P. M., Gupta, P. K., & Bilmen, J. G. (2018). Malignant hyperthermia. In *Handbook of clinical neurology* (Vol. 157, pp. 645-661) Amsterdam, Netherlands: Elsevier.
- Jaffe, R. A., Schmiesing, C. A., & Golianu, B. (2014). Appendix D: Standard pediatric anesthetic management. In Maas, B. (Ed.), *Anesthesiologist's manual of surgical procedures* (5th ed., pp. D-1-D-5). Philadelphia, PA: Wolters Kluwer Health.
- Lauder, G. R. (2014). Total intravenous anesthesia will supersede inhalational anesthesia in pediatric anesthetic practice. *Pediatric Anesthesia*, 25, 52-64.
doi:10.1111/pan.12553
- Lerman, J., & Johr, M. (2009). Inhalational anesthesia vs total intravenous anesthesia (TIVA) for pediatric anesthesia. *Pediatric Anesthesia*, 19, 521-534.
doi:10.1111/j.1460-9592.2009.02962.x
- MHAUS. (2019). Healthcare professionals. Retrieved from <https://www.mhaus.org/healthcare-professionals/>
- Miller, R. D. (2015). Malignant hyperthermia and muscle-related disorders. In Zhou, J., Bose, D., Allen, P. D., & Pessah, I. N. (Eds.), *Miller's anesthesia* (8th ed., pp. 1287-1311). Philadelphia, PA: Elsevier Churchill Livingstone.
- Mullins, M. F. (2017). Malignant hyperthermia: A review. *Journal of PeriAnesthesia Nursing*, 33(5), 582-589. <http://dx.doi.org/10.1016/j.jopan.2017.04.008>
- Nagelhout, J., & Elisha, S. (2018). Musculoskeletal system anatomy, physiology, pathophysiology, and anesthesia management. In Karlet, M. C. (Ed.), *Nurse anesthesia* (6th ed., pp. 773-777). St. Louis, MO: Elsevier.

- Orliaguet, G. A., Gall, O., Savoldelli, G. L., & Couloigner, V. (2012). Case scenario: Perianesthetic management of laryngospasm in children. *Anesthesiology*, *116*(2), 458-471. doi:10.1097/ALN.0b013e318242aae9
- Rosenberg, H., Sambuughin, N., Riazi, S., & Dirksen, R. (2013). Malignant hyperthermia susceptibility. In M. P. Adam, H. H. Ardinger, R. A. Pagon, et al. (Eds.), *GeneReviews* (Internet). Seattle, WA: University of Washington, Seattle.
- Rosenberg, H., Pollock, N., Schiemann, A., Bulger, T., & Stowell, T. (2015). Malignant hyperthermia: A review. *Journal of Rare Diseases*, *10*(93), 1-19. doi: 10.1186/s13023-015-0310-1
- Schuster, F., Johannsen, S., Schneiderbanger, D., & Roewer, N. (2013). Evaluation of suspected malignant hyperthermia events during anesthesia. *BMC Anesthesiology*, *13*(24), 1-7. Retrieved from <http://www.biomedcentral.com/1471-2253/13/24>
- Smith, J. L., Tranovich, M. A., & Ebraheim, N. A. (2018). A comprehensive review of malignant hyperthermia: Preventing further fatalities in orthopedic surgery. *Journal of Orthopaedics*, *15*, 578-580. <https://doi.org/10.1016/j.jor.2018.05.016>
- Stillwell, S. B., Fineout-Overholt, E., Mazurek Melnyk, B., & Williamson, K. M. (2010). Evidence-Based practice step by step: Searching for the evidence. *American Journal of Nursing*, *110*(5), 41-47. doi:10.1097/01.NAJ.0000372071.24134.7e
- Tobias, J. D. (2007). Dexmedetomidine: Applications in pediatric critical care and pediatric anesthesiology. *Pediatric Critical Care Medicine*, *8*(2), 115-131. doi:10.1097/01.PCC.0000257100.31779.41
- Tobias, J. D. (2017). Current evidence for the use of sugammadex in children. *Pediatric Anesthesia*, *27*, 118-125. doi:10.1111/pan.13050

Malignant Hyperthermia Precautions in the Pediatric Patient


Amanda Versteeg, SRNA



Malignant Hyperthermia

- An “uncommon, life-threatening, hypermetabolic disorder of skeletal muscle”
- First case witnessed in 1920s
- Gold standard of diagnosis is the halothane and caffeine muscle contracture test or the caffeine halothane contracture test
 - **Cannot be completed in patient less than 5 years old or those that weigh less than 20kg**
- Clinical presentation mimics many other disease states, complicating the differential diagnosis


(Nagelhout & Elisha, 2018; Miller, 2015; Hopkins et al., 2018; Rosenberg et al., 2013)



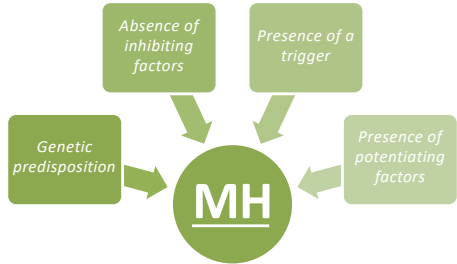
Epidemiology

- Incidence is approximated to be 1:4,500 when using a triggering anesthetic
- **The pediatric patient population accounts for roughly 52.1% of all MH reactions**
- Males have a higher incidence than females
- **Most common in patients under the age of 15**
- Known MH clusters exist in the U.S.
- The prevalence in relatives that are known carriers is 1:2,000


(Nagelhout & Elisha, 2018; Miller, 2015; Hopkins et al., 2018; Mullins, 2017)



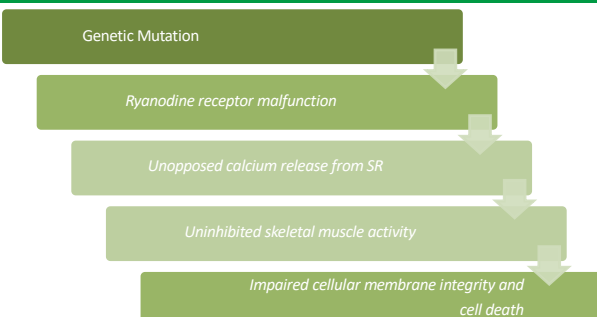
Pathophysiology




(Nagelhout & Elisha, 2018; Miller, 2015; Hopkins et al., 2018; Mullins, 2017)



Pathophysiology




(Smith et al., 2018; Miller 2015)



Morbidity and Mortality

- Has decreased from nearly 60% when MH was first discovered to less than 5%
- Mortality increases:
 - 2.9 times per 2°C increase in maximum core body temperature
 - 1.6 times per 30-min delay in dantrolene administration
 - In ambulatory surgery settings
- Complications include:
 - Acute renal failure
 - Compartment syndrome
 - Cardiac dysfunction
 - DIC
 - Multi-system organ failure
- Untreated MH reactions will be fatal 100% of the time

(Miller, 2015; Rosenberg, 2013)



PEDIATRIC MALIGNANT HYPERTHERMIA

Case Information

- **Surgical Procedure**
 - Tonsillectomy & Adenoidectomy
- **Pertinent patient information**
 - 8 y/o Male - ASA 1
 - 37.8kg; 58in - No Known Allergies
- **PMH: Recurrent Strep Tonsillitis; Lyme disease (2017); Left arm fracture**
- **PSH: None**
- **Family history revealed MH in both the boy's mother and maternal grandmother**
- **Pre-op VS and ROS WNL**
- **Mallampati I; >3 FB; Full Neck ROM**

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Preparatory Steps

- **First case of the day**
- **A safe OR environment was able to be prepared:**
 - Vaporizers were removed from the anesthesia machine
 - New pediatric-sized breathing circuit and breathing bag applied
 - New CO₂ absorbent placed
 - Charcoal filters to the inspiratory and expiratory limbs of the machine
 - Machine flushed with high fresh gas flows for 90 seconds per recommendations
- **Dantrolene is the only medication known to reverse an MH reaction**
 - Dantrolene dose was calculated to be 95 mg (2.5mg/kg)
 - 5 vials reconstituted with 300 mL sterile water

(MHAUS, 2019)

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Anesthetic Course

- **Preoperatively**
 - 20mg PO Midazolam
 - 70/30 N₂O/O₂ used for 24g IV placement
- **Induction**
 - 30mg Lidocaine
 - 100mg Propofol
 - 20mcg Fentanyl
- **Technique**
 - 5.0 Oral RAE ETT
 - Miller 2 blade used to establish Grade 1 view
- **Ventilator Settings**
 - +BBS, +EtCo₂, Leak <20mmHg
 - PSV-PRO to achieve tidal volumes of 4-6mL/kg
- **Maintenance**
 - **Propofol infusion at 140mcg/kg/min**
 - 10mcg Fentanyl
 - PONV Prophylaxis
 - 4mg Ondansetron
 - 8mg Dexamethasone
- **Initial temperature = 37°C**

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Intraoperative Issues

- **Surgical course was uneventful**
- **Vital signs, including temperature, remained WNL for the duration of the surgery**
- **Fluid Administration**
 - 150mL lactated ringer's
- **Blood loss ~1mL**

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

PACU

- **Extubated drowsy, but awake, after thorough oral suctioning prior to arrival in PACU**
- **6L oxygen via simple facemask**
- **Immediate post-op temperature was 36.6°C**
- **No apparent anesthetic complications**
- **Vitals remained WNL**
- **Discharged home after 2 hour stay**

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Genetic Considerations

- **There are six noted forms of MH**
- **The most widely accepted opinion is that MH is an inherited disorder**
- **Autosomal dominant with incomplete penetrance**
 - Each child or sibling of a carrier has a 50% chance of being MH susceptible
- **RYR1 genetic mutation accounts for 70% of the occurrences of the disorder**


(Rosenberg et al., 2013; Nagelhout & Elisha, 2018)

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Triggering Agents

- **Environmental Triggers**
 - Heat exposure
 - Exercise
 - Anoxia
 - Excitement
- **Anesthetic Triggers**
 - Ether
 - Halothane
 - Enflurane
 - Isoflurane
 - Desflurane
 - Sevoflurane
 - Succinylcholine


(Miller, 2015)



Preoperative Considerations for the Pediatric Patient

- Thorough family history is very important
- **Even if a pediatric patient has had an uneventful prior exposure to a triggering agent, there is a chance that the patient may develop an MH reaction to a subsequent anesthetic**
- Oral anxiolytics in the preoperative area
 - i.e. Midazolam 0.5-0.7 mg/kg up to 20mg
- Non-triggering anesthetic should be prescribed
- Preparatory steps should be taken to make the OR safe for the child's anesthetic


(Bassi & Smith, 2017; Hines & Marshall, 2018; Chan et al., 2017)



Intraoperative Considerations for the Pediatric Patient

- Standard monitors, including [core] temperature
- Induction will look different from commonly used inhalational induction
- Avoidance of succinylcholine for pediatric patients
- Utilization of TIVA
- If MH event is suspected based on clinical presentation, treatment should not be delayed
 - Have MH resources available
 - Dantrolene 2.5 mg/kg is the only definitive treatment of MH
 - Reconstitute with **sterile water**


(Smith, Tranovich & Ebraheim, 2018)



TIVA for the Pediatric Patient

- **Advantages**
 - Decreased airway reactivity
 - Decreased incidence of emergence delirium
 - Neuroprotection
- **Disadvantages**
 - Need for IV prior to the initiation of the anesthetic
 - Pain on injection of the medication
 - Less predictable responses to the medications
- Due to larger volume of distribution, may need increased induction doses


(Lauder, 2015)



TIVA for the Pediatric Patient Cont.

- Use of propofol, ketamine, or dexmedetomidine infusions as wells as adjunct medications
- **Propofol**
 - Induction dose: 2.5 mg/kg (or 2-3 mg/kg)
 - Infusion rate: 15 mg/kg/h for 15 minutes working down to a dose of 9 mg/kg/h to finish out the case
 - **OR** Infusion rate: 100-200 mcg/kg/min
 - +Remifentanil infusion: 0.1-0.2 mcg/kg/min
 - +N2O
 - Increase dose in children less than 3 years old


(Lauder, 2014; Jaffe, 2015)



TIVA for the Pediatric Patient Cont.

- **Dexmedetomidine**
 - Not FDA approved for use in children
 - *Loading dose: 1.0 mcg/kg over 10 min
 - Infusion rate: 0.2-0.7 mcg/kg/h
 - +Remifentanil infusion: 0.05-0.1 mcg/kg/min
- **Ketamine**
 - Induction dose: 3-5 mg/kg
 - Infusion: 0.2-1.5 mg/kg/h
 - +Morphine infusion: 0.05 mg/kg/h
 - Fentanyl or hydromorphone infusions are also options
- **BIS monitoring**
 - Not reliable in patients less than 5 years old

(Tobias, 2007; Jaffe 2015)



Considerations for Emergence

- Laryngospasm
 - Common complication/concern for the pediatric population
 - Less common when using a TIVA
 - Standard treatment includes the use of succinylcholine
 - In lieu of succinylcholine, **rocuronium can be used to treat laryngospasm refractory to standard treatments**
 - Only other paralytic agent that can be given IM
 - 0.9-1.2mg/kg (two to three times ED₉₅)
 - Reversal may be needed

(Lauder, 2015; Orilaguet et al., 2012; Tobias 2017)

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Postoperative Considerations for the Pediatric Patient

- Safe discharge home after appropriate Phase 1/Phase 2 stay after receiving a non-triggering anesthetic
 - Minimum 1 hour, possibly up to 4 hours
 - Facility specific predetermined discharge criteria has been successfully met
- MH symptoms that have not manifested after 1 hour are likely to not occur

(Hines & Marschall, 2018; Barnes et al., 2015)

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Case Review & Conclusions

- A thorough preoperative assessment prevented a potentially fulminant MH crisis
- Preparation is key
- If MH is ever suspected, do not delay treatment
- Be aware of your resources and stay educated
- Successful management of MH susceptibility is attainable in all phases of care
- Unrecognized and untreated MH reaction will be fatal 100% of the time!

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

References

- Barnes, C., Stowell, K. M., Bulger, T., Langton, E., & Pollock, N. (2015). Safe duration of postoperative monitoring for malignant hyperthermia patients administered non-triggering anaesthesia: An update. *Anaesthesia and Intensive Care Journal*, 43(1), 98-104.
- Basli, S., & Smith, C. (2017). Two occurrences of malignant hyperthermia in a pediatric patient following adenotonsillectomy and subsequent control of tonsillar bleed. *Middle East Journal of Anesthesiology*, 24(2), 143-145.
- Chan, T. Y., Bulger, T. F., Stowell, K. M., Gillies, R. L., Langton, E. E., Street, N. E., & Pollock, N. A. (2017). Evidence of malignant hyperthermia in patients administered triggering agents before malignant hyperthermia susceptibility identified: Missed opportunities prior to diagnosis. *Anaesthesia and Intensive Care Journal*, 45(6), 707-713.
- Hines, R. L., & Marschall, K. E. (2018). Pediatric diseases. In Dlu, M. W., & Mancuso, T. J. (Eds.), *Stoelting's anesthesia and co-existing disease* (7th ed., pp. 666-669). Philadelphia, PA: Elsevier.
- Hopkins, P. M., Gupta, P. K., & Bilmen, J. G. (2018). *Malignant hyperthermia*. Amsterdam, Netherlands: Elsevier.
- Jaffe, R. A., Schmielesing, C. A., & Gollanu, B. (2014). Appendix D: Standard pediatric anesthetic management. In Maas, B. (Ed.), *Anesthesiologist's manual of surgical procedures* (5th ed., pp. D-1-D-5). Philadelphia, PA: Wolters Kluwer Health.
- Lauder, G. R. (2015). Total intravenous anesthesia will supercede inhalational anesthesia in pediatric anesthetic practice. *Pediatric Anesthesia*, 25, 52-64. doi:10.1111/pan.12553
- MHAUS. (2019). Healthcare professionals. Retrieved from <https://www.mhaus.org/healthcare-professionals/>
- Miller, R. D. (2015). Malignant hyperthermia and muscle-related disorders. In Zhou, J., Bose, D., Allen, P. D., & Pessah, I. N. (Eds.), *Miller's anesthesia* (8th ed., pp. 1287-1311). Philadelphia, PA: Elsevier Churchill Livingstone.
- Mullins, M. F. (2017). Malignant hyperthermia: A review. *Journal of PeriAnesthesia Nursing*, 33(5), 582-589.

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

References

- Nagehout, J., & Elisha, S. (2018). Musculoskeletal system anatomy, physiology, pathophysiology, and anesthesia management. In Karlet, M. C. (Ed.), *Nurse anesthesia* (6th ed., pp. 773-777). St. Louis, MO: Elsevier.
- Orilaguet, G. A., Gall, O., Savoldelli, G. L., & Couloigner, V. (2012). Case scenario: Perianesthetic management of laryngospasm in children. *Anesthesiology*, 116(2), 458-471. doi:10.1097/ALN.0b013e318242ae9
- Rosenberg, H., Sambaughin, N., Riazi, S., & Dirksen, R. (2013). Malignant hyperthermia susceptibility. In M. P. Adam, H. H. Ardinger, R. A. Pagon, et al. (Eds.), *GeneReviews* (Internet). Seattle (WA): University of Washington, Seattle.
- Smith, J. L., Tranovich, M. A., & Ebraheim, N. A. (2018). A comprehensive review of malignant hyperthermia: Preventing further fatalities in orthopedic surgery. *Journal of Orthopaedics*, 15, 578-580. <https://doi.org/10.1016/j.jor.2018.05.016>
- Tobias, J. D. (2007). Desmedetomidine: Applications in pediatric critical care and pediatric anesthesiology. *Pediatric Critical Care Medicine*, 8(2), 115-131. doi:10.1097/01.PCC.0000257100.31779.41
- Tobias, J. D. (2017). Current evidence for the use of sugammadex in children. *Pediatric Anesthesia*, 27, 118-125. doi:10.1111/pan.13050

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

Thank You!

Are There Any Questions?

UND NURSE ANESTHESIA
UNIVERSITY OF NORTH DAKOTA

